THE DIAGNOSIS AND TREATMENT OF SPASTICITY

A Practical Guide

Edited by **Ivano Dones** and **Vincenzo Levi**

The Diagnosis and Treatment of Spasticity

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CHAPTER 1

SPASTICITY

IVANO DONES

Introduction

The term spasticity comes from the Greek word 'spasmos' meaning cramp and it was first introduced in English by Good in 1829 and then by Little in 1843 to define a syndrome in which a marked increase in muscle tone occurs together with spasms. The clinical picture of spastic paraplegia was then described together with symptoms of multiple sclerosis by Charcot in 1868.[1]

The latter and universally adopted definition of spasticity by Lance (1980) is 'a motor disorder characterised by velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex as one component of the upper motor neuron syndrome' and, although there have been several more recent attempts to rename spasticity as the result of spastic muscle overactivity, the concept of a velocity-dependent increase in muscle tone remains the core meaning of the term spasticity.[2] From the clinical viewpoint spasticity is a disabling neurological clinical sign observed in many neurological disorders and characterised by muscular velocity-dependent hypertonus, osteotendinous hyperreflexia, presence of abnormal spinal reflexes such as the Babinski sign and clonus. These signs frequently come together with muscle spasms and pain localised at the most involved body segments.

Spasticity has long been considered as an incurable condition that only motor rehabilitation and orthopaedic procedures might correct by improving the patient's consequent motor disability. Moreover, unfortunately, spasticity, as a clinical sign frequently causing severe motor impairment,

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[1] Rowland, Pedley, and Kneass, *Merritt's Neurology*.

[2] Lance, 'Symposium Synopsis'.

has always been underestimated. That is why spasticity as a disabling trait has always been mostly considered, both by general practitioners and neurologists, as something to live with without any attempt to improve the spastic trait thus improving both motor performance and quality of life in a spastic patient. Weakness, always present together with spasticity, is usually the major problem when dealing with the effort to improve motor performance in a patient affected by spasticity. It is frequently worth treating in order to give the patients an improvement of their motor performance and of their quality of life as well. While a separation between spasticity of cerebral and spinal origin still exists in the literature, a more helpful distinction between focal and diffuse spasticity is worth considering for practical use when planning its possible treatment. Moreover, an additional distinction must be made between spasticity in patients who are bedridden or in a wheelchair and patients who, despite their spasticity and motor impairment, are still able to move autonomously even with a cane or crutches.[3] Spasticity may have different aetiologies. The associated spinal and cerebral forms of spasticity are frequently due to the development of multiple sclerosis. Patients who underwent a spinal cord injury due to a trauma will soon develop spasticity. Spinal cord neoplasms, transverse myelitis, different myelopathies due to spondylosis may present together with a relevant and progressive clinical picture of spasticity (30% of patients). Cerebral palsy (70% of patients), cranial traumas with brain injury, brain bleeding or strokes and degenerative disorders at the brain level may as well be the cause of a stable clinical picture of diffuse or focal spasticity (50% of patients).[4] Spasticity can show both positive and negative clinical signs together with some alterations of the skeletal muscle occurring on a long-term history of spasticity. The positive clinical signs are the increase of muscle tone, increased tendon reflexes, stretch reflex spread to extensors and repetitive stretch reflex discharges and clonus. Negative signs are the loss of motor dexterity, weakness and slow movements. Muscle alterations are stiffness, contracture, fibrosis and atrophy appearing in the long term **(Table 1).**

The large diffusion of spasticity as caused by such a great variety of diseases can give an idea of the high number of patients that are affected by spasticity all over the world. From the early orthopaedic and rehabilitating approaches to treating spasticity, the medical sciences moved forward to the introduction of many pharmacological, surgical and neuromodulation procedures to adequately treat spasticity regardless of its

[3] Daroff and Bradley, 'Bradley's Neurology'.

[4] Daroff and Bradley; Albright, 'Spasticity and Movement Disorders'.

aetiology. These present different therapeutic strategies are described in this handbook.

Table 1: Positive signs, negative signs and muscle alterations associated with spasticity

Positive signs	Negative signs	Muscle alterations
Increased muscle tone	Loss of motor dexterity	Stiffness
Increased tendon reflexes	Weakness	Contracture
Stretch reflex spread to extensors	Slow movements	Fibrosis
Repetitive stretch reflex discharges and clonus		Atrophy

Diagnosis

Spasticity, as defined by Lance in 1980, is a clinical sign characterised by a velocity-dependent increase in muscle tone involving both agonist and antagonist muscles together with increased osteotendinous reflexes as a consequence of the hyperexcitability of stretch reflexes. It largely interferes with the normal motor function of many body segments and almost every time it is accompanied by muscle weakness and loss of motor dexterity.

It can be considered part of the first motor neuron syndrome.[5] Spasticity is a predominant positive clinical sign of the upper motor neuron syndrome although it is often able to decrease motion, thus bringing it to relative disability. Its negative signs are weakness and loss of dexterity.

The increased excitability of the group of alpha-motor neurons at the segmental spinal level or the increase of afferent excitatory inputs coming

[5] Brooks and Stoney, 'Motor Mechanisms'.

from the motor cortex to the second motor neuron are the causes of spasticity.

Whatever the cause, the final result is an imbalance between the gamma-aminobutyric acid (GABA) mediated inhibitory afference on the second motor neuron and the glutamate mediated excitatory afference on the same neurons, with the excitatory afference prevailing.

Moreover, the decrease in the inhibitory GABA-mediated afference, in the first motor neuron syndrome, occurs together with a decrease of dendrites from descending fibres from the motor neurons to the dorsal roots and the concomitant collateral sprouting of nerve fibres, causing an increase in the excitatory afference on the second motor neuron thus increasing muscle tone[6] **(Figure 1-1).**

It is present in many clinical pictures as a predominant sign of different neurological disorders such as multiple sclerosis (around 34% of cases) with both brain and spinal localisation of demyelinating areas, degenerative brain disorders, brain bleeding or ischaemia, spinal cord injury or myelopathies from different causes. Thus, it may affect a wide range of patients at different ages.

The most frequent causes of spasticity are reported in **Table 2** together with the site of the lesion responsible for spasticity and the dedicated tests that are needed to ascertain the disease.

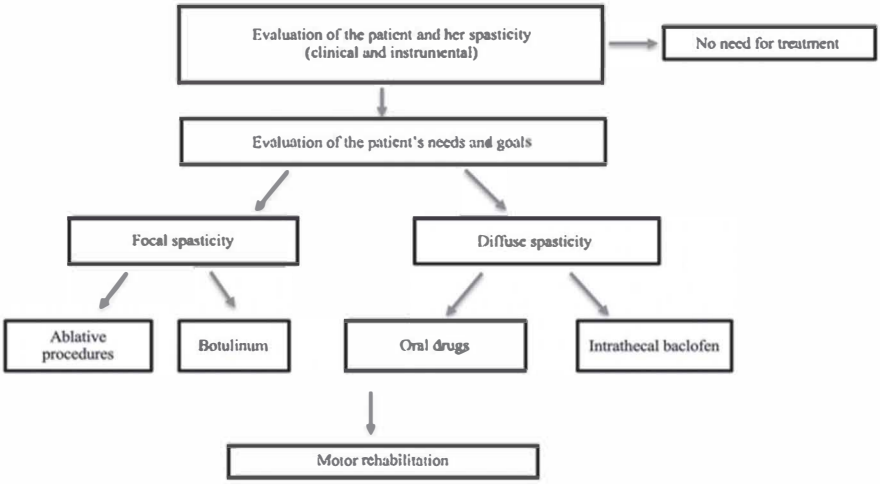

Figure 1-1 *Spasticity treatment flowchart*

[6] Akert et al., 'Motor Performance'; Ashby et al., 'Pyramidal and Extrapyramidal Control'.

*Table 1 Neurological disorders causing spasticity. *A careful clinical assessment is always mandatory*

Name of the disease	Site of lesion	Tests needed *
Infantile cerebral palsy	Brain	Brain MRI
Myelopathies	Spinal cord	CSF test, spinal MRI
Leukoencephalopathies	Brain	brain MRI, biochemistry
Primary lateral sclerosis	Brain	Brain MRI, MEP
Sjogren-Larsson syndrome	Brain	Brain MRI, biochemistry
Familial spastic paraplegia	Brain	Brain MRI, molecular bio
Infantile cervical malformations	Atloccipital	Atlooccipital CT and MRI
Spinal cord trauna	Spinal cord	Spinal cord MRI, SSEP
Multiple sclerosis	Brain, spinal cord	Spinal and brain MRI, CSF
Acute myelitis	Spinal cord	Spinal cord MRI, CSF
Brain trauma	Brain	Brain CT and MRI, MEP
Spinal cord injury	Spinal cord	Spinal cord MRI, SSEP
Amyotrophic lateral sclerosis	Brain, spinal cord	Cervical MRI, EMG, MEP
Cervical myelopathy	Spinal cord	Cervical MRI, SSEP
Spinal cord tumours	Spinal cord	Spinal cord MRI
Adrenoleukodystrophy	Brain	Biochemistry
Joseph disease	Brain	Brain MRI

Due to its appearance when a pyramidal injury is observed, spasticity as a compensatory trait originated by the central nervous system is considered as a positive sign although it is always matched to the negative sign of an associated muscle weakness. However, spasticity has been considered a parapyramidal clinical sign of dysfunction as it refers to both an impairment of the pyramidal corticospinal pathway, an involvement of the brainstem to spinal cord circuitry and the system of gain-setting originating from the inferior brainstem nuclei under limbic control. That is the reason why when a pure pyramidal lesion occurs the loss of muscle strength and dexterity appear without spasticity that, on the contrary, will occur later in the progression of the pyramidal disorder as a compensatory involvement of the parapyramidal system originating at the brainstem and controlled by an excitatory afference coming from the cortical pre-motor

and supplementary motor areas of the brain cortex. Moreover, a lesion in these latter circuits will produce spasticity although the involvement of the pyramidal tract is poor. Rigidity, contracture, muscle atrophy and fibrosis may then, in the long term, interfere with the pathological regulatory mechanisms by hampering the normal control of limb position in space and movement. Thus, when assessing a spastic patient, the proper distinction between the resistance to movement caused by spasticity and the resistance due to rheologic changes is important to tailoring the proper treatment. In this regard, diagnostic nerve blocks and dynamic EMG are used to separate those two causes of rigidity.[7]

Co-activation of agonist muscles and abnormal activation of antagonist muscles are one of the elements causing muscle weakness together with weakness originating from a poor signal from the motor cortex both decreasing the net force at a joint and impairing movement. The clinical evaluation of a patient with spasticity should include the complete assessment and scoring according to the common scales internationally used for spasticity, together with the general neurological evaluation of the patient. Muscle tone is assessed by having the patient completely relaxed while the examiner moves each patient's body segment to full flexion and extension. By increasing the passive movements of these body segments the examiner appreciates a progressive increase in the muscle tone proportional to the speed of passive movement. A comparison is carefully made of both sides of the body. In a completely relaxed non-spastic patient, no increase in resistance is felt at the wrist, elbow, knee and ankle while in a spastic patient the 'clasp-knife phenomenon' is felt proportional to the speed of the passive movement. Pain and joint fixations can confuse the examination of the resistance due to spastic hypertonus. Active movements are then made to assess muscle strength. The flexor reflex (Babinski sign), indicating an alteration of the descending projections from the first cortical and brain stem motor neurons and the alpha and gamma motor neuron in the spinal cord, is always present in a patient affected by upper motor neuron syndrome.

The Ashworth scale is used at the different body segments, to score spasticity according to five degrees of muscle tone. From 0 as a condition of normal muscle tone, to 5 as no movement can be induced even passively due to a very severe muscle tone on both agonist and antagonist muscles. **(Table 3)**

[7] Bones, Nazzi, and Broggi, 'Guidelines for the Diagnosis'.

Table 2 The Ashworth scale to score spasticity

Grade	Condition
1	Normal tone
2	Slight increase in muscle tone with easy flexion and extension and initial 'clasp-knife' phenomenon
3	Marked increase in muscle tone but flexion and extension easily possible
4	Severe increase in muscle tone with difficulties in passive movements
5	Total rigidity both in extension and flexion

An additional scale to grade spasticity in a more dynamic context, is the Tardieu scale which quantifies spasticity through the assessment of the muscle response to stretch applied at different velocities at each limb with a constant position of the body. **(Table 4)**

There are two more scales to grade spasticity. The first is the scale for osteotendinous reflexes and the second is the scale for muscle spasms. **(Tables 5-6)** The FIM (functional independence measure) and the index Index complete the scoring of a spastic patient by measuring their autonomy in the conventional actions of daily living. The evaluation of the quality of life of a spastic patient together with the knowledge of their social environment is helpful in tailoring a bespoke treatment for their spasticity.

Motor impairment due to increased muscle tone is the consequence of enhanced motor neuron activity, co-activation and increased stretch reflexes together with enhanced postural reflex activity even in children affected by cerebral palsy. Spastic still-ambulant patients need a computerised gait analysis to record both the gait trait and the EMG activity of different muscles during gait in order to evaluate the opportunity of possible combined treatments for both diffuse and focal spasticity to optimise the patient's motor performance.[8]

[8] Dones et al., 'A Neurophysiological Method'.

Table 3 The Tardieu scale

This scale quantifies muscle spasticity by assessing the response of the muscle to stretch applied at specified velocities. Grading is always performed at the same time of day, in a constant position of the body for a given limb. For each muscle group, reaction to stretch is rated at a specified stretch velocity with two parameters, x and y.

VELOCITY TO STRETCH	
V1	as slow as possible
V2	speed of the limb segment falling
V3	as fast as possible
QUALITY OF MUSCLE REACTION	
0	no resistance throughout passive movement
1	slight resistance with no clear catch at a precise angle
2	clear catch at a precise angle followed by release
3	fatigable clonus (< 10/sec) occurring at a precise angle
4	indefatigable clonus (>10/sec) occurring at a precise angle
5	immobile joint
ANGLE OF MUSCLE REACTION	
Measure relative to the position of minimal stretch of the muscle (corresponding to angle)	
SPASTICITY ANGLE	
R1	Angle of catch seen at velocity V2 or V3
R2	Range of motion achieved when muscle is at rest and tested at V1 velocity

Table 4 The scale of osteotendinous reflexes

0	Absent
1	Hyporeflexia
2	Normal
3	Hyperreflexia
4	Extinguishable clonus
5	Unextinguishable clonus

Table 5 Penn's scale of muscle spasms

Penn's scale of muscle spasms	
0	No spams
1	Absence of spontaneous spasms. A relevant sensory or motor stimulation provokes spasms
2	Occasional spontaneous spasms
3	Hourly spontaneous spasms
4	More than 10 spasms per hour

In the correct assessment of a patient affected by spasticity, it is mandatory to decide whether patients actually need their spasticity to be treated. In fact, there are many conditions where spasticity must be preserved in order to help the patient in keeping their standing position or to use their spasticity to keep a desired posture.

Treatment

Spasticity, as a clinical sign of upper motor neuron syndrome, may variously interfere with any motor function. To plan any possible treatment of spasticity a few concepts have to be considered: severity of spasticity, its chronicity, extension throughout the body, the level of lesion in the central nervous system responsible for its appearance, co-morbidities, the availability of social support from both the family and centres of motor rehabilitation, and the real goal of treatment that should be clearly explained to the patient. The treatment of spasticity is aimed to improve motor performance, patient's comfort and nursing, decrease pain and prevent fixed abnormal postures and joint blockade. In fact, spasticity must be treated only if it severely interferes with motor performance or positioning, care and comfort.

As spasticity is one of the prevailing clinical signs as a consequence of stroke, brain injury, spinal cord injury of different origin, neurodegenerative disorders, cerebral palsy and multiple sclerosis, it is frequently associated with other clinical signs and symptoms such as sensory disturbances, perception abnormalities, cognitive impairment, and additional motor disturbances such as dystonia and extrapyramidal rigidity that always appear together with muscle weakness, spasms and loss of dexterity. Spasticity can even increase the energy a patient must spend to move as it hampers both agonists and antagonists, thus braking any voluntary movement. It usually limits the fitting of orthotic devices including a real limitation in even using exoskeletons and it can lead to pressure sores,

contractures and related pain. All these additional signs and symptoms create a general state of inadequacy in performing even simple daily motor tasks. Thus, when explaining any antispastic treatment to a patient, we must be careful in depicting any miraculous future scenario obtainable with the antispastic treatment alone.

Spasticity can give many different motor patterns: co-contractions of agonist and antagonist muscles with limitation of extremity movements and poor agonist activation together with other overactive agonist muscles, with a resulting limited ability to voluntarily contract single muscles. Moreover, muscle tone varies according to the state of movement or rest. Thus, the patient must be carefully evaluated during activity and at rest. Standard electromyography (EMG), dynamic EMG and quantitative gait analysis together with a careful clinical examination are helpful tools to draw an accurate clinical picture of the spastic patient.

In addition, evaluating and treating a patient affected by spasticity is a matter of multidisciplinary interaction between neurosurgeons, neurologists, rehabilitation physicians, physiotherapists, nurses, urologists, psychologists and, sometimes, orthopaedic specialists. Motor rehabilitation, wherever indicated, must be mandatory to obtain the maximal effect of any treatment together with a careful analysis of the social environment of the patient.

The type of treatment of spasticity is indicated not only by the degree of spasticity, but also by using a scale of invasiveness of any treatment ranging from oral drug therapy to dorsal root entry zone lesions at the spinal cord. It is often a multimodal treatment consisting of non-pharmacological and pharmacological approaches associated with physical therapy.[9]

Finally, as already mentioned, focal and diffuse spasticity must have different treatments. It is then worth separating spastic patients into two different groups: the first being bedridden or wheelchair patients and the second of still-ambulatory patients as the spasticity assessment tools and the goal of any treatment are different in the two groups. **(Table 7)**

Oral drugs

The pharmacological treatment of chronic spasticity is mainly a symptomatic treatment, which is rarely able to solve the chronic degenerative disease of the central nervous system that causes spasticity.

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[9] Dimitrijevic and Sherwood, 'Medical and Surgical Treatment'.

As spasticity is variously present in many neurological diseases, the common goal of any of its treatments is the relief of subjective discomfort, improvement in patient care, and occasionally in the patient's functional performance and prevention of long-term complications due to prolonged excessive muscle tone such as joint ankylosis, tendon retractions and skeletal muscle fibrosis.

While spasticity can be improved by the drug treatment, the coexisting loss of dexterity and weakness cannot be treated, thus implying a limitation of the outcome of any drug treatment presently available.

Mephanesin was the first drug, introduced in 1946, to treat spasticity by blocking spinal interneurons. Since then, a large variety of antispastic agents have been developed. Most of them can even be used in combination. Unfortunately, they show relevant efficacy in only a small percentage of cases and in some of them the antispastic effect comes together with the onset of undesired side effects.[10]

When observing a lack of effect or a loss of effect of these drugs even at their highest daily dosage, a further treatment must be thought of and set, and the oral treatment consequently withdrawn accordingly.

These drugs are part of the two groups GABAergic and central alpha2-adrenergic, acting on the inhibitory afference of the second motor neuron at different levels. GABA agonists are diazepam (maximal daily dosage 60 mg), clonazepam (maximal daily dosage 3 mg) and baclofen (maximal daily dosage 75 mg) while central alpha2 adrenergic agonists are tizanidine (maximal daily dosage 36 mg) and clonidine (maximal daily dosage 3 mg). Dantrolene as a calcium channel blocker at the muscle fibre not only always gives muscle weakness but it is even hepatotoxic, thus it should not be considered as a useful drug for spasticity.[11]

The fact that all drugs, when orally administered, distribute everywhere in the central nervous system and not only at the spinal cord level, where their concentration is needed to decrease spasticity, is responsible for the occurrence of undesired side effects due to their action on analogous receptors that, at the brain level, are not strictly connected to the control of muscular tone.

Benzodiazepines

The antispastic effect of benzodiazepines is mediated by a functionally coupled benzodiazepine-GABA-A receptor chloride ionophore complex.

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[10] Young and Delwaide, 'Drug Therapy: Spasticity'.

[11] Elovic, 'Principles of Pharmaceutical Management'.

They have no primary presynaptic GABA-mimetic effect but an indirect postsynaptic action only in the case where GABA action is functional. Benzodiazepines are largely metabolised by the liver and they differ in long-acting and short-acting molecules. They cross the placental barrier and are secreted into breast milk.[12] Diazepam is the oldest drug used to decrease spasticity: this molecule has great affinity for the GABA-A receptors thus give an increase in the presynaptic inhibition and a decrease of mono and polysynaptic reflexes excitability. Diazepam overdose may bring the patient to CNS depression and coma. Its effect on spasticity is often hampered by the onset of side effects such as somnolence, light-headedness, fatigue, muscular weakness, dizziness, ataxia, vertigo and addiction. Drug tolerance to diazepam may occur in the long term.

Anxiety, agitation, irritability, increased tremor, muscular fasciculations and twitching, nausea, insomnia, psychotic manifestations and death can be experienced in case of rapid or abrupt withdrawal of diazepam administration.

The action of diazepam on spasticity has been reported in double-blind studies on spastic patients of both spinal and cerebral origin. Sedation has been observed more frequently than during baclofen treatment although side effects and their efficacy in reducing spasticity were equally observed with the oral administration of both molecules.[13]

It is always advisable to begin treatment with diazepam with a bedtime dose of 5 mg and extending its use at daytime with 2 mg twice/day progressively reaching a maximum of 60 mg per day when needed. Control studies on the use of diazepam in spastic patients ceased in 1991. Besides its well-known anticonvulsant action, clonazepam can also decrease rigidity and muscle spasms similarly to baclofen but with higher sedation and muscle weakness.[14] It is primarily used for the suppression of night-time spasms.

