

Pathophysiology of Spasticity

Spasticity is a major neuromuscular problem in CP. It is so deeply engrained in medical and public literature that a spastic child has come to mean a child with CP for most people around the world. Spasticity is difficult to define. The pathophysiology is obscure, findings on examination are inconsistent, and treatment is not always successful. Understanding the physiology of normal movement may help the physician in the management of spasticity.

Physiology of movement

Afferent input from the internal organs, the musculoskeletal system, and the skin converge on the medulla spinalis. This afferent input activates the stretch reflex, both directly and through

the interneuron, and results in a reflex motor response [A].

The same afferent information goes to the cerebellum and the somatosensory cortex. It is processed in those centers as well as in the basal ganglia. The resulting motor response is relayed to the lower motor neuron through the pyramidal and extrapyramidal system tracts. The pyramidal tracts go directly to the lower motor neuron whereas the extrapyramidal tracts end at the interneuron. The cerebellum, basal ganglia, and extrapyramidal system nuclei modify the motor response as it goes to the medulla spinalis. In this way all motor output is influenced by the incoming sensory input and converges on the lower motor neuron. The interneurons in the medulla spinalis regulate the activity of the motor neuron.

A

Neural pathways regulating muscle contraction

The motor cortex is responsible for planning voluntary movement.

The corticospinal tracts carry movement order to the lower motor neuron.

The nerve impulse arising from the cerebral motor cortex is also sent to the basal ganglia and the extrapyramidal system nuclei.

The basal ganglia correct the timing of movement.

The extrapyramidal system corrects the force of contraction of the muscles involved.

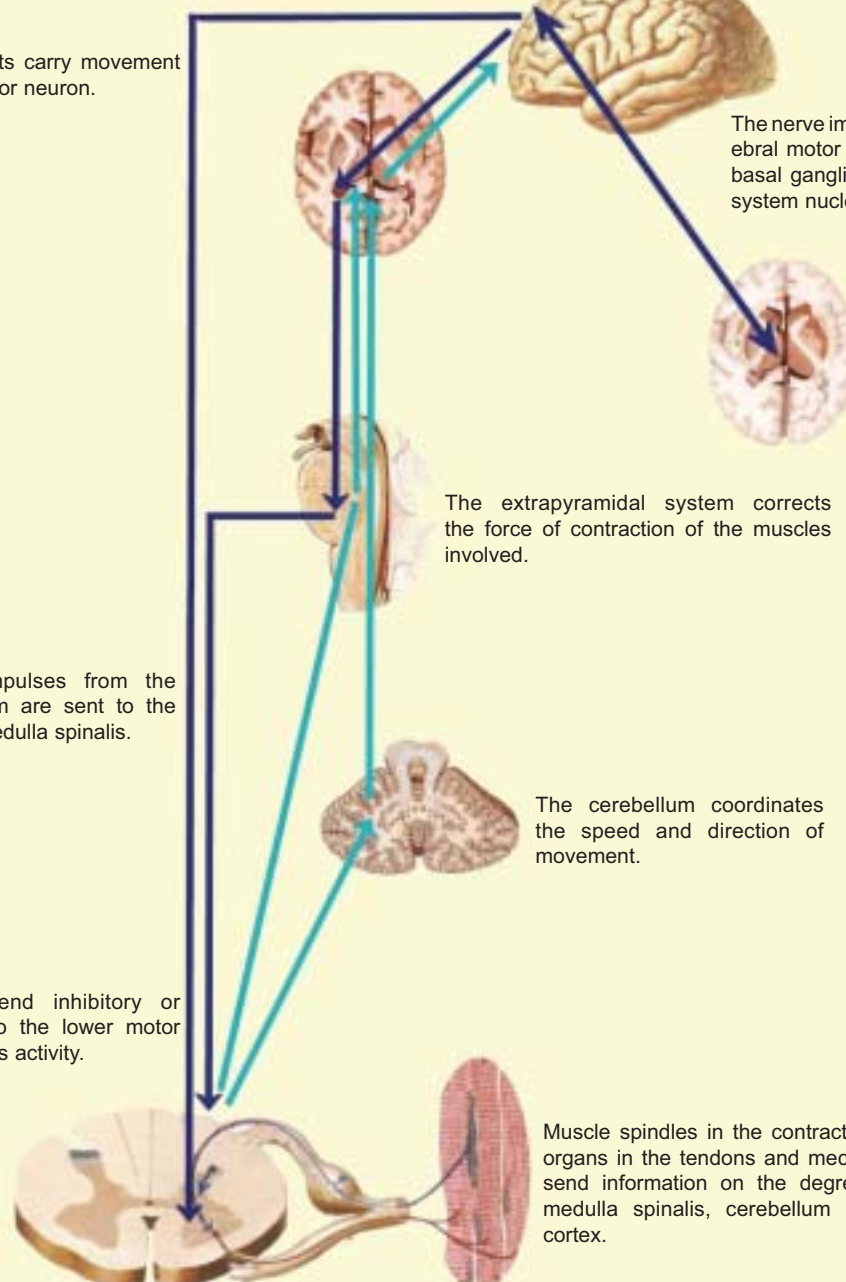
These corrective impulses from the extrapyramidal system are sent to the interneurons in the medulla spinalis.

The cerebellum coordinates the speed and direction of movement.

The interneurons send inhibitory or excitatory impulses to the lower motor neuron and regulate its activity.

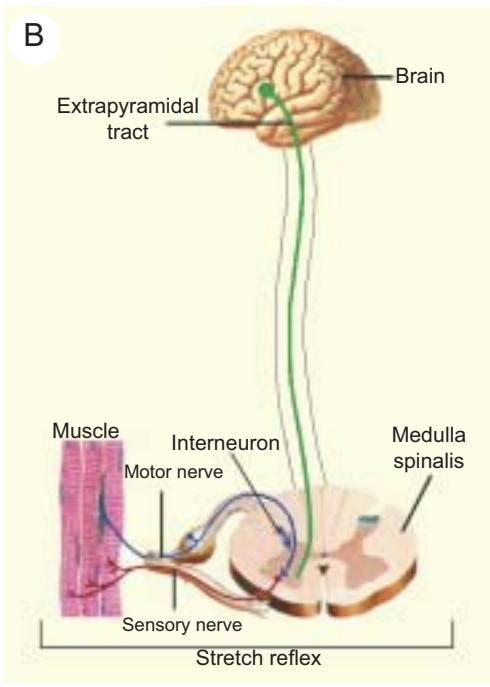
Muscle spindles in the contracting muscle, golgi tendon organs in the tendons and mechanoreceptors in the joints send information on the degree of contraction to the medulla spinalis, cerebellum and the somatosensory cortex.

The lower motor neuron sends contraction impulse to the muscle through the peripheral nerve. This is the final common pathway from the nervous system to the muscle.



The upper motor neuron syndrome	
A	<i>Positive findings</i>
	1. Increased muscle tone
	2. Exaggerated tendon reflexes
	3. Clonus
	4. Babinski positive
Negative findings	1. Loss of selective motor control
	2. Loss of hand and finger dexterity
	3. Muscle weakness
Results in muscle	1. Stiffness
	2. Contracture
	3. Fibrosis
	4. Atrophy

Table modified from: Mayer NH: Clinico-physiologic concepts of spasticity, Spasticity: Etiology, Evaluation, Management and the Role of Botulinum Toxin. Eds. Mayer NH, Simpson DM, WEMOVE, 2002



The hyperexcitability of the lower motor neuron is presumed to be the cause of spasticity. This hyperexcitability is evident in the increase in deep tendon reflexes.

D Modified Ashworth Scale	
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end range of motion when the part is moved in flexion or extension/abduction or adduction, etc.
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but the affected part is easily moved
3	Considerable increase in muscle tone, passive movement is difficult
4	Affected part is rigid in flexion or extension (abduction, adduction, etc.)

The upper motor neuron syndrome

CP results in an upper motor neuron syndrome [A] characterized by spasticity, exaggerated tendon reflexes, clonus, pathological reflexes, mass synergy patterns, muscle weakness, loss of selective motor control and loss of hand dexterity. Spasticity is a component of the upper motor neuron syndrome.

Definition of spasticity

Muscles show a physiological resistance to passive motion. This is called muscle tone. Spasticity is the increase in this physiological muscle tone. The terms “spasticity” and “increased tone” may be used interchangeably. Spasticity is velocity dependent. The faster the passive movement, the greater the resistance of the muscle. The increase in muscle tone causes loss of trunk balance and difficulty of active movement in the extremities.

Pathogenesis

The pathogenesis of spasticity is presumed to be an increase in the excitability of the lower motor neuron. This presents as hyperactive stretch reflexes [B] at clinical examination. Many hypotheses attempt to explain this hyperexcitability. One suggests a change in the balance of excitatory and inhibitory inputs to the motor neuron pool. When the inhibitory inputs are reduced, the interneurons send excitatory impulses to the lower motor neurons and they become hyperexcitable.

Measuring spasticity

Spasticity can be measured by clinical examination, mechanical instruments, and electrophysiological techniques [C]. The modified Ashworth and Tardieu scales are commonly used for clinical evaluation. They measure tone intensity but do not evaluate the effect of spasticity on function. Mechanical instruments measuring the resistance of the muscle to passive stretch and electrophysiological measures showing the hyperexcitability of the stretch reflex are used only for research purposes.

The Ashworth scale The Ashworth scale [D] is by far the most commonly used evaluation method for spasticity. Always test the patient while he or she is in a relaxed supine position. Passively move the joint rapidly and repeatedly through the available range of motion and grade the resistance using the definitions.

C Measurements in spasticity	
<i>Clinical measures</i>	
Range of motion	
Tone intensity measures	
Modified Ashworth Scale	
Tardieu Scale	
<i>Mechanical instruments</i>	
The pendulum test	
<i>Electrophysiological measures</i>	
The H reflex	
Vibration inhibition index	
<i>Functional measures</i>	
Upper extremity function	
Gait	

The Tardieu scale The Tardieu scale measures the intensity of muscle tone at specified velocities [A]. Note the joint angle at which the catch is first felt. Always grade the Tardieu Scale on the same day. Keep the body in a constant position for a given extremity. Keep the other joints, particularly the neck in a constant position throughout the test and from one test to another. Perform the test at a reproducible velocity of stretch.

