SECOND EDITION

Edited by Michael P. Barnes and Garth R. Johnson

Upper Motor Neurone Syndrome and Spasticity

Clinical Management and Neurophysiology

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Preface to the second edition

The first edition of this textbook provided a practical guide and source of references for physicians, surgeons, therapists, orthotists, engineers and other health professionals who are involved in the management of the disabled person with spasticity. The second edition follows the same format. We have updated the chapters and provided new references and described new techniques. We hope we have covered all aspects of management from physiotherapy, seating and positioning and orthoses to the use of drugs, intrathecal techniques and surgery. We have also stressed the importance of adequate measurement techniques and, indeed, Chapter 3 has been completely rewritten by Garth R. Johnson and Arnand D. Pandyan. We hope that clinicians will continue to find this book helpful and a useful source of reference in their own practise and that it will continue to provide a solid base for a greater understanding of the management of spasticity.

1

An overview of the clinical management of spasticity

Michael P. Barnes

Spasticity can cause significant problems with activity and participation in people with a variety of neurological disorders. It can represent a major challenge to the rehabilitation team. However, modern approaches to management, making the best use of new drugs and new techniques, can produce significant benefits for the disabled person. The details of these techniques are outlined in later chapters and each chapter has a thorough reference list. The purpose of this initial chapter is to provide a general overview of spasticity management, and it attempts to put the later chapters into a coherent context.

Definitions of spasticity and the upper motor neurone syndrome

Spasticity has been given a fairly strict and narrow physiologically based definition, which is now widely accepted (Lance, 1980):

> Spasticity is motor disorder characterised by a 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 neurone syndrome.

This definition emphasizes the fact that spasticity is only one of the many different features of the upper motor neurone (UMN) syndrome. The UMN syndrome is a somewhat vague but nevertheless useful concept. Many of the features of the UMN syndrome are actually more responsible for disability, and consequent problems of participation, than the more narrowly defined spasticity itself. The UMN syndrome can occur following any lesion affecting some or all of the descending motor pathways. The clinical features of the UMN syndrome can be divided into two broad groups – negative phenomena and positive phenomena (Table 1.1).

Negative phenomena of the UMN syndrome

The negative features of the UMN syndrome are characterized by a reduction in motor activity. Obviously this can cause weakness, loss of dexterity and easy fatiguability. It is often these features that are actually associated with more disability than the positive features. Regrettably the negative phenomena are also much less easy to alleviate by any rehabilitation strategy.

Positive phenomena of the UMN syndrome

These features can also be disabling but nevertheless are somewhat more amenable to active intervention. At the physiological level there are increased tendon reflexes, often with reflex spread. There is usually a positive Babinski sign and clonus may be elicited. These may be important diagnostic signs for the physician but are of little relevance with regard to the disability. The exception is sometimes the presence of troublesome clonus. This can be triggered during normal walking, such as when stepping off a kerb, or can occasionally occur with no obvious trigger, such as in bed. In these circumstances clonus can sometimes be a significant disability and

Table 1.1. Features of the upper motor neurone syndrome

Negative	Positive
• Muscle weakness	• Increased tendon reflexes with radiation
• Loss of dexterity	• Clonus
• Fatiguability	• Positive Babinski sign
	• Spasticity
	• Extensor spasms
	• Flexor spasms
	• Mass reflex
	• Dyssynergic patterns of cocontraction during movement
	• Associated reactions and other dyssynergic and stereotypical spastic dystonias

occasionally needs treatment in its own right. The other positive features of the UMN syndrome cause more obvious disability.

Spasticity

A characteristic feature of spasticity is that the hypertonia is dependent upon the velocity of the muscle stretch – in other words, greater resistance is felt with faster stretches (this results in the clinical sign of a 'spastic catch'). Thus, spasticity resists muscle stretch and lengthening. This has two significant consequences. First, the muscle has a tendency to remain in a shortened position for prolonged periods, which in turn may result in soft tissue changes and eventually contractures (Goldspink & Williams, 1990). The second consequence is that attempted movements are obviously restricted. If, for example, the individual attempts to extend the elbow by activation of the triceps, this will stretch the biceps, which in turn will induce an increase in resistance and indeed may prevent full extension of the elbow. However, it is worth emphasizing that the situation is usually more complex. In the above example, relief of the spasticity in the biceps may not lead to improvement in the function of the arm, as other features of the UMN syndrome, particularly muscle weakness, may have a part to play.

Soft tissue changes and contractures

Restriction of the range of movement is not always simply due to increase of tone and spasticity in the relevant muscles. The surrounding soft tissues, including tendons, ligaments and the joints themselves, can develop changes resulting in decreased compliance. It is likely that such contractures and changes in the soft tissues arise from the muscle being maintained in a shortened position. It is possible, but not absolutely proven, that maintaining a joint through a full range of movement may prevent the longer-term development of soft tissue contractures. The frequency of the stretch, either actively or passively, that is required to prevent contractures is unknown. However, it is important to emphasize good posture and seating such that the muscles, as far as possible, are maintained at full stretch for at least some of every day. The recommendation is that muscles be put through a full stretch for 2 hours in every 24 hours (Medical Disability Society, 1988). However, more research is needed in this field to determine the degree and frequency of stretch with more certainty.

Thus, hypertonia often has both a neural component (secondary to the spasticity) and a biomechanical component (secondary to the soft tissue changes). Obviously biomechanical hypertonia is not velocity dependent and restricts movements even at slow velocities. Furthermore, biomechanical hypertonia will not respond to antispastic agents; the only treatment possibilities relate to physiotherapy, stretching, good positioning, splinting and casting. Ultimately surgery may be needed to relieve advancing and disabling soft tissue contracture. In practical terms there is often a mixture of neural and biomechanical hypertonia, and it is very difficult clinically to determine the relative contribution of each of the components. Thus, active intervention for spasticity (e.g. by antispastic medication or local treatment such as phenol block or botulinum toxin injection)

is worth undertaking simply to be sure of alleviating at least the neural component of the hypertonia. There is often a gratifying response even in limbs that appear to have fixed contractures.

In advanced spasticity, it is often the soft tissue changes that contribute most to the disability and are resistant to treatment. Increasing deformity of the limbs will clearly lead to rapidly decreasing function and often result in problems with regard to hygiene, positioning, transferring and feeding and make the individual more prone to pressure sores (O'Dwyer *et al.*, 1996).

Flexor and extensor spasms

Severe muscle spasms are often found in UMN syndrome. These can be in either a flexor pattern or an extensor pattern.

The commonest pattern of flexor spasm is flexion of the hip, knee and ankle. The spasms can sometimes occur spontaneously or, more commonly, in response to stimulation, are often mild. Simple movement of the legs or adjusting position in a chair can be enough to induce the spasm. The spasms themselves can be painful and are sometimes so frequent and severe that a permanent state of flexion is produced. If spasms worsen suddenly, it is worth looking for aggravating factors such as pressure sores, bladder infections, irritation from a catheter or even such apparently mild stimulants such as an ill-fitting orthosis or a tight-fitting catheter leg bag. Occasionally constipation or bladder retention can also produce a flexor spasm, which can then be associated with a reflex emptying (mass reflex) of the bowel or bladder.