Baclofen

The drug used the most to treat spasticity is a GABAb agonist, inhibiting spinal mono and polysynaptic reflexes. It was first synthesised in the 1960s as a GABA agonist for the treatment of epilepsy. Its anti-epileptic effect was poor, while a marked antispastic effect was observed.[15] It is able to decrease spasticity and muscle spasms but, when

[12] Young and Delwaide, 'Drug Therapy: Spasticity'.
[13] Cocchiarella, Downey, and Darling, 'Effect of Diazepam'.
[14] From and Heltberg, 'A Double-Blind Trial'.
[15] Van Hemert, 'Comparison of Baclofen'.

given orally, its response can be interfered with by undesired side effects related to central depression such as confusion, sedation, drowsiness, fatigue and coma, due to its concentration at the GABA receptors in the brain. Therefore, patients must be cautioned about any activity made hazardous by decreased alertness (above all, driving). In this regard it is always advisable to begin baclofen by prescribing one single dose at night and then increase the dosage and spread the administration evenly in the morning and at lunch time.

Baclofen is believed to exert a major action on spasticity of spinal origin and not on the one of brain origin although the decrease in spasticity on patients affected by cerebral palsy has been observed.[16] Baclofen might even cause lack of memory and attention in elderly and brain-injured patients. An excess daily dosage of baclofen may cause trunk hypotonia, altering posture in patients in wheelchairs. In patients who are still able to walk despite their spasticity, baclofen might induce muscle weakness by an independent peripheral mechanism, thus reducing their walking ability.[17]

Spastic patients affected by asthma should be carefully evaluated before the use of oral baclofen as it increases airway bronchial constriction responsiveness. Cough reflex is also inhibited. Moreover, patients who are additionally affected by epilepsy should be monitored as baclofen can interact with anti-epileptic drugs, thus losing seizure control. Possible interaction of baclofen with pregnancy is largely unknown. Baclofen withdrawal syndrome appearing with the abrupt decrease or discontinuation of baclofen is characterised by seizures, confusion, rebound muscle activity and hypertonia, hallucinations and fever.[18] Patients experiencing oral baclofen overdosage may present with hypoventilation, low blood pressure, small pupils, hypothermia and bradycardia and, occasionally, unresponsiveness. Baclofen oral daily dosage ranges from 10 to 75 mg with increases of 10 mg every 10 days if needed.

Tizanidine

Tizanidine is an alpha-2 adrenergic central agonist that interferes with the release of excitatory amino acids (aspartate and glutamate) from the presynaptic endplates of spinal internuclear neurons and enhances the action of glycine as an inhibitory neurotransmitter. Its antispastic action is

[16] Pedersen, Arlien-Soborg, and Mai, 'The Mode of Action'.
[17] Hulme et al., 'Elderly Stroke Patient'.
[18] Garabedian-Ruffalo and Ruffalo, 'Baclofen Withdrawal'.

mediated by the increase of the noradrenergic presynaptic inhibition. The antinociceptive effect is due to the inhibition of the synaptic transmission of nociceptive stimuli in the spinal pathways through an alpha-2 adrenergic receptor – mediated action was reported by Davies in 1984.[19]

Its use at 6–36 mg/day has been found equal or superior to baclofen in reducing passive stretch responses in patients affected by stroke, spinal cord lesions or multiple sclerosis although no differences between the two molecules were observed in gait and functional measures.

Moreover, there is a discrepancy in the findings on a large cohort of patients on tizanidine and placebo in two reports, one a UK study reporting a significant reduction in muscle tone with tizanidine, while in the other, a US study, no differences in response were found between patients on tizanidine and on placebo.[20] A transient increase in hepatic transaminase levels restored after discontinuation of treatment with tizanidine was reported.

Clonidine

Clonidine is an alpha2 noradrenergic agonist having both hypotensive and antispastic properties. It is rarely used due to the frequent appearance of low blood pressure, bradycardia and somnolence. About half of its dosage is metabolised in the liver while the other half is excreted in the urine as an unchanged drug. Autoradiographic studies of clonidine demonstrate its binding not only in the brain but even at the dorsal horns of the spinal cord.

In spinalised animals, clonidine was reported to induce a reduction in motoneuronal excitability. The antispastic effect of clonidine in humans affected by spinal cord injury was ascribed to an enhancement of alpha-2 mediated presynaptic inhibition of sensory afferents.

Bradycardia, hypotension, depression, constipation and dry mouth are relevant undesired side effects of clonidine. Blood pressure and pulse must be periodically monitored. Main side effects such as syncope seizures, cerebrovascular accidents, deep vein thrombosis, nausea, vomiting and autonomic hyperreflexia have also been reported.[21]

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[19] Davies et al., 'Tizanidine (DS103-282)'.

[20] Kamen, Henney, and Runyan, 'Overview of Tizanidine Use'.

[21] Elovic, 'Principles of Pharmaceutical Management'.

Dantrolene

The use of dantrolene as an inhibitor of calcium release at the sarcoplasmic reticulum of muscle fibres in the skeletal muscle has been mostly withdrawn due to its hepatotoxicity and poor action on spasticity. Together with a relevant decrease in muscle strength and motor performance, dantrolene is also sedating and can cause lethargy, drowsiness, malaise, nausea, vomiting, diarrhoea and paraesthesia. Its weakening effect can cause postural complications. Its use as an antispastic should not be encouraged at present.[22]

[22] Ward, Chaffman, and Sorkin, 'Dantrolene. A Review'.

CHAPTER 2

THE TREATMENT OF FOCAL SPASTICITY: THE BOTULINUM TOXIN

GRAZIA DEVIGILI

Introduction

The use of botulinum neurotoxins (BoNTs) is a well-established treatment in the management of focal spasticity, both for the lower and upper limbs. There is now consistent knowledge about its indications, effects and safety in clinical practice. The BoNTs are neurotoxins produced by neurotoxigenic strains of anaerobic bacteria of the genus Clostridium, that cause the flaccid paralysis of botulism by inhibiting the neurotransmitter release mainly at the peripheral cholinergic nerve terminals at the neuromuscular junction. [1] This causes a reversible reduction in muscle contraction and a dose-dependent reduction in muscle strength. There is also some evidence for other sites of action including the cholinergic autonomic terminals, and the more recently discovered inhibition of the release of peripheral neurotransmitter and inflammatory mediators in the nociceptive system.[2] The mechanism of action consists of the high-affinity binding to a receptor of the presynaptic membrane of peripheral cholinergic nerve terminals, and its entry into their cytosol where they cleave the SNARE proteins (VAMP/synaptobrevin, SNAP-25, and syntaxin) thus blocking the neurotransmitters' release.[3] The clinical effect is temporary, as the BoNTs degrade and become inactive in 48 hours and the neuromuscular junctions regenerates with sprouting within a

[1] Burgen, Dickens, and Zatman, 'The Action of Botulinum'; Rossetto, Pirazzini, and Montecucco, 'Botulinum Neurotoxins'; Pirazzini et al., 'Biology, Pharmacology, and Toxicology'.

[2] Pirazzini et al., 'Biology, Pharmacology, and Toxicology'; Luvisetto, Vacca, and Cianchetti, 'Analgesic Effects of Botulimun'.

[3] Rossetto, Pirazzini, and Montecucco, 'Botulimun Neurotoxins'.

few weeks. Generally, the muscle weakness and hypotrophy regress over three to five months. The BoNTs have been traditionally classified into seven serotypes, from A to G. However, there are many variants for each serotype and some chimeric BoNTs were also identified, i.e. BoNT/CD, BoNT/FA and BoNT/DC. Several BoNT preparations were licensed for clinical use. They are nearly all based on serotype A1, with only one on serotype B1. Details are summarised in **Table 7**. The duration of clinical effects varies between different serotypes, animal species and kind of cholinergic terminals, e.g. in humans the duration of action is three times longer than in mice, and the skeletal muscles recover about three times faster than autonomic nerve terminals. The BoNTs are potent and neurospecific drugs, and when they are correctly injected they show limited diffusion; their effect is reversible over time. For all these reasons BoNT/A1 is considered as the safest and most efficacious treatment for a variety of human syndromes characterised by hyperfunction of selected nerve terminals, including spasticity.

Botulinum as treatment of spasticity

Several open and placebo-controlled studies reported the efficacy and safety of local botulinum toxin injections in reducing spasticity.[4] Recent systematic reviews have concluded that BoNT/A1 injections have to be considered as the pharmacological treatment of choice in focal spasticity to improve limb mobilisation and posture and functional ability, and to reduce pain, whereas limited data are still available on the effectiveness of BoNT/B1 on spasticity.[5]

The principal goal of BoNT/A treatment of spasticity is to reduce motor overactivity to improve movement without worsening weakness. BoNTs treatment can reduce muscle tone, improving function and pain due to shortening of muscle fibres and ligaments, and ameliorate nursing. However, this treatment should be included in a multidisciplinary approach where all physical, medical and surgical treatments need to be combined.

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[4] Elia et al., 'Post-Stroke Spasticity'; Hara et al., 'Botulinum Toxin A.'; Hara et al., 'Therapy and Multidisciplinary Rehabilitation'; Kaji et al., 'Botulinum Toxin Type A'.

[5] Esquenazi et al., 'Evidence-Based Review'; Zakin and Simpson, 'Evidence on Botulinum Toxin'; Bentivoglio et al., 'Clinical Differences between Botulinum'.

Table 6 Technical details of botulinum neurotoxin products marketed in North America and Europe

	Botox®	Xeomin®	Dysport®	Neurobloc®
Generic name	Onabotulinum toxinA	Incobotulinum toxinA	Abobotulinum toxinA	Rimabotulinu mtoxinB
Manu-facturer	Allergan (USA)	Merz Pharma (Germany)	Ipsen Pharmaceutica ls (France)	US WorldMeds (USA)
Toxin type	A1	A1	A1	B1
MW	900 kDa complex	150 kDa	MW not reported	MW not reported
Pharmace utical form	Vacuum-dried powder for reconstitution	Freeze-dried powder for reconstitution	Freeze-dried powder for reconstitution	Ready-to-use solution
Shelf life	2 8°C	Room temperature	2 8°C	2 8°C
	36 months	36 months	24 months	24 months
pH after reconstitut ion	7.4	7.4	7.4	5.6
Unit/vial	100 U or 200 U Botox	100 U or 200 U Xeomin	300 U or 500 U Dysport	2,500 U/0.5 ml
				5,000 U/1 ml
				10,000 U/2 ml
Clinical activity compared to Botox	1	1	1:2 1:3	1:40 1:50

In post-stroke spasticity, the BoNT treatment should be considered in the early phases of rehabilitation as well as in the long-standing spasticity. After a stroke, an early treatment in selected muscles may prevent soft tissue shortening caused by spasticity and limb immobility.

The BoNT effect associated with the rehabilitative treatment may potentially improve the neurological recovery. Otherwise, the treatment of long-standing spasticity is focused on functional improvement, symptom control (clonus, pain) and passive function outcomes e.g. wearing splints and nursing. For instance, as far as the lower limb area is concerned, BoNT injections improve pes varus and equino-varus foot, which cause ankle instability during the loading response phase and poor toe clearance during the swing phase of gait, improving walking velocity.[6] The target muscles as well as the frequency of BoNT treatments in spasticity should be evaluated in every single case by the rehabilitation team. In **Table 8** are summarised the most common patterns of focal spasticity, muscles that are mainly involved and common targets of BoNT.

Table 7 Common pattern of focal spasticity, the muscles mainly involved and target of BoNT treatment

Pattern of spasticity	**Muscles involved**
Upper limb	
Shoulder adduction, internal rotation and retraction	Pectoralis major Latissimus dorsi Teres muscle group Subscapularis Rhomboids and interscapular muscles
Elbow flexion	Biceps brachii Brachialis Brachioradialis
Pronation of the forearm	Pronator teres Pronator quadratus
Flexed wrist and clenched hand	Flexor carpi ulnaris and radialis Flexor pollicis longus Flexor digitorum superficialis and profundus

[6] Rosales and Chua-Yap, 'Evidence-Based Systematic Review'.

Thumb in palm	Adductor pollicis Opponens pollicis Flexor pollicis brevis Lumbricals interossei
Lower limb	
Hip adductor spasticity	Adductor magnus, longus and brevis
Hip and knee flexion	Psoas major Biceps femoris Medial hamstring group (gracilis, semimembranosus and semitendinosus)
Knee extension	Quadriceps
Equinus-varo foot	Gastrocnemius, soleus and posterior tibialis
Toe clawing	Flexor hallucis longus, flexor digitorum longus

Level of evidence

For the treatment of adult upper-limb spasticity, OnaBoNT, AboBoNT and IncoBoNT are safe and effective for the reduction of spasticity and improvement of passive function (Level A evidence), while RimaBoNT has a Level B of evidence.[7] For the lower limb spasticity, there is inadequate data for IncoBoNT and RimaBoNT, but good evidence in terms of safety and effectiveness both for OnaBoNT and AboBoNT.[8]

Dilution and technical issues

In clinical practice, the treatment can be tailored to individual patients' functional targets choosing the proper BoNT dose for each muscle, the

[7] Simpson et al., 'Practice Guideline Update Summary'.
[8] Zakin and Simpson, 'Evidence on Botulinum Toxin'.

injection site and number of injections per site, together with the planning of target muscles. A key issue that may influence the outcome is the dilution rate of the solution to be injected. In general, the dilution in saline solution for larger muscles (e.g. quadriceps) ranges from 2.0 ml to 3.0 ml for 100U of OnaBoNT and/or IncoBoNT, and from 2.5 ml to 4.0 ml for 500U of AboBoNT. For smaller muscles the volume of dilution is nearly halved. The use of higher dilution leads in larger injection volumes and higher risk of diffusion and excessive muscle weakness.[9] The needle size should be carefully selected according to the muscle to be injected: a 26- or 27.5-gauge injecting needle is generally used, while for small muscles such as facial or lumbrical muscles, a 30-gauge needle seems to be more appropriate. Despite the safety of this treatment, BoNT should be injected by clinicians with the appropriate skills and training only.

Planning and sites of injections

To reach the proper goal in treating spasticity with BoNT, a correct plan of administration of the solution on the right panel of muscles has to be carefully scheduled. BoNT injections for upper and lower limb spasticity usually need to be guided through electromyography (EMG), electrical stimulation or ultrasound guidance (US), particularly when dealing with the small size and complexity of hand, forearm and foot muscles.

Larger and superficial muscles, though, may be easily identified with inspection and palpation, unless anatomical deformity and postural deformities prevent the visual evaluation. EMG and electrical muscle stimulation can provide valuable assistance by confirming the correct placement of the needle before injection.

The EMG can also give additional information about the motor end-plate zones, theoretically considered as the best site for injection. Conversely, the US guide mainly provides information about muscle size and fibrosis as factors that can be important in the therapeutic decision-making. Moreover, particularly in children, the US guided injection technique gives some advantages, because it is better tolerated and relatively faster, and provides a real-time assessment of the location of the target muscle during injection as well as the position of neurovascular structures. The choice of EMG or US guide mostly depends on the operator's confidence and experience in using the instrument.

[9] Kutschenko et al., 'Neurotoxic Potencies'.

Doses and duration

The treatment of focal spasticity usually requires larger doses than those used to treat dystonia or other neurological conditions. For focal spasticity at the upper or lower limb the mean doses are: 300–500 U for OnaBoNT (Botox) or IncoBoNT (Xeomin) or 600–1000 U for AboBoNT A (Dysport). However, evidence of higher doses in post-stroke patients with up to 800 U of OnaBoNT, 1800 U AboBoNT and up to 1200 U of IncoBoNT without signs of systemic toxicity have been recently reported.[10]

Conversely, in children with cerebral palsy the dosage recommendations start from ≤12U/kg body weight for OnaBoNT/IncoBoNT for the first injection, and subsequent treatments ≤15U/kg (maximun total dose of 300 U), and ≤20U/kg body weight for AboBoNT for the first injection, and subsequent treatments of ≤30U/kg (maximum total dose of 1000 U).[11]

Other technical details including the dose conversion ratio between BoNTs/A1 are summarised in **Table 8**.

The clinical effect starts gradually over 5–7 days from the injection of BoNT/A1. It interferes with neuromuscular synaptic transmission for about 10–17 weeks and causes clinically detectable weakness for 3–4 months in most cases.

Adverse events

Adverse events may include excessive local muscle weakness.[12] Generalised muscle weakness can rarely occur, in particular if high doses are given in multiple muscles. Weakness arises as a consequence of the potential local spreading or diffusion into the systemic circulation. To avoid this risk, one should take into account the appropriate volume and speed of injection, the right dose and site of injections. The clinical effect outside the targeted muscles is due to local diffusion and is generally limited to adjacent muscles.

Autonomic side effects are also rare and more frequently occur after BoNT/B1 rather than BoNT/A1 treatment, and they are probably due to the higher affinity of BoNT/B1 for cholinergic autonomic nerve endings.[13]

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[10] Santamato et al., 'Employment of Higher Doses'.
[11] Strobl et al., 'Best Clinical Practice'; Wissel et al., 'Botulinum Toxin A Dose'; Heinen et al., 'The Updated European Consensus'.
[12] Bhatia et al., 'Generalised Muscular Weakness'.
[13] Aoki, 'A Comparison of the Safety Margins'.

Other rare effects reported are mild flu-like symptoms for a week during the first month after treatment; brachial neuritis following local injections and altered taste. These adverse events are usually mild and self-limiting.

The contraindications are limited to the rare cases of hypersensitivity to the toxin, or inflammation or infection involving the site of injection. Moreover, although there is no evidence of risk during pregnancy, BoNT is placed in pregnancy risk category C and the FDA advocates that it should be 'administered during pregnancy only if the potential benefit justifies the potential risk to the foetus.'[14]

[14] Pirazzini et al., 'Botulinum Neurotoxins'.

CHAPTER 3

THE TREATMENT OF FOCAL SPASTICITY: NEUROSURGICAL PROCEDURES

IVANO DONES

Peripheral neurotomy

Peripheral neurotomy is a neurosurgical procedure, first described by Stoffel in 1911, aimed at pauperising part of the nerve fibres of the motor component of mixed nerves, thus decreasing the motor innervation of selected muscles. The earliest surgical neurotomies were performed without any neurophysiological monitoring thus frequently causing chronic neuropathic pain due to the concomitant section of sensory nerve fibres. For this reason, and because of the advent of chemical nerve blocks, the procedure was nearly abandoned until the 1990s, when French and Belgian neurosurgical groups successfully reintroduced this technique by using electrical intraoperative stimulation and the operative microscope to avoid major damage.[1] Peripheral neurotomy usually leads to the permanent correction of posture and decrease in focal spasticity, without the need for repetitive injections such as the treatment with botulinum toxin.[2] The procedure can be performed at both upper and lower limbs and it is usually performed under general anaesthesia by avoiding muscle relaxants to allow intraoperative peripheral nerve electrical stimulation induced muscle contracture, thus localising and isolating motor nerve fibres bundles to be sectioned. A percentage of motor fibres is cut and discontinued for a few millimetres, keeping in mind that at least 2/5 of the motor nerve fibres should be preserved to avoid the complete paralysis of one muscle. Patients are allowed to move the day after surgery without immobilisation of the operated part. In the long term, a relevant sprouting

[1] Decq, '[Peripheral neurotomies]'.

[2] Deltombe, Lejeune, and Gustin, 'Botulinum Toxin Type A'.

of nerve fibres innervating the skeletal muscle occurs. This usually restores movement but without spasticity to become visible again.

Preoperative tests with botulinum toxin or bupivacaine blocks can give an indication regarding whether the limited movement is due to the spastic component or to joints blockade. Occasional section of sensory nerve fibres may inadvertently lead to the appearance of focal pain, paraesthesia and dysesthesia. While the sectioning of alpha-motor fibres causes a transient muscle weakness that restores after nerve fibre sprouting, the effect of selective neurotomy on spasticity is usually permanent as the sprouting of Ia nerve fibres mediating the monosynaptic stretch reflex arc, causing spasticity and clonus, at the level of muscle spindles are ineffective.

Posterior spinal rhizotomy

This surgical ablative procedure can be considered as a heritage of the past, when no neuromodulation procedures were available.[3] It consists of the complete section of one or more spinal posterior roots with the purpose of extinguishing all the afferences to the stretch monosynaptic and relaxation polysynaptic reflexes. Unfortunately, all the sensory afferences are usually lost, giving anaesthesia and severe impairment of sphincter functions.

Selective posterior rhizotomy

This consists of the section of ⅓ to ⅔ of the rootlets part of a single posterior root from L1 to S1. The mechanism of action is similar to the one described for the posterior spinal rhizotomy, but with the preservation of the sensory afference.[4] A further development of this technique is the functional posterior rhizotomy, in which rootlets are sectioned from L2 to S1 levels under neurophysiological monitoring in order to separate rootlets causing contraction greater than their expected area of innervation from those only innervating a small group of muscles, which must be carefully preserved.[5] This technique was formally introduced in 1996, although its sporadic use for the treatment of spasticity dates back to the beginning of the last century, when it was first used in Germany by Foerster to reduce hypertonia in a patient.

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[3] Chambers, 'Surgical Treatment of Spasticity'.
[4] Abbott, Forem, and Johann, 'Selective Posterior Rhizotomy'.
[5] Moreta, Ihara, and Ogiwara, 'Management of Childhood Spasticity'.

Selective posterior rhizotomy is mainly used in children with spasticity due to cerebral palsy.[6] The main goal of this procedure is to decrease pain, improve nursing with a concomitant decrease of the physical and psychological burden on the patient's family. In patients who are still able to walk with or without support, a further purpose of the procedure is to reach an additional improvement of joint motion, while in those patients who are bedridden or using a wheelchair the aim is to improve posture, pain and nurse care.