Determine the effect of spasticity on the child's function, ease of care and quality of life by using various functional scales. This guides the treatment.

Effects of spasticity

Adverse effects Spasticity causes [B] difficulty in movement, abnormal posture in sitting and standing, contractures leading to deformities, pressure sores and pain. Increase in tone is uncomfortable. Sitting is difficult for the nonambulatory child because of increased adductor and hamstring muscle tone. The child slides out of the wheelchair and cannot be positioned properly. He cannot transfer to and from the bed, wheelchair and bathtub. Perineal hygiene and dressing the child require more effort. The ambulatory child has trouble initiating movement. He cannot wear his braces. Energy cost of movement increases. Loss of function results and parents have difficulty caring for the child.

When muscle tone increases, muscles become tight. This inhibits normal gait and posture. Normal movement patterns do not develop. Instead, the child shows abnormal or compensatory movement patterns. Spasticity affects muscle growth. Muscles need to be stretched while relaxed; failure to do this results in poor growth. Spasticity initially causes apparent muscle shortening but the passive range of motion is full. This abnormal permanent resistance is dynamic contracture. If uncorrected, fibrosis and eventually bony deformity lock the joint into a fixed contracture. How fast a contracture will develop depends on the severity of spasticity and the muscles involved: contractures progress more quickly in some muscles.

Bone growth is distorted by the abnormal resistance of the shortened muscles. Growing bone is easily distorted by sustained pressure. Untreated spasticity puts excessive stress on bone that produces abnormal rotation or it inhibits physiological derotation of long bones. If not relieved at an early stage, bone deformities occur. Prolonged equinovarus caused by triceps surae and tibialis posterior spasticity might rotate the tibia inwards. Spasticity of hip adductors can rotate the femur inwards. This inhibits the physiological derotation process of infantile femoral anteversion.

Beneficial effects Increased tone may be useful for the child. It helps maintain to keep the legs straight, thereby supporting the child's weight against gravity. The child with increased tone in trunk extensors may stand and take a few steps. Spasticity may help preserve muscle bulk and bone density.

References

- 2002 Mayer NH 'Clinicophysiological concepts of spasticity, Spasticity: Etiology, Evaluation, Management and the Role of Botulinum Toxin' Eds. Mayer NH, Simpson DM, WEMOVE
- 2002 Sheean G. 'The pathophysiology of spasticity' Eur J Neurol. 9 Suppl 1:3-9
- 2001 Gracies JM 'Pathophysiology of impairment in patients with spasticity and the use of stretch as a treatment of spastic hypertonia' Phys Med Rehabil Clin N Am 12(4):747-768
- 2001 Meythaler JM 'Concept of spastic hypertonia' Phys Med Rehabil Clin N Am 12(4):725-732
- 2001 Hinderer SR, Dixon K 'Physiologic and clinical monitoring of spastic hypertonia' Phys Med Rehabil Clin N Am 12(4):733-746
- 1992 Rymer WZ 'The neurophysiological basis of spastic muscle hypertonia' In The Diplegic Child: Evaluation and Management Sussman MD 21-30 American Academy of Orthopaedic Surgeons Rosemont
- 1986 Bohannon RW, Smith MB. 'Interrater reliability of a modified Ashworth scale of muscle spasticity' Phys Ther 67:206-207

A Tardieu scale	
Quality of muscle reaction is measured as:	
0	No resistance throughout the course of the passive movement
1	Slight resistance throughout the course of the passive movement
2	Clear catch at precise angle, interrupting the passive movement, followed by release
3	Unsustained clonus (less than 10 sec when maintaining the pressure) occurring at a precise angle, followed by release
4	Sustained clonus (more than 10 sec when maintaining the pressure) occurring at a precise angle

Angle of muscle action is measured relative to the position of minimal stretch of the muscle (corresponding to angle zero) for all joints except the hip where it is relative to the resting anatomical position.

B Effects of spasticity	
<i>Positive effects</i>	
	Extensor tone in the limbs help standing
	Preserve muscle bulk
	Preserve bone density
<i>Negative effects</i>	
	Masks contraction in the antagonist
	Difficulty in movement
	Abnormal posture
	Difficulty in sitting and transfers
	Inhibits muscle growth
	Leads to contractures
	Difficulty in hygiene and dressing
	Pressure sores
	Pain

A	Goals of spasticity treatment
	Increase function
	to perform better in activities of daily living
	to walk better
	Increase sitting ability and balance
	Prevent deformity & decrease contractures
	Pain relief
	Improve hygiene and patient care

B	Treatment methods
	<i>Physiotherapy</i>
	Positioning
	Exercises
	Stretching
	Neurofacilitation
	Electrostimulation
	<i>Splinting & Casting</i>
	<i>Oral medications</i>
	Baclofen
	Diazepam
	Clonazepam
	Dantrolene
	Tizanidine
	<i>Intrathecal medications</i>
	Baclofen
	Morphine
	Clonidine
	<i>Neuromuscular blocks</i>
	Local anesthetics
	Phenol
	Botulinum toxin
	<i>Orthopedic surgery</i>
	<i>Selective dorsal rhizotomy</i>

Essentials of Spasticity Treatment

Indications for treatment

Consider treating spasticity when it causes loss of function or produces contractures, deformities, pressure sores, or pain [A]. Additional indications include difficulty in positioning or caring for the total body involved child. Even though a wide range of treatments exist, none of them is fully satisfactory. Unwanted side effects limit the use of certain modalities. Some children do not respond to any of the antispasticity measures. The success of treatment depends on having specific goals in treatment, choosing the correct method according to the child’s problem and monitoring for side effects and complications.

Treatment methods

Treatment options are divided into reversible and permanent (surgical) procedures [B]. They can also be classified as systemic or local treatments. All treatment procedures aim to modulate the stretch reflex. In mild spasticity, basic measures such as positioning, exercises and bracing may be sufficient whereas in more severe cases, interventions can be more invasive. Often, treatments are combined to decrease side effects and to improve outcome.

Physiotherapy

Physiotherapy is a fundamental part of spasticity management. Muscle overactivity produces muscle shortening and muscle shortening increases spindle sensitivity. Muscle contracture and stretch sensitive muscle overactivity are intertwined. Therefore physical treatments aimed at lengthening the overactive muscles are fundamental. Address both shortening and overactivity. Consider applying various techniques such as positioning, ice, and exercises for these purposes.

Positioning Position the child to stretch the spastic muscles and decrease the sensitivity of the stretch reflex and the brain stem reflexes that trigger spasticity [C]. The therapists should teach these positions to the family so that the child lies and sits this way most of the time at home. Head supports may improve tone in the trunk muscles by providing a sense of safety and inhibiting the tonic neck reflexes. Advise use of the tailor-sitting position to reduce adductor spasticity [D]. Good seating provides a stable platform and facilitates good upper extremity function.

Stretching exercises Stretching muscles may prevent contractures and promote muscle growth. Spasticity decreases with slow and continuous stretching. This effect lasts from 30 minutes to 2 hours. Use stretching exercises before bracing and serial casting to obtain the necessary joint position.



Have the child sit with legs in front, knees extended and ankles in neutral to stretch the hamstring and gastrocnemius muscles. This position is difficult to maintain for long periods.



Sitting in a cross legged position applies slow static stretch to the adductors and decreases spasticity.

Neurofacilitation techniques Most neurofacilitation techniques are used to reduce muscle tone [A]. With the Bobath method, the therapist positions the child in reflex inhibitor positions and provides kinesthetic stimulation to inhibit the primitive reflexes and elicit advanced postural reactions to normalize muscle tone. With the Vojta method [B], different positions and proprioceptive stimulation are used for the same effect. Tone reduction lasts for a relatively short period of time with both methods.

Inhibitive (Tone Reducing) Casting and Bracing

Muscle relaxation after stretching exercises lasts for a short period of time. For longer duration the stretch on the muscle should be maintained for several hours every day. This is possible with the use of rigid splints or serial casting [C]. The effects are maximal if the cast or the splint is applied after the muscle is relaxed.

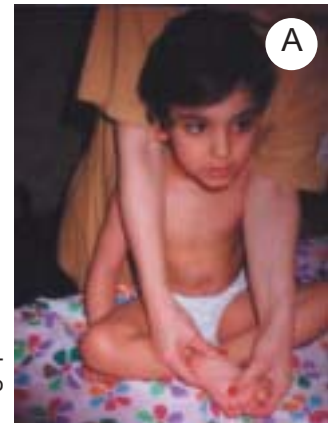
The tone-reducing effect of casts and splints is controversial. Some think that casts decrease muscle tone by creating atrophy in the already weak spastic muscle. Casts also cause pressure sores in children who are malnourished and have severe spasticity. Patient compliance may be poor because of difficulties of living with the cast.

Consider casting as an adjunct to treatment with local antispastic medications in the young diplegic or hemiplegic child with severe spasticity interfering with ambulation to delay orthopaedic surgery.

At present, the most common methods of spasticity management in cases of CP are oral medications, botulinum toxin, phenol or orthopaedic surgery [D].

References

- 2004 Tilton AH 'The management of spasticity' *Semin Pediatr Neurol* 11(1):58-65
 2001 Gracies JM 'Pathophysiology of impairment in patients with spasticity and the use of stretch as a treatment of spastic hypertonia' *Phys Med Rehabil Clin N Am* 12(4):747-768
 2001 Hinderer SR, Dixon K 'Physiologic and clinical monitoring of spastic hypertonia' *Phys Med Rehabil Clin N Am* 12(4):733-746
 2001 Meythaler JM 'Concept of spastic hypertonia' *Phys Med Rehabil Clin N Am* 12(4):725-732
 1988 Hinderer KA, Harris SR, Purdy AH, et al 'Effects of 'tone-reducing' vs. standard plaster-casts on gait improvement of children with cerebral palsy' *Dev Med Child Neurol* 30(3):370-7
 1998 Tilton AH, Ried S, Pellegrino L, et al 'Management of spasticity in children with cerebral palsy' In *Caring for Children with Cerebral Palsy: A Team Approach* Dormans JP, Pellegrino L, 99-123 Paul H Brookes Co Baltimore
 1991 Price R, Bjornson KF, Lehmann JF, et al 'Quantitative measurement of spasticity in children with cerebral palsy' *Dev Med Child Neurol* 33(7):585-95



The Bobath method uses positioning and kinesthetic stimulation to reduce muscle tone.