Similar problems can occur with extensor spasms, which are commonest in the leg and involve extension of the hip and knee with plantar flexion and usually inversion of the ankle. Once again, such spasms can be triggered by a variety of stimuli and sometimes can be so severe as to produce a permanent extensor position. Extensor spasms are probably more common than flexor spasms in incomplete spinal cord lesions and cerebral lesions, but there is no clear association with any particular pathology. Occasionally a spasm can be useful from a functional point of view. Placing pressure on the base of the foot in order to stand can sometimes produce a strong extensor spasm of the leg, effectively turning it into a rigid splint, which, in turn, aids walking. Occasionally individuals can make positive use of self-induced spasms, such as for putting on trousers. This emphasizes the importance of detailed discussion with the disabled person and his or her carer before assuming that the spasm will need treatment. Finally, extensor and flexor spasms can be extremely painful; even if not causing undue functional disturbance, they can need treatment in an attempt to relieve the associated acute pain.

Spastic dystonia and associated reactions

Most of the previously described positive phenomena of the UMN syndrome can occur at rest. Another range of problems can occur on movement. For example, there is the classic hemiplegic posture, commonly occurring in stroke, that often occurs when the individual tries to walk. This posture consists of a flexed, adducted, internally rotated arm with pronated forearm and flexed wrist and fingers. The leg is extended, internally rotated and adducted, and the ankle is plantar flexed and inverted, often with toe flexion. Other patterns occurring on movement are sometimes called spastic dystonias (Denny-Brown, 1966). This is a term that probably ought to be avoided, given the potential confusion with extrapyramidal disease.

Other problems that occur on movement or attempted movement involve co-contraction of the agonist and antagonists. Simultaneous contraction of agonist and antagonist muscles is a normal motor phenomenon and is required for the smooth movement of the limb. However, in the UMN syndrome, agonist and antagonist muscles may co-contract inappropriately and thus disrupt normal smooth limb movement (Fellows *et al.*, 1994). Sometimes involuntarily activation of muscles remote from the muscles involved in a particular task also contract. For example, if the individual attempts to move an arm, then a leg may extend or flex. Conversely the

arm can flex when attempting to walk (Dickstein *et al.*, 1996). These 'associated reactions' (Walshe, 1923) can interfere with walking by unbalancing the individual or, for example, making it impossible to do any task with the arms while standing. Various other patterns of dyssynergic and stereotypical contractions have been described, such as extensor thrust (Dimitrijevic *et al.*, 1981). However, the labelling of these problems is less helpful than a prolonged period of observation and discussion with the disabled person, the family and the person's carers. Simple bedside testing is usually inadequate to determine an overall treatment strategy. The pattern of spasticity and the functional consequences during attempted movement as well as at rest all need careful assessment, often over prolonged periods of time. Reports from a well-educated disabled person who can describe the problems in different circumstances are of far more value than a single examination in the outpatient clinic.

Clinical consequences

The above description of the different patterns of the UMN syndrome make it clear that there is a potentially wide range of functional problems. In order to draw the discussion together, the major consequences can be annotated as follow.

Mobility

Probably the most common consequence of the UMN syndrome is difficulty walking. The gait can be clumsy and uncoordinated, and falling can become a common event. Eventually walking may become impossible owing to a combination of soft tissue contractures, flexor or extensor spasms and unhelpful associated reactions. It is also worth bearing in mind that individuals with UMN syndrome may often have a whole variety of other neurological problems, such as cerebellar ataxia or proprioceptive disturbance, which further compounds the problem. Even if the individual cannot walk, the UMN syndrome can cause further problems with regard to difficulty maintaining a suitable seating posture. Spasticity may make it difficult to self-propel a wheelchair. Extensor spasms may constantly thrust the individual forward while sitting in the chair, giving rise to an increased risk of shear forces that can cause pressure sores. Seating will often require a considerable range of bracing, supports and adjustments in order to allow the person to maintain a useful and comfortable position.

Loss of dexterity

In the arm, the UMN syndrome can cause further difficulties with, for example, feeding, writing, personal care and self-catheterization. Mobility in bed may be hampered and loss of dexterity in the arm may make it difficult to self-ambulate in a wheelchair. All these problems can slowly lead to decreased independence and a consequent increased reliance on a third party.

Bulbar and trunk problems

Although most of the functional consequences of spasticity occur in the arm or leg, it is worth remembering that truncal spasticity can cause problems with seating and maintaining an upright posture – necessary for feeding and communication. Bulbar problems can give rise to difficulty swallowing, with consequent risk of aspiration or pneumonia. Further problems can arise with communication, secondary not only to inappropriate posture but also to spastic forms of dysarthria.

Pain

It is not widely recognized that spasticity and the other forms of UMN syndrome can be extremely painful. This is particularly the case with flexor and extensor spasms, and sometimes treatment is needed simply for analgesia rather than improvement of function. Abnormal postures can also give rise to an increased risk of musculoskeletal problems and osteoarthritic change in the joints. Any peripheral stimuli from problems such as ingrowing

toenails or small pressure sores can, in turn, exacerbate the spasticity, and a vicious circle of increased pain and increased spasticity can ensue.

Carers and nursing problems

Spasticity is one of the unusual conditions that can sometimes require treatment of the disabled person for the sake of the carer. Individuals, particularly with advanced spasticity, can be extremely difficult to move and nurse. Transfers from bed to toilet or bed to wheelchair can be laborious. Hygiene can be a problem with, for example, marked adductor spasticity, causing problems with perineal hygiene and catheter care. Flexion of the fingers can cause particular difficulties with hygiene in the palm of the hand. Thus, aggressive treatment of spasticity can sometimes be a factor in reducing carer stress, which in turn can make the difference between the individual remaining at home or moving into an institution.

An approach to management

The previous section indicated the complexity and functional consequences of spasticity. The following chapters in the book outline the detail of the different approaches to the management, but this section attempts to provide an overview of the process (Fig. 1.1).

Aims of treatment

The first question to ask is whether treatment is needed at all. The previous section has shown that occasionally a spastic pattern can be functionally useful, such as an aid to walking or dressing. Spasticity in the UMN syndrome may be abnormal from a neurophysiological point of view, but this does not mean that treatment is always required. The aims of treatment will always need careful annotation and discussion with the individual. The commoner aims are to improve a specific function, reduce pain, ease the task of caring or prevent long-term problems, such as soft tissue contractures. The specific aims of a particular treatment strategy always need clear explanation. This also implies that there should be an appropriate method of measuring outcome, so that one knows when the aim is fulfilled. Chapter 3 discusses the topic of measurement in spasticity. Outcomes clearly need to be geared to the aim of treatment. For example, if the aim of the treatment is to improve hand function, a simple, reproducible and valid test of hand function will be required. If the outcome is a reduction of pain, perhaps use of a visual analogue scale will be helpful. The use of a global disability or activities of daily living (ADL) scale is usually inappropriate, as subtle treatment effects may be masked.

It is important, particularly in people needing long-term treatment, that the aims and purposes of treatment be reviewed regularly and new goals set or old goals adjusted. This is particularly the case with the use of long-term antispastic medication when the side effects of treatment may at some point outweigh its benefits (see Chapter 7).