The surgical procedure of functional posterior rhizotomy consists of two phases. The first is performed by a preliminary L1–L5 laminotomy and laminectomy below S1 to reach the caudal end of the dural sac. The lower age limit for this procedure has been set to 30 months. In children affected by cerebral palsy with predominant presence of choreoathetosis, this treatment should be avoided as a decrease in their spasticity may worsen involuntary movements. A similar careful preoperative evaluation is mandatory in older children who can still walk, as a decrease in their spasticity might deteriorate their motor function. A preoperative CT and MRI of the spine is recommended to rule out any malformation or adhesion of the cauda equina that might cause more difficulties in separating each spinal nerve root. A preoperative neurophysiological assessment with evoked potentials, H and F waves is also highly recommended. Patients are intubated using short-acting muscle relaxants, while during surgery anaesthesia is kept intravenously to avoid interference of the anaesthetics with the neurophysiological intraoperative monitoring. The patient must be positioned then in the prone position. The medial skin incision extends from T12 to S3, laminae from L1 to S2 are exposed and laminotomy is performed from L1 to L5. The dura is opened in the epiarachnoid space to avoid nerve roots to emerge from the dural opening. L2–S3 roots are separated from the others and posterior roots are dissected free from the anterior ones between L2 to S2 under constant neurophysiological monitoring. The pudendal afferent fibres are avoided from lesioning. Electric stimulation at 10 Hz for 1 second is made to identify the roots.[7]

DREZotomy

This is a neurosurgical procedure, originally introduced to treat chronic neuropathic pain, which was successively used in the treatment of focal

[6] Walker, 'Selective Dorsal Rhizotomy'.

[7] Peacock and Staudt, 'Selective Posterior Rhizotomy'.

spasticity. It consists in the ventromedial incision of the dorsal root entry zone (DREZ) followed by the sectioning and coagulation of both myelinated and unmyelinated nerve fibres through a longitudinal incision of the dorso-lateral sulcus of the spinal cord.[8]

Tenotomy and tendon elongation

This is the oldest surgical procedure used to correct focal abnormalities of posture in patients affected by spasticity. It is used to correct focal postural abnormalities by sectioning muscle tendons in those patients in whom a long-term existing spasticity brought to the joint deformity and block with no chances of restoring the correct position due to tendon retraction and joint ankylosis. These orthopaedic procedures are still particularly used in young patients affected by cerebral palsy, as the abnormal postures and deformities may give pain which in tum increases spasticity.[9]

[8] Mertens and Sindou, '[Microsurgical dorsotomy]'.
[9] Bouttens and Delecourt, '[upper limb spasticity]'; Denormandie et al., '[spasticity in the lower limb]'.

CHAPTER 4

THE TREATMENT OF DIFFUSE SPASTICITY

IVANO DONES, VINCENZO LEVI

Introduction

When spasticity is severe and diffuse to both upper and lower limbs and the trunk, it may even cause the patient to be bedridden or confined to a wheelchair. In these severely disabled cases the treatment of diffuse spasticity is aimed both to decrease pain due to joints fixation and muscle contracture, give better nursing and, rarely, improve the patient's motor performance. Even in these patients, the first step in any treatment of spasticity must be the oral administration of drugs and, only when this kind of treatment shows to be useless, major and more invasive treatments must be recommended.

Oral drugs

The pharmacological treatment of chronic spasticity is mainly a symptomatic treatment, which, unfortunately, never solves the chronic degenerative disease of the central nervous system that causes spasticity. The ordinary drugs used to decrease spasticity are the first choice of treatment for all the patients affected by spasticity, regardless its degree. They are those previously described in this book, such as baclofen, a GABAb agonist acting at the inhibitory afference of the second motor neuron that, when given orally, may cause undesired side effects due to its action on the brain GABA receptor not strictly involved in the control of muscle tone. The second molecule that is used to decrease spasticity is diazepam, whose sedative action can sometimes prevail on its antispastic action. Tizanidine is the third most used molecule to treat spasticity through a direct action on the central nervous system, unlike dantrolene that may decrease spasticity by interfering with the calcium release from the sarcoplasmic reticulum of the skeletal muscle fibre. All these drugs

can be really effective in improving spasticity in less than half of the patients affected by different forms of diffuse spasticity or, when effective, they frequently cause undesired side effects. Thus, there is a need for further surgical options, such as intrathecal baclofen, to enhance the drug effect and minimise its undesired side effects.

Intrathecal baclofen

The first implant of a device to intrathecally administer a drug began in the early 1980s by delivering morphine or clonidine in intractable cancer pain.

Intrathecal baclofen therapy for spasticity was introduced in 1985 by Penn and Kroin, and then quickly spread to other countries.[1] At its inception, it was used mainly to treat spasticity in patients affected by spinal cord injury, while the first use of intrathecal baclofen was in 1985 in a 4-year-old child suffering from hypertonicity due to near-drowning syndrome.[2] In 1991, the first use of intrathecal baclofen in children with spastic cerebral palsy was reported by Albright. Since then, more than 60,000 patients have been treated with intrathecal baclofen worldwide.[3] Nowadays, this kind of pharmacological neuromodulation can be considered as the gold standard for the treatment of diffuse spasticity. This treatment has to be considered when both oral drug therapy is ineffective and spasticity in a patient really deserves a treatment to improve their quality of life. Most of the child candidates for intrathecal baclofen are patients with spasticity and dystonia due to cerebral palsy as well as children affected by spasticity due to different pathological conditions. Examples are brain injury, severe hypoxic damage, spinal cord trauma, multiple sclerosis and many other severe metabolic neurodegenerative disorders where spasticity may be relieved with intrathecal baclofen.[4] Moreover, as far as dystonia is concerned, cases responding to intrathecal baclofen are those affected by dystonia secondary to brain lesions whereas primary dystonias, such as DTY-1, are usually unresponsive.

The use of intrathecal baclofen in adults affected by spasticity of different causes is definitely considered to be the present gold standard of treatments for diffuse spasticity.[5] An additional analgesic effect of baclofen has been reported in patients affected by complex regional pain

[1] Penn and Kroin, 'Intrathecal Baclofen'.
[2] Penn, 'Drug Pumps'.
[3] Bones, 'Intrathecal Baclofen'.
[4] Lee et al., 'Early Outcomes'.
[5] Hsieh and Penn, 'Intrathecal Baclofen'.

syndrome refractory to other treatments and post-herpetic neuralgia. Moreover, a facilitating effect on spinal cord stimulation by intrathecal baclofen was reported to persist in the long term.[6]

High drug concentrations are obtained at the required site of action at the spinal cord level while avoiding relevant concentrations at the brain level. A gradient of 4:1 between the baclofen concentration at the spinal level within the caudal and rostral ends demonstrated why the intrathecal baclofen infusion through a spinal catheter can give a high concentration of this drug at the spinal level while avoiding its concentration at the brain level, thus avoiding the undesired side effects due to the action of this drug on the brain GABA receptors.[7]

Baclofen is a highly hydrophilic molecule that passes poorly through the blood brain barrier. This is why the oral administration of baclofen needs a high dosage (up to 75 mg/day) while its intrathecal administration needs a much lower daily dosage (20 to 1000 mg/day). Each spastic patient, regardless of weight, degree of spasticity and aetiology of spasticity has their own daily dose, thus the correct dose must be carefully set. There are many clinical conditions in which spasticity has to be considered as a positive sign of a reaction of the central nervous system to an injury, thus needing its preservation to keep the patient able to stand or even to move. One common example is the spasticity occurring on two ipsilateral limbs in a patient who has hemiplegia due to ischaemic brain injury. The patient uses the spastic lower limb as a cane to move and keep the standing position. Thus, if spasticity markedly improves, the patient will experience a worsening of motor performance and autonomy due to the lack of muscle strength.[8] For those patients who need to treat their diffuse spasticity, a test by injecting a bolus of a minimal quantity of baclofen (25, 50, 75 and 100 micrograms) through lumbar puncture is necessary to assess the effect of this GABAb agonist in improving spasticity without major undesired side effects. Once the test positively indicates a real improvement to the patient in a reasonable time on the day of the test, the implant of a programmable system for the infusion of intrathecal baclofen is performed after written consent. A bolus test can occasionally be repeated over a number of days with increasing dosage to obtain the proper effect and estimate the real therapeutic window of the needed daily dosage.[9] The bolus test is considered positive if a relevant decrease in spasticity with possible concomitant improvement of motor

[6] Lind et al., 'Spinal Cord Stimulation'; Kumru et al., 'Intrathecal Baclofen Bolus'.
[7] Lazorthes et al., 'Drug Delivery Systems'.
[8] Bones et al., 'Cautious Use of Intrathecal Baclofen'.
[9] Winter, Beni-Adani, and Ben-Pazi, 'Intrathecal Baclofen Therapy'.

performance is observed persisting at least four hours after the injection, without undesired side effects such as nausea, somnolence or dizziness. To be considered for the implant of an administration device, the patient must be free from active infections and pressure sores and, in particular, the skin in the lumbar and abdominal region should be intact. Although these pumps still have a relevant size and weight, they can be implanted even in children either under the skin or under the muscular fascia of their abdomen. The drug administration device system consists of an implantable pump connected to an intradural catheter inserted into the lumbar intradural space. There are two main types of implantable pumps presently available on the market: constant flow pumps and programmable pumps. The first are pumps in which the drug solution filling the reservoir is propelled by a positive pressure induced by a compressed gas chamber adjacent to the reservoir. The solution flow is constant, while variation of the daily dosage can be obtained by changing the drug concentration in the solution at every refill. [10] The three programmable pumps presently available on the market differ in their mechanism of action. In one type of pump (Siromedes, Germany and Prometra, USA) there is a valve regulating the drug solution flow from a high-pressure, gas-driven reservoir. The second most frequently used type of pump (Synchromed, [Medtronic] USA) is a peristaltic pump consisting of a 20–40 ml drug solution reservoir connected to a rotor that can be programmed to varying delivery rates and patterns through a microprocessor inside the pump. **(Figure 4-1)**

Figure 4-2 Intrathecal baclofen: different infusion modes

This is an unconditionally 3 Tesla MR compatible pump which the patient can be submitted to. This pump has a battery lasting approximately 7 years depending on the drug infusion rate. After that, the pump must be

[10] Koulousakis and Kuchta, 'Intrathecal Antispastic Drug Application'.

replaced, even under local anaesthesia, by simply reopening the abdominal skin incision, exposing the implanted pump and replacing it with a brand new pump that has been previously refilled and programmed according to the patient's requirements.

It is personal experience that at any pump replacement, the baclofen daily dosage should be lowered by at least 30% to avoid initial overdosage. In fact, as reported in the literature, these peristaltic pumps could lose their physical properties of elasticity of the internal soft tubes and the rotor could be losing its thrust in the long term, thus giving a dosage lower than that reported by electronic telemetry.[11] These pumps are remotely controlled by telemetry through an external programmer to change their parameters. **(Figure 4-2)**

Before any implant procedure begins, the pump is refilled with a drug solution that usually, at the beginning of the treatment, is a 500 micrograms/ml baclofen solution that can be replaced by a higher concentration of 2000 micrograms/ml of baclofen according to the daily dosage used.

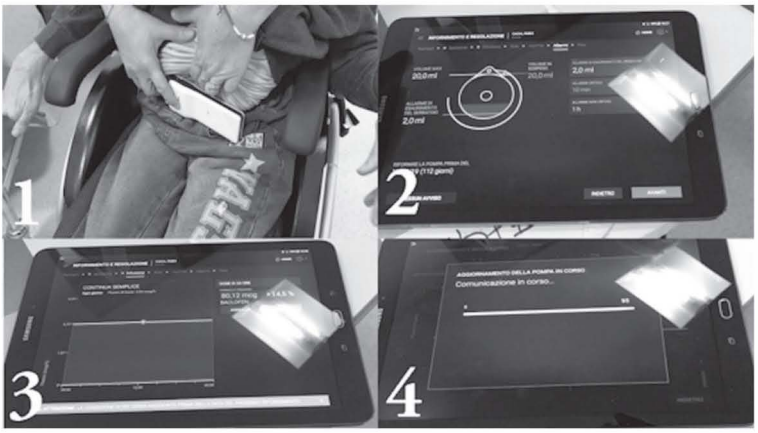

Figure 4-3 External programmer (1) and verification of pump parameters at refill (2–4).

The initial daily dosage set at the implant is conventionally calculated as twice the amount of drug used at the effective bolus test. This calculation prevents any problem related to initial drug overdose.[12]

[11] Winter, Beni-Adani, and Ben-Pazi, 'Intrathecal Baclofen Therapy'.
[12] Dones, 'Intrathecal Baclofen'.

The surgical procedure must be performed in the operating theatre under sterile conditions and with access to the common surgical resources such as bipolar coagulation and fluoroscopy. The procedure is usually performed under general anaesthesia. An intradural catheter is usually inserted by lumbar puncture with a Tuohy needle at the L4 level. One should enter paramedian with angle of about 30° and reach the mid-thoracic level with the tip of the catheter. Unlike the opinion of some other authors, we reckon the rostral location of the catheter's tip is not crucial to guarantee the baclofen's maximum effectiveness. [13] Considering our experience based on almost 1000 cases with different clinical pictures of spasticity variously localised throughout the body, indeed, the tip of the catheter was always placed mid-thoracic and the efficacy in reducing spasticity was always obtained at different daily dosages.

Moreover, in a very small number of patients, due to their physical activity and to traumas, the tip of the catheter dislodged from the mid-thoracic to the sacral region with an intradural coiling of the catheter but without any difference in the control of their spasticity or additional neurological damage at a stable daily dosage of baclofen. **(Figure 4-3)**

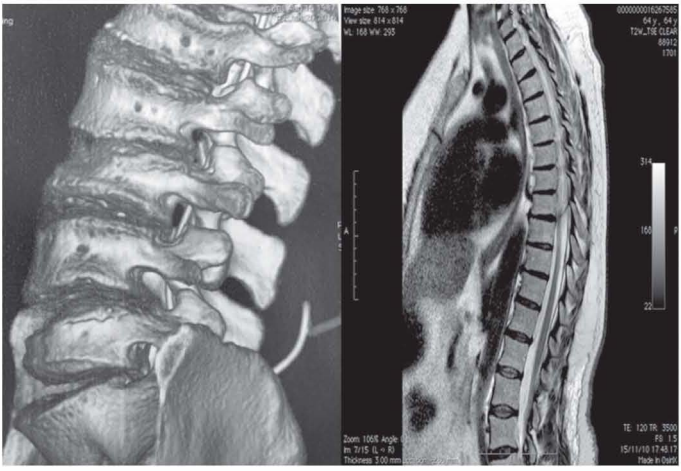

Figure 4-4 3D-CT scan of the intrathecal catheter positioning (left panel) and its terminal loop at the tip (right panel).

[13] Sivakumar et al., 'Intrathecal Baclofen Therapy'.

Basic surgical instruments for spine surgery must be available when a partial laminectomy is occasionally needed to easily create the access to the intradural catheter.

Minimising the cerebrospinal fluid (CSF) leakage during the catheter insertion procedure can avoid post-surgical headache.

The only occasion when the intradural catheter has to be replaced is when it becomes obstructed by biological debris or, as it emerged from our more than 25 years experience, when at pump replacement, the catheter appears to be physically deteriorated (usually not before 14 years). **(Figure 4-4)**

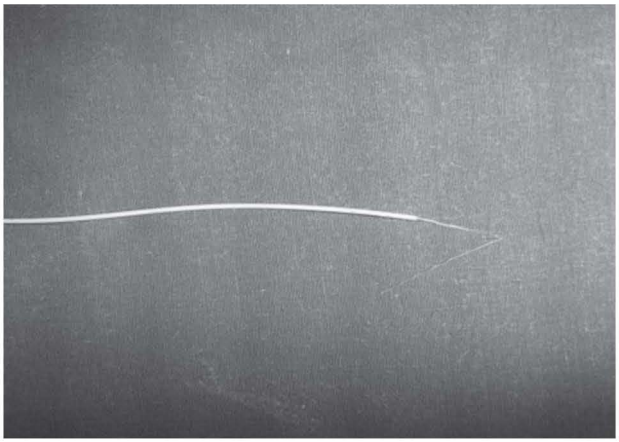

Figure 4-5 A physically deteriorated catheter, incidentally found during a pump replacement.

Biological debris can commonly occur in patients with hyperproteic CSF, when scattered sepimentations of the CSF space in the spinal cord are provoked by traumas or previous infections. A jacketed catheter is normally used to prevent kinking and accidental puncture of the catheter. There might be difficulties in inserting the catheter due to concomitant scoliosis or spinal deformities, or in patients who underwent instrumented thoracolumbar fusion or arthrodesis. For this reason, a fluoroscopic control might be helpful in some procedures. CT-guided procedures aimed at easing the insertion of the catheter intradurally have also been reported, but CT-guided imaging may actually be redundant in most of the cases as

well as the use of sonograms to refill pumps.[14] In fact this procedure, when performed by experienced hands, is usually quite simple. The fixation of the catheter can be performed via an anchoring system provided by the catheter manufacturer or, alternatively, leaving a catheter loop that, once the scar tissue is formed, locks the catheter in its position and avoids any catheter dislodgement. Then the catheter is tunnelled subcutaneously up to an abdominal subcutaneous pocket created at the lower left abdominal quadrant. The catheter is then connected to the pump which is eventually inserted in the abdominal pocket. Although not mandatory, a bridge bolus can be programmed to quickly fill the catheter with the drug solution.

A constant flow pump is rarely used in the chronic treatment of spasticity as any variation in the daily dosage would imply the replacement of an expensive baclofen solution and variations in the daily dosage are frequently needed even in the long term.

Any variation in the daily dosage of baclofen should be programmed at least every 15 days with an increase of not more than 10% of the daily dosage each time to avoid abrupt drug overdosage. Patients are assessed according to the clinical evaluation described before, both during the bolus test and at refills or dosage variations on long-term follow-up. Possible periodic variations in the daily dosage of baclofen may occur depending on different conditions such as disease progression, variation in the motor rehabilitation programme, climate variations and concomitant infections that may temporarily worsen spasticity.

Like many other treatments implying the use of any internal device, intrathecal baclofen should be recommended to patients who have an appropriate social support, particularly if they are affected by additional cognitive impairment. An extended network of 'service stations' near their domestic territory must be granted to promptly face any complication in case of device malfunction or additional hardware problems. Unfortunately, patients who live in rural areas far from well-equipped medical centres cannot be easily proposed for any device implant as they cannot be provided with a remote control able to manage every function of these devices even in case of any emergency. Unfortunately, the pumps used for this treatment are presently not yet able to remotely connect to the implanting centre to check functions and modify parameters.

Anecdotal improvement of motor performance was reported in association with an increase in physical therapy of the patient. Thus, it was impossible to define a real improvement of mobility only due to intrathecal baclofen treatment. Nevertheless, physical therapy can be

[14] Hsieh and Penn, 'Intrathecal Baclofen'.

improved by intrathecal baclofen-induced decrease in spasticity and sometimes tools to keep the standing position and exoskeleton can only be used when the patient shows a decreased spasticity with minor postural abnormalities.

Moreover, urge incontinence and uninhibited bladder contractions are diminished by intrathecal baclofen. Despite an associated decrease in urethral pressure, intrathecal baclofen may result in a progressive increase in the residual volume of urine in the spastic patient's bladder. Areflexic bladder and retention in patients under intrathecal baclofen were also occasionally reported. Thus, post-void residual urine volume should be checked before and during intrathecal baclofen. Constipation may occur during intrathecal baclofen. An improvement in sleep was reported due to the effect of intrathecal baclofen on night-time muscle spasms.

When performed by experienced physicians this treatment is quite safe, but many life-threatening complications are reported in the literature and most of them are due to human error during implant, refill and reprogramming of the pump.[15]

There is no antagonist clinically useful for baclofen overdose. Some cases of baclofen overdose or withdrawal due to human or mechanical failure led the patient to coma with respiratory depression and some of them were also reported to have a lethal outcome.

Baclofen overdose may induce bradycardia, hypotension and drowsiness that can precede the onset of coma. Although the use of intravenous physostigmine has been reported as a possible tool to reverse the chain of events bringing the overdosed patient to coma, other drugs such as ondansentron have been reported to be helpful in reversing the progression of clinical worsening in these patients. Patients showing signs of possible baclofen overdose should be admitted to an intensive care unit, their pumps should be emptied and stopped, and possibly a great amount of CSF should be withdrawn through a lumbar puncture.[16]

Baclofen withdrawal due to wrong pump refill, mechanical stall of the pump, obstruction of the catheter and lack of refill of the pump in due time may present with hyperthermia, rhabdomyolisis and disseminated intravascular coagulation.[17] Intravenous diazepam and oral baclofen may be useful in reversing the clinical picture before the correct intrathecal baclofen administration is restored.

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[15] Winter, Beni-Adani, and Ben-Pazi, 'Intrathecal Baclofen Therapy'.

[16] Bones, Messina, and Franzini, 'Correction to:'Careful' Reprogramming'; Broggi et al., 'A Possible Pharmacological Treatment'.

[17] Frizon et al., 'Removal of Intrathecal Catheters'.

Drug tolerance during a long-term intrathecal baclofen treatment has been occasionally reported, forcing the progressive increase in baclofen daily dose.[18] A 'therapy holiday' from baclofen for at least two months is often recommended to re-establish the population of baclofen receptor and restoring drug sensitivity. An alternative drug may be used as a substitute to preserve the antispastic treatment in the patient. Daily dosage seasonal variations according to climate and variations in physical activity can be helpful in avoiding any drug tolerance in the long term.

The use of intrathecal baclofen in children is reported to give remarkable improvement of the functional outcomes with improvement of gait and upper extremity function, and better activities of daily living. Additional advantages regarding sleep, pain, speech and in terms of prevention of the worsening of hip deformities have also been described in children on intrathecal baclofen. [19]

Epidural spinal cord stimulation

Before the use of intrathecal baclofen, many cases of spinal cord stimulation to treat spasticity were reported. Some papers recently suggested the possible enhancement of the electrical modulation by adding intrathecal baclofen, although technical and economic issues do discourage the simultaneous use of both treatments in the spastic patient.[20]

The mechanisms of such an effect have been ascribed to the role of the sensory feedback through the chain of interneurons at the spinal level.