The Vojta method has two basic positions of reflex rolling and crawling used both to initiate movement and to diminish muscle tone.



Long leg casts keep the knees in extension and the ankles at 90° flexion.

D Treatment options in spasticity						
	Age	Patient group	Indication	Follow-up care	Result	Side-effect
Oral medications	Any age 2-5 most common	Total body involved	Severe spasticity	Rehabilitation	Mild reduction	Sedation, weakness
Botulinum toxin A	Any age 2-10 most common	All spastic types	Focal spasticity too young for other interventions	Range of motion, stretching, strengthening exercises	Effective for 3-6 months good results in walking and ADLs	None obvious
Intrathecal baclofen	Above age 3 Abdomen large enough for pump insertion	Total body involved spastic or dystonic	Severe spasticity interfering with function or patient care	Range of motion exercises	Less need for orthopaedic surgery easier care better sitting	Infection Cerebrovascular fluid leak
Orthopaedic surgery	5-15 years	All spastic types	Contractures & deformities	Strengthening	Better walking	Recurrence, weakness
Selective dorsal rhizotomy	3-7 years	Diplegic patient with pure spasticity	Spasticity interfering with walking	Intensive physiotherapy	Controversial	Increasing scoliosis, hip instability risk of incontinence

Oral Medications

Various pharmacological agents decrease spasticity. Baclofen, benzodiazepines (diazepam, clonazepam), dantrolene sodium and tizanidine are commonly used in children [A].

Indications

Consider systemic oral antispastic drugs in total body involved nonambulatory children with generalized spasticity. They are also useful for short periods after orthopaedic surgery. Systemic side effects such as drowsiness, sedation, and generalised weakness are common, so they generally are not recommended for ambulatory children. Keep the initial dose low and gradually titrate to a level at which the effect is maximal and the side effects are minimal. The responses of the children to oral antispastic drugs are not consistent. Try different drugs to achieve a satisfactory clinical effect.

Oral antispastic drugs

Baclofen

Baclofen is an agonist of the main inhibitory CNS neurotransmitter gamma aminobutyric acid (GABA). It shows its effect mainly on the spinal cord. It decreases spasticity by increasing the inhibitory effect of the interneuron on the alpha motor neuron. The lipid solubility of baclofen is poor, so it cannot easily cross the blood brain barrier. High oral doses are necessary to achieve a therapeutic dose in the cerebrospinal fluid (CSF). The effect starts 1 hour after ingestion and lasts for 8 hours. The drug must be taken three to four times daily in divided doses. Daily dose for children between ages 2 to 7 is 10 to 15 mgrs per day with a maximum of 40 mgrs per day. After the age of 8 years, the dose may be increased to 60 mgrs per day. Maximum doses range between 80 to 120 mg. per day in adults. Side effects including sleepiness, sedation, drowsiness, fatigue, headache, nausea, and a decrease in seizure threshold are commonly associated with increasing doses. Baclofen also causes generalised muscle weakness. All side effects are dose dependent. Sudden withdrawal may cause hallucinations and seizures sometimes accompanied by extreme hyperthermia and increased spasticity called the baclofen withdrawal syndrome. The dose of the drug must be decreased gradually.

Diazepam

Diazepam is a benzodiazepine tranquillizer that works as a GABA agonist. It enhances the presynaptic inhibitory effect of GABA and decreases spasticity. It is absorbed faster than baclofen, acts faster, and has a longer lasting effect. Doses in children range between 0.12 to 0.8 mg/kg body weight with a maximum of 20 mg. daily divided into two or three equal doses. Diazepam decreases painful muscular spasms and improves sleep. Sedation and other CNS side effects are very common, so this drug is not recommended for treating ambulatory children except after orthopaedic surgery when it improves the child's tolerance and participation in the rehabilitation program. CNS side effects are weakness, memory loss, ataxia, depression, and dependency.

Clonazepam

Clonazepam has an effect similar to that of diazepam, but it has a slightly longer half-life. It is preferred over diazepam because its side effects are fewer. Initial dose is 0.1 to 0.2 mg/kg/day. This dose is titrated for an optimal effect.

Dantrolene sodium

Dantrolene sodium inhibits muscle contraction by blocking calcium release from the sarcoplasmic reticulum in the muscle fiber. Initial dose is 0.5 mg/kg of body weight with a maximum dose of 3 mg/kg of body weight. Total daily dose should not exceed 12 mg per day administered in four divided doses. Side effects include muscle weakness, sedation, diarrhoea, and hepatotoxicity. CNS side effects are rare. Liver function tests should be performed two to four times a year, and the total treatment duration should not exceed 2 years.

Tizanidine

Tizanidine is an alpha adrenergic receptor agonist. It shows its effect at the brain and the spinal cord level. Tizanidine decreases the release of excitatory neurotransmitters and increases the release of inhibitory neurotransmitters. Guidelines for use in children are not well established. In adults the initial dose is 2 to 4 mg. administered at 4 hour intervals and increased to 36 mg. as needed. It may cause drowsiness, nausea, hallucinations, and is hepatotoxic.

References

2001 Elovic E 'Principles of pharmaceutical management of spastic hypertonia' Phys Med Rehabil Clin N Am 12(4):793-816

A Oral antispastic agents in CP			
	<i>Baclofen</i>	<i>Diazepam</i>	<i>Dantrolene</i>
<i>Mechanism</i>	GABA analogue	Postsynaptic GABA-mimetic	Inhibits Ca ⁺⁺ release from sarcoplasmic reticulum
<i>Dose</i>	2.5 mg/day increased to 30 mg for 2 - 7 years 60 mg for 8 and above	0.12 - 0.8 mg/kg/day divided doses	0.5 mg/kg twice daily 3 mg/kg q.i.d.
<i>Duration</i>	2 - 6 hours	20 - 80 hours	4 - 15 hours
<i>Side Effect</i>	Seizure activity	Cognitive	Hepatotoxicity

Neuromuscular Blocking Agents

Local Anesthetics, Phenol, Botulinum Toxin

Consider using local anesthetics, alcohol, phenol and most recently, botulinum toxin as neuromuscular blocking agents [A] when treating focal spasticity.

Local anesthetics

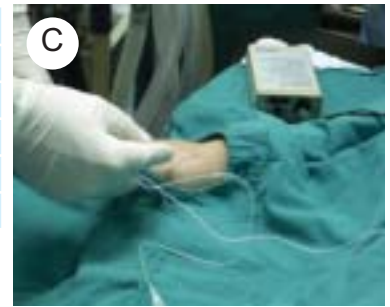
Mechanism of effect

Local anesthetics block nerve conduction by changing membrane permeability to sodium ions. They affect both sensory and motor function in the area innervated by the nerve. This effect is completely reversible and causes no structural damage to the nerve. The effect starts within 3-15 minutes after the injection and lasts from 45 minutes to 8-12 hours depending on the type of drug used. Median nerve in the upper extremity and many nerves in the lower extremity are available for local anesthetic blocks [B].

Dosing and administration

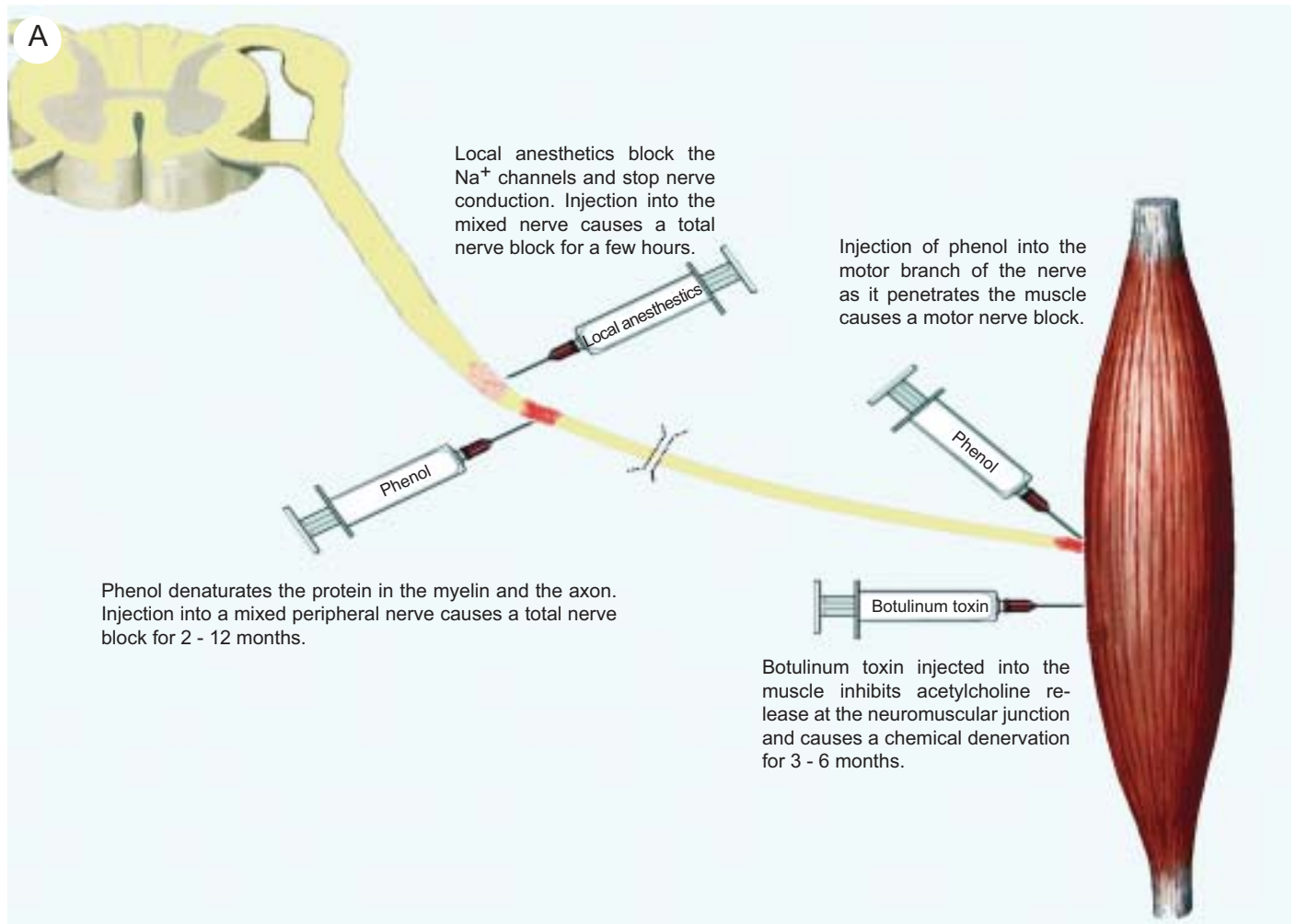
Lidocaine, etidocaine and bupivacaine are used for nerve blocks. Prefer bupivacaine because it is more potent and its duration of action is longer. It can be injected in amounts up to 3 mg/kg of 0.25 to 0.75% of a solution. Do a perineural injection when you want to block the motor, sensory and autonomic fibers in the nerve. A motor point block affects the motor fibers only. A peripheral nerve stimulator that gives a low intensity electrical current through a needle electrode is used for blocks [C]. Use small needles and give short-lasting stimuli to localize the nerve more accurately. This makes the procedure less painful [D].