Self-management

Education of the disabled person and his or her family is vital, as in all rehabilitation management. Spasticity and the UMN syndrome involve complex phenomena. The individual needs to be aware of some of the factors that may aggravate the problem, such as inappropriate positioning, tight-fitting shoes, or even heavy bedclothes. A detailed appraisal of the pattern of spasticity may enable the individual to relieve many of the functional problems. Both the clinician and the individual should be aware of potential aggravating factors, such as the worsening effect on spasticity of bladder infection or constipation.

The physiotherapist and the orthotist

The early involvement of an experienced physiotherapist is invaluable. There are many potential interventions, ranging from simple passive range-of-motion exercises to more complex antispastic physiotherapy approaches (see Chapters 4 and 5). The physiotherapist can also administer symptomatic

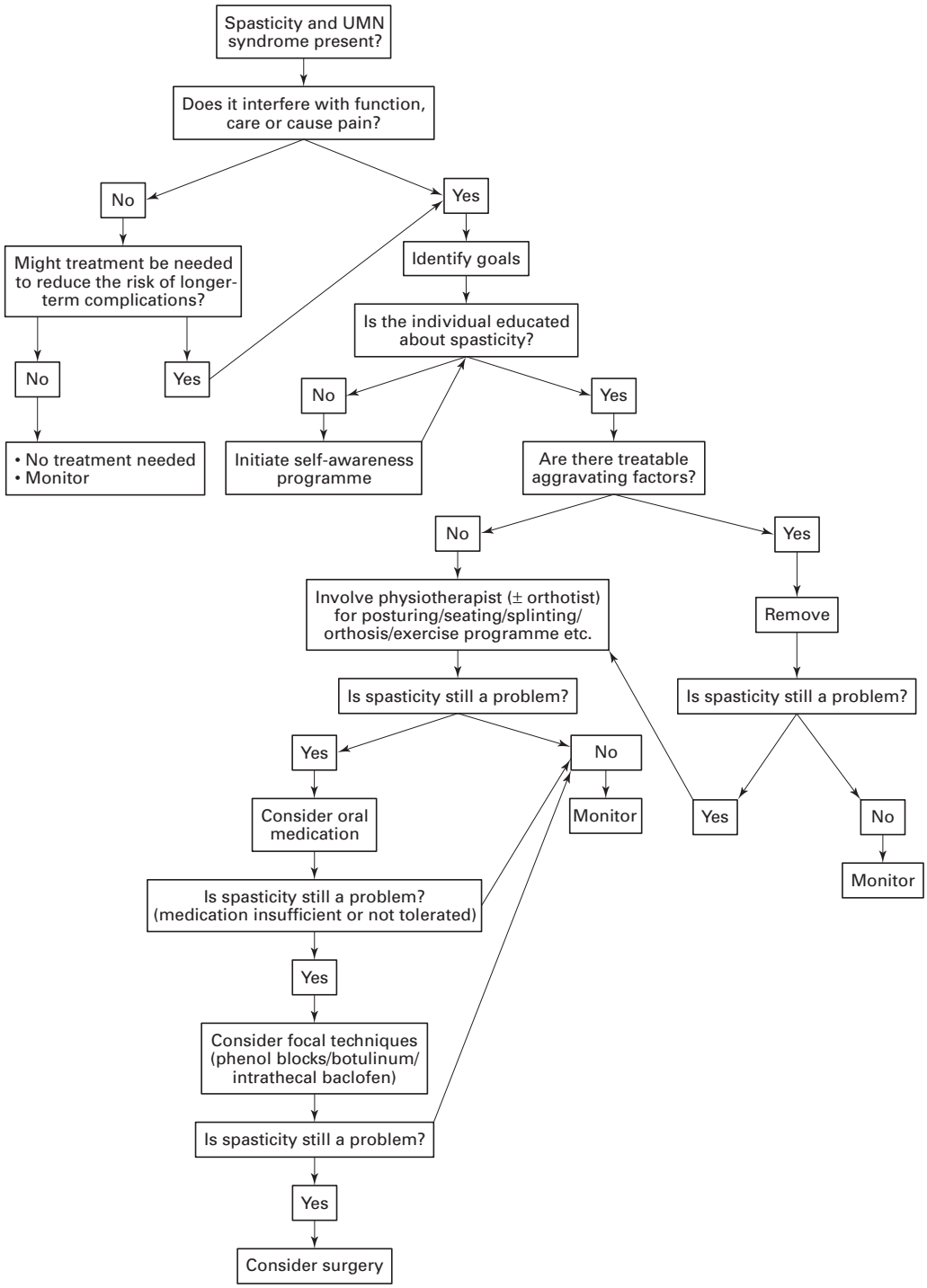

Figure 1.1. Flowchart outlining the approach to the overall management of spasticity.

treatment such as heat and advice on the use of hydrotherapy as well as the prescription of splints and casts. At this point the input of an orthotist is essential, as many situations are helped by the judicious application of a suitable orthotic device (see Chapter 6). Much can be achieved by these noninvasive techniques before resorting to medication or invasive focal treatments.

Oral medication

Chapter 7 outlines the various pharmacological possibilities of antispastic medication. Medication should rarely be used in isolation but usually is just part of a whole treatment strategy. Medication can provide a useful background effect, which makes, for example, the fitting of an orthosis or positioning in a chair easier and more comfortable. Occasionally, particularly in mild spasticity, the use of antispastic medication can be sufficient in isolation to reduce a functional problem, such as troublesome clonus. The problem with medication is that it is often associated with side effects. These particularly focus around increased weakness and fatigueability. Spasticity is often a focal problem, and medication will clearly give a systemic effect. Thus, muscles that are not troublesome can be inappropriately weakened and the overall functional effect can be made worse.

Medication may reduce some of the positive effects of the UMN syndrome but at the same time make some of the negative effects worse. The purposes and goals of medication need to be carefully annotated and the use of medication constantly reviewed.

Focal techniques

The need for intervention in spasticity is often concentrated on one or a few muscle groups. Thus, a focal approach is often more appropriate than the systemic effect induced by oral medication. In recent years increasing value has been placed on focal techniques such as phenol and alcohol nerve blocks (see Chapter 8) and the use of botulinum toxin (see Chapter 9). The latter, in particular, is a remarkably safe and useful technique, but once again it is important to emphasize that it is not often used in isolation but rather as part of an overall treatment package. For example, the use of botulinum can facilitate positioning in physiotherapy or ease the fitting of an orthosis. Fortunately, the effect of botulinum toxin is reversible over a period of 2 to 3 months, which enables reappraisal and reassessment on a regular basis. Phenol nerve blocks are equally efficacious but more difficult to administer, and there is the risk of a permanent effect. However, phenol is very significantly cheaper than botulinum toxin and thus is more relevant and practical in developing countries.

Intrathecal and surgical techniques

Occasionally spasticity is very resistant to intervention and further invasive techniques need to be considered. Intrathecal baclofen (see Chapter 10) is now a well-recognized and relatively safe procedure. In some centres, it is used in preference to other focal techniques, such as botulinum toxin. The technique is generally safe, although it can occasionally be associated with unwanted complications such as pump failure, infection or movement of the catheter tip.

Finally, there is the possibility of surgical intervention (see Chapter 11). There are some surgical techniques, such as rhizotomy, that relieve spasticity in their own right, but surgery is now often reserved for the unwanted complications of spasticity, particularly soft tissue contracture. If soft tissue contracture is advanced and disabling, there is often no option but to resort to surgical release and repositioning of the limb. However, it is probably true that if spasticity is treated appropriately and actively at the outset, it is only the very rare individual who will need surgery.