Tetrahydrocannabinol

The plant Cannabis sativa has a very long history of medical use in the treatment of pain and spasms. A renewed interest in its active molecule delta-9-tetrahydrocannabinol (THC) has lately come to attention. There is fuzzy evidence in the literature about THC having a role even in improving spasticity in some subjects. A heterogeneous group of patients affected by multiple sclerosis has been described to show both improvement of pain and of their spasticity. Mammalian tissues contain at least two types of cannabinoid receptors, CB1 and CB2, both couplet to G

[18] Bones and Broggi, 'Long-Term Appearing Drug'.
[19] Harat et al., 'Deep Cerebellar Stimulation'; Leary et al., 'Intrathecal Baclofen Therapy'; Gilmartin et al., 'Intrathecal Baclofen for Management'.
[20] Sivaramakrishnan, Solomon, and Manikandan, 'Transcutaneous Electrical Nerve Stimulation'; Nagel et al., 'Spinal Cord Stimulation'.

proteins. CB1 receptors are mainly found in the neurons of the central and peripheral nervous system, while CB2 receptors are mainly found in the cells of the immune system. CB1 receptors have been found in the brain where spasticity, pain, abnormal involuntary movements, seizures and anmesia develop. Cannabinoids are NMDA receptors and glutamate antagonists.

THC is used in the control of nausea, as an analgesic and in glaucoma. The antispastic action of cannabis was described more than a century ago. Anecdotal reports on the relaxing action of smoking marijuana on muscles in spastic patients affected by multiple sclerosis or spinal cord injury have been reported. Doses higher than 5 mg of THC had more effect on spasticity than the placebo. Immediate adverse effects of cannabinoid ingestion are hypotension, increased heart rate, reddened conjunctivae, dry mouth, light-headedness, sedation, psychomotor slowing, depersonalisation and panic attacks.

Acute intoxication leads to euphoria, loss of short-term memory and impaired linear thinking while chronic high doses may cause impairment of cognitive abilities. Moreover, cannabinoids cause dependence.[21]

Cerebellar neuromodulation

Brain neuromodulation for spasticity has always been controversial and its application fell into oblivion for many years. Nowadays, due to the great improvements in neuroimaging and surgical technique, brain neuromodulation might soon be newly rediscovered and potentially become a useful option in cases of drug-resistant diffuse spasticity.[22]

Unlike other common movement disorders, which have benefited from deep-brain stimulation (DBS) and ablative procedures applied to basal ganglia targets, neuromodulation techniques for the treatment of spasticity have traditionally focused their field of investigation on the cerebellum. Anatomically, the cerebellum can exert a modulative role on spinal neurons responsible for muscle tonus control through one of two different pathways:

- Direct efferences towards the spinal cord. The spinocerebellum, constituted by the vermis and paravermis zones, is the most important cerebellar structure involved in this direct pathway. The vermis, after receiving visual, auditory, vestibular and somatic

[21] Fraguas-Sanchez and Torres-Suarez, 'Medical Use of Cannabinoids'.
[22] Sindou and Mertens, 'Neurosurgery for Spasticity'.

sensory input from the head and proximal parts of the body, projects by way of the fastigial nucleus to the reticular formation in the brainstem, which gives rise to the reticulospinal tract, involved in controlling axial muscles and proximal limb extensors tone, thus assuring balance during stance and gait. The paravermal zones, on the other side, connect through the interposed nuclei and the superior cerebellar peduncle to the contralateral red nucleus. This nucleus is the origin of the rubrospinal tract, responsible for the activity of limb flexor muscles. Considering this anatomical information, the spinocerebellum is mainly involved in both muscle tone and coordination of the extremities.[23]

- The dentatorubrothalamic indirect pathway. This tract originates in the dentate nucleus of the neocerebellum and influences the activity of the motor cortex and descending motor systems. Although the dentate nucleus is mainly implicated in planning, initiation and control of voluntary movements as well as in cognition and visuospatial functions, some evidence suggests its possible role in mediating muscle tone.[24]

Cerebellar control of muscle tonus was first observed by Jean Babinski in 1899.[25] In 1963, Schneider and Crosby, after removing a large area of cerebellar cortex in a patient with cerebral palsy, were the first to link clinical signs of increasing spasticity to the cerebellum.[26] Two years later, in 1965, Heimburger and Whitlock published their results on stereotactic dentatotomy performed for the first time on 12 patients with hypertonic and dyskinetic manifestations of cerebral palsy. All 12 patients improved after the procedure showing a prevailing marked reduction in muscle tone.[27] In 1972, Cooper and colleagues pioneered chronic cortical cerebellar stimulation (CCS) for the alleviation of spasticity in 11 patients affected by cerebral palsy and head injury.[28] Since then, several neuromodulation and ablative procedures targeting different cerebellar structures have been proposed, with varying degrees of success.

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[23] Asanome, Matsuyama, and Mori, 'Postural Muscle Tone'.
[24] Safronov, Vasin, and Lesov, '[Effect of dentatotomy]'; Tona et al., 'Role of Cerebellar Dentate'.
[25] Teixeira, Schroeder, and Lepski, 'Evaluating Cerebellar Dentatotomy'.
[26] Schneider and Crosby, 'Between Cerebral Hemispheres'.
[27] Heimburger and Whitlock, 'Stereotaxic Destruction'.
[28] McLellan, Selwyn, and Cooper, 'Clinical and Physiological Effects'.

The main currently available techniques (anterior lobe cerebellar stimulation, superior cerebellar peduncle stimulation and dentatotomy) will be briefly described along with their results and potential complications.

Chronic cortical cerebellar stimulation

Chronic cortical cerebellar stimulation (CCS), initially performed by mean of external radio frequency-linked systems and later by the safer totally implanted controlled-current stimulators, was the first brain modulation technique used to treat severe spasticity. Initially performed by Cooper in subjects affected by cerebral palsy and severe brain injury, it then made more widespread by Davis in the 1980s. CCS employed four-in-line leads electrode pads implanted via a suboccipital bilateral craniotomy and aimed to stimulate the superomedial aspect of the cerebellar anterior lobe cortex.[29] Eighteen papers describing a total of 600 patients were published on CCS from 1976 to 1984.[30] Considering the 568 patients (95%) who were able to be followed up, a relevant degree of spasticity reduction was noticed in 85% of cases (classified as marked in 25%, moderate in 34% and mild in 27%). In the remaining subjects, no clinical worsening was reported after stimulation and only one post-operative death, from extradural posterior fossa hematoma, was observed. The following cycling parameters (1 min ON and 8 min OFF) were clinically shown to be the safest and most effective: 150–200 Hz; 0.2–0.5 msec, charge density 1–4 mC/sq cm/ph.[31] Despite the initial interest and the promising results, CCS was then progressively replaced by less invasive surgical procedures.

Deep superior cerebellar peduncle stimulation

Superior cerebellar peduncle stimulation (SCPS) consists of the direct mini-invasive stereotactic approach to the medial anterior lobe of the cerebellum. Its aim is to deliver high-frequency stimulation (185–200 Hz) by means of deep-implanted leads. This technique, proposed for the first time by Galanda et al., was initially performed through a transtentorial approach using the radiofrequency system TESLA LSP 330.[32] After noticing frequent radio receiver malfunction in 30 patients, the radiofrequency

[29] McLellan and Cooper; Davis, Schulman, and Delehanty, 'Cerebellar Stimulation'.
[30] Davis, 'Cerebellar Stimulation'.
[31] Davis, 'Cerebellar Stimulation'.
[32] Galanda and Hovath, 'Chronic Electrical Stimulation'.

technology was progressively replaced by totally implanted stimulation hardware, similar to the one commonly used for basal ganglia DBS.[33] In SCPS, the four contact leads are inserted bilaterally into the target (set on the midline MRI section, 8 mm above the fastigium, parallel to the floor on the fourth ventricle) after performing a small craniectomy with the entry point localised 1 cm below and 1 cm medial to the sigmoid sinuses. The optimal threshold for stimulation (0.5–2.5 V, 150–210 μsec, 20 min ON 2–6 OFF) is usually 0.1–0.2 mA lower than the intensity at which a sudden increase in muscle tone is observed, and it is commonly accompanied by immediate relaxation and a feeling of pleasure, followed by a gradual decrease of hypertonus in muscles within 15–20 min. Between 2003 and 2007, Harat and colleagues treated 13 patients with SCPS suffering from severe spasticity due to cerebral palsy.[34] They observed remarkable improvement of both spasticity, mostly in the first six months, and associated pain. Infection of the hardware resulting in the removal of the entire neuromodulation system occurred in 23.1% of cases. Similar results were found by Sokal et al., who reported the outcomes of SCPS in a group of 13 young patients with dystonic and spastic features due to cerebral palsy.[35] A significant reduction of spasticity in upper (from 3 to 1.5, Ashworth scale) and lower extremities (from 3 to 1.75) was obtained in 8 and 7 patients respectively. The decrease in muscle tone, however, did not lead to a concomitant improvement of preoperative pain, and, as previously mentioned, 3 patients (23.1%) underwent the entire stimulation hardware removal due to severe infection.

Dentatotomy

Surgical ablation of the dentate nucleus, better known as dentatotomy, was widely used in the past for the treatment of several spastic disorders.[36] This technique, usually performed under local anaesthesia, involves the stereotactic introduction of an electrode and its exposed tip through a suboccipital burr hole and the cerebellum, with the aim of lesioning the intermediate anterior part of the dentate nucleus (coordinates: 10–12 mm behind the fastigial point, 3–5 mm below the fastigial line an 8–10 mm from the midline). Once the target is reached, physiological monitoring is

[33] Galanda and Horvath, 'Stereotactic High-Frequency Stimulation'.
[34] Harat et al., 'Clinical Evaluation.'
[35] Sokal et al., 'Deep Anterior Cerebellar Stimulation.'
[36] Heimburger and Whitlock, 'Stereotaxic Destruction'; Gornall, Hitchcock, and Kirkland, 'Stereotaxic Neurosurgery'; Galanda and Hovath, 'Chronic Electrical Stimulation'; Siegfried and Verdie, 'Long-Term Assessment'.

usually performed to rule out adverse events and the lesion is eventually made at 75°C for 60 sec, until a satisfactory decrease of homolateral muscle tone is achieved. Complications are rare and include aseptic meningitis and temporary neurological deficits (in particular dysarthria, hypotonia and ataxia).

In 2015, Teixeira and colleagues reviewed 12 consecutive patients who underwent unilateral or bilateral dentatotomy.[37] All the patients were affected by severe spasticity due to different brain injuries (spontaneous or traumatic intracerebral bleeding, birth trauma and degenerative disease of unknown aetiology). Immediate spasticity relief was observed in ten patients (83.3%) and lasted for a minimum of 12 months following the procedure. This benefit, though, persisted in only five of them (41.6%) at the last follow-up (mean 31.6 months). No mortality and adverse events related to the procedure were described.

Although not routinely performed nowadays, dentatotomy may still be considered a valuable resource in case of severe drug-resistant hemi- or bilateral spasticity. In addition, the valuable insights gained in terms of cerebellar physiology with dentatomy could be of paramount importance in the very near future, with the potential introduction of new neuromodulative and ablative procedures (such as adaptive DBS and high-frequency focused ultrasound).

The literature and data available about the different techniques of cerebellar neuromodulation for the treatment of severe spasticity clearly present several methodological pitfalls (retrospective and anecdotal reports, inadequate patient selection criteria, coexistence of patients affected by severe dystonia and spasticity, lack of appropriate functional grading scales). Despite their controversial results though, these procedures should not be completely neglected because, if performed by expert hands, they may still represent an effective therapy in cases of spasticity refractoriness compared to other well-established procedures (intrathecal baclofen infusion, dorsal rhizotomy and selective neurotomy). Second, in the very near future, new neuromodulative and ablative procedures (adaptive DBS and high-frequency focused ultrasound) might increase the efficacy and safety of the currently available surgical techniques.

[37] Teixeira, Schroeder, and Lepski, 'Evaluating Cerebellar Dentatotomy'.

CHAPTER 5

SPASTICITY IN CHILDREN: A WORLD APART

GIOVANNA ZORZI

Introduction

Spasticity is a consequence of lesions of the upper motor neuron and it is one feature of upper motor neuron syndrome, together with exaggerated tendon reflexes, involuntary spasm and motor weakness **(Table 9).** Spasticity in children results from congenital abnormalities, injury or degeneration of motor pathways in the cortex, basal ganglia, brainstem, central white matter or spinal cord. It is therefore seen in a wide range of paediatric neurological conditions, acquired or genetic in nature, with a static or progressive course **(Table 10)**. Spasticity can be the sole or prominent clinical manifestation, or it can be part of more complex phenotypes, associated with other neurological and extraneurological signs. Spasticity can have little or even no impact on motor function, or it may cause severe motor impairment. Spasticity can increase over time through delayed complications of the primary pathology or through progression of the underlying disease. Diagnosis of the underlying condition causing spasticity in children is a multistep process: familial and perinatal history, age at onset, disease course, associated signs and magnetic resonance imaging are the most important clues for the diagnosis.

Table 8 Components of upper motor neuron syndrome

Positive components
Exaggerated tendon reflexes
Released reflexes
Babinski sign
Increased tone
Clonus
Spasm
Negative components
Motor weakness
Slowed movements
Loss of dexterity
Loss of selective motor control

As a second step, extensive metabolic and genetic investigations may be necessary. In clinical practice, it is important to remember that cerebral palsy is by far the most common cause of spasticity in the paediatric population.[1]

Table 9 List of neurological conditions causing spasticity in the paediatric population

Acquired condition
Cerebral palsy
Cerebral and spinal tumours
Encephalitis
Stroke
Brain and spinal cord injury
Acute myelitis
Multiple sclerosis and other demyelinating disorder
Genetic/inherited conditions
• Progressive
Leukodystrophies
Hereditary spastic paraparesis
Ceroid lipofuscinoses
Mitochondrial disorders

[1] Bax et al., 'Proposed Definition and Classification'.

	Neurodegeneration with brain iron accumulation
	Gangliosidosis
	Organic acidurias
	Peroxisomal disorders
• Not progressive	
	Cortical malformation (pachygyria, polymicrogyria)
	Congenital muscular dystrophies
	Ponto-cerebellar atrophy
	Spinal malformation

Differential diagnosis and clinical evaluation

Spasticity has to be differentiated from other types of hypertonia in children, mainly dystonia and rigidity.[2] Dystonia is defined as a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, alone or in association with abnormal postures.[3] Dystonia is triggered or worsened by voluntary and task-specific movement (action dystonia) and may vary with body position, stress, fatigue or emotional state. Dystonic movements are usually distinguishable from the involuntary flexor and extensor spasms seen in patients with spasticity: they are twisting with the overflow of muscle contraction.[4] Rigidity is a common clinical sign in adults as a feature of Parkinsonism, but only rarely reported in young children. It is defined as increased resistance to passive movement independent of posture and speed of movement. Unlike dystonia or spasticity, rigidity is not influenced by voluntary movements or postures. Myotonia and neuromyotonia can also cause increased muscle tone in children. Other causes of hypertonia, that can be frequent in adult patients such as catatonia, are extremely rare in children.[5] Spasticity is a velocity-dependent resistance of a muscle to stretch. One or both of the following signs has to be present: 1) resistance to externally imposed movement increases with increasing speed of stretch, and/or 2) resistance to externally imposed movement rises rapidly above a threshold speed or joint angle. Spastic hypertonia usually predominates in antigravity muscles and can be increased by anxiety, emotional state, pain, surface contact or

[2] Sanger et al., 'Classification and Definition'.
[3] Albanese et al., 'Phenomenology and Classification'.
[4] Sheean and McGuire, 'Spastic Hypertonia'.
[5] Preston and Shapiro, *Electromyography and Neuromuscular Disorders*; Daniels, 'Catatonia: Clinical Aspects'.

other non-noxious sensory input. As a part of the upper motor neuron syndrome, spasticity is usually associated with other positive and negative symptoms. The negative symptoms, in particular dexterity or fine motor control, may be difficult to evaluate in young patients or in those with mental impairment. Spasticity can be measured, and any objective assessment is essential for clinical evaluation and monitoring treatment. It is well known that the degree of spasticity is also influenced by external factors such as temperature, time of the day, fatigue, posture and position of the limb. All these factors are particularly relevant for the paediatric population, so it is important to create an adequate and positive clinical setting in evaluating a child with spasticity.[6] There are several scales for the quantitative assessment of spasticity. The modified Ashworth score is the most frequently used clinical measure because it is easy to administer and has good reliability.[7] The sole quantification of spasticity in a child does not always correlate with the disability, since increased tonus has a variable functional impact on a child's motor function. In some patients, hypertonia allows a reduction in the impact of weakness, in other cases hypertonia causes painful contractures that negatively impact the child's motor ability. It is therefore of paramount importance to recognise that a comprehensive clinical assessment should also include functional and quality of life scales such the Pediatric Evaluation of Disability Index, Peabody Developmental Motor Scale, Functional Independence Measure for Children, Gross Motor Function Measure and Child Health Questionnaire.[8]

Treatment

The goal of any treatment is to cure a disease, but for the majority of disorders causing spasticity in children treatment is still aimed at reducing symptoms, mainly pain and musculoskeletal deformities, with variable effects on motor function. Most of the paediatric studies were conducted in children with CP and there are limited data regarding treatment of spasticity in other non-progressive motor disorders, or in degenerative conditions.[9] In general, any treatment of spasticity requires specific experience and knowledge regarding correct indication, dosage and different therapeutic options that are represented by oral pharmacological agents, focal treatment and surgical interventions. **(Table 11)** Pharmacological

[6] Yelnik et al., 'How to Clinically Assess'.
[7] Scholtes et al., 'Assessment of Spasticity'.
[8] Sanger et al., 'Definition of Disorders'.
[9] Delgado et al., 'Pharmacologic Treatment of Spasticity'.

treatment options are more restrictive compared to adults because of possible side effects of many drugs that are not tolerated by children. Among oral agents, the most used drugs are benzodiazepine (in particular diazepam) and oral baclofen. Diazepam has been shown to be effective for short-term treatment but there is no evidence about a positive impact on motor function. Most frequent side effects are ataxia and drowsiness.[10]

Table 10 Treatment options for spasticity in children

Oral medications
Baclofen
Diazepam
Dantrolene
Tizanidine
Injectable (focal treatments)
Botulinum toxin A
Botulinum toxin B
Ethanol
Phenol
Surgical treatments
Orthopaedic surgery
Intrathecal baclofen
Selective dorsal rhizotomy
Deep-brain stimulation

Oral baclofen is widely used; it reduces spasticity but its efficacy to improve motor function has not been definitively proved in controlled studies. Drowsiness and sedation are common side effects, so it is important to start at the lowest possible dose and avoid rapid discontinuation due to the risk of withdrawal symptoms.[11]

[10] Mathew et al., 'The Efficacy of Diazepam'; Delgado et al., 'Pharmacologic Treatment of Spasticity'

[11] Verrotti et al., 'Pharmacotherapy of Spasticity'.

Dantrolene and tizanidine have also been used, but in small set of children and there are not sufficient data to support or to refute their use in treating spasticity. The most widely used therapy for spasticity in children is botulinum neurotoxin A injections, an effective and generally safe treatment as also demonstrated by controlled studies.[12]

Side effects are the same as those seen in adults; they depend on the dosage and the site of injection, and are mainly pain and excessive weakness. In some children, it is necessary to perform the procedure under anaesthesia. Selective dorsal rhizotomy is a procedure that interrupts motor nerve signal transduction to reduce spasms and pain. It is used in children, especially in those with CP. It has been shown to reduce in spasticity in children in the long term.[13]

Intrathecal baclofen has gained an important role in treating children with different forms of spasticity, mainly due to CP, but also in brain and spinal cord injury and progressive neurological conditions. [14] It is recommended for children older than 4 years and after a trial with oral baclofen.[15] Controlled studies have shown reduction of spasticity in CP in the short term, while the long-term efficacy or the results in patients with spasticity not due to CP is less clear. [16] Finally, in recent years the advanced technique of pallidal deep-brain stimulation has become the standard of care to treat different forms of paediatric dystonia, being most effective in genetic isolated dystonia.[17]

It is also effective, but to a lesser extent, in other dystonic syndromes combined with spasticity such as dystonic cerebral palsy, but it must be emphasised that more studies with larger numbers of cases are needed to better define surgical target and selection criteria for children with combined spasticity eligible for neuromodulation.[18]

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[12] Wallen, O'Flaherty, and Waugh, 'Intramuscular Botulinum'; Kawamura et al., 'A Randomized Controlled Trial'.
[13] Nordmark et al., 'Long-Term Outcomes'.
[14] Margetis et al., 'Intrathecal Baclofen Therapy'.
[15] Berweck et al., 'Use of Intrathecal Baclofen'.
[16] Hasnat and Rice, 'Baclofen for Treating Spasticity'.
[17] FitzGerald et al., 'Deep Brain Stimulation'.
[18] Marks et al., 'Dystonia Due to Cerebral Palsy'; Keen et al., 'Deep Brain Stimulation'.

CHAPTER 6

BLADDER SPASTICITY: THE OVERACTIVE BLADDER

MICHELE SPINELLI

Introduction

'Bladder spasticity' is an old-fashioned term that has been lately abandoned. It has been replaced by the correct definition of overactive bladder (OAB), a medical condition characterised by urgency, with or without urging urinary incontinence, frequency and nycturia, in the absence of genitourinary pathologies or metabolic factors that could explain these symptoms.[1] The key symptom of OAB is urgency as the sudden compelling and hardly deferrable desire to pass urine. OAB affects one sixth of the European population older than 40 years and similar data were also reported in the United States where around one sixth of adults older than 18 years have symptoms of OAB with an estimated prevalence of 33 million US residents aged over 18 years.[2] Erwin reported a cross-sectional population-based survey of people over 18 years, showing that the total prevalence in four European countries is 12.2% and confirmed that OAB is a common condition in men and women across all adult age groups.[3] One third of the population affected by an overactive bladder has urge urinary incontinence and studies on large case series reported that the prevalence of symptoms of OAB increases with age.[4] The aim of this chapter is to critically address the different therapies of OAB providing an up-to-date insight on alternative strategies to antimuscarinics.