Local anesthetic blocks	
B	Median block
	Tibial block
	Obturator
	Femoral
	Sciatic



Electrical stimulation is used to locate the median nerve. Local anesthetic block to the median nerve results in total sensory and motor loss in the area innervated by the nerve. The effect lasts for a couple of hours.

D Electrical stimulation technique	
1.	Locate the motor point or the nerve with the help of a stimulator. Charts exist for the location of each nerve.
2.	Cleanse the skin. Choose the injection site and start stimulating the nerve. Adjust stimulation intensity first to a maximum, when the muscles innervated by the nerve begin to twitch, lower the intensity to 0.2-0.5 miliamperes.
3.	If the muscle is still contracting, aspirate first and then inject the local anesthetic or phenol until the muscle is silent.
4.	Increase the stimulus intensity to control the block. If there is no contraction at maximum stimulus intensity, the block is efficient. If not, inject more until the contraction stops.



Indications for local anesthetic blocks	A
Differentiate spasticity from contracture	
Predict functional changes	
Distinguish the muscles that contribute to spasticity	
Evaluate the presence of selective motor control	

Advantages of local anesthetic blocks	B
Reversible short duration effect	
Relatively painless	
Helps differentiate contracture from spasticity	
Unmasks activity in the antagonists by relaxing the spastic muscles.	

Side effects and precautions	C
Hypersensitivity reaction	
Hematoma at injection site	
Sudden weakness may cause injuries in the unprepared patient	
Systemic toxicity (dose related)	



The injection may be painful and is best performed under general anesthesia in young children.

Phenol blocks for lower extremity spasticity	E
The rectus femoris motor point block	
The hamstring motor point block	
Adductor muscle motor point block	
Tibial nerve block	

Indications

Local anesthetic blocks may be used as a diagnostic tool to differentiate spasticity from contracture and to predict functional changes with long term therapy [A]. The block may clarify which muscles contribute to spasticity and unmask selective motor control in the antagonist muscles if there is any. Block the median nerve at the elbow to evaluate the upper extremity. The hand relaxes completely a couple of minutes after the injection if the flexion in the wrist and fingers is because of spasticity. Bring the fingers into extension while holding the wrist in extension. The joint will not relax if there is a contracture. Thus, a local anesthetic block aids the physician in the decision making process of treatment of the spastic hand.

Advantages

Local anesthetics have a short and reversible effect, so they are useful for diagnosis of the problem and differentiating contracture from dynamic spasticity [B].

Side effects and precautions

Local anesthetics rarely cause a hypersensitivity reaction in the form of a mild rash. Fatal anaphylactoid reactions have been reported. Hematoma may occur at the injection site. There can be significant changes in walking and transfers after a nerve block. The sudden decrease in muscle tone may result in falls and injuries in the few hours after the block. In high doses, local anesthetics may have systemic toxic side effects if they enter the systemic circulation by mistake. This is uncommon in children and in doses used for peripheral nerve blocks [C].

Chemical neurolysis: alcohol and phenol

Alcohol and phenol are chemical agents that block nerve conduction by creating a lesion in a portion of the nerve.

Alcohol

Ethyl alcohol acts as a local anesthetic by decreasing sodium and potassium conductance at the nerve membrane at low concentrations. It causes protein denaturation at higher concentrations such as 50%. Intramuscular injection of ethyl alcohol causes burning pain, therefore children must be injected under general anesthesia [D].

Even though alcohol has fewer adverse effects and is safer than phenol it has not been used as extensively in spasticity treatment possibly because of the pain it causes during the injection. Phenol blocks are generally used for lower extremity spasticity [E]. Recently botulinum toxin was added to the armamentarium of focal spasticity treatment [F].

	Local Anesthetics	Phenol (6%)	Botulinum toxin A (Botox®)	F
<i>Mechanism</i>	Blocks sodium channels	Denatures protein	Inhibits acetylcholin release	
<i>Onset</i>	Minutes	Less than an hour	Days	
<i>Duration</i>	Hours	2-36 months	3-6 months	
<i>Dose</i>	Bupivacaine (0.25-0.75%) <3mg/kg	Less than 10 ml (1 gm)	400 units at one single time	
<i>Precaution</i>	Hypersensitivity	Pain-dysesthesia	None	
<i>Indication</i>	Differentiate spasticity from contracture Test effects before long term blocks Relax muscles before casting	Proximal large muscles mainly motor nerves (no mixed nerve) More for hygiene and comfort In combination with BTX-A	All muscles accessible for injection Especially smaller muscles Active function Combination with phenol	
<i>Technique</i>	Stimulation - motor point	Stimulation - motor point	Stimulation - EMG guide Motor point or end-plate targeting	

Phenol

Mechanism of effect Phenol is benzyl-alcohol or carbolic acid with the old terminology. It has been used as a disinfectant and antiseptic. It causes protein denaturation and non-selective tissue destruction in the injected area. Wallerian degeneration of neurons occurs in the weeks following injection. Most axons regrow, over a period of time [A]. The effect of phenol starts rapidly because of its local anesthetic properties and lasts for up to 2 to 12 months.

Dosing and administration The usual dilution is 3 to 6% depending on the technique and the injection site. There are two techniques to apply phenol blocks: the motor point block and the motor nerve block. Motor point and motor nerve injection sites must be identified using electrical stimulation as explained in local anesthetic blocks. Electrically stimulating to find the motor points enables the physician to use very small quantities of the drug to obtain good clinical response [B].

Indications The advantages [C] include an early onset of action, longer duration of effect and low cost. In addition, there is no antibody formation to phenol so that larger, more powerful muscles may be treated without dosing considerations. Although the injection is painful at first, pain resolves in seconds because of its analgesic effects and injections are as easy as botulinum toxin injections for the experienced physician.

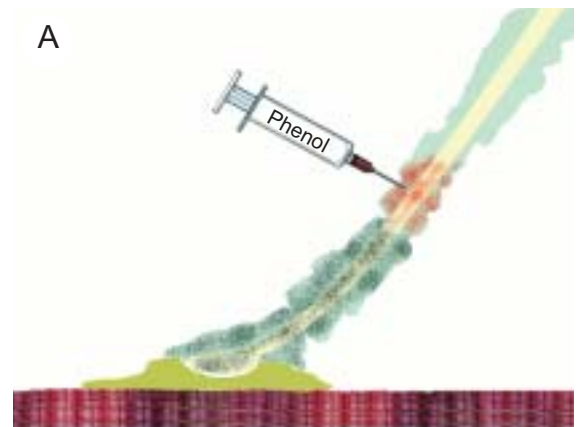
Side effects and precautions The main risks to be aware of when using phenol for spasticity management are permanent nerve injury, causalgia or neuropathic pain because of sensory fiber damage, tissue edema, venous thrombosis, and compartment syndrome resulting from large amounts of phenol in constrained space [B].

Avoid using phenol in the upper extremity because nerves in the upper limb are mainly mixed nerves and motor point blocks are difficult. Risks of dysesthesia, causalgia, venous thrombosis, and compartment syndromes are higher. Phenol is destructive to tissues, intramuscular administration in the small child may lead to unwanted and irreversible muscle fiber atrophy.

Combination treatment At present phenol has a rather small but useful place in spasticity treatment [D]. State-of-the-art treatment for focal spasticity relief is botulinum toxin. However, there is an upper limit to the amount of botulinum toxin that can be used in a single setting so a combination of phenol with botulinum toxin is preferred to better control multisegmental focal spasticity and to provide a longer duration of effect. Use phenol for large lower extremity muscles and botulinum toxin for smaller lower and all upper extremity muscles for multilevel injections whenever the necessary botulinum toxin dose exceeds the maximum amount you can use.

Botulinum toxin

Botulinum toxin, produced by the anaerobic bacteria *Clostridium botulinum*, is one of the most potent poisons known to man. In the past two decades it has been transformed into one of the most useful antispastic agents. Of the seven distinct toxins from A to G, only type A and B are used for therapeutic purposes. The structure of all toxins and their mechanism of action are similar, only their site of action is different.