Overall, we hope that this book gives a practical and straightforward account of the various treatment approaches to spasticity as well as emphasizing the importance of setting clear goals with clear outcome measures. We trust the book makes it clear that spasticity is a highly variable and dynamic phenomenon. Treatment needs careful planning, careful monitoring and above all the input and involvement not only

of the physician, physiotherapist and orthotist but also of the person with the spasticity and his or her carer.

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2

Neurophysiology of spasticity

Geoff Sheean

Introduction

The pathophysiology of spasticity is a complex subject and one frequently avoided by clinicians. Some of the difficulties relate to the definition of spasticity and popular misconceptions regarding the role of the pyramidal tracts. On a more basic level, the lack of a very good animal model has been a problem for physiologists. Nonetheless, a clear concept of the underlying neurophysiology will give the clinician better understanding of their patients' clinical features and provide a valuable basis upon which to make management decisions.

Definition

Some of the difficulty that clinicians experience with understanding the pathophysiology of spasticity is due to the definition of this condition. Most textbooks launch the discussion with a definition offered by Lance (1980) and generally accepted by physiologists:

> Spasticity is a motor disorder characterized by a 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 neurone syndrome.

It may be difficult for clinicians to correlate this definition with a typical patient. They may see instead a patient with multiple sclerosis who has increased muscle tone in the legs, more in the extensors than the flexors, that appears to increase with the speed of the testing movements. They also recall a clasp-knife phenomenon at the knee, tendon hyperreflexia with crossed adductor reflexes, ankle clonus, extensor plantar responses, a tendency for flexor spasms and, on occasion, extensor spasms. Or perhaps they picture the stroke patient with a hemiplegic posture, similar hypertonia in the upper limbs but more in the flexors, a tendency for extension of the whole leg when bearing weight and increasing flexion of the arm as several steps are taken.

Lance's definition has been criticized for being too narrow by describing spasticity only as a form of hypertonia (Young, 1994). However, Lance's definition points out that this form of hypertonia is simply one component of the upper motor neurone (UMN) syndrome (Table 1.1, p. 2). The clinician tends to picture the whole UMN syndrome and regard all the 'positive' features of the syndrome as 'spasticity'. For example, increasing flexor spasms is often recorded as worsening spasticity. Because these positive features do tend to occur together, the clinician often uses the presence of these other signs (tendon hyperreflexia, extensor plantar responses, etc.) to conclude that a patient's hypertonia is spasticity rather than rigidity or dystonia.

However, these positive features do not always occur together, and other factors may contribute to a patient's hypertonia. Furthermore, the pathophysiology of the positive features of the UMN syndrome is not uniform, as explained subsequently, and their response to drug treatment may also be different. Thus, there is merit in treating each of the positive

features of the UMN syndrome as separate but overlapping entities and in particular to restrict the definition of spasticity to a type of hypertonia, as Lance has done.

Chapter overviews

Because this is a chapter on spasticity, the 'negative' features of the UMN syndrome, such as weakness and loss of dexterity, are not discussed. The majority of the 'positive' features of the UMN syndrome are due to exaggerated spinal reflexes. These reflexes are under supraspinal control but are also influenced by other segmental inputs. The spinal mechanisms or circuitry effecting these spinal reflexes may be studied electrophysiologically. This discussion of the neurophysiology of spasticity begins, then, with the descending motor pathways comprising the upper motor neurones, which, when disrupted, produce the UMN syndrome. Following that, the spinal reflexes responsible for the clinical manifestations are explained. This section includes the nonreflex or biomechanical factors that are of clinical importance. The final section deals with the spinal mechanisms that may underlie the exaggerated spinal reflexes.

Descending pathways: upper motor neurones

Spasticity and the other features, positive and negative, of the UMN syndrome (as listed in Table 1.1) arise from disruption of certain descending pathways involved in motor control. These pathways control proprioceptive, cutaneous and nociceptive spinal reflexes, which become hyperactive and account for the majority of the positive features of the UMN syndrome.

Extensive work was done, mostly on animals, in the latter part of the last century and the early years of this century to discover the critical cortical areas and motor tracts. These experiments involved making lesions or electrically stimulating areas of the central nervous system (CNS) and observing the results. Human observations were usually afforded by disease or trauma and occasionally by stimulation. One of the difficulties with the animal studies, especially with cats, was in translating the findings to humans. Monkey and chimpanzee experiments are thought to have greater relevance. The studies chiefly focused on which areas of the CNS, when damaged, would produce motor disturbances and which other areas, when ablated or stimulated, would enhance or ameliorate the signs. Lesion studies, both clinical and experimental, may also be difficult to interpret, given that the lesions may not be confined to the target area; histological confirmation has not always been available.

One early model was the decerebrate cat developed by Sherrington. A lesion between the superior and inferior colliculi resulted in an immediate increase in extensor (antigravity) tone. For several reasons, this model is not especially satisfactory as a model of human spasticity (Pierrot-Deseilligny & Mazieres, 1985; Burke, 1988).

This vast body of work was reviewed by Denny-Brown (1966) and integrated with his findings. It has been excellently summarized more recently by Brown (1994).

Fibres of the pyramidal fibres arise from both precentral (60%) and postcentral (40%) cortical areas. Those controlling motor function within the spinal cord arise from the precentral frontal cortex, the majority from the primary motor cortex (Brodmann area 4, 40%) and premotor cortex (area 6, 20%). Postcentral areas (primary somatosensory cortex, areas 3, 1, 2, and parietal cortex, areas 5 and 7) contribute the remainder but these are more concerned with modulating sensory function (Rothwell, 1994). At a cortical level, isolated lesions in monkeys and apes of the primary motor cortex (area 4) uncommonly produce spasticity. Rather, tone and tendon reflexes are more often reduced. It seems that lesions must also involve the premotor cortex (area 6) to produce spasticity. Such lesions made bilaterally in monkeys are associated with greater spasticity, indicating a bilateral contribution to tone control. Subcortical lesions at points where the motor fibres from both areas of the cortex have converged (e.g. internal capsule) are

more likely to cause spasticity. Even here, though, some slight separation of the primary motor cortex (posterior limb) and premotor cortex (genu) fibres allows for lesions with and without spasticity (Fries *et al.*, 1993).

Although both cortical areas 4 and 6 must be affected to produce spasticity and both contribute to the pyramidal tracts, isolated lesions of the pyramidal tracts in the medullary pyramids (and in the spinal cord) do not produce spasticity. Hence, there are nonpyramidal UMN motor fibres arising in the cortex, chiefly in the premotor cortex (area 6), that travel near the pyramidal fibres which must also be involved for the production of spasticity. It is debatable whether these other motor pathways should be called extra-pyramidal or parapyramidal. Denny-Brown (1966) preferred the former but I favour the latter, as does Burke (1988), to emphasize their close anatomical location to the pyramidal fibres and to avoid confusion with the extrapyramidal fibres from the basal ganglia that produce rigidity. This close association of pyramidal and parapyramidal fibres continues in the spinal cord where lesions confined to the lateral corticospinal tract (pyramidal fibres) produce results similar to those of the primary motor cortex and medullary pyramids, without spasticity. More extensive lesions of the lateral funiculus add spasticity and tendon hyperreflexia.