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[1] Abrams et al., 'The Standardisation of Terminology'.
[2] Milsom et al., 'Symptoms of an Overactive Bladder'; Stewart et al., 'Burden of Overactive Bladder'.
[3] Irwin et al., 'Urinary Incontinence'.
[4] Irwin et al., 'Urinary Incontinence'.

Pathophysiology of micturition reflex

The lower urinary tract serves two main functions: the storage of urine without leakage (storage phase) and the periodic release of urine (voiding phase). During the storage phase the detrusor muscle is relaxed, and the outlet region is contracted to maintain continence. During the voiding phase the detrusor muscle contracts and the outlet region relaxes, facilitating bladder emptying. These two functions are dependent on central, peripheral autonomic and somatic neuronal pathways and local peripheral factors. During the storage phase the afferent impulses reach the CNS from the lower urinary tract and afferent activity sends information to the periaqueductal grey of pons. In the pontine tegmentum there are two regions: a medially located one (M-region), which corresponds to Barrington's nucleus or pontine micturition centre which is responsible for the coordination of micturition reflex, and a laterally located one (L-region), which is involved in the storage phase by suppressing the bladder contraction and improving external sphincter muscle activity during this phase.[5] The development of functional imaging such as single photon emission tomography (SPET), positron emission tomography (PET) and functional MRI has shown several sovraspinal-sovrapontine (cortical) areas involved in the micturition reflex.[6]

Three different sets of peripheral neuronal systems are involved in the micturition reflex: the parasympathetic system, the sympathetic system and the somatic system. The parasympathetic system originates in the sacral level of the spinal cord (S2–S4) and provides an excitatory input to the bladder by the postganglionic nerve terminal release of acetylcholine (Ach), which excites muscarinic receptors (M2, M3) in the detrusor smooth muscle leading to the bladder contraction. The sympathetic system originates in the thoracolumbar cord (T11–L2) and provides an inhibitory input to the bladder by the postganglionic nerve terminal release of norepinephrine (NA) which excites β3 receptors in the body of the detrusor leading to the bladder relaxation. The sympathetic system also provides an excitatory input to the urethra smooth muscle by the postganglionic nerve terminal release of NA, which excites α1 receptors in the urethra leading to the urethral closure. The somatic system provides an excitatory input to the urethral striated muscle; in this case the motor neurons are located along the lateral border of the ventral horn of the

[5] Barrington, 'The Effect of Lesions'; Blok, Willemsen, and Holstege, 'A PET Study'.

[6] Fukuyama et al., 'Neural Control of Micturition; Nour et al., 'Cerebral Activation'; Athwal et al., 'Brain Responses to Changes'.

sacral spinal cord, which is known as Onuf's nucleus. They release Ach, which acts on nicotinic receptors to induce muscle contraction. Immunohistochemical and morphological studies which have been conducted on the bladder wall showed a lot of neuronal terminal endings that do not correspond to cholinergic and adrenergic innervations.[7] These nerves, which are non-adrenergic non-cholinergic, are peptide-containing fibres and they are selectively sensitive to capsaicin. They are primary afferents and may play an important role in the regulation of lower urinary tract functions.[8] These nerves consist of small myelinated Aδ and unmyelinated C fibres, which are, however, 'silent' under normal conditions.

Current therapies for overactive bladder

Anticholinergics

Anticholinergics, which antagonise Ach for the muscarinic receptors, are the first line pharmacological treatment for an OAB. The indication for the treatment of OAB derives from a high level of evidence (Level 1) and high grade of recommendation (Grade 1).[9] Anticholinergics produce significant symptom improvements in OAB syndromes when they are compared to a placebo, and the number of anticholinergic drugs available on the market is increasing. However, the debate about the pathophysiological rationale and the clinical use of antimuscarinic agents remains an unsolved issue. Herbison reported a systematic review of anticholinergic drug treatment compared to a placebo therapy in the treatment of an OAB, as a result from randomised controlled trials.[10] He found that patients receiving active treatment were more likely to subjectively improve and they had a lower number of leakage episodes every 48 hours than those taking a placebo.

Urodynamic assessment showed larger increases in maximum cystometric capacity in those receiving active treatment and a greater volume at first contraction in the group under drug treatment, compared to the placebo group. Dry mouth was the most frequently reported side effect. Herbison concluded that although statistically significant, the differences between anticholinergic drugs and a placebo were small, apart from the increased rate of dry mouth in patients receiving active treatment.

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[7] Holzer, 'Local Effector Functions'.
[8] Maggi and Meli, 'The Sensory-Efferent Function'.
[9] Abrams, Cardozo, and Wein, '3rd International Consultation'.
[10] Herbison et al., 'Effectiveness of Anticholinergic Drugs'.

For many of the outcomes studied, the observed difference between anticholinergics and a placebo may be of questionable clinical relevance. After the publication of this paper, many urologists felt that Herbison had inappropriately removed this class of drugs and that the author had a preconceived notion about anticholinergics. Chapple et al. carried out a systematic review and a meta-analysis on the effects of antimuscarinics in the ●AB therapy.[11] His review was supposed to assess the safety, tolerability and efficacy of antimuscarinics in the ●AB therapy, considering the effects on quality of life (●oL), differences between different antimuscarinics and, finally, addressing criticism of Herbison's review. Chapple's review is different from Herbison's study in several aspects. A systematic analysis of ●oL data was performed along with a differentiation between individual antimuscarinics, following a 'splitting' approach and not a 'cumulative' one. Chapple et al. reported that antimuscarinic formulations, apart from ●xybutynin (immediate release), were actually well tolerated with a negligible risk of death. Dry mouth was again the most commonly reported adverse effect, even though other adverse reactions were noticed (such as blurred vision, constipation, dyspepsia, nausea, vomiting, and urinary retention). Antimuscarinics were able to reduce frequency and urgency episodes to one episode per day, incontinence by half an episode or more per day with a concomitant increase in the volume voided per micturition. Eventually, patients receiving antimuscarinics had greater improvements in ●oL than those on a placebo version. Chapple et al. concluded that there is a quantifiable, objective clinical benefit provided by antimuscarinics for the therapy of ●AB. Most of the studies regarding this topic though, including Chapple's review, have several limitations in terms of outcome assessment measures, trial length, sample size, placebo effect and economic issues. For all these reasons, nowadays there is an ongoing, systematic debate among urologists aimed at establishing the more appropriate and rational use of anticholinergic drugs for the treatment of ●AB, while finding potential alternative therapeutic strategies.

Botulinum toxin

Botulinum toxin (BTX) is a complex protein, produced by the anaerobic bacterium clostridium botulinum. Previously known only as a cause of a serious and often fatal paralysis acquired through ingestion of contaminated food, the neuromuscular blocking effect of the toxin has

[11] Chapple et al., 'The Effects of Antimuscarinic'.

since been discovered to alleviate muscle spasm due to excessive neural activity of central origin as well. Local injections of BTX have been shown as effective in the treatment of strabismus, essential blepharospasm and hemifacial spasm. Further studies indicate that BTX injections can also provide useful symptomatic relief in a variety of other conditions characterised by involuntary spasms of certain muscle groups, notably in focal or segmental dystonia, including spasmodic torticollis, oromandibular dystonia (orofacial dyskinesia, Meige syndrome), and spasmodic dysphonia.

'Botox: penicillin for the twentieth century.' This quote derives directly from Brigitte Schurch, one of the pioneers of the use of BTX in urology, and well explains the influence that BTX has had in treating OAB. This sentence may be even more explicative if one considers the prevalence of the problem. Speaking of OAB, in fact, a prevalence of 11.8% was found in the Epic study, with a slight difference between men and women (10.8% and 12.8% respectively). In addition, 49% of women and 28.7% of men suffering from OAB reported urinary incontinence.[12] These numbers increase when neurological patients are taken into account (spinal cord lesions, Parkinson's disease, multiple sclerosis).

Given the low adherence to antimuscarinics treatment (estimated to be around 21% at 6 months), the advent of BTX has revolutionised OAB treatment. Approved in 2011 by the Food and Drug Administration, the main indication for detrusor BTX injection is the treatment of neurogenic detrusor overactivity in patients who have an inadequate response or intolerance to antimuscarinics. [13] Recently, the range of urological indications for BTX injections has even been increasing, because of its application to patients with painful bladder symptoms and different voiding dysfunctions.

The BTX mechanism of action consists of the inhibition of neuromuscular junctions by blocking acetylcholine release. Its action, though, is not only limited to this aspect. BTX also modulates sensory nerve functions by altering neurotransmitter release and reducing receptor expression in the urothelium. Furthermore, recent studies revealed some anti-inflammatory effect and a global improvement of urothelium function, thus helping to restore bladder functions.[14]

From a technical point of view, BTX injection is a safe procedure, which can be easily performed under local anaesthesia on an outpatient basis. Local complications including haematuria, urinary tract infections and increase of post-void residue, are uncommon and can be easily

[12] Giannantoni et al., 'Real-Life Clinical Practice'.
[13] Veenboer and Bosch, 'Long-Term Adherence'.
[14] Jhang and Kuo, 'Botulinum Toxin A'.

managed. Systemic and severe complications are even more rare. Due to the temporary action of the toxin, its injection must be periodically repeated, every 6–9 months. In terms of effect, BTX leads to an improvement in daily incontinence and catheterisation episodes, increase in maximum cystometric capacity, reflex volume and maximum detrusor pressure. In OAB patients, it improves bladder diary (daily frequency and urgency) and daily incontinence.[15]

Two types of toxins are available:

- Onabotulinumtoxin A (Botox®, Allergan Inc, Irvine, CA)
- Abobotulinumtoxin A (Dysport®, Ipsen bipharmaceuticals, Inc, Basking Ridge, NJ)

Botox has been more frequently used in larger studies because it is the only approved toxin for urological use. Nevertheless, some authors have challenged its superiority in comparative studies, demonstrating similar effects between the two products with longer intervals between injections for Dysport.[16] However, it is important to point out that the exact dose equivalency between Botox and Dysport has never been acknowledged, making the objective comparison of these two toxins difficult. The other open debate is about the dose necessary for the proper management of the neurogenic detrusor overactivity, which ranges in the literature from 50 U to 300 U (guidelines nowadays recommend doses of about 200 U). Given all the previous considerations, BTX appears to be at the present moment the best and more versatile therapeutic option for OAB management, apart from electricity modulation therapy.

Sacral neuromodulation

Impaired bladder and sphincter function can be improved by different treatment modalities. Electrostimulation is one of the therapeutic options that has been used in urology for many years. Sites of stimulation include the anal, vaginal, vesical and tibial districts where transcutaneous or direct application can be performed. The success rate of these stimulation techniques varies to some degree and this may be the reason why most of the stimulation treatment options did not gain wide acceptance. Thanks to the work of Tanagho and Schmidt at the beginning, which was supported by many other urologists in the following years, chronic stimulation of the

[15] Mangera et al., 'An Updated Systematic Review'.
[16] Tanagho and Schmidt, 'Bladder Pacemaker'.

sacral nerves by sacral neuromodulation (SNM) has become one of the most accepted stimulation treatment modalities in functional urology today.

SNM uses mild electrical pulses to activate or inhibit neural reflexes by continuously stimulating the sacral nerves innervating the pelvic floor and lower urinary tract; it is also referred to as the pacemaker of the bladder. SNM was introduced in 1979 by Tanagho and Schmidt at the University of California in San Francisco. From this first experimental use of SNM by surgically implanting an electrode around selected sacral nerves in dogs, InterStim™ [17] therapy was developed by Medtronic Inc. (Minneapolis, USA) for human use. It first received CE marking in Europe in 1994 and obtained FDA approval for the first urological indication in October 1997. Since then, InterStim therapy has continuously evolved in terms of knowledge of its mode of action as well as in technical and surgical aspects. Although its mechanism of action is still not completely understood, investigational studies suggest its action is not just on efferent electrostimulation of sacral nerves, but also in somatosensory bladder afferences projecting into the pontine micturition centre in the brainstem.[18]

In the field of lower urinary tract dysfunctions, no other treatment has experienced such a wide diffusion in the last few years as the SNM. Major hardware developments, evidence from literature, FDA approval and increased knowledge on the physiological mechanisms of action, all played a major role in the growth of the therapy's acceptance.

Many studies have described the advantages of having a trial test stimulation, often described as peripheral nerve evaluation (PNE), before the permanent implant. This would help in improving the accuracy of patient selection, based on the positive response to the acute and subchronic phase of the test. Some patients, though, have been shown to gain excellent benefits from definitive therapy despite an initial unsuccessful test. Given this last consideration, different alternative methods to test stimulation and thus changing in the methodology of patient selection started to develop.

One-stage vs. two-stage implantation

To assess SNM effectiveness and allow good patient selection, an acute stimulation trail followed by a subchronic stimulation period is usually performed (two-stage implantation). Under local anaesthesia, an

[17] Tanagho and Schmidt, 'Electrical Stimulation'.
[18] Blok et al., 'Different Brain Effects'.

insulated thin wire is placed into the S3 foramen. The temporary unipolar lead is then connected to an external neurostimulator and fixed to the skin surface. If the chronic stimulation, which can last up to two weeks, shows good response, the patient will be then submitted to permanent implantation.

In case the acute intraoperative test shows at least 50% symptom improvement, it is possible to proceed with the removal of the temporary lead and the insertion of a quadripolar permanent lead with consequent implantable neurostimulator (INS) placement (1-stage implantation). There are some patients who have a sustained chronic clinical benefit from SNM despite an initial unsuccessful acute trial. An explanation for these potential false negatives is that the temporary electrode is often prone to migration during the acute/chronic test phase.

The probability of displacement is even higher if one considers the unipolar structure of the temporary lead compared to the quadripolar permanent lead. In addition, the trial duration is limited to 2 weeks, as a longer test duration increases the probability of bacterial infection. Moreover, other significant restrictions, such as no showering, suggest the short-term testing. Similarly, up to 33% of patients who have a positive trial do not report a successful outcome after INS definitive implantation (false positives).

Considering these data, a better patient selection aimed at reducing false negative and false positive responders is of paramount importance to improve SNM outcome. This could be achieved by finding predictive factors and/or by improving the classical testing technique.

To minimise technical-related failures and increase test efficacy, several further technological modifications were made, finally leading to the development of the currently practised InterStim therapy. The most significant change was the shift from PNE (1-stage implant) to a 2-stage procedure. The first stage refers to the implanting of a permanent lead for testing the response to SNM.

In the second stage, patients who are responsive after testing have the INS implanted. The latter only consists of a minor surgical intervention.

Development of the tined lead

At first, the permanent lead placement was secured by fascial fixation with the patient under general anaesthesia. A refined fixation method with twist locks or silicone anchors allowed a smaller incision under conscious sedation as a less invasive approach.

To further improve the technical features of the lead, a self-anchoring tined lead was designed, which received CE marking and FDA approval in

2002. The tined lead comprises four sets of silicone tines proximal to the electrodes as an integral part of the lead body, with each tine element consisting of four flexible, pliant tines. **(Figure 7-1)**

Figure 7-6 The tined lead.

The system engages subcutaneous tissue, particularly muscle tissue, to decrease axial movement of the lead and consequent dislodgment of the stimulating electrodes.

The particularity of the tined lead is that the 2-stage implant can be conducted in a fully percutaneous and simplified way.

Furthermore, this technique does not preclude other treatment options and, in contrast to surgical interventions, it can be easily reversed.

Thus, it offers the advantage of a truly minimally invasive approach for SNM, performed under local anaesthesia even as day surgery. Besides fluoroscopy and motor responses (bellows contractions of the perineum, plantar flexion of the great toe), the patient's conscious sensory responses (vaginal, perineal or rectal) may help in reaching a more accurate placement of the permanent tined lead. A positive outcome during screening with the tined lead was reported in 77–90% of cases. SNM with the tined lead resulted in permanent implant of the INS in significantly

more urinary urge incontinent patients than with PNE (88% vs. 46%, p=0.02).

The minimally invasive operative procedure to test and apply InterStim therapy with the tined lead is performed with an insertion kit consisting of a foramen needle, a directional guide wire, a dilator with a concentric plastic sheath and the tined lead.[19] The patient is placed in the prone position with a 45° flexion of the hips and knee joints. By using local anaesthesia and intravenous conscious sedation, the foramen needle is inserted in the S3 foramina.

After ensuring correct sensory and motor responses, the inner stylet of the needle is removed and replaced with the directional guide. The foramen needle is then replaced by the dilator and introducer sheath, and thereafter the directional guide and dilator are removed, leaving the introducer sheath in position. Finally, the tined lead is inserted until the proximal electrode enters the foramen. **(Figure 7-2)**

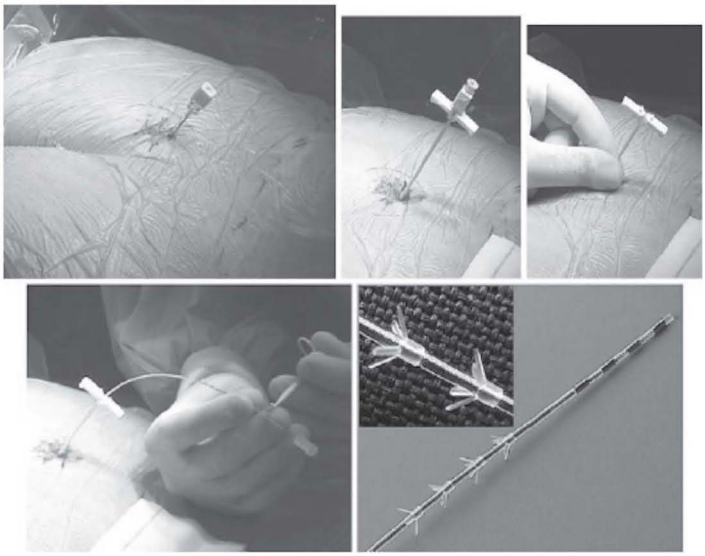

Figure 7-7 The minimally invasive operative procedure to test and apply InterStim therapy with the tined lead

[19] Spinelli et al., 'New Sacral Neuromodulation Lead'; Spinelli et al., 'New Percutaneous Technique'.

To verify the lead's position both fluoroscopy and an electrical signal to evoke motor and sensory responses is applied. With the lead held in place, the introducer sheath is retracted.

The tined lead is tunnelled subcutaneously to the future implant pocket of the INS. Through a small incision, an extension cable is subcutaneously introduced to connect the tined lead to the external pulse generator, which is located on the contralateral side. This transposition with long tunnelling is chosen to prevent infection. In the second stage, the INS is implanted into the upper gluteal region in a subadipose pocket.

It is also recommended that sacral x-rays are performed at the end of each stage of the procedure, and whenever there is a decrease in symptomatic response. Buttock placement of the INS has become an alternative to subcutaneous implant in the lower part of the anterior abdominal wall because of the lower incidence of adverse events, shorter (approximately half) operation time and avoidance of patient repositioning during the operation.

In a prospective European multicentre study in 94 patients with different types of voiding dysfunction, screening with the tined lead was performed for about 30 days. This was successful in 72 patients (76.6%) and in 70 patients (74%) if defined as ≥ 50% improvement in symptoms compared to baseline after 6 weeks; these 70 patients received the INS. After 6 months, follow-up data were available for 20 patients with UUI and 21 patients with UR. Patients with UUI had a significant reduction in the number of daily voids ($p < 0.001$), incontinent episodes ($p < 0.005$) and replaced pads ($p = 0.0069$). Patients with UR experienced improvements in the number of self-catheterisations ($p < 0.001$), voids per day ($p < 0.001$) and in the catheterisation volume ($p < 0.001$).[20]

A small but longer-term study with the tined lead showed that 31 of 39 patients with OAB or UR (79%) showed a good outcome; 90% of these 31 patients had >50% improvement in at least one of the relevant voiding diary variables after a mean follow-up of 15.5 months. In the 21 patients with UUI or urgency-frequency, the mean number of voids and incontinence episodes per day decreased; the difference was probably not significant due to the small sample size. The mean voided volume significantly increased by about 44%.

Several technical aspects of SNM were markedly improved by the InterStim therapy. This led to the development of the InterStim II system, which has been designed to eliminate the need for extension cables and it

[20] Spinelli and Sievert, 'Technologic and Surgical Developments'.

is also almost 50% lighter and smaller in volume compared to the initial INS model.[21]

Electrical modulation of the pudendal nerve

As the pudendal nerve (S2–S4) is one of the major nerves stimulating the pelvic floor muscles, external urethral, anal sphincters and pelvic organs, it is being increasingly investigated as a treatment option, particularly in patients with neurogenic OAB.

The pudendal nerve contains both somatic and autonomic fibres. It leaves the pelvis via the infrapiriform foramen, it extends dorsally in an arc around the ischial spine, and enters the ischiorectal fossa through the lesser sciatic foramen. Before leaving the Alcock's canal (pudendal canal), it eventually divides into two terminal branches: the perineal nerves and the inferior rectal nerves.

These nerves supply motor and sensory innervation to the striated muscles (bulbocavernosus muscle and external anal sphincter) and partly to the urethra and the dorsal nerve of the penis or clitoris. The caudal portion of the pudendal nerve runs through the pudendal canal, which lies against the sidewall of the pelvis and duplicates the fascia of the obturator internus muscle.

The anatomy, physiology and neurophysiology of the pudendal nerve have been studied extensively, particularly once its role in continence mechanisms had been better elucidated.[22] One of the first works investigating the clinical significance of pudendal nerve anatomy was produced by Juenemann et al.[23] The authors demonstrated that in patients with neurogenic lower urinary tract dysfunction, electrostimulation of the sacral root and pudendal nerve markedly increased intra-urethral closure pressures.

Nowadays, there is extensive knowledge regarding the pudendal nerve anatomy and the role of its innervation.