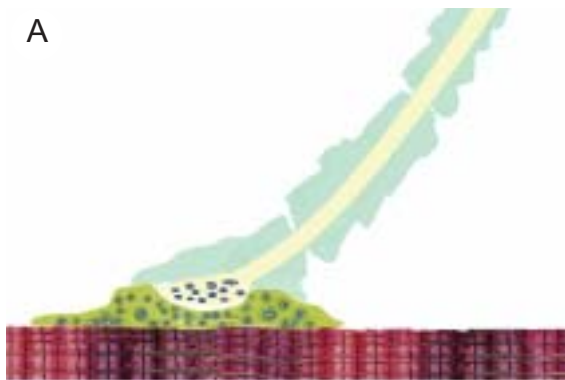


Phenol denaturates proteins in the myelin sheath and the axon. It also causes nonselective tissue destruction. The effects are reversible, most axons regrow.

Advantages of phenol	
Rapid action	B
Longer duration	
Low cost	
No antibody formation	

Dysadvantages and precautions	
Relatively painful injection	C
Chronic dysesthesia and pain	
Peripheral edema, deep venous thrombosis	
Reversible sensory loss	
Systemic side effects (dose related)	
Relatively difficult technique	

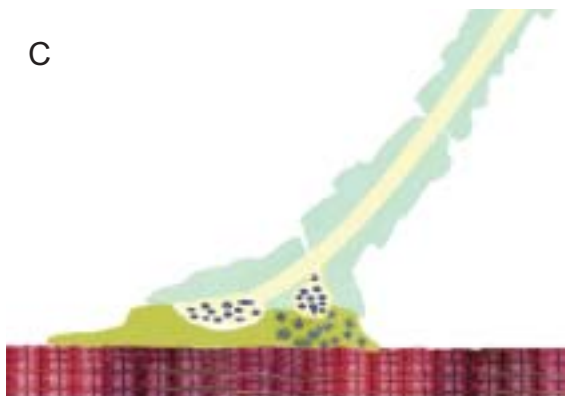
Hints on using phenol	
Avoid using in the upper extremity	D
Do not inject mixed peripheral nerves	
Only inject motor nerves	
The most common uses are rectus femoris motor point block obturator nerve block hamstring motor point block tibialis posterior nerve block (mixed nerve!) gastrocnemius motor point block	
Use 6 % concentration of phenol	
Maximum dose 1 ml/kg body weight	
The effects are immediately obvious	
Use 0.5-1 ml for motor point blocks	
Use up to 3 ml for nerve blocks	



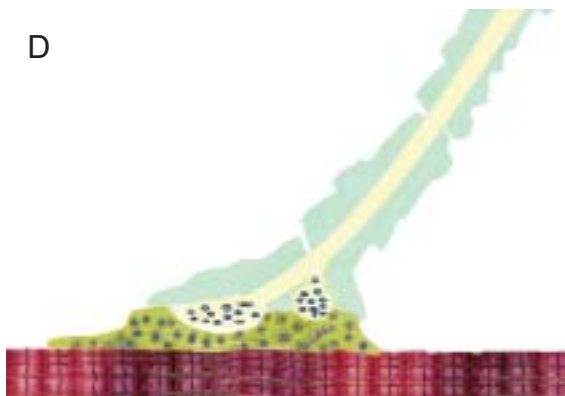
Muscle contraction depends on acetylcholine release from the axon terminal into the synaptic cleft.



Botulinum toxin blocks acetylcholine release. The axon terminal has normal amount of acetylcholine but the end-plate is not functional.



A nerve sprout forms immediately proximal to the dysfunctional end-plate and innervates the muscle fiber.



Eventually the original end-plate regains function as the effect of toxin wears off.

The mechanism of effect

The toxin inhibits acetylcholine release at the neuromuscular junction causing a reversible chemodenervation. Studies suggest that the toxin affects the muscle spindle and afferent nerve fibers as secondary actions.

Effect at the neuromuscular junction The toxin must enter the nerve endings to exert its effect. It becomes fully active once inside the cholinergic nerve terminal.

When the impulse for contraction arrives at the axon terminal acetylcholine (ACh) vesicles fuse with the nerve membrane and the ACh is released into the synaptic cleft. This causes excitation in the muscle fiber and muscle contraction [A]. The various serotypes of botulinum toxin act on different portions of the acetylcholine vesicle complex. Botulinum toxin inhibits the fusion of acetylcholine vesicles at the pre-synaptic membrane. ACh cannot be released into the synaptic cleft, the impulse from the nerve to the muscle fiber is blocked and the muscle fibers innervated by that axon cannot contract. This is chemical denervation [B]. The extent of muscle weakness created by the botulinum toxin depends on the serotype, dose and volume of toxin used.

The effect of botulinum toxin is reversible. Nerve sprouts form at the unmyelinated terminal axon immediately proximal to the end plate. These sprouts innervate the muscle fiber [C]. Eventually, the original neuromuscular junction regains function [D]. This terminates the clinical effect in 3 - 6 months and spasticity reappears.

Afferent effect The toxin may block the sensory afferents from the muscle spindle. This reduces spindle sensitivity and consequent reflex action.

Analgesic effect There is an analgesic effect of the toxin explained by a couple of mechanisms. First, decreasing spasticity decreases pain. Second, botulinum toxin affects afferent transmission and inhibits the release of substance P. Substance P is the primary mediator of pain in the spinal cord and the brain. Inhibition of its release together with the block in afferent transmission result in pain relief.

Specific pharmacology

The potency of the toxin is defined by mouse units. One mouse unit is the amount required to kill 50% of a group of female Swiss-Webster mice. There are two different commercial preparations for botulinum toxin; Botox® (Allergan), and Dysport® (Speywood) [B]. BTX-B is available as Myobloc™ in the United States and NeuroBloc® in Europe and elsewhere.

There are 100 units of botulinum toxin in one vial of Botox and 500 units in one vial of Dysport. The clinical potency of Botox and Dysport are influenced by numerous factors including the way they are produced. Therefore, the units are not interchangeable and there is no equivalence ratio between the two products [A on opposite page].

Indications

Botulinum toxin injections have been used as a safe and effective treatment for spastic CP for the past 10 years. Botulinum toxin B is also becoming commercially available.

The general indication for botulinum toxin injections in CP is 'the presence of a dynamic contracture, interfering with function, in the absence of a fixed muscular contracture'. If botulinum toxin injections are started at an early age and repeated as necessary, they can help prevent the development of muscle contractures and bony deformities. This helps to delay orthopaedic surgery until the gait is mature. The need for extensive surgical procedures may be eliminated if bony deformities are prevented by botulinum toxin.

The success of botulinum toxin administration depends on many factors. Patient selection is critical [B]. Children with spasticity who do not have fixed contractures benefit a great deal from treatment whereas patients with dyskinesia have a variable response and athetoids do not benefit at all.

The timing of the injections is controversial. Most clinicians agree that the earlier the spasticity is reduced, the better the outcome. Botulinum toxin can be injected as early as 18 months of age. There is no upper age limit, however, once the muscle is shortened as occurs with age, the effect of spasticity relief will not be apparent because of contracture.

Dosing and administration

Botulinum toxin dosing depends on which preparation is used. Dysport dosing is different than Botox and there is no equivalence ratio between the two preparations in terms of clinical effect. The doses mentioned here refer to Botox injections [C,D]. The amount changes according to the number of muscles to be treated, prior response of the patient if there are any prior injections and functional goals.

The dose limits range from 2 units to 29 units/kg of body weight, most common range being between 10-20 units/kg of body weight. Avoid injecting more than 400 to 600 units of total dose at any one time, injecting more than 50 units at one injection site and exceeding 20 units per kilogram per muscle at any one time. If there is a need for more toxin because of multilevel involvement, combine treatment with phenol. Inject larger muscles with phenol and use botulinum toxin for more distal and smaller muscles [E].

Targeting the neuromuscular junction during the injection using electrical stimulation guide may result in more effect for less volume. Even though no serious complications have been reported, it is a good idea to apply high doses under general anesthesia in the operating theatre. Reduce the dose if the child is small and has atrophic muscles, if the treatment is going to be repeated for a number of times and if multiple muscles are being injected. Severely spastic and larger muscles should receive a larger dose whereas less spastic and small muscles receive a smaller dose [F].

The amount of toxin given to one muscle must be divided into more than two injection sites, depending on the dose. Put a safe distance between two injection sites with high doses. This increases the diffusion of the toxin in the muscle and prevents it from entering the systemic circulation. Divide the total dose per muscle over more sites as much as possible. For example, for a 20 kg child who has a very spastic gastrocnemius muscle, the dose should be 6 U/kg/muscle, 120 U total. This dose should be divided into 4 injection sites, 30 units per site in the muscle.

E Recommended dosages	
Per muscle of lower limb	3-6 U/kg
Per kg total body weight:	12 U/kg proven dosage
Maximum dose per session	400 U
Frequency:	Not more than once every 3 months Usually at least 6 month intervals
Dilution	100 U in 1 or 2 ml 0.9% NaCl
Maximum dose per site	50 U

Comparison of botulinum toxin A preparations		
<i>Preparation</i>	Dysport	Botox
<i>Company</i>	Ipsen	Allergan
<i>1 ng toksin-hemagglutinin</i>	20 m.u.	> 5 m.u.
<i>Contents of one vial</i>	500 m.u. (12,5 ng)	100 m.u.(40 ng)

The relative potency of these preparations has not been established yet.

Specific goals for botulinum toxin A treatment
To improve walking in the spastic diplegic and hemiplegic child
To minimise adductor tone in the child with early hip subluxation
To decrease the spasms and pain in the spastic-athetoid patients
To reduce tone in the psoas muscle in patients with back pain because of hyperlordosis
As a simulation for orthopedic surgery, to have a general idea of how the child will be when spasticity is reduced.