Given these findings, just what are the consequences of a pure pyramidal lesion? In primates, there is only a loss of digital dexterity (Phillips & Porter, 1977) and, in humans, mild hand and foot weakness, mild tendon hyperreflexia, normal tone and an extensor plantar response (Bucy *et al.*, 1964; van Gijn, 1978). Although there are reports that suggest that spasticity might arise from 'pure' lesions, such as strokes, of the pyramidal tracts (Souza *et al.*, 1988, abstract in English), there is always the concern that these lesions might really have affected adjacent parapyramidal fibres to some degree. Thus, the bulk of the UMN syndrome, both positive and negative features, is not really due to interruption of the pyramidal tracts, save perhaps for the extensor plantar response, but of the parapyramidal fibres (Burke, 1988). Although this implies that the term 'pyramidal' syndrome is a misnomer, it is so ingrained in clinical terminology that to attempt to remove it appears pedantic.

Brainstem areas controlling spinal reflexes

The following discussion is readily agreed to be somewhat simplistic but is conceptually correct. From the brainstem arise two balanced systems for control of spinal reflexes, one inhibitory and the other excitatory (Fig. 2.1). These are anatomically separate and also differ with respect to suprabulbar (cortical) control.

Inhibitory system

The parapyramidal fibres arising from the premotor cortex are cortico-reticular and facilitate an important inhibitory area in the medulla, just dorsal to the pyramids, known as the ventromedial reticular formation (Brown, 1994). Electrical stimulation of this area inhibits the patella reflex of intact cats. In decerebrate cats, the previously rigid legs become flaccid (Magoun & Rhines, 1947) and muscle tone is reduced in cats that have been made spastic with chronic cerebral lesions (cited in Magoun & Rhines, 1947). In the early spastic stage of experimental poliomyelitis in monkeys, the most severe damage was found in this region (Bodian, 1946). Stimulation of this region in intact cats also inhibits the tonic vibration reflex (discussed further on). Flexor reflex afferents are also inhibited (Whitlock, 1990) (see below). That this inhibitory centre is under cortical control was verified by the finding of potentiation of some of these effects by stimulation of the premotor cortex or internal capsule (Andrews *et al.*, 1973a,b). There may also be some cerebellar input (Lindsley *et al.*, 1949). The descending output of this area is the dorsal reticulospinal tract located in the dorsolateral funiculus (Engberg *et al.*, 1968).

Excitatory system

Higher in the brainstem is a diffuse and extensive area that appears to facilitate spinal stretch reflexes.

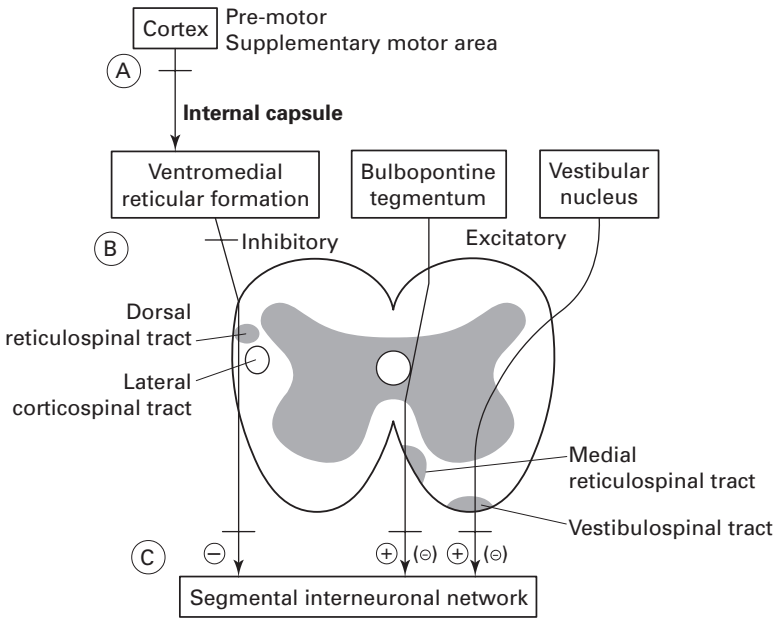

Figure 2.1. A schematic representation of the major descending systems exerting inhibitory and excitatory supraspinal control over spinal reflex activity. The anatomical relations and the differences with respect to cortical control between the two systems mean that anatomical location of the upper motor neurone lesion plays a large role in the determination of the resulting clinical pattern. (A) Lesion affecting the corticospinal fibres and the cortico-reticular fibres facilitating the main inhibitory system, the dorsal reticulospinal tract. (B) An incomplete spinal cord lesion affecting the corticospinal fibres and the dorsal reticulspinal tract. (C) Complete spinal cord lesion affecting the corticospinal fibres, dorsal reticulospinal fibres and the excitatory pathways. (+) indicates an excitatory or facilitatory pathway; (−) an inhibitory pathway. The excitatory pathways have inhibitory effects on flexor reflexes. (From Sheean, 1998a.)

Stimulation studies suggest that its origin is in the sub- and hypothalamus (basal diencephalon), with efferent connections passing through and receiving contributions from the central grey and tegmentum of the midbrain, pontine tegmentum and bulbar (medullary) reticular formation (separate from the inhibitory area above). Stimulation of this area in intact monkeys enhances the patella reflex (Magoun & Rhines, 1947) and increases reflexes and extensor tone and produces clonus in the chronic cerebral spastic cat mentioned above (see 'Inhibitory system' on p. 11) (Magoun & Rhines, 1947). Lesions through the bulbopontine tegmentum alleviate spasticity (Schreiner *et al.*, 1949). Although input is said to come from the somatosensory cortex and possibly the supplementary motor area (SMA) (Whitlock, 1990), stimulation of the motor cortex and internal capsule does not change the facilitatory effects of this region (Andrews *et al.*, 1973a,b). Thus, this excitatory area seems under less cortical control than its inhibitory counterpart. Its descending output is through the medial reticulospinal tracts in the ventromedial cord (Brown, 1994).

The lateral vestibular nucleus is another region facilitating extensor tone, situated in the medulla close to the junction with the pons. Stimulation produces disynaptic excitation of extensor motoneurones (Rothwell, 1994). Its output is via the lateral vestibulospinal tract, located in the ventromedial cord near the medial reticulospinal tract. Although long recognized as important in decerebrate rigidity, it appears less important in spasticity. An isolated

lesion here has little effect on spasticity in cats (Schreiner *et al.*, 1949) but enhances the antispastic effect of bulbopontine tegmentum lesions. Similarly, lesions of the vestibulospinal tracts performed to reduce spasticity had only a transient effect (Bucy, 1938).

Although both areas are considered excitatory and facilitate spinal stretch reflexes, they also inhibit flexor reflex afferents (Liddell *et al.*, 1932; Whitlock, 1990), which mediate flexor spasms (see below). The lateral vestibulospinal tract also inhibits flexor motoneurones (Rothwell, 1994).

Other motor pathways descending from the brainstem

Rubrospinal tract

Despite its undoubted role in normal motor control in the cat, there is some doubt about the importance and even existence of a rubrospinal tract in man (Nathan & Smith, 1955). In cats, this tract is well developed and runs close to the pyramidal fibres in the spinal cord. It facilitates flexor and inhibits extensor motoneurones (Rothwell, 1994) via interneurones. In contrast, in man, very few cells are present in the area of the red nucleus that gives rise to this tract. However, the rubro-olivary connections are better developed in man than in the cat (Rothwell, 1994).