Due to the Alcock's canal anatomy, the once technically difficult surgical exposure of the nerve is presently facilitated by recent developments in the implant procedure and equipment – chronic pudendal nerve stimulation (PNS). The anatomy of the pudendal nerve with its terminal branches was carefully described in 28 cadavers by Schraffordt et

[21] Spinelli and Sievert, 'Technologic and Surgical Developments'.
[22] Fall and Lindstrom, 'Electrical Stimulation'; Hollabaugh et al., 'Neuroanatomy of the Pelvis'.
[23] Juenemann et al., 'Sacral and Pudendal Nerve'.

al. in 2004.[24] Today, chronic PNS can easily be performed using the InterStim device. The treatment is minimally invasive, as it relies on a percutaneous approach to reach Alcock's canal. A permanent tined lead can be implanted in the first implant stage to evaluate the clinical efficacy and to avoid any undesired loss of efficacy after INS definitive implantation. The tined lead, which was originally developed for sacral nerve stimulation to create a more secure lead position, has also contributed to making the PNS a safe option for surgeons and patients.[25] Neurophysiological monitoring ensures lead correct placement, testing at the same time the effectiveness of stimulation. It is done by assessing the electromyographic activity (EMG) of the external anal sphincter. A cadaver study, published by Reitz in 2007, provides evidence for safe needle placement via the posterior approach, the one used by the author.[26]

Surgical technique: lead implant

The patient is placed in the prone position. Bony topography is drawn with the use of a fluoroscopy x-ray device in order to spot the greater trochanter and the ischial tuberosity. **(Figure 7.3)** These two reference marks are used to find the two points as schematic images show below **(Figures 7-4)**. The fluoroscopy system should be ready to perform anterior and posterior images of the pelvis. Then the ischial tuberosity tip and the greater trochanter are located with a pair of 90° angle crossed stylets placed on the patient's skin, the intersection of the lines representing the entry point for the lead. It is recommended to avoid veins and arteries along the trajectory and possible injections of anaesthesia directly into the vascular system.

[24] Schrafford et al., 'Anatomy of the Pudendal Nerve'.
[25] Spinelli et al., 'New Minimally Invasive Procedure'.
[26] Reitz et al., 'Topographic Anatomy'.

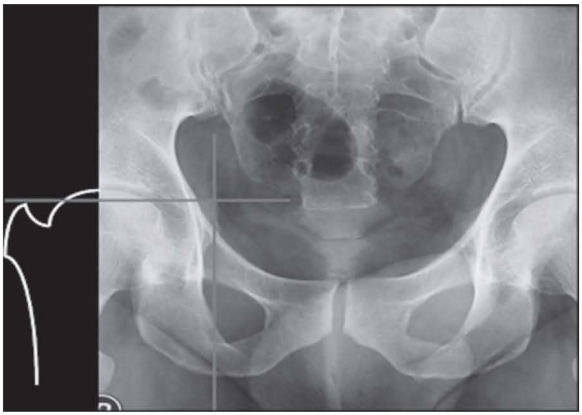

Figure 7-8 X-ray showing lead insertion position.

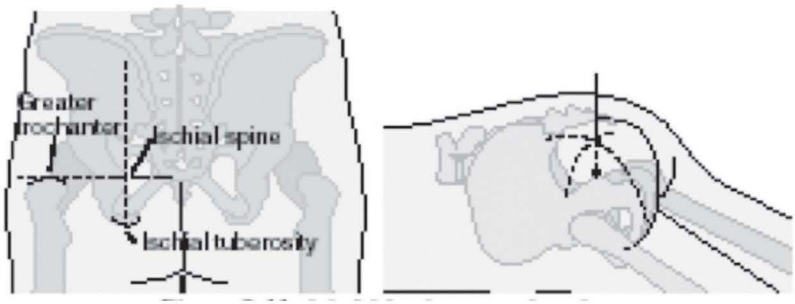

Figure 7-9 Diagrammatic view of lead puncture insertion site

Muscle relaxants should be avoided, while local anaesthetics include lidocaine (maximum dose is 500 mg for healthy patients) and bupivacaine (maximum dose of 200 mg). Their dosage should be kept at the lowest in order to preserve the nerve response. After establishing the lead optimal position with the aid of acute electrophysiological testing, the patient is placed in the prone position and the lower quadrant, perineum, gluteus and sacrum are prepared for surgery. Drape to allow observation of the pelvic floor for muscle response to test stimulation. Clean and dry the skin area and affix the ground pad to it. An electromyography recording needle is gently inserted in the anal sphincter, and the patient stimulation cable is connected to the electromyography output. Vertically insert the insulated

foramen test needle. Connect the mini-hook from the patient cable to the non-insulated part of the foramen needle and stimulate. **(Figure 7-5)**

Figure 7-10 Acute test with test needle.

Increasing pulses of current in 1 mA steps are used to locate the tip of the needle adjacent to the pudendal nerve by comparing the generated compound muscle action potential (CMAP) with the reference trace. An acceptable CMAP should be comprised within 2 ms if compared to the reference trace.

Once the best the needle position has been achieved, the needle stylet should be replaced with the directional guide. Make a small incision on either side of the directional guide. Fit the dilator and introducer sheath over the directional guide and advance to the third most proximal depth marker on the directional guide with the top of the dilator **(Figure 7-6)**.

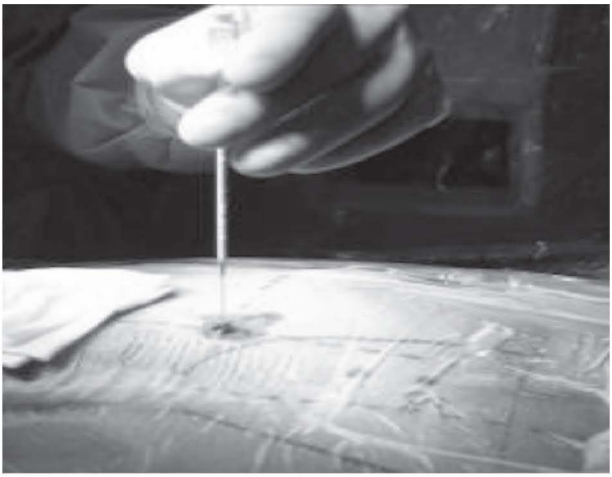

Figure 7-11 Tined lead insertion.

While holding the lead in place, retract the introducer sheath until the second visual marker lines up with the top of the introducer sheath handle. A 1 mA step increasing pulse current from 0 is used to locate the tip of the needle adjacent to the pudendal nerve by comparing the generated CMAP with the reference trace. Stimulate the various electrodes and observe the generated CMAP. **(Figure 7-7)** Hold the sheath and lead together when adjusting the lead position. When satisfied with the lead position, hold the lead in place and carefully withdraw the introducer sheath and the lead stylet. Ensure the lead is in the correct position before deploying the tines. Do not dislodge the lead as tines are deployed. Stimulate the four electrodes to confirm the CMAP previously observed.

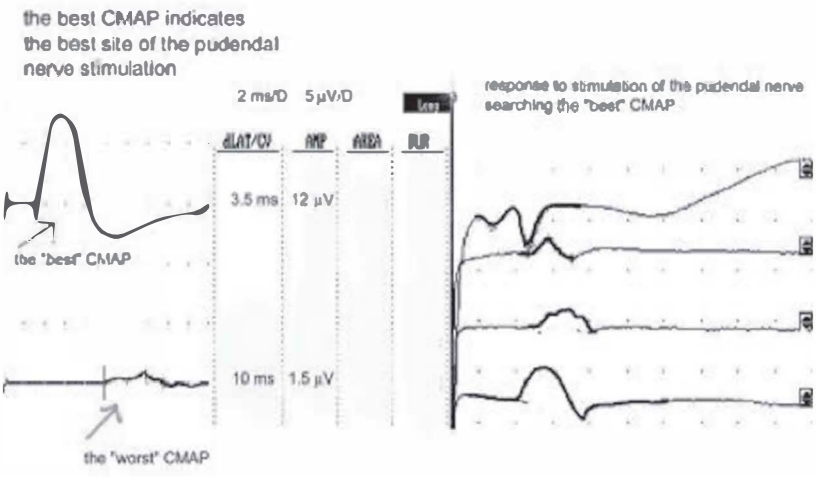

Figure 7-12 CMAP aids to locate best tined lead position.

If you need to advance the lead after tines are deployed do so after the lead stylet is inserted. If you need to retract do so completely, using gentle traction and place it again.

For tunnelisation from the pocket site to the incision site and lead connection to the test stimulator, first identify the site for the neurostimulator subcutaneous pocket. Make a small opening large enough for the percutaneous extension-lead connector at the future neurostimulator pocket site. Either abdomen or buttocks are suitable sites. Make a tunnel from the pocket site to the incision site. Lead tunnelling should not be too deep. Gently feed the lead through the tube, remove the tube and keep the lead in place, close the lead implant incision and dress the wound appropriately. Make a small incision contralateral to the neurostimulator pocket site where the percutaneous extension will exit the skin, tunnel at the subcutaneous level from the pocket to the stab wound. Connect the lead and the percutaneous extension, position the lead and extension in order to avoid sharp bends or kinks. Insert the lead into the percutaneous extension screw set connector. The connection to the test stimulator is now available for test stimulation. Tunnel the lead to the future neurostimulator pocket site. Close the initial incision and staple the wound leaving only the fine percutaneous extension wires, and pin the connector protruding from the skin.

Parameter settings: suggested parameter settings in the test stimulator are: bipolar stimulation between the best stimulating electrodes, frequency

of 5 Hz, pulse width 210 ms, continuous mode, amplitude as low as possible (1 to 5 V below patient's sensitivity). It is not suggested to seek patient sensory responses.

Conclusions

The discovery of electricity brought to enormous changes to human civilisation, but true medical advantages happened in the eighteenth century when the first relationship was made between electricity and the nerves. Since then, knowledge of muscle stimulation, discovery of the connection between electricity and magnetism, the creation of the first electric generator and later electric oscillators, stimulators and amplifiers for neuropsychological studies in the early twentieth century led the way to modern electrical stimulation and its use in the urology field. In 1963, two noteworthy papers were published. Caldwell et al. used electrical stimulation to control sphincter incompetence by using the first pelvic floor stimulator. The device was designed for the treatment of faecal incontinence, but he also successfully treated urinary incontinence.

The milestone in the use of sacral nerve stimulation in humans has been the adoption of the implantable Brindley system, able to restore bladder voiding in complete spinal injury with a direct intradural or extradural stimulation of S2, S3 and S4 bilateral.

According to Brindley's lessons, physicians involved in this field learnt what is possible with a direct stimulation of sacral area in terms of efferent responses.

Based on their findings that bladder contractions can be achieved separately from sphincteric activity, it was possible to work on and develop a true bladder pacemaker. Thanks to their work it was possible to treat neurogenic bladder dysfunction and take a true step forward in functional urology.

Nowadays, SNM is one of the most important tools for the urologist interested in functional pathologies. Despite good evidence from literature and the great evolution in the surgical technique, however, SNM applications still encounter difficulties in treating bladder symptoms due to spinal injuries, or neurodegenerative or auto-immune disease, such as multiple sclerosis.

CHAPTER 7

THE REHABILITATION OF THE SPASTIC PATIENT

M. ALI JAMOUS , SHIVA JAMWAL, EVA SOBONOVA

Introduction

Spasticity or spasm originates from the Greek word *spasmos* that means convulsion. It denotes a sudden abnormal involuntary muscular contraction that could be either tonic (continuous) or clonic (alternating contraction and relaxation). 'Pure spasticity' could be defined as the early involuntary muscular overactivity, taking place during the fast passive movement manifested as a 'catch', while the elasticity of soft tissues is preserved and the passive movement is fully completed.

Types

Spasms could be the result of various neurological disorders that differ depending on the underlying neurological disorder.

1. Spasticity following a stroke

When spasticity is present following a stroke, the abnormal movements of the limbs are due to synergistic movements. They are characterised as primitive movements that dominate reflex and voluntary effort. Their presence interferes with coordinated voluntary movements such as eating, dressing and walking.

2. Spastic dystonia

In contrast to what has been termed pure spasticity, when muscles at rest are overactive without any triggering factor, parts of the body assume

abnormal postures, which are a major cause of disfigurement and social handicap. As a result, changes in muscle composition occur, so the muscle becomes shortened and the range of motion is limited. Muscles may reach a state of permanent contraction, or joints may become completely immobile.

3. Spasticity due to upper motor neuron lesions

In this type, the spasms could be due to brain or spinal injuries. Spasticity of spinal origin can be simply defined as a 'simplified reflex arc that is maintained in the hyperactive state in response to a painful stimulus by the lack of the cortico-spinal inhibition.'

Incidence

The literature indicates that the percentage of patients suffering from spasms differs according to their underlying pathologies; spinal cord injury/disease patients suffer more severe spasticity than multiple sclerosis patients, and cerebral palsy patients suffer a more severe degree of spasms than brain injury patients.

- Multiple sclerosis: 62% (12% severe, 50% mild/moderate).
- Spinal cord injury/disease: 68% (21% severe, 47% mild/moderate).
- Cerebral palsy: 75% (29% severe, 46% mild/moderate).
- Brain injury: 48% (14% severe, 34% mild/moderate).

Underlying causes

The spinal cord damaged patient is vulnerable to many complications that could cause increased spasms. These include, to name but a few, skin complications such as pressure ulcers, ingrowing toenails, anal fissures, stones in the kidneys, bladder or gall bladder, severe constipation or a distended bladder from a blocked urinary catheter as well as skeletal fractures and hip joints dislocation. The clinical signs of spasticity can be different depending on the injury type (sudden or progressive), site and extent of the injury (brain or spinal cord), and whether it is complete or incomplete. In this chapter, we intend to concentrate on the management of spasms of spinal origin. In localised incomplete spinal cord injury, the degree of increased muscular tone is different for various joints, while non-injured antagonist muscles also play an important role for the position of the joint. In this case, the risk of deformation of the joint is higher. In

contrast, when spinal cord injury is diffuse or complete, spasticity is much more homogeneous.[1]

Another significant factor to consider is the chronicity of the injury, spasticity over time can lead to the development of permanent contractions in muscle.[2] Therefore, the type and rate of treatment depend on the presentation (diffuse versus focal) and the degree of disability (mild vs. severe) caused by spasticity.[3]

It has been generally accepted that there are positive aspects to having spasms; some degree of spasms is good for the patient. For patients with complete spinal cord dysfunction, transferring with a degree of increased tone in their lower limbs is much easier than if the tone is flaccid. Spasticity in the legs can provide a stable base and therefore can be helpful for both dressing and transferring.[4] On the other hand, for patients with incomplete neurology, the spastic lower limbs can enable them to stand or even walk with a pair of crutches.

However, the constant contraction of 'spastic' muscles renders opposing muscles inactive, and the latter grow weak due to disuse. Severe and possibly moderate degrees of spasms could cause difficulty in carrying out the activities of daily living (ADL), difficulty in pushing the wheelchairs on rough ground as well as driving cars. In the high-level patients, severe spasticity can cause difficulties in delivering the care for the individual. In addition, spasms can cause pain, abnormal posture, difficulty with movement as well as reduced range of movement and shortening of muscles.

Spasticity usually affects the antigravity muscle groups in the upper and lower limbs.[5] In the upper limbs, shoulder adductors, elbow, wrist and finger flexors, forearm pronators and thumb adductors are commonly the affected muscle groups. In the lower limbs, spasticity often affects the hip adductors, knee flexors, ankle plantar flexors and invertors, and big toe extensors. Spasticity can even affect muscles in the neck.

Management

Elimination of underlying causes is a common-sense first step. However, the difficulty in spinal lesions is that the motor neurons are so excitable that when a muscle is activated, all the muscles of the limb tend

[1] Petropoulou et al., 'Spasticity'.
[2] Petropoulou et al., 'Spasticity'.
[3] Barnes and Johnson, 'Upper Motor Neurone Syndrome'.
[4] Cheung et al., 'Patient-Identified Factors'.
[5] Nair and Marsden, 'The Management of Spasticity'.

to contract together. Although spasticity management is not a linear or hierarchical process (monotherapy or in combination), it has been commonly accepted that as a good practice, the first step of managing spasticity after eliminating any underlying cause is physical therapy. Oral medications, surgical procedures, injecting botulinum toxin into various muscles and intrathecal therapy are all standard forms of treatment for spasticity that are discussed in detail in other chapters.

As members of the multidisciplinary team undertaking the rehabilitation of individuals with spinal cord dysfunction and to enable them to go through their rehabilitation programme and achieve their ultimate functional goals, managing their spasms is an essential part of their daily programme. We therefore aim to discuss in this chapter the physical therapy treatment that we undertake as part of the patients' overall therapy, either to treat their spasms or to manage their spasticity so that it does not hinder achieving their functional goals during their rehabilitation programme.

It is essential to understand the following, before prescribing a management programme for an individual:

- the nature of the spasticity
- the differential diagnosis from other muscle tone disorders
- the cause of spasticity according to the site and degree of the injury
- its changing effects over time
- its changes throughout the day and during the night
- its coexistence with other symptoms such as pain, mood etc.
- changes in its intensity due to external and internal sensory stimuli

As spasticity management is a problem-solving approach, it is essential to identify the purpose of the management and the goals of the treatment, and establish functional gains and improve quality of life as a whole. In many cases, spasticity does not affect function, and likewise, the multidisciplinary team (MDT) may decide it is best not to intervene. It is when spasticity is too high that it interferes with function or poses a threat to safety and wellbeing that consideration is made to undertake a management programme. It is important to highlight that management of spasticity does not necessarily restore lost abilities entirely and has to follow, therefore, a combination of compensatory and restorative approaches.

Contrary to the general belief that upper motor neuron lesions do not result in wasted muscles, atrophy of some of the muscles below the level of injury does occur. Atrophy is more pronounced in muscles that cross a

single joint, which are primarily responsible for maintaining posture and bearing weight.[6] For example the soleus muscle, which is used for control of position, undergoes significant atrophy while the tibialis anterior muscle, which does not contract against resistance, shows very little atrophy. This important fact needs to be taken into account when managing the spastic patient.

Evaluation of spasticity

At the time of evaluation, the influencing factors must be considered that can affect the decision-making process and management. These include understanding the pros and cons of spasticity specific to the patient, the timing of medical interventions, distribution (focal, multifocal, diffused), the age of the patient, prognosis, time since onset and other medical conditions. Evaluation is carried out by the MDT as each discipline has a significant role to play.

1. MDT assessment

It is essential to take note of the clinical presentation of the patient – postural changes and seating balance, gait, transfers, any abnormal or involuntary movements, muscle bulk, skin integrity, continence and pain. Besides physical presentation, it is also essential to observe the patient's mood, level of alertness and fatigue.

2. Physical examination

This is then followed by a physical examination in supine lying or in a sitting position. The physical evaluation includes neuromuscular assessment involving the range of motion (ROM), strength, posture, skin integrity, coordination, balance, transfers, sensation, cranial nerve testing, functional mobility, gait and reflexes. Standardised assessment tools like the modified Ashworth scale and the Tardieu scale are the most validated scales used to record and measure the level of spasticity.[7] Task-specific assessment tools for upper-limb function most commonly cited for this population are the Action Research Arm Test (ARAT), and the Wolf Motor Function Test (WMFT). Walking function assessed by gait speed is

[6] Popovic-Maneski et al., 'Assessment of Spasticity'.

[7] Pandyan et al., 'Properties and Limitations'; Haugh, Pandyan, and Johnson, 'A Systematic Review'.

proposed as the most meaningful objective assessment of active lower limb function for patients undergoing spasticity treatment.

3. Patient's self-reported assessment

The patient's own version and record of experience is paramount as this can give a clearer picture of the overall effect of spasticity on the patient's ability and day-to-day functions. Research suggests that clinical examination results do not always correspond to the person's self-report of spasticity and with their reported functions.[8]

The Patient Reported Impact of Spasticity Measure (PRISM), the Goal Attainment Scale (GAS), the Canadian Occupational Performance Measure (COPM), the Arm Activity Measure (ArmA), Functional independence measure/Functional assessment measure (FIM/FAM), the Barthel Index, and the Disability Assessment Scale (DAS) are valuable self-report tools. The COPM is a client-centred outcome tool that measures a patient's self-perception of their most meaningful everyday tasks.[9]

The PRISM is a self-report evaluation tool created to measure both positive and negative effects of spasticity in patients with SCI.[10] In addition, there is significant literature to support the usefulness of GAS goals for the decision-making process and person-centred outcome measure in rehabilitation and has been widely practised by MDTs; GAS goals are a measure of recording the achievement of an individual's personalised goals in the course of the intervention. Furthermore, Ashford et al. define the Arm activity measure as:

> The ArmA is a measure of difficulty in passive and active function for application following focal therapy intervention and in particular for spasticity interventions, both physical and with botulinum toxin injection. It is a relatively new measure that has a set of questionnaires to record changes in active and passive functions of the upper limbs following spasticity management intervention.[11]

[8] Lechner, Frotzler, and Eser, 'Self- and Clinically Rated Spasticity'.
[9] Reeves and Lambeth, 'Physical and Occupational Therapy'.
[10] Cook et al., 'Development and Validation (PRISM)'.
[11] Ashford, Alexandrescu, and Siegert, 'The Arm Activity Measure'.

4. Functional assessment

Spasticity cannot be an isolated dysfunction. It has direct and indirect effects that need to be recorded over time in a functional-based assessment to fully appreciate its impact on the overall functional abilities of the patient. The Barthel Index and FIM/FAM are outcome measures that measure global disability and function. Evaluated items are self-care and activities that require physical effort including dressing, bathing, feeding, gait and stair mobility. On the other hand, the Spinal Cord Injury Independence Measure (SCIM) is a validated tool for the spinal cord injury population. The DAS is a four-item self-report/observation tool that primarily addresses upper extremity functional difficulties and the patient's rate of perceived difficulty in the areas of hand hygiene, including washing hands, cutting nails and dressing, which includes putting on gloves, limb position and pain.[12] Whereas walking speed correlates with most kinematic measures of gait in spastic paresis and can be quantified in a number of ways, the 10m walk test is validated in populations of individuals with spasticity and therefore, is a clinically useful tool.[13]

Management techniques

Current interventions and modalities to treat spasticity lack a robust evidence base, and guidelines and techniques often depend on expert recommendations.[14] The following techniques or interventions are widely used in rehabilitation applied in combination with other therapies for maximum therapeutic benefit.