General guidelines for upper extremity spasticity		
<i>Muscles injected</i>	<i>Dose range (units/kg of bw)</i>	<i>Number of sites per muscle</i>
Biceps	2	2-3
Pronator teres	1	1
Flexor carpi radialis	2	1
Flexor carpi ulnaris	2	1
Flexor digitorum superficialis	2	1-2
Flexor digitorum profundus	2	1-2
Flexor pollicis longus	0.5-1	1
Adductor pollicis	0.5-1	1

General guidelines for lower extremity spasticity		
<i>Muscles injected</i>	<i>Dose range (units/kg of bw)</i>	<i>Number of sites per muscle</i>
Iliopsoas	2	2
Quadriceps	3-6	4
Medial hamstrings	3-6	3-4
Lateral hamstrings	2-3	2
Adductors	3-6	2
Gastrocnemius	3-6	1-2
Soleus	2-3	1
Tibialis posterior	1-3	1

In general maximum of 50 U/site

F Botox® dose modifiers		
	<i>Decrease dose if</i>	<i>Increase dose if</i>
<i>Patient weight</i>	Low	High
<i>Duration of therapy</i>	Chronic	Acute
<i>Muscle bulk</i>	Very small	Very large
<i>Number of muscles injected simultaneously</i>	Many	Few
<i>Ashworth score</i>	Low	Very high
<i>Concern about weakness</i>	High	Low
<i>Results of previous therapy</i>	Too much weakness	Inadequate response

Table reproduced with permission from WE MOVE New York www.mduv.org.

General guidelines for spastic CP A		
Type of CP	Muscles involved	Problem
Hemiplegic	Rectus femoris	Stiff knee gait
	Gastrosoleus & tibialis posterior	Pes equinovarus
	Flexor – pronator spasticity	Thumb in palm deformity, flexion of the wrist and digits
Diplegic	Multilevel lower extremity injections	Adductor - flexor spasticity of the hip
		Hamstring spasticity causing knee flexion
		Gastrosoleus spasticity causing pes equinus
Quadriplegic	Hip adductors	Prevent hip subluxation
	Hamstring spasticity	Sacral sitting
		Sitting balance



Examine the child once again under general anesthesia. If there is no limitation of passive range of motion under general anesthesia, there are no contractures and the botulinum toxin injections will be useful. If there is limitation in joint motion indicating a fixed contracture, there will be a limited response to botulinum toxin.



Injection to the belly of the medial gastrocnemius with EMG guidance



Injecting the flexor pollicis brevis muscle using electrical stimulation

Patient Selection

Botulinum toxin is useful in various upper and lower extremity problems in spastic cerebral palsy cases [A].

Muscle selection

Choosing the right muscles to inject depends on a good clinical evaluation [B]. Evaluate passive range of motion at the ankle, knee and hip; measure spasticity using the modified Ashworth or the Tardieu scale and determine strength and selective motor control of different muscle groups of the lower limbs. Gait analysis using dynamic EMG may be helpful in complex cases.

Injection technique

Needle size depends on site of injection and physician preference. 1.0 ml tuberculin type syringes and 26-30 gauge, 1/2 inch (1.5 cm) needles are used. Teflon-coated monopolar injection needles are necessary for stimulation and injection with EMG or electrical stimulation guide [C].

Targeting Botulinum toxin dosing and injection technique is relatively easy. For optimal results the physicians must be experienced in managing children with CP. Difficult-to-localize muscles often require adjunctive methods to confirm injection sites and to target the region of the neuromuscular junctions. Electromyography (EMG), electrical stimulation [D], computerized tomography (CT), fluoroscopy, and ultrasound have been used to target the region of maximum muscle activity. The technique of electrical stimulation is the same as in local anesthetic blocks. Efficacy is maximal and adverse effects minimal if the muscles are targeted properly.

Sedation The injection is not painful, but may be a cause of distress in young children and in multilevel injections. It is rather difficult to inject certain muscles such as the hamstrings or iliopsoas in a fully awake and frightened child in the outpatient setting. Consider a simple sedative like diazepam or chloral hydrate when injecting single muscles in the outpatient clinic. Using EMG or ES guide and injecting multiple muscles is a considerable stress on the child so perform these under local anesthesia, conscious sedation using midazolam or general anesthesia.

Preparation Keep the toxin frozen in vial. Dilute with normal saline to the desired concentration prior to usage [E]. The toxin is in a vacuumed vial, when diluting hold the piston of the syringe steady because sudden inflow of saline into the vial may cause protein denaturation and loss of pharmacological activity. Then put a second needle through the lid to balance the negative pressure inside the vial before drawing back the diluted toxin.

Injection Clean the area, put sterile gloves on, localize the target muscle [A - L on opposite page], inject the desired amount into the muscle belly. You may need to inject at two or more sites depending on the dose and muscle size.

E Dilutions	
For 100 units of Botox preparation	
Aimed final dilution	Saline added to vial
2.5 U/0.1 ml	4 ml.
5.0 U/0.1 ml	2 ml.
10.0 U/0.1 ml	1 ml.



A Adductor longus muscle: Patient lies supine. Abduct the leg to 15°. Palpate the tendon arising from the pubic tubercle and insert the needle 2-4 finger breadths distal to the tubercle into the muscle belly.



B Adductor magnus muscle: Patient lies supine. Abduct and externally rotate the leg. Insert the needle midway between the medial femoral epicondyle and the pubic tubercle.



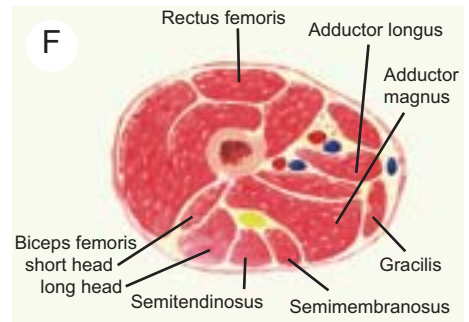
C Rectus femoris: Patient lies supine. Insert the needle on the anterior aspect of the thigh, midway between the superior border of patella and the anterior superior iliac spine.



D Medial hamstring muscles: Patient lies prone. Insert the needle at the midway on a line between the medial femoral epicondyle and the ischial tuberosity.



E Lateral hamstring muscles: Patient lies prone. Insert the needle at the midway on a line between the fibula head and the ischial tuberosity.



F Coronal view of commonly injected thigh muscles



G Gastrocnemius, medial head: Patient lies prone, leg extended. Insert at the most prominent point of the medial muscle mass (approximately 3 fingers to one handbreadth below the popliteal crease.)



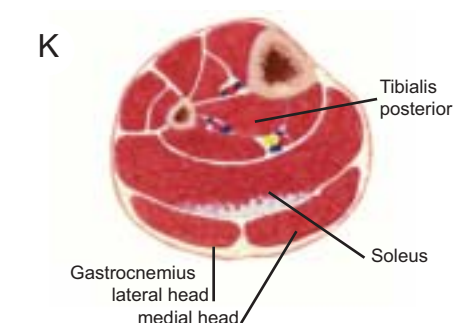
H Gastrocnemius, lateral head: Patient lies prone, leg extended. Insert at the most prominent point of the lateral muscle mass (approximately 3 fingers to one handbreadth below the popliteal crease.)



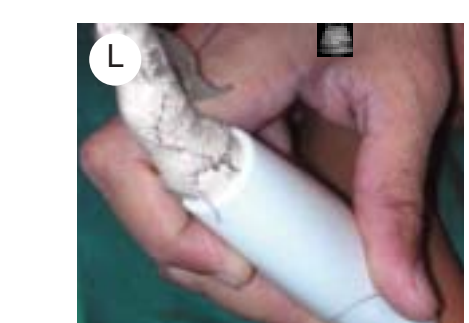
I Soleus: Patient lies prone, the leg is extended. Insert the needle deep just distal to the belly of the gastrocnemius muscle, medial and anterior to the Achilles tendon.



J Tibialis posterior: Patient lies prone, with the leg in internal rotation. Draw a line from the popliteal crease to the medial malleolus. Inject one finger breadth off the medial edge of the tibia, directly obliquely through the soleus and the flexor digitorum longus, just posterior to the tibia.



K Coronal view of commonly injected calf muscles



L Ultrasonographic guidance can be helpful especially when injecting deep muscles. Courtesy D. Ganjwala



Put the cast on and bivalve it if possible while the patient is still sedated so that the trauma of casting will be minimal.

B Resistance	
<i>Primary nonresponder</i>	<i>Secondary non responder</i>
No response to initial injection	Relative or complete loss of effect after second injection
Presence of antibodies	Low dose Poor technique Change in spasticity Inappropriate reconstitution Inappropriate storage Antibody formation

C Advantages	Dysadvantages
The minimality of side effects	Cost
Ease of application	Availability
Relatively painless injection	
Reversible effect (may not be an advantage)	
No permanent injury to tissues	

D Side effects
(Rare, all reversible)
Slight weakness at site of injection
Local pain
Flu-like syndrome
Generalized weakness
Incontinence

E Contraindications & precautions
Aminoglycoside antibiotic use
Pregnancy (for adult CP patients)
Lactation (for adult CP patients)

Post-injection treatment

The antispastic effect appears within 24 hours to 3 days after injection and becomes maximum at 10 days to a month. It lasts for 3 to 6 months. Some patients are golden responders in whom the antispastic effect lasts for over a year. Proper exercises, splinting and casting may increase the number of golden responders.

Casting for 2 to 3 weeks after injections may improve the results. Botulinum toxin relieves dynamic spasticity whereas casting addresses fixed contracture. Consider casting for two weeks beginning on the third day after the injection in severe cases. If injecting under conscious sedation or general anesthesia, put the cast on when the child is sedated or asleep [A].

Problems related to casting are psychological trauma of putting the cast on and taking it off and muscle atrophy.

Physical therapy Perform range of motion and strengthening exercises in an intensive manner to obtain maximum benefits from the injection. Intensive exercises and electrical stimulation after the injection may increase toxin uptake by the nerve terminal and potentiate the effect.

Orthotic management Continue bracing as prior. Brace tolerance generally increases after the injection.