Coerulospinal tract

The clinical benefits of drugs such as clonidine (Nance *et al.*, 1989) and tizanidine (Emre *et al.*, 1994) and of therapeutic stimulation of the locus coeruleus have refocused attention on the noradrenergic coerulospinal system. The locus coeruleus resides in the dorsolateral pontine tegmentum and gives rise to the coerulospinal tract. Coerulospinal fibres terminate in the cervical and lumbar regions and appear to facilitate presynaptic inhibition of flexor reflex afferents (Whitlock, 1990). As tizanidine reduces spasticity as well as flexor spasms, it must also modulate spinal stretch reflexes. However, there is no evidence that the coerulospinal tracts play a role in the production of spasticity or flexor spasms. Degeneration of the locus coeruleus is also seen in Parkinson's disease and Shy-Drager syndrome and neither have spasticity as a sign. Furthermore, the putative mechanism of tizanidine in spasticity is such that would be mimicked by increased coerulospinal activity. However, the coerulospinal tract appears to provide excitatory drive to alpha motoneurones (Fung & Barnes, 1986) and inhibit Renshaw cell recurrent inhibition (Fung *et al.*, 1988), effects, which would be expected to increase stretch reflexes.

Descending motor pathways in the spinal cord

As indicated above, the principal descending motor tracts within the spinal cord in the production of spasticity is the inhibitory dorsal reticulospinal tract (DRT) and the excitatory median reticulospinal tract (MRT) and vestibulospinal tract (VST) (Fig. 2.1). As already discussed, isolated lesions of the lateral corticospinal (pyramidal) tract in monkeys do not produce spasticity but rather hypotonia, hyporeflexia and loss of cutaneous reflexes. Extending the lesion to involve more of the lateral funiculus (and hence the dorsal reticulospinal tract) results in spasticity and tendon hyperreflexia (Brown, 1994). Similar lesions in man of the dorsal half of the lateral funiculus produced similar results (Putnam, 1940). Curiously though, bilateral lesions of the intermediate portion of the lateral column resulted in tendon hyperreflexia, ankle clonus and Babinski signs immediately, but rarely spasticity. Brown (1994) points out, however, that there was no histological confirmation of the extent of these lesions. In the cat, dorsolateral spinal lesions including the DRT produce spasticity and extensor plantar responses (Babinski sign) but not clonus or flexor spasms (Taylor *et al.*, 1997). Furthermore, these positive UMN features appeared rapidly. These results support the idea that the DRT is critical in the production of spasticity in man and also show that lesions in the region can result in restricted forms of the UMN syndrome, especially the dissociation of tendon hyperreflexia and spasticity.

Concerning lesions of the excitatory pathways made in attempt to reduce spasticity, cordotomies

of the anterior portions of the ventral columns to interrupt the vestibulospinal tracts were only transiently successful in reducing spasticity in the legs (Bucy, 1938). These lesions were said to spare the deeper sulcal regions where the medial reticulospinal tract resides. After more extensive cordotomies were performed, which included these tracts, and following a period of flaccidity, spasticity was markedly reduced but tendon hyperreflexia, clonus and adductor spasms persisted. These findings reinforce the more dominant role that the MRT plays and the relatively less important role of the VST and once again illustrates that the positive feature of the UMN syndrome may occur independently. Furthermore, these findings in man tend to support the ideas on the pathophysiology of spasticity developed from animals.

In summary, cortical lesions producing spasticity must involve both the primary motor and premotor cortices. Such lesions affect both pyramidal and parapyramidal cortico-reticular reticular fibres, which run adjacent to each other in the corona radiata and internal capsule. Conceptually, there is a system of balanced control of spinal reflexes that arises within the brainstem. There is an inhibitory area in the medullary reticular formation that largely suppresses spinal reflex activity. This region receives cortical facilitation from the motor cortex (mainly premotor) via cortico-reticular fibres, which comprises the suprabulbar portion of the inhibitory system. The output of this medullary inhibitory centre is the dorsal reticulospinal tract, which runs in the dorsolateral funiculus, adjacent to the lateral corticospinal (pyramidal) tract. Two other areas comprise the excitatory system that facilitates spinal stretch reflexes and extensor tone. The main one arises diffusely throughout the brainstem and descends as the medial reticulospinal tract. The other is the lateral vestibular nucleus, giving rise to the vestibulospinal tract. Both are located in the ventromedial cord, well away from the lateral corticospinal tract and the inhibitory dorsal reticulospinal tracts.

Thus, spasticity arises when the parapyramidal fibres of the inhibitory system are interrupted either of the cortico-reticular fibres above the level of the medulla (cortex, corona radiata, internal capsule) or of the DRT in the spinal cord. Theoretically, isolated lesions of the inhibitory medullary reticular formation could do the same but as Brown (1994) points out, strokes in this area tend to be fatal. It is attractive to presume that spasticity develops in this situation simply due to the effects of the excitatory system, which is now unbalanced by the loss of the inhibitory system but the situation is not so simple (see p. 15, 'Mechanism of the change in excitability of the spinal reflexes').

Clinicopathological correlation

The clinical picture of the UMN syndrome seems to depend less upon the etiology of the lesion and more upon its location in the neuraxis. It has been long recognized that the UMN syndrome following cerebral lesions is somewhat different to that of spinal lesions. Similarly, there are differences between partial or incomplete spinal lesions and complete lesions. With cerebral lesions, spasticity tends to be less severe and more often involve the extensors with a posture of lower limb extension. Flexor spasms are rare and the clasp-knife phenomenon is uncommon. Clonus tends also to be less severe. In contrast, spinal lesions can have very severe spasticity, more often in flexors with a dominant posture of lower limb flexion (paraplegia in flexion); prominent flexor spasms, clasp-knife phenomenon is more common, as is clonus.

The pathophysiological substrate for these differences may reside in three factors. The existence of cortico-reticular drive to the inhibitory brainstem centre, the anatomical separateness of the inhibitory and excitatory tracts in the spinal cord and the fact that both the excitatory and inhibitory systems inhibit flexor reflex afferents, which are responsible for flexor spasms.

A suprabulbar lesion, say, in the internal capsule, would deprive the inhibitory brainstem centre of its cortical facilitation. This inhibitory centre could, however, continue to contribute some inhibition of spinal stretch reflexes and flexor reflex afferents. With a partial reduction in inhibitory drive, the excitatory

system would still dominate, facilitating extensors while also inhibiting flexor reflex afferents. Hence, the whole syndrome would be milder in form and more extensor in type with few flexor spasms.

The chief clinical difference between complete and incomplete spinal cord lesions is that incomplete lesions more often show a dominant extensor tone and posture with more extensor spasms than flexor spasms, as opposed to the complete spinal lesion, which is strongly flexor (Barolat & Maiman, 1987). An incomplete cord lesion might affect the lateral columns (including the inhibitory DRT) and spare the ventral columns (along with the excitatory system). Thus, the incomplete cord lesion would abolish all inhibition of spinal stretch reflexes and leave the excitatory system unopposed to drive extensor tone but still inhibit flexor reflex afferents ('paraplegia in extension'). With complete spinal cord lesions, all supraspinal control is lost, and both stretch reflexes and flexor reflex afferents are completely disinhibited; a strong flexor pattern follows ('paraplegia in flexion').