A) Physical Therapies

1) Manual Therapy for Realignment of soft tissues

Manually base therapies are generally beneficial and widely practised as their related side effects are fewer even though the evidence behind their effectiveness is limited. The programme can be jointly carried out by physiotherapists, occupational therapists, nurses, healthcare assistants and

[12] Fujimura et al., 'Disability Assessment Scale'; Brashear et al., 'Reliability of the Ashworth Scale'.
[13] Pozo-Cruz et al., 'Whole-Body Vibration Training'.
[14] Nair and Marsden, 'The Management of Spasticity'.

family members as a team for the treatment programmed to be consistent and effective.[15] Stretching the muscle to maintain optimal length is a universally practised technique, but available evidence on its clinical benefit is overall inconclusive.[16] The Cochrane review on this type of management also concluded that there is no clinically significant short-term effect of stretch on pain, spasticity, activity limitation, participation restriction or quality of life.[17] In her review of the interventions used in spinal cord injury, Lisa Harvey concluded that there are only four physical therapy interventions that have initial evidence of their effectiveness, but they all are still widely followed with some benefits. More robust research is required to place a strong evidence base for other interventions.[18] However, in our opinion, the therapist can reduce spasticity at the non-neural level by influencing the muscle length and the joint's range of movement.

2) Muscle strengthening

Muscle weakness and fatigue are among the negative effect of spasticity. In a study by a Cheung et al, significant percentage of patients perceived muscle fatigue as a causative factor for increased spasticity.[19] Muscle weakness results in reduced functional ability. Research now states that the strengthening of the spastic muscles does not increase muscle tone but has beneficial effect on the strength of spastic muscles and hence strengthening interventions are widely used.[20] Such training is best performed within the context of functional skills with repetitive practice, following the principles of progressive resistance training.

3) Normal movement patterns

Spasticity can cause selected muscles to contract continuously thereby causing muscle stiffness and interfering in their normal movement pattern. Active participation in normal movement patterns in a repetitive, task-

[15] D'Amico et al., 'Neuronal and Network Excitability'.
[16] Bovend'Eerdt et al., 'The Effects of Stretching'
[17] Harvey et al., 'Stretch for the Treatment'.
[18] Harvey, Glinsky, and Bowden, 'Commonly Administered Physiotherapy Interventions'.
[19] Cheung et al., 'Patient-Identified Factors'.
[20] Aparecida Silva Borges et al., 'Effect of Resisted Exercise'.

oriented exercise programme can lead to maximal efficiency of the muscles which can positively influence tone and spasticity.[21]

4) Functional re-education and activity-based training

The current neurorehabilitation approach is rooted in the fact that activity is beneficial to individuals with central nervous system injury and therefore focus is on the improvement of functional performance in goal-oriented functional tasks with repetitive practice.

Changes in cortical representations are linked with task-specific skill training consistent with learning dependent models of neural plasticity.[22] Activity-based training attempts to restore function using standardised therapeutic activities based on principles of experimental psychology, exercise physiology and neuroscience. Robotic therapy directed at the hemiplegic arm, and treadmill training techniques aimed at improving gait in persons with stroke and spinal cord injury are some of the best-developed activity-based therapies.[23] The core of the therapy intervention is the training for functional tasks that are meaningful to the individual to gain maximal independence. Evidence that task-specific or functional training is not only well established but gives a practical and meaningful translation of skills learnt via rehabilitation to life skills. Here, the individuals are taught to manage the effects of spasticity and continue to focus on their abilities as opposed to disabilities. This means learning wheelchair transfers and mobility skills, bed mobility, gait training and participation in activities of daily living (ADL) as well as instrumental activities of daily living (IADL). Functional training in ADL influences the quality of life tremendously, especially when spasticity is considered to be associated with worse health status.

B) Splinting

According to the Association of Chartered Physiotherapists Interested in Neurology (ACPIN) guidelines, splinting is defined as a term used to describe the process of applying a prolonged stretch through the application of a range of devices.[24] Splinting can provide extended stretch

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[21] Meadows, Raine, and Lynch-Ellerington, *Bobath Concept.*
[22] French et al., 'A Systematic Review'; Hubbard et al., 'Task-specific Training'.
[23] Dromerick, Lum, and Hidler, 'Activity-Based Therapies'.
[24] Lannin and Ada, 'Neurorehabilitation Splinting'; Basaran et al., 'Hand Splinting for Poststroke Spasticity'.

to the muscle-tendon unit (MTU) which may influence the stretch reflex, but in practice, this intervention is useful only if delivered as a part of a patient-centred and goal-oriented rehabilitation programme. Splinting can help to improve participation in functional activities or increase the ease of care by maintaining or improving the range of movement (passive function), but this does not mean that the splints reduce spasticity in the long term, especially after they are taken off. It should be kept in mind that spasticity from different upper motor neuron lesions might be of varying nature due to the cause and location of the lesion, and hence the observed responses to prolonged stretching might be different for different pathologies.[25]

C) Positioning and Posture Management

Spasticity may also result in abnormal trunk posture resulting in asymmetry of posture and in some cases the inability to sit, which may lead to restricted mobility and even social isolation. Also, such difficulties can lead to the development of pressure sores, which may further increase the severity of spasticity and spasms. In these circumstances, spasticity is best managed by maintaining the length of vulnerable tissues. Therefore, appropriate seating and positioning is paramount to maintain joint integrity, appropriate soft tissue length, prevent further contractures and enhance an individual's engagement in the day-to-day functions. As emphasised by Barnes and Johnson in their book, positioning is an essential intervention to address spasticity early on. Early intervention can bring a long-term effect and can limit contractures and consequent deformities.[26] Posture management is a 24-hour approach with input from all disciplines but most importantly from the carers and family members. The aim of posture management in upper motor neuron lesions is to manage an individual's posture and to position the subject in such a way that it maintains an optimal length of vulnerable tissues and reduces spasticity. The seating system is set up not only to support the individual in a position that inhibits or decreases the spasticity but also make sure that the materials or parts of the chair do not cause pain that may trigger the spasticity. MDT members should consider the future progression of spasticity in the individual and likewise plan changes to the seating systems too. In some cases, seating systems are set up so they allow

[25] Tsao and Mirbagheri, 'Upper Limb Impairments'.
[26] Barnes and Johnson, *Upper Motor Neurone Syndrome*.

spasms to occur, but on relaxation, the posture returns to the desired position.[27]

D) Standing

Supported standing and a weight-bearing therapy have potential benefits in managing spasticity in the early and late stage of rehabilitation following spinal cord injury.[28] The remaining sensory pathways may increase the inhibition of the stretch reflex while the subject is in the standing position that result in decreased motor neuron excitability.[29] Standing can be static or dynamic. A static standing uses traditional standing equipment where the position of limbs does not change while dynamic standing can be achieved by using more advanced equipment or standing frames whereby an individual can move around within a safe environment. However, studies have shown that there is no difference in spasticity reduction when using static or dynamic standing.[30] The National Institute of Health and Clinical Excellence (NICE) guidelines in the United Kingdom recommend that standing should be performed at least three times per week between 30 minutes and 1 hour.

E) Hydrotherapy

Hydrotherapy or aqua therapy is an effective therapeutic modality delivered by a hydrotherapist in the water with a temperature from 33.5 to 35.5°C. There is evidence that it is useful in improving strength and joint range of movement, decreasing muscle fatigue and joint pain, enhancing cardiorespiratory function, and reducing spasticity.[31] Kesiktas et al. also found that the intervention for 20-minute sessions three times per week leads to improvement in spasticity. The water environment has broad potential for those with SCI. There are many influencing aspects. The first element is water temperature; water is an efficient conductor, which transfers heat faster than an equivalent volume of air. However, future studies are needed to determine whether it is the water temperature or the exercise in this enviroment of warm temperature that helps reduce spasms.

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[27] Turner-Stokes, 'Goal Attainment Scaling (GAS)'.
[28] Sadeghi et al., 'Static Standing, Dynamic Standing'.
[29] Newman and Barker, 'Effect of Supported Standing'.
[30] Boutilier et al., 'Spasticity Changes in SCI'.
[31] Kesiktas et al., 'The Use of Hydrotherapy'; Ellapen et al., 'The Benefits of Hydrotherapy'.

F) Functional Electrical Stimulation

An evoked action potential in a nerve is crucial for an effector to contract. This action is disturbed when a spinal cord is damaged. By delivering these stimuli with the application of external neuromuscular electrical stimulation, we provide an effective rehabilitation strategy in managing spasticity.[32] From a therapeutic point of view, the three distinct types of electrical stimulation used in activity-based restorative therapy include Neuromuscular Electrical Stimulation (NMES), Functional Electrical Stimulation (FES) and Transcutaneous Electrical Nerve Stimulation (TENS). They provide sensory stimuli to the nervous system and are used in tone and spasticity management. FES alternates the muscle stimulation between the agonist and the antagonist muscles based on the principle that reciprocal inhibition can be a useful treatment of spasticity. The variable responses to electrical stimulation depend on parameters such as amplitude, pulse width and frequency of current. However, literature is inconclusive about what are these optimal parameters. The most used or commonly applied method to deliver electrical stimulation is the commercially available surface stimulators that have four channels and up to twelve channels. Implanted stimulators used for standing and walking are currently only available on a research basis.[33]

The future

It is now acknowledged that an insult to the central nervous system can result not only in spasticity but also in functional spastic movement disorders, which lead to muscle paresis as well as maladaptation of the movement pattern. [34] It is suggested that the reduced inhibitory mechanisms observed in spastic muscles under passive conditions do not further decrease during voluntary contractions, meaning that inhibitory mechanisms in voluntary muscle contractions are at similar levels in a healthy individual as they are in individuals with spasticity.[35] Some of the latest technologies are exploiting these aspects to enhance and improve the quality of movements by facilitating active or active-assisted movements in normal motor patterns.

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[32] Van der Salm et al., 'Comparison of Electric Stimulation Methods'.
[33] Dutta, Kobetic, and Triolo, 'Incomplete Spinal Cord Injury'.
[34] Dietz and Sinkjaer, 'Spastic Movement Disorder'.
[35] Duffell, Brown, and Mirbagheri, 'Effects of Anti-Spastic Medication'.

Robotics

Robotic devices are to assist therapists in performing the types of activities and exercises they believe give their patients the best chance of functional recovery. These devices allow patients to begin therapy sessions quickly after the injury, in a safe environment which means early intervention and more time for repetitive activities which can translate to greater functional outcomes. Not only are they being useful in providing early intervention but they are also proving to be useful in extended rehabilitation in the chronic stages, providing continuation of therapy input. They are easy to use, but unfortunately, 'easy to use' does not necessarily translate into low cost.

In recent years a high number of robotic devices have been developed to improve the quality of movements for both upper limbs and lower limbs.

Some of the robotic devices used are exsoskeletons for gait training, and Hocomas and Tyromotion products for upper and lower limb exercises. NICE guidelines in the UK also acknowledge the benefits of exoskeletons and recommend further research on their physiological benefits. The level of scientific evidence on the benefits of an exoskeleton on spasticity is low and limited to single intervention trials or single case studies, although users have reported some carry over of reduction in spasticity and pain after its regular use.[36]

All exoskeleton technologies can accommodate low to moderate spasticity levels but severe spasticity can damage gait kinematics during training. Currently, there are three systems used as class II medical devices approved for community or clinic use. Another nine systems are in research and trials only. The primary objective of all these exoskeletons is to improve or achieve a near normal walking pattern. However, their comparison is hindered since there are no standardised approaches to the assessment of their efficiency and safety.[37] More studies are needed to provide further information about performance and the physiological benefits of exoskeletons and other robotic devices over the longer term, spasticity being one of them.[38]

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[36] Kolakowsky-Hayner et al., 'Safety and Feasibility'; Kozlowski, Bryce, and Dijkers, 'Time and Effort Required'; Lajeunesse et al., 'Exoskeletons' Design'.
[37] Ekelem and Goldfarb, 'Supplemental Stimulation'.
[38] Cheung et al., 'Patient-Identified Factors'.

Vibration Therapy

There is sufficient evidence for the beneficial use of whole-body vibration in children with cerebral palsy to reduce spasticity in the legs, improve standing and gait function, and to incorporate it as a part of rehabilitation in this population.[39]

The evidence so far is very limited to support or refute its benefit on the adult population with upper motor neuron lesions and future research on its usefulness is needed.[40]

Virtual Reality (VR)

VR-based technologies create a simulated interactive environment with the additional benefit of providing feedback while the movement is performed. They are an emerging technology with a variety of potential benefits for many aspects of rehabilitation. The ability of VR technologies to provide feedback is considered useful in force correction of inaccurate voluntary movements generated due to the effect of spasticity. VR can also facilitate the repetition of movements following a normal motor pattern and can provide a safe yet challenging environment to perform carefully selected activities on the screen which have been evidenced to increase participants' confidence and motivation.[41] The Cochrane review in the field has also supported the use of VR as a beneficial adjunct to rehabilitation therapies.

Lycra Garments

These garments are made to measure with elasticated dynamic materials such as Lycra. They are close fitting garments that include full body suits, vests, sleeves and gloves. A different thickness of material provides dynamic compression and offers more support in a specific area. Lycra garments have been widely used in cerebral palsy to manage spasticity, but according to NICE the evidence available on the benefits of their use is limited, especially in the adult population. Some studies have concluded that the garment can produce continuous stretch to the muscles

[39] Huang, Liao, and Pang, 'Effects of Whole Body Vibration'.
[40] Pozo-Cruz et al., 'Using Whole-Body Vibration Training'; Hylton and Schoos, 'Deep Pressure Sensory Input'.
[41] Hylton and Schoos, 'Deep Pressure Sensory Input'.

for several hours and provide proximal stability, hence can be useful in the management of spasticity in the upper limbs.[42]

The Mollii Suit

The Mollii suit is a garment that is designed to apply low-frequency electrical stimulation to antagonistic muscles, thereby reducing the tone of a spastic muscle. The garment produces a whole-body response to reduce spasticity through a mechanism called reciprocal inhibition. It has been used successfully to reduce spasticity in children with cerebral palsy.[43] It has been used on the adult population in the UK but even though available, research is quite minimal. NICE guidelines in the UK suggest that the Mollii suit could be an effective option for conditions that cause spasticity in adults, but evidence collected so far is very limited and more research is needed in the future.

Summary

Spasticity manifesting itself in spasms, pain and contractures is a debilitating secondary complication of SCI. Identification of potential mechanisms and their significance to the pathophysiology of spasticity is critical for the design of rehabilitation programmes. The pathogenesis of spasticity resulting from SCI is multifactorial and extends beyond the stretch reflex. It also depends on the type, site and duration of injury. The alteration in excitability of various inhibitory pathways has historically been studied the most, with less focus until recently on the alterations in excitability of motoneurons and interneurons themselves. This latter alteration appears to play critical roles in the manifestation of spasticity after SCI and could become the target of new pharmacological and clinical treatments. The new electrical stimulation interventions suggested by computer simulations for suppressing motoneuronal excitability seem promising, but more careful studies are needed in the future to establish their benefits.

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[42] Knox, 'Use of Lycra Garments'; Gracies et al., 'Lycra Garments'; Nicholson et al., 'Assessment of Upper-Limb Function'.

[43] Ellapen et al., 'The Benefits of Hydrotherapy'; Torabi et al., 'The Mollii-Suit®'.

CHAPTER 8

SURGICAL TREATMENT OF PRESSURE ULCERS IN PATIENTS WITH SPINAL INJURIES

RAFFAELE ATTOLINI

Introduction

This is a possible cause of complication and discomfort for any spastic patient and sometimes it may be worsened by an exceedingly effective treatment for spasticity causing generalised hypotonia.

The annual incidence of pressure ulcers has been reported at between 23% and 37%. According to Model Spinal Cord Injury Care Systems in the United States, 33% of people with spinal cord injury develop at least one pressure ulcer during initial hospitalisation. The prevalence of pressure ulcers in those with spinal cord injury was 8% after 1 year, increasing to 9% after 2 years and 32% at 20 years post spinal cord injury.[1] In community-dwelling individuals with SCI, 25% of pressure ulcers are classified as severe stage III or IV.[2]

Which pressure ulcer to operate on?

The pressure ulcers of NPUAP stages III and IV do not respond to optimal care according to the guidelines.[3] The preoperative approach with the patient should consist of information about the available surgical procedures, expected benefits and potential risk. A correct post-operative course is essential to promote healing and avoid recurrence. The most effective and least traumatic method should be used to treat pressure ulcers

[1] Houghton, Campbell, and CPG Panel, *Canadian Best Practice Guidelines*.
[2] Fuhrer et al., 'Pressure Ulcers'.
[3] Agency for Healthcare Research Quality, 'Clinical Practice Guidelines Archive'.

to reduce the risk of recurrence, and the choice of surgical technique must be based on the needs and the general goals of the individual patient.

Patient selection

- Need and adaptability to surgical treatment
- Tolerance to post-operative posture
- Improvement of the quality of life
- Evaluation of the risk of relapse

Evaluation of the patient

a) ulcer assessment
- pressure ulcer scale for healing (PUSH tool 3.0 – NPUAP)
- topographic survey
- photographic image

b) blood tests (delay of cell regeneration if blood tests are markedly alterated)
- haemoglobin
- platelet count
- creatinine
- blood glucose
- prothrombin time (INR), partial thromboplastin time (aPTT)
- albuminemia
- lymphocytes

c) infectious evaluation
- CRP
- ferritin, fibrinogen
- blood count
- protein electrophoresis
- culture tests (ulcer culture, blood culture, urine culture, strep test)

d) radio-diagnostic evaluation (for diagnosis of osteitis)[4]
- conventional radiography
- contrast-enhanced CT scan and contrast-enhanced NMR (in the study of patients with osteitis, these two investigations resulted in a sensitivity of 98% in the most reliable methods)
- fistulography

[4] Stalcup, Pathria, and Hughes, 'Musculoskeletal Infections of the Extremities'.

- bone scintigraphy or with marked leukocytes (a highly sensitive examination in the study of infection; its limitation is given as the lack of discriminating an infectious process of soft tissues from one of the bone).[5]

e) neurological evaluation

- neurological classification of spinal cord injury (ASIA)
- spasticity spinal cord injury scale (Ashworth scale)

f) nutritional evaluation

- blood tests (albumin, blood count, transferrin, serum iron)
- nutritional indexes (PNI: Prognostic Nutritional Index and Septic Risk Index; BMI: Body Mass Index)

Preoperative treatment

- enzymatic and/or surgical debridement
- antithrombotic prophylaxis
- antibiotic therapy on antibiogram (ulcer culture)
- empirical antibiotic therapy for ostectomy
- nutrition therapies (nutritional supplements and/or integrated parenteral nutrition)
- therapy of spasticity
- bladder catheterisation
- anal plug

Intraoperative treatment

- ulcer culture
- bone culture after ostectomy
- histological examination of the ulcer (for diagnosis of neoplasia)
- histological examination of the bone (for diagnosis of osteitis)

[5] Oyen et al., 'Diagnosis of Bone'

Surgical treatment

a) Pressure ulcer curettage (Figure 9-1)

Figure 9-13 Sacral pressure ulcer before (left panel) and after curettage (right panel).

b) Partial ostectomy (Figure 9-2)

Figure 9-14 Ischial pressure ulcer: partial osteoctomy of ischial bone.

c) Surgical technique

- suture
- skin grafting
- cutaneous flaps
- fasciocutaneous flaps
- muscle-cutaneous flaps
- free flaps

Surgical technique

a) Direct closure (Figure 9-3)

Although suture is the simplest method of repair, this type of approach creates a skin tension that frequently leads to wound dehiscence; therefore suture is rarely used except for small and superficial pressure ulcers.[6]

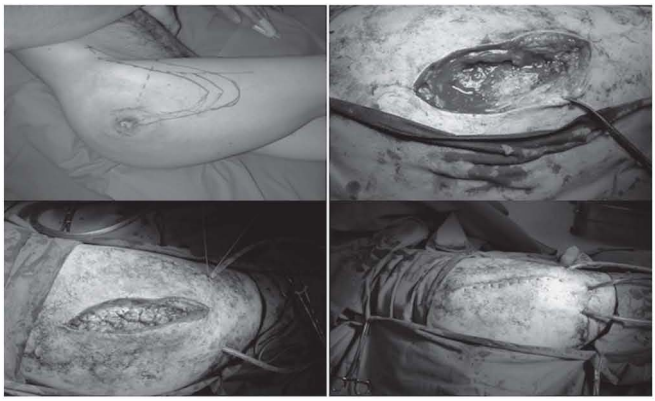


Figure 9-15 Trochanteric pressure ulcer curettage (upper panels) and direct closure (lower panels).

b) Skin grafting (Figure 9-4)

The skin grafts are the second easiest method of repair and are used for the treatment of shallow pressure ulcers; however, skin grafts only provide a skin barrier. When applied to the bone, skin grafts are quickly eroded, precluding healing.[7]

[6] Anthony, Huntsman, and Mathes, 'Changing Trends'; Lewis, 'Tensor Fasciae Latae'.

[7] Sundell, Pentti, and Langensiöld, 'Surgical Treatment'.