Resistance

A small percent of children may not respond to initial injection of botulinum toxin. Consider one or more treatments before classifying patient as a “non-responder”. A secondary non-responder is a child who shows a relative or complete loss of effect after a second injection. The reasons are too low a dose, poor injection technique, a change in the spastic muscles during treatment, inappropriate reconstitution or storage of toxin and the presence of neutralizing antibodies.

Development of resistance to botulinum toxin therapy is characterized by absence of any beneficial effect and by lack of muscle atrophy following the injection. Antitoxin antibodies are presumed responsible for most cases of resistance. Use the smallest possible effective dose and extend the time interval between treatments to at least 3 months to reduce the likelihood of antibody development. Botulinum toxin B or F may benefit those who have developed antibody resistance.

Advantages and disadvantages

Side effects are few, mild and rare. The injection is relatively easy compared to phenol. There is no permanent tissue injury and all the effects are reversible. The cost is the only factor limiting toxin use [C].

Contraindications

Side effects are extremely few [D]. Slight weakness at injection site, local pain, fever, generalised weakness and fatigue presenting as a flu-like syndrome, respiratory tract infections, temporary incontinence and constipation have been reported with an incidence of 2-3%.

Contraindications include patients who are hypersensitive to any ingredient in botulinum toxin, who are using aminoglycoside antibiotics, pregnant or may become pregnant, or in lactation [E]. These contraindications are not absolute and not really relevant for children with CP. Patients who have a neuromuscular junction disease such as myasthenia like syndrome are not appropriate candidates for botulinum toxin therapy.

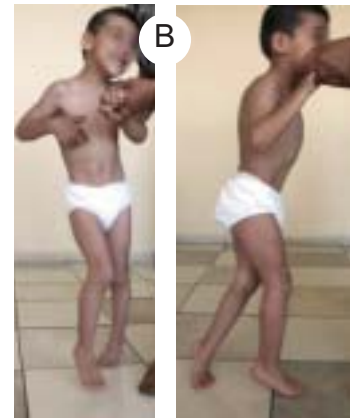
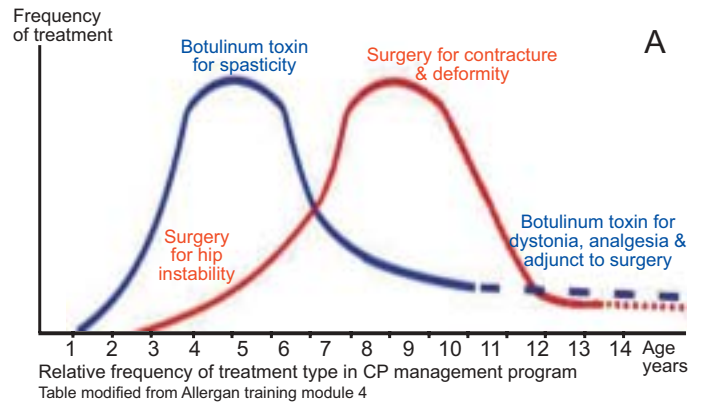
Conclusion

Botulinum toxin has an established place in the treatment of spasticity in cerebral palsy. Consider botulinum toxin treatment as early as two years of age and combine with other treatment options as the child grows older and spasticity begins to cause contractures and deformities [A].

The only factors limiting its use are high cost and restriction on the maximum dose per treatment session. The most common indications are young diplegic [B] and hemiplegic [C] children.

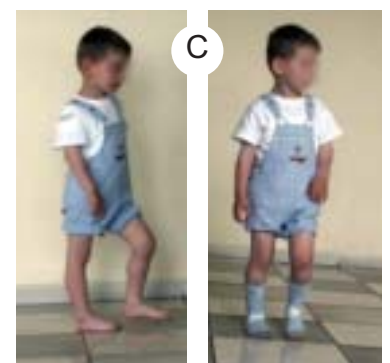
References

2004 Berweck S, Heinen F 'Use of botulinum toxin in pediatric spasticity (cerebral palsy)' *Mov Disord.* 19 Suppl 8:S162-7
 2004 Gooch JL, Patton CP 'Combining botulinum toxin and phenol to manage spasticity in children' *Arch Phys Med Rehabil.* 85(7):1121-4
 2001 Boyd RN, Hays RM 'Outcome measurement of effectiveness of botulinum toxin type A in children with cerebral palsy: an ICIDH-2 approach' *Eur J Neurol* 8 Suppl 5:167-77.
 2001 Koman LA, Brashear A, Rosenfeld S, et al 'Botulinum toxin type A neuromuscular blockade in the treatment of equinus foot deformity in cerebral palsy: a multicenter, open-label clinical trial' *Pediatrics* 108(5):1062-71
 2001 Zafonte RD, Munin MC 'Phenol and alcohol for the treatment of spasticity' *Phys Med Rehabil Clin N Am* 12(4):817-832
 2001 Molenaers G; Desloovere K; De Cat J; et al 'Single event multilevel botulinum toxin type A treatment and surgery: Similarities and differences' *Eur J Neurol*;8(Suppl 5):88-97
 1999 Molenaers G, Desloovere K, Eysen M, et al 'Botulinum toxin type A treatment of cerebral palsy: An integrated approach' *Eur J Neurol* 6(Suppl 4):S51-S57
 1999 Wissel J; Heinen F; Schenkel A; et al 'Botulinum toxin A in the management of spastic gait disorders in children and young adults with cerebral palsy: A randomized, double-blind study of 'high-dose' versus 'low-dose' treatment' *Neuropediatrics*;30(3):120-124
 1997 MF Brin: Botulinum Toxin: Chemistry, Pharmacology, Toxicity, and Immunology *Muscle Nerve* 20 (suppl 6): S146-S168.
 1995 Chutorian A, Root L, BTA Study Group 'A multi-centered, randomized, double-blind placebo-controlled trial of botulinum toxin type A in the treatment of lower limb spasticity in pediatric cerebral palsy' *Mov Disord* 10:364



Diplegic 5 year old patient with jump gait, body weight 18 kilograms

Muscles to be injected	Dose	Total dose per muscle	Number of injection site
Right medial hamstring	4	72	2
Left medial hamstring	4	72	2
Right lateral hamstring	3	54	1
Left lateral hamstring	3	54	1
Right gastrocnemius	4	72	2
Left gastrocnemius	4	72	2
Total		396 units	10



Hemiplegic 4 year old patient with stiff knee and pes equinovarus, body weight 15 kilograms

Muscles to be injected	Dose	Total dose per muscle	Number of injection sites
Right quadriceps	4	60	4
Right gastrocnemius	5	75	2
Right tibialis posterior	2	30	1
Total		165 units	7

Intrathecal Baclofen (ITB)

Baclofen is one of the most potent antispastic drugs. It cannot easily cross the blood brain barrier because of its poor lipid solubility. This makes it difficult to reach therapeutic doses in the CNS. A novel method of introducing the baclofen directly into the CSF through an implantable pump and catheter system has been devised in the past decade and has become increasingly popular. Intrathecal administration enables the drug to reach the receptor site quicker with a much lesser side effect profile.

Indications for ITB

ITB is useful for the severely involved spastic, dystonic or mixed child [A]. The aim is to enable sitting in the wheelchair, make transfers easier, decrease spinal deformity, increase the comfort level and ease of care through a decrease in spasticity. ITB pumps have been used in severe spastic diplegia, but more research is needed before one can definitely recommend this form of therapy for this particular problem.

Factors to consider

Consider several factors before the implantation [B]. Look for spasticity interfering with function and patient care. Define the type of involvement and the expected outcome after the intervention. Family cooperation is absolutely essential because complications of ITB pumps are potentially life threatening. The pump can be inserted in cases above the age of three, with an abdomen large enough for implantation. Check for hydrocephalus. It should be under control if present, otherwise it increases the chance of CSF leak. Get appropriate medical treatment for seizure activity because baclofen decreases the seizure threshold. Examine the skin of the back. It must be intact, there must be no pressure sores or active infection anywhere in the body. Financial resources must be sufficient because both the implantation and maintenance cost a substantial amount.

Performing the test dose

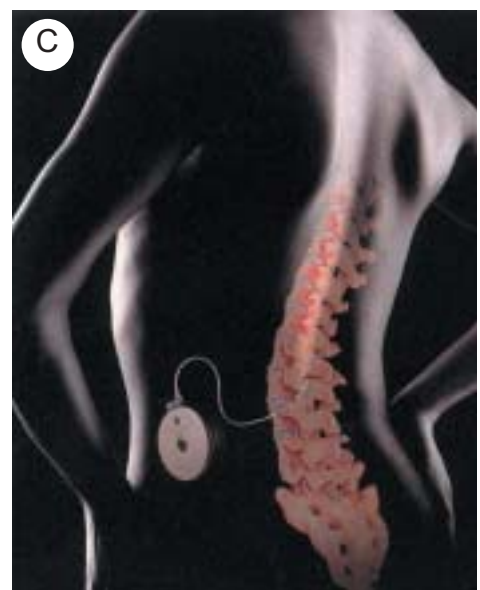
After the initial decision to implant a baclofen pump, perform a test to evaluate the effect of the drug when given intrathecally. Introduce 50 micrograms of baclofen into the intrathecal space by bolus injection through a lumbar puncture in the spastic total body involved child. Implant the pump if the child responds to this dose. If the child does not respond, use 75 to 100 micrograms in the consecutive trials on the following days. The effect of intrathecal baclofen starts at 1-2 hours after the injection, reaches a maximum at 4-6 hours and gradually diminishes after 8 hours. Perform the test with an intrathecal catheter placed at the level of the 9th thoracic vertebra for the dystonic child. Give a continuous infusion of baclofen. Children who show a decrease of one or more in the Ashworth scale for a six to eight hour period are good candidates for pump implantation.