Mechanism of the change in excitability of the spinal reflexes

The above outline of a balanced system of suprasegmental inhibitory and excitatory influences on spinal segmental reflexes could imply that the increased excitability of spinal reflexes is simply a matter of release or disinihibition. However, following acute UMN lesions there is frequently a variable period of reduced spinal reflex activity ('shock') and it is only following resolution of this that hyperactive reflexes appear. This raises the possibility that some structural and/or functional reorganization within the CNS ('plasticity') is responsible. The human CNS has been shown to be quite capable of such plasticity involving both motor and sensory pathways following limb amputation (e.g. Chen *et al.*, 1998 & Elbert *et al.*, 1994) and brain injury (Nirkko *et al.*, 1997). For the somatosensory pathways, reorganization occurs at cortical, brainstem and spinal levels (Florence & Kaas, 1995). Possible contributory processes include collateral sprouting of axons, receptor hypersensitivity following 'denervation' (Brown, 1994) and unmasking of previously silent synapses (Borsook *et al.*, 1998). The idea of collateral sprouting as the basis of spasticity was first proposed by McCouch more than 40 years ago (McCouch *et al.*, 1958), but later reports that the CNS was capable of sprouting were disputed (Noth, 1991). Subsequently, better evidence appeared that axon terminals in the mammalian spinal cord could sprout and form new synapses (Hulseboch & Coggeshall, 1981; Krenz & Weaver, 1998). Burke (1988) believes that new synapses may simply act to reinforce existing spinal circuits rather than create entirely new circuits, a quantitative rather than a qualitative change. Thus, the positive features of the UMN syndrome involve two main mechanisms (1) disruption of descending control of spinal pathways and (2) structural and/or functional reorganization at the spinal level (Pierrot-Deseilligny & Mazieres, 1985).

In some patients, hyperactive reflexes appear remarkably quickly, lending some credence to the idea of a 'release' effect. In support of this, CNS plasticity has been seen within 24 hours of human limb amputation (Borsook *et al.*, 1998); such rapidity suggests the unmasking of silent connections, rather than the formation of new ones. In addition, electrical stimulation of skin overlying the spastic biceps can produce longer-lasting reductions in spasticity, indicating a therapeutically useful short-term plasticity (Dewald *et al.*, 1996).

The mechanism of reduced spinal reflexes in spinal shock deserves some discussion in this context. Vibratory inhibition is increased in spinal shock, suggesting presynaptic mechanisms (Calancie *et al.*, 1993). However, it the acute spinal rat, polysynaptic excitatory postsynaptic potentials (pEPSPs) are markedly prolonged (Li *et al.*, 2004), which argues against increased presynaptic inhibition. It has been proposed that plasticity may play a role, involving down-regulation of receptors (Bach-y-Rita & Illis, 1993). Recovery from spinal shock could involve up-regulation of receptors, making them more sensitive to neurotransmitters (Bach-y-Rita & Illis, 1993). The supersensitivity to monoamines of spinal interneurones involved in extensor reflexes in chronic spinal

rats compared with the acute preparation is an example of this (Ito *et al.*, 1997). Nonsynaptic transmission could also play a role in spinal shock and its recovery (Bach-y-Rita & Illis, 1993). Finally, postsynaptic mechanisms may be involved. In the spinal shock phase of rats with cord lesions, the motorneurone becomes poorly excitable, especially in extensor motoneurones, as a result of reduced persistent inward currents (see 'Alpha motoneurone excitability' on p. 47, and Heckman *et al.*, 2005, for a review).

There may be some additional therapeutic relevance to understanding the underlying cellular processes behind the hyperreflexia of the UMN syndrome (Noth, 1991). If collateral sprouting is responsible, it may be possible to inhibit this process (Schwab, 1990).

Spinal segmental reflexes

Hyperexcitability of spinal reflexes forms the basis of most of the 'positive' clinical signs of the UMN syndrome, which have in common excessive muscle activity. These spinal reflexes may be divided into two groups, proprioceptive reflexes and nociceptive/cutaneous reflexes (Table 2.1). Proprioceptive reflexes include stretch reflexes (tonic and phasic) and the positive supporting reaction. Nociceptive/cutaneous reflexes include flexor and extensor reflexes (including the complex Babinski sign). The clasp-knife phenomenon combines features of both groups, at least in the lower limbs.

Table 2.1. Classification of positive features of upper motor neurone syndrome by pathophysiological mechanism

A. *Afferent – disinhibited spinal reflexes*
   1. Proprioceptive (stretch) reflexes
      - Spasticity (tonic)
      - Tendon hyperreflexia and clonus (phasic)
      - Clasp-knife reaction
      - Positive support reaction?
   2. Cutaneous and nociceptive reflexes
      (a) Flexor withdrawal reflexes
      - Flexor spasms
      - Clasp-knife reaction (with tonic stretch reflex)
      - Babinski sign

      (b) Extensor reflexes
      - Extensor spasms
      - Positive support reaction

B. *Efferent – tonic supraspinal drive?*
   - Spastic dystonia?
   - Associated reactions/synkinesia?
   - Cocontraction?

Proprioceptive reflexes

Proprioception is the sensory information about movement and position of bodily parts and is mediated in the limbs by muscle spindles. Stretch of muscle spindles causes a discharge of their sensory afferents that synapse directly with and excite the motoneurones in the spinal cord innervating the stretched muscle. This stretch reflex arc is the basis of the deep tendon reflex, referred to as a phasic stretch reflex because the duration of stretch is very brief. Reflex muscle contractions evoked by longer stretches of the muscle, such as during clinical testing of muscle tone, are referred to as tonic stretch reflexes. The positive support reaction may be in part due to stretch of muscle proprioceptors in the foot (Bobath, 1990).

Phasic stretch reflexes

The clinical signs arising from hyperexcitability of phasic stretch reflexes include deep tendon hyperreflexia, irradiation of tendon reflexes and clonus. The traditional view is that percussion of the tendon causes a brief muscle stretch, a synchronous discharge of the muscle spindles and an incoming synchronized volley of Ia afferent activity that monosynaptically excites alpha motoneurones. However, Burke (1988) points out that the situation is more complex. The following summarizes his explanation. In addition to muscle stretch, the percussion of a tendon causes a wave of vibration through the limb that is also capable of stimulating muscle spindles in the muscle percussed, as well as others in the limb. This is the basis of tendon reflex 'irradiation', discussed later. Spindle activity from these other muscles could

contribute to the tendon reflex. Furthermore, percussion also stimulates mechanoreceptors in the skin and other muscles. The discharge from the muscle spindles evoked by percussion is far from synchronous and spindles may fire repetitively. Finally, the reflex is unlikely to be solely monosynaptic. The rise time observed in the excitability of the soleus motoneurones following Achilles tendon percussion is around 10 ms, which is ample time for oligo or polysynaptic pathways to be involved. These do exist for the Ia afferents and could include those from the percussed muscle as well as from other muscles in the limb excited by the percussion. Cutaneous and other mechanoreceptor afferents also have polysynaptic connections. H reflexes are commonly used to examine the phasic stretch reflex pathways in the UMN syndrome and considered equivalent to the tendon reflex. This is not the case for many of these same reasons (see p. 38, 'Electrophysiological studies of spinal reflexes in spasticity').