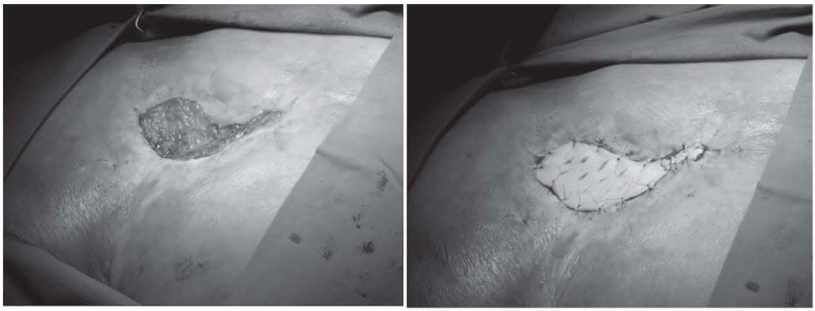
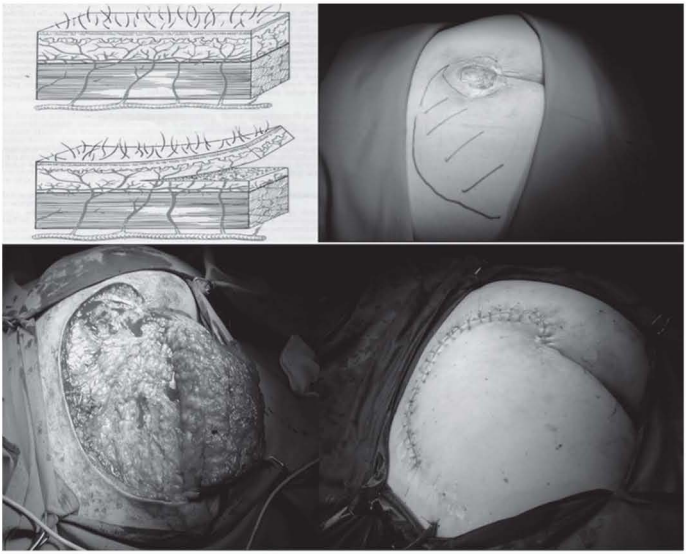


Figure 9-16 Sacral pressure ulcer before (left panel) and after skin grafting (right panel).

c) Cutaneous flaps (Figure 9-5)

Before 1970 the repair of pressure ulcers with skin flaps constituted the surgical treatment of choice; today they are used as an alternative to second-choice repair. [8] The skin flaps receive an occasional vascular supply, and blood vessels may not flow into the lesion area.



[8] Sanchez, Eamegdool, and Conway, 'Surgical Treatment of Decubitus Ulcers'.

Figure 9-17 Sacral pressure ulcer (upper panels) and cutaneous flap (lower panels)

d) Fasciocutaneous flaps (Figure 9-6)

Beam-cutaneous flaps are normally used in pressure sores where muscle loss does not occur. They are formed by skin, subcutaneous and aponeurotic fascia. **The beam-cutaneous flaps have a well-defined vascular supply placed on the aponeurosis.**

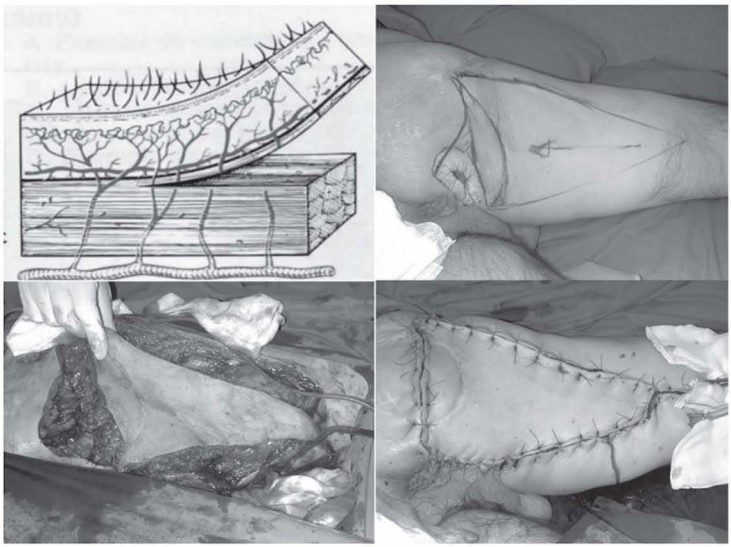


Figure 9-18 Ischial pressure ulcer (left upper panel) and fasciocutaneous flap.

e) Myocutaneous flaps (Figure 9-7)

Myocutaneous flaps are normally the first choice of surgical treatment if muscle loss does not favour the onset of concomitant pathologies.[9] Myocutaneous flaps can limit damage caused by stretching forces, friction and pressure.[10]

[9] Koshima et al., 'The Gluteal Perforator-Based Flap'; Kroll and Rosenfield, 'Perforator-Based Flaps'; Vyas, Binns, and Wilson, 'Thoracolumbar-Sacral Flaps'.
[10] Daniel and Kerrigan, 'Skin Flaps'; Mathes, Feng, and Hunt, 'Coverage of the Infected Wound'; Vasconez, Schneider, and Jurkiewicz, 'Pressure Sores'.

Figure 9-19 Myocutaneous flaps for a trochanteric pressure ulcer.

f) Free flaps

Free flaps are muscle flaps in which the vein and the artery are disconnected from the donor site and reconnected to the blood vessels of the recipient site. This is the most complex method and has not been described in the literature dedicated to the treatment of pressure ulcers (Agency for Health Care Policy and Research – AHCPR).

Surgical treatment for ulcer localisation

Before advising the patient about a surgical technique, the clinician should also consider the site of the lesion (AHCPR)

a) Sacral ulcer

- Limberg skin flap. **(Figure 9-8)**

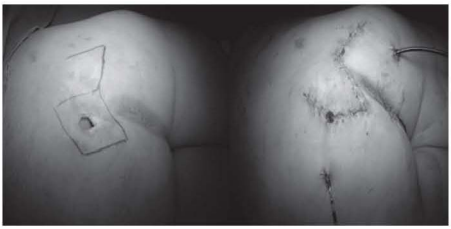


Figure 9-20 Limber skin flap

- Griffith skin flap
- Gluteus fasciocutaneous flap to V–Y
- Gluteus maximus myocutaneous flap to V–Y **(Figure 9-9)**
- Gluteus maximus island myo-ocutaneous flap

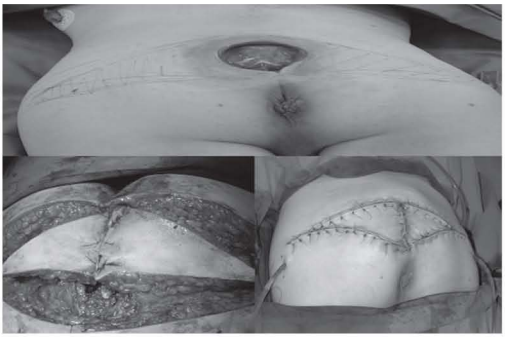


Figure 9-21 Double gluteus maximus myocutaneous flap to V–Y.

b) Ischial ulcer

- Fasciocutaneous posterior thigh flap
- biceps myocutaneousc flap **(Fig 9-10)**
- gluteus maximus island myo-cutaneous flap

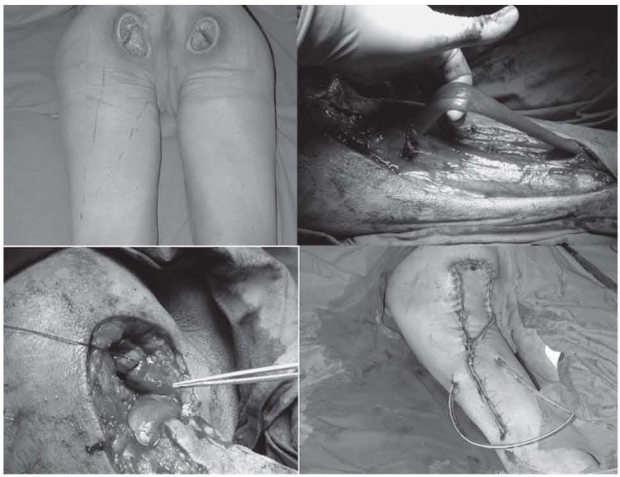


Figure 9-22 Biceps myocutaneous flap for ischial pressure ulcer.

c) Trochanteric ulcer

- Incision + suture
- Myocutaneousc flap of the fascia lata
- Myocutaneousc flap lap of vast lateral **(Figure 9-11)**

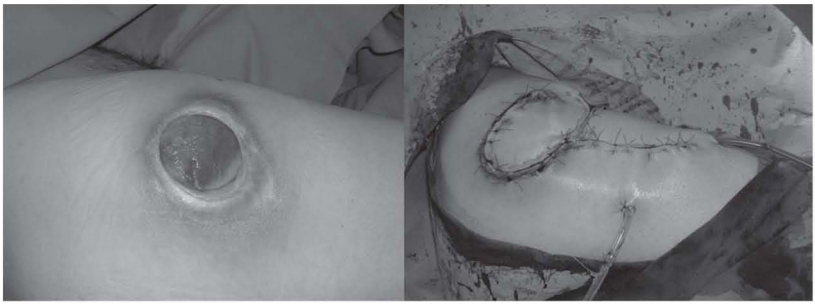


Figure 9-23Myocutaneous flap of vast later for trochanteric pressure ulcer

d) Heel ulcer

- Medial plantar fasciocutaneous flap

Complications

a) Soft tissue infection

- necrotising cellulites
- necrotising fasciitis

b) Bone infections (osteitis)

Acute osteitis therapy

- abscess cavity drainage
- removal of necrotic tissues
- antibiotic therapy (until CRP normalisation)
- possible application of negative pressure therapy

Chronic osteitis therapy

- sequestrectomy and/or partial ostectomy of the infected bone
- removal of necrotic tissues
- antibiotic therapy (until CRP normalisation)
- possible application of negative pressure therapy
- fasciocutaneous or myocutaneous flaps

Table 11 Classification of osteitis localisations

PRESSURE ULCER	OSTEITIS LOCALISATION
sacral	sacral osteitis coccyx osteitis
ischial	ischial osteitis superior femur osteomyelitis + coxofemoral septic arthritis
trochanteric	large trochanter osteitis superior femur osteomyelitis + coxofemoral septic arthritis
inguinal	superior femur osteomyelitis + coxofemoral septic arthritis
leg	tibia and fibula osteomyelitis
heel	heel osteitis
foot	metatarsal osteitis phalanxes osteitis

Table 12 Classification of surgical treatment for pressure ulcer and osteitis localisation

PRESSURE ULCER OSTEITIS	SURGICAL TREATMENT
sacral ulcer + sacral osteitis	a) sequestrectomy + gluteus fasciocutaneous flap to V Y b) sacral partial ostectomy + gluteus fasciocutaneous flap to V Y
sacral ulcer + coccyx osteitis	coccyx ostectomy + gluteus fasciocutaneous flap to V Y
ischial ulcer + ischial osteitis	a) ischial partial ostectomy + fasciocutaneous posterior thigh flap b) ischial partial ostectomy + biceps myocutaneous flap
ischial ulcer + superior femur osteomyelitis	superior femur ostectomy + synovectomy + biceps myocutaneous flap
trochanteric ulcer + superior femur osteomyelitis	superior femur ostectomy + synovectomy + myocutaneous flap of the fascia lata
trochanteric ulcer + large trochanter osteitis	a) trochanteric partial ostectomy + incision + suture b) trochanteric partial ostectomy + myocutaneousc flap of the fascia lata
inguinal ulcer + superior femur osteomyelitis	superior femur ostectomy + synovectomy + sartorius muscle flap + myocutaneousc flap of the fascia lata
leg ulcer + leg osteitis	sequestrectomy+leg fasciocutaneous

heel ulcer + heel osteitis	heel partial ostectomy + medial plantar fasciocutaneous flap
PRESSURE ULCER OSTEITIS	**SURGICAL TREATMENT**
foot ulcer + metatarsal osteitis	metatarsal partial ostectomy
foot ulcer + phalanxes osteitis	Phalanxes partial ostectomy

c) Neoplastic degeneration

The carcinomatous degeneration (or Marjolin ulcer) of a pressure ulcer (not healed, or held in a large keloid) is a rare event with a latency period ranging between 20 and 30 years. The Marjolin ulcer comes in two forms: a) superficial ulcer, b) exophytic tumour, whose growth occurs outside the ulcer.[11]

Histologically, it is a squamous cell carcinoma that originates from keratocytes or squamous epithelium. The Marjolin ulcer metastasises between 18% and 31%.

The treatment modalities depend on the degree of differentiation and on the presence or absence of metastases:

- well differentiated and absence of metastasis: surgical radical exeresis
- little differentiation and presence of metastases: radical exeresis is impossible and the treatment will be palliative

Surgical excision of tumour < 2 cm should have a resection margin of 3 to 5 mm, while for a tumour of the size > 2 cm it must be at least 6 mm.

Post-operative course

This is based on our experience with over 400 surgical treatments of pressure ulcers in patients with spinal injuries.

GUIDELINES

2000–2005: Consortium for Spinal Cord Medicine (CSCM)

[11] Königová, Matoušková, and Broz, 'Burn Wound Coverage'.

IMMEDIATE POST-OPERATORY

- antithrombotic prophylaxis
- antibiotic therapy on antibiogram
- nutrition therapies (nutritional supplements and/or integrated parenteral nutrition)
- therapy of spasticity
- bladder catheterisation
- anal plug
- drainage assessment
- patient positioning on fluidised bed air

1st day (possible complication: tissue necrosis)

- wound dressing
- blood count + PCR

3rd day (possible complication: anaemia)

- wound dressing
- blood count + CRP
- intestinal re-education

7th day (possible complication: wounded dehiscence with purulent secretion)

- wound dressing
- blood count + CRP
- drainage removal

10th day (possible complication: haematoma)

- wound dressing
- blood count + CRP

14th day (possible complication: seroma)

- wound dressing
- blood count + CRP
- suture stitch removal

15th day

- discontinuation of antibiotic
- upper-limb physiokinesis therapy
- patient positioning on a low air loss mattress

POSTURE IN BED

a) Sacral and trochanteric ulcers

18th DAY	19th DAY	20th DAY
Supine with inclination of 30°	Supine with inclination of 45°	Supine with inclination of 60°

b) Ischial ulcers

21st DAY	24th DAY	27th DAY
Supine with inclination of 30°	Supine with inclination of 45°	Supine with inclination of 60°

c) Ulcers with osteitis

28th DAY	31st DAY	34th DAY
Supine with inclination of 30°	Supine with inclination of 45°	Supine with inclination of 60°

SACRAL AND TROCANTERIC ULCERS

21st day

- postural evaluation of sitting
- choice of anti-decubitus cushion or postural unit
- lower limb physiotherapy
- CRP

25th day

- patient positioning on polyurethane foam mattress

Layout of patient positioning in a wheelchair on an anti-decubitus cushion with sacral and trochanteric ulcers

21st DAY	22nd DAY	23th DAY	24th DAY	25th DAY
1 hour	2 hours	3 hours	4 hours	5 hours

ISCHIAL ULCERS

28th day

- postural evaluation of sitting
- choice of anti-decubitus cushion or postural unit
- lower limb physiotherapy
- CRP

30th day

- patient positioning on polyurethane foam mattress

Layout of patient positioning in a wheelchair on an anti-decubitus cushion with sacral and trocanteric ulcers

28th DAY	29th DAY	30th DAY	33th DAY	35th DAY
1 hour	2 hours	3 hours	4 hours	5 hours

ULCERS WITH OSTEITIS

35th day

- discontinuation of antibiotic (CRP with normal values)
- postural evaluation of sitting
- choice of anti-decubitus cushion or postural unit
- lower limb physiotherapy
- CRP

40th day

- patient positioning on polyurethane foam mattress

Layout of patient positioning in a wheelchair on an anti-decubitus cushion with sacral and trochanteric ulcers

35th DAY	36th DAY	37th DAY	40th DAY	42nd DAY
1 hour	2 hours	3 hours	4 hours	5 hours

CHAPTER 9

THE DARK SIDE OF THE MOON

IVANO DONES

Beyond all the extravaganza that is commonly shown at congresses and in the scientific literature regarding any medical or surgical procedure, there is actually a number of complications, side effects and general problems that sometimes do hamper a good result of any possible treatment of spasticity, and create a wide backstage behind the fireworks. These are commonly neglected but need to be extensively explored to minimise their presence in our common practice.

Undue or inaccurate drug therapy

As previously mentioned, the general careful evaluation of patients affected by spasticity should pertain not only to their spasticity but to their general clinical condition, social environment and expectations. In fact, there are many patients who lose time and faith after long-term antispastic treatments that turned to be useless for their clinical condition and possible motor performance. This is particularly observed in patients undergoing different cocktails of oral antispastic drugs before they are addressed to other useful treatment or to motor rehabilitation only.

CSF leakage in patients with intrathecal drug delivery devices

CSF leakage has been occasionally reported in patients undergoing the implant of a drug delivery intrathecal device. This is almost always due to a longitudinal laceration of the dura at the point the Tuohy needle enters the intradural space. It may happen when having difficulties in finding the right point of entrance of the needle, which is being tilted around to search the right point so its entrance may be assured. The tip of the needle might then scrape the dural surface and lacerate it. Thus, it is always advisable to

insert the needle in one direction and, possibly, repeat the procedure without tilting the needle but creating a new approach to insert the needle the proper way.

Fluid collection around the pump can be occasionally observed due to a seroma as a reaction to the material the pump is made of, and to a collection of CSF leaking from the connection between the pump and the catheter. It could also be due to a perforation of the catheter if a simple silicon non-jacketed catheter is used.

Skin erosions at the subcutaneous pocket with a pump

When dealing with thin patients and patients affected by diabetes mellitus there is the relevant risk of skin erosions located where the pump is implanted due to the sharp edges of the pumps and their size. When a skin erosion occurs in proximity with either the pump or the catheter, there is high risk of infection from the infusion system and frequently this has to be totally removed.

Intrathecal drug administration devices failure

Catheter obstruction

The catheter obstruction can be caused by the deposit of biological debris inside the cateter or at the tip of the catheter. This was a frequent complication before the introduction of jacketed catheters to prevent their obstructive kinking. It has been recently reported by Shao et al. as the result of a pump-related twiddler's syndrome due to the patient's twisting of the pump inside the subcutaneous pocket with related twisting of even a jacketed catheter and its obstruction.

Removal of intrathecal catheters from long-term implants of pumps

In a recent paper by Frizon et al. on 59 patients, complications due to the removal of an intrathecal catheter after long-term treatment with intrathecal baclofen are described as pertaining to the retention of the intrathecal catheter or persistent cerebrospinal leakage after catheter removal. In fact, it is very easy for the intrathecal catheter to become anchored and cannot simply be removed after a long-term permanence in the intradural space. Any major traction to try to remove the catheter can result in a dural laceration with CSF leakage that has to be repaired with

further surgery. In those cases where the catheter appears to be tightly anchored, it is always better to cut the intradural catheter extradurally and close it with a double suture to avoid CSF leakage. The remaining intradural part of the catheter is almost never disturbed during the patient's life as the distal closure of the catheter with a double suture can prevent the intradural portion of catheter from migrating cranially, as occasionally reported in the literature. It will then be possible to insert a new intradural catheter through another way.

Human errors in reprogramming a pump

Despite the really friendly software available on the market to program the different pumps for intrathecal drug administration, there are still reported cases of complications due to a bad programming of the pumps both at implant and at refills. These problems arise with the wrong use of measures during the resetting of drug concentration and daily dosage, and they can easily result in drug overdosage that maybe harmful or fatal. In fact, there is not yet an antagonist of baclofen for clinical use able to restore a condition of overdosage.

Human errors in refilling a pump for intrathecal baclofen

When refilling a pump there are a few things to take care of. The first is the need to perform any refill under sterile conditions. The second is to carefully evaluate the real drug concentration and daily dosage to avoid any dangerous over- or underdosage **(Figure 10-1).**

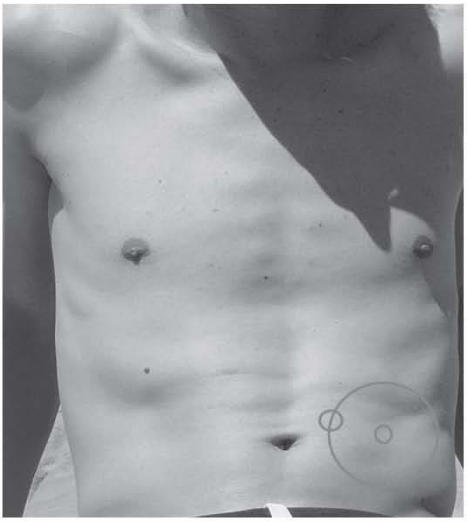


Figure 10-24 Correct site for pump placement and reservoir identification (inner circle) at implant.

Neglecting dystonia

Patients who are affected by different neurological disorders in which spasticity occurs together with other clinical pictures such as dystonia, should be carefully assessed both prior and during any treatment, and possible additional treatments for dystonia should be considered.

Scorning motor rehabilitation

Regardless of any pharmacological or surgical treatment, a spastic patient must be addressed to a continuous and intense programme of motor rehabilitation to optimise the outcome of any treatment.

The real dark side of the moon

There is still a real lack of knowledge and capability to treat muscle weakness associated with spasticity, although many attempts are being made in developing new trends of motor rehabilitation and the use of orthosis in patients who could go back to autonomous movements although their spasticity and lack of muscle strength. Moreover, although spasticity is largely distributed worldwide regardless of the economic

condition of patients, there are still relevant parts of this planet where any of the above-described treatments are not yet available. Poor people have to deal with their spasticity as well, as it used to be in the Middle Ages and this is definitely one of the shames of mankind.

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There are thousands of learned references which have not been mentioned. They have not been scorned or neglected, though. They can all be found by reading the references reported and cited all over the book.

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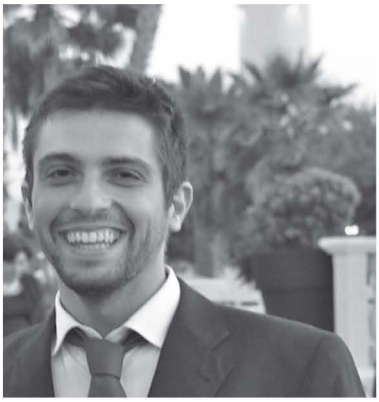

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