Implanting the pump

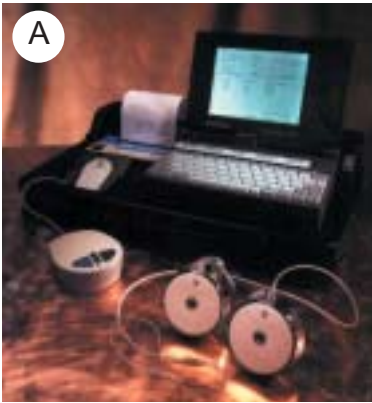
A minor surgical procedure is necessary for pump implantation [C]. Introduce the catheter into the intrathecal space at the distal thoracic or lumbar spine. Push the catheter tip to upper thoracic levels in cases of upper extremity spasticity and dystonia. The catheter is attached to an externally programmable pump implanted into the abdominal wall. The pump is filled transcutaneously every 2-3 months depending on the dosing schedule.

A	Indications
	Severe total body involved child
	Severe dystonic or mixed CP
	To ease burden of care
	To enable sitting and transfers
	To decrease spinal deformity
	Diplegic children with severe spasticity interfering with ambulation

B	Before the implantation
	Answer these questions
	Is tone interfering with function ?
	Is tone interfering with patient care ?
	Define type of involvement and clarify expected outcome
	Evaluate family resources and cooperation
	Evaluate the medical status of the child
	Age
	Is the abdomen large enough?
	Is there recurrent infection?
	Hydrocephalus?
	Seizure activity ?
	Evaluate financial resources
	Perform test dose



Baclofen is injected through the skin into a reservoir placed in the abdominal wall. The reservoir also contains a programmable pump which is connected to the lumbar epidural space via a catheter. Courtesy of Medtronic Inc.



The intrathecal baclofen pump is remotely controlled by a computer. This enables the physician to increase or decrease the dose if necessary. Bolus injections may also be given.

Courtesy of Medtronic



The child's abdomen must be large enough for the pump. Sometimes the pump protrudes from under the skin and becomes vulnerable to trauma or infection.



Follow-up

Dosing and clinical evaluation

Intrathecal administration of baclofen provides a continuous infusion of the desired amount of baclofen into the CSF. A computer based remote control system makes it possible to regulate the daily dose [A]. The antispastic effects of intrathecal baclofen are obtained at 1% of the daily oral dose.

Begin with an initial daily dose of 25 micrograms and titrate up until there is a satisfactory reduction in spasticity. The dose is usually between 100 to 500 micrograms per day. A static dose is generally achieved within a year after implantation. The pump should be refilled at 1-3 month periods. Refills are made through a transcutaneous injection. The battery life of the pump is approximately 4-5 years.

Begin an intensive physiotherapy program after pump implantation to reach functional goals [B,C]. Muscle weakness becomes prominent after a decrease in spasticity. Strengthening is important.

Complications

ITB pump implantation is expensive and the complication rate is moderately high. Complications include CNS infections, CSF leaks, and catheter related problems. Acute baclofen withdrawal syndrome [D] characterized by hallucinations, seizures, psychosis and rebound spasticity occurs if the baclofen flow to the CSF is interrupted. Signs of overdose are drowsiness, dizziness, somnolence, seizures, respiratory depression and loss of consciousness progressing to coma.

References

- 2003 Albright AL, Gilmartin R, Swift D, et al 'Long-term intrathecal baclofen therapy for severe spasticity of cerebral origin' *J Neurosurg.* 98(2):291-5
- 2003 Bjornson KF, McLaughlin JF, Loeser JD, et al 'Oral motor, communication, and nutritional status of children during intrathecal baclofen therapy: a descriptive pilot study' *Arch Phys Med Rehabil* 84(4):500-6
- 2002 Campbell WM, Ferrel A, McLaughlin JF, et al 'Long-term safety and efficacy of continuous intrathecal baclofen' *Dev Med Child Neurol* 44(10):660-5
- 2001 Albright AL, Barry MJ, Shafton DH, et al 'Intrathecal baclofen for generalized dystonia' *Dev Med Child Neurol* 43(10):652-7
- 2000 Butler C, Campbell S 'Evidence of the effects of intrathecal baclofen for spastic and dystonic cerebral palsy' *Dev Med Child Neurol* 42: 634-645
- 1999 Krach LE 'Management of intrathecal baclofen withdrawal: a case series' *Develop Med Child Neurol. Suppl* 80:11
- 1996 Albright AL 'Intrathecal baclofen in cerebral palsy movement disorders' *J Child Neurol.* 11 (Suppl 1): S29-S35

D Symptoms of acute baclofen withdrawal

- Acute increased tone
- Spasms
- Paresthesias
- Profuse sweating
- Dysphoria
- Hallucinations
- Seizures

Selective Dorsal Rhizotomy and Other Neurosurgical Treatment Modalities

Selective dorsal rhizotomy (SDR) involves sectioning of the dorsal column rootlets to interrupt the spinal reflex arc [A]. This inhibits the afferent input from the muscle and tendons and reduces the efferent activity at the level of the spinal cord. The advantage of SDR is a global muscle tone reduction in lower extremities without producing weakness. All the lower extremity muscles are affected. The effects are permanent and weakness is not a major issue, however, there is loss of superficial and deep sensation.

Indications

Patient selection is important for success of the intervention. The ideal patient [B] is an independent ambulatory diplegic child between the ages of 3-10 with pure spasticity, no fixed contractures, good strength and balance with spasticity being the major limitation to function. Family commitment is essential for success because there is a need for long term intensive physiotherapy after the procedure. The extent of functional improvements cannot always be related to SDR itself because the patients also receive long and intensive hours of physiotherapy after the procedure for at least a year.

Technique

A laminectomy is done under general anesthesia and the posterior roots are exposed. EMG monitorization is recommended to determine which rootlets should be cut. The rootlets are stimulated electrically and the response from the muscles are observed. This way, the most active rootlets are localized. Up to 30-50% of the dorsal rootlets at each level from L2 to S1 are cut. In some centers, the L1 rootlets are also cut to assist in reduction of psoas activity. S2-S4 rootlets must be spared to preserve bladder function.

Follow-up

Expected results of the procedure are a loss of deep tendon reflexes, decrease in muscle tone, an improved gait pattern and smoothness of gait. Energy consumption may improve if walking is very inefficient prior to surgery. Sensory loss is usually transient though long term effects are not clear.

There is a need for extensive postoperative rehabilitation. After surgery, the therapy must focus on strengthening. Orthopaedic surgery is still necessary usually for foot instability (excessive valgus), rotational abnormalities and contractures. Continued gait improvements are minimal between 1 and 2 years after surgery.

Contraindications

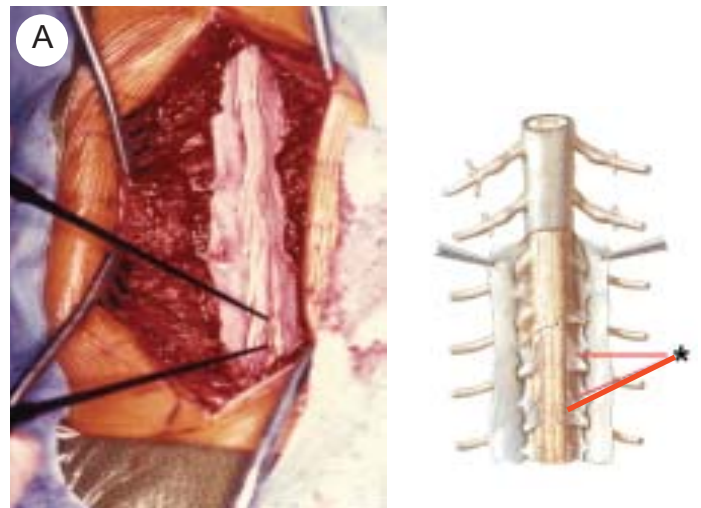
SDR is contraindicated in patients who have extrapyramidal findings, significant weakness or contractures, spinal abnormality and poor family support and commitment.

Side effects & Precautions

There are concerns regarding the development of hip instability and spinal deformity after SDR. Proprioceptive sensory loss is common and the long term effects are unknown.

Other neurosurgical treatment modalities

Deep brain stimulation and magnetic repetitive stimulation have all been tried in the CP patient with limited success [C]. Certain neurosurgical procedures such as thalamotomy and stereotaxic surgery have not produced satisfactory results.



Selective dorsal rhizotomy is technically difficult. The surgeon must be familiar with the anatomy of the spine and the spinal cord, must use electrophysiological monitoring to determine which and how many of the rootlets (*) he wants to cut and must be careful not to damage the cord in any way. The long term effects of SDR on joint integrity and muscle function are yet unknown.

B The ideal SDR candidate

Diplegic child
Age 3-10
Independent ambulator
Pure spasticity
No fixed contractures
Good strength and balance
Reasonable selective motor control
Family commitment

C Neurosurgical procedures in spasticity

Procedure	Target	Result
Stereotaxic encephalotomy	Globus pallidus Ventrolateral thalamic nuclei	Variable-poor
Cerebellar stimulation	Cerebellum	Poor
Cervical rhizotomy	C1-C3	Variable-complications
Selective dorsal rhizotomy	L2-S2 selected rootlets	Variable-good
Neurectomy	Peripheral nerves	Variable, may cause chronic pain

References

- 2002 Buckon CE, Thomas SS, Harris GE, et al 'Objective measurement of muscle strength in children with spastic diplegia after selective dorsal rhizotomy' Arch Phys Med Rehabil 83(4):454-60
- 2002 McLaughlin J, Bjornson K, Temkin N, et al 'Selective dorsal rhizotomy: meta-analysis of three randomized controlled trials' Dev Med Child Neurol 44(1):17-25
- 2002 Steinbok P, McLeod K 'Comparison of motor outcomes after selective dorsal rhizotomy with and without preoperative intensified physiotherapy in children with spastic diplegic cerebral palsy' Pediatr Neurosurg 36(3):142-7
- 2000 Graubert C, Song KM, McLaughlin JF, et al 'Changes in gait at 1 year post-selective dorsal rhizotomy: results of a prospective randomized study' J Pediatr Orthop 20(4):496-500
- 1998 McLaughlin JF, Bjornson KF, Astley SJ, et al 'Selective dorsal rhizotomy: efficacy and safety in an investigator-masked randomized clinical trial' Dev Med Child Neurol 40(4):220-32.