In the UMN syndrome, percussion of one tendon often produces similar brief reflex contractions of other muscles in the limb, a phenomenon known as reflex irradiation. This is not due to the opening up of synaptic connections between various muscles in the limb (Burke, 1988) but to a simpler mechanism. As mentioned, tendon percussion sets up a wave of vibration through the limb that is capable of exciting spindles in other muscles (Lance & De Gail, 1965; Burke *et al.*, 1983). If the stretch reflexes of those muscles are also hyperexcitable, phasic stretch reflexes will be evoked.

Clonus is a rhythmic, often self-sustaining contraction evoked by rapid muscle stretch, best seen in the UMN syndrome at the ankle, provoked by a brisk, passive dorsiflexion. It tends to accompany marked tendon hyperreflexia and responds similarly to factors that reduce hyperreflexia (Whitlock, 1990). The rhythmicity suggested a central oscillatory generator, an idea supported by the inability to modify the frequency by external factors (Walsh, 1976; Dimitrijevic *et al.*, 1980). However, Rack and colleagues found that the frequency of the ankle clonus did vary with the imposed load, as had also been found at other joints countering the central oscillator notion (Rack *et al.*, 1984). By changing the mechanical load, the frequency of spontaneous ankle clonus in spastic patients could vary from 2.5 to 5.7 Hz. It was also possible to inhibit clonus with strong loads. Load-dependent spontaneous clonus could also be induced in normal subjects (after prolonged sinusoidal joint movements) at similar frequencies. This is no surprise as a great many normal people have experienced ankle clonus at some stage in their lives under certain conditions. The conclusion drawn by Rack *et al.* (1984) was that clonus is a manifestation of increased gain of the normal stretch reflex and that central mechanisms are less dominant in determining the frequency of clonus.

The mechanism underlying clonus is similar to that of tendon hyperreflexia, increased excitability of the phasic stretch reflex. A rapid dorsiflexion of the ankle by an examiner produces a brisk stretch of the gastrocnemius-soleus. A reflex contraction in the gastrocnemius-soleus is elicited, plantar flexing the ankle. This relieves the stretch, abolishing the stimulus to the stretch reflex and so the muscle relaxes. If this relaxation is sufficiently rapid while the examiner maintains a dorsiflexing force, another stretch reflex will be elicited and the ankle again plantar flexes. Thus, a rhythmic, pattern of contraction and relaxation is set up that will often continue for as long as the dorsiflexion force is maintained, referred to as sustained clonus. However, unsustained clonus can also occur in UMN lesions. Burke (1988) comments that the much of the eliciting and maintaining of clonus lies in the skilled technique of the examiner and, as Rack *et al.* (1984) noted, it was possible to suppress clonus with stronger loads.

Tonic stretch reflexes

Muscle tone is tested clinically by passive movement of a joint with the muscles relaxed and refers to the resistance to this movement felt by the examiner. The hallmark of the UMN syndrome is a form of hypertonia, called spasticity. It had been observed clinically that slow movements would often not reveal hypertonia but faster movements would and that thereafter this resistance increased with the speed of the passive movements. Electromyographically such resistance correlated with reflex contraction of the

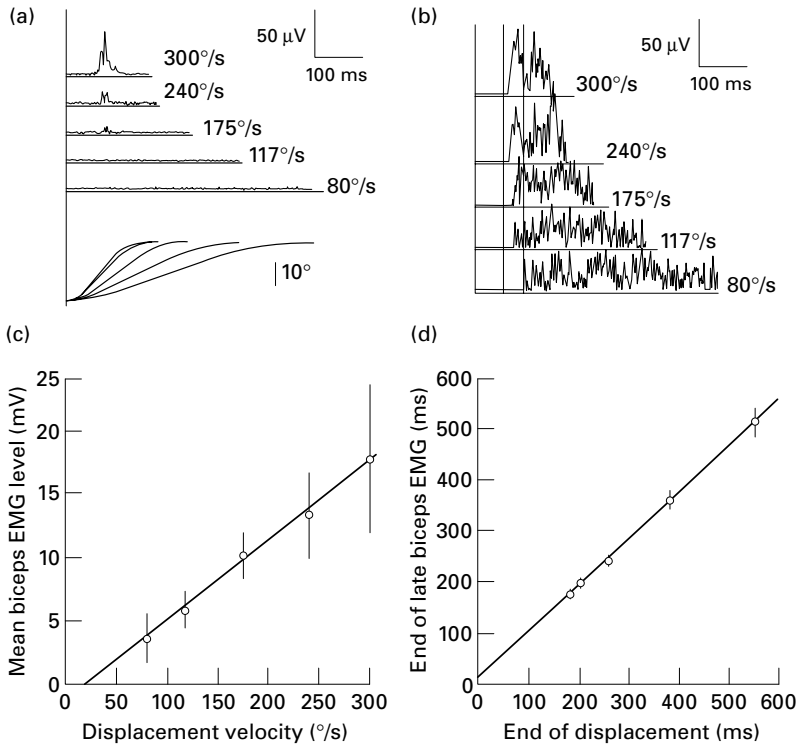

Figure 2.2. Surface electromyography (EMG) recordings of the biceps during passive displacements of the elbow of various angular velocities. (a) Normal subjects. No EMG activity (stretch reflex) is elicited until very fast displacements are made (175°/s and faster). The reflex responses then are brief and terminate before the movement is complete (angular displacement represented below). (b) Spastic subjects show stretch reflexes, even at low angular velocities, which continue for the duration of the movement. (c) The magnitude of the EMG response increases linearly with the speed of the movement. (From Thilmann *et al.*, 1991a.)

stretched muscle, which opposes the stretch (Herman, 1970). These contractions of stretched muscle are referred to as tonic stretch reflexes to distinguish them from the brief stretches that elicit phasic stretch reflexes. Tonic stretch reflexes have also been studied during active muscle contraction, in part to determine the role that hyperexcitability of such reflexes might play in the impairment of movement in the UMN syndrome (see following).

In an elegant experiment, Thilmann and colleagues (1991) found stretch reflexes in the relaxed biceps in only half their normal subjects (Fig. 2.2) and then only with very fast movements; the threshold was an angular velocity of around 200 degrees per second. The latency of the reflex was 61 to 107 ms, some of which probably includes the time it takes for the mechanical displacement of the elbow to stretch the muscle and excite the spindles (Rothwell, 1994). The reflex contraction was brief and was not maintained throughout the stretching movement and is probably a phasic stretch reflex, analogous to the tendon reflex (Rothwell, 1994).

This was an important finding because it indicated that at the velocities of movement usually used to test tone in normal, relaxed muscle (much slower than 200 degrees per second), there is no stretch reflex. Thus, tonic stretch reflexes do not contribute to muscle tone, which therefore must come from the

viscoelastic properties of the muscle. This is discussed in more detail further on.

The situation was found to be quite different in hemiparetic spastic (stroke) patients (Thilmann *et al.*, 1991a) in whom stretch reflexes could be elicited with relatively slow movements – as slow as 35 degrees per second. Reflex activity usually began at a relatively constant latency, at the end of the 61- to 107-ms window found in normal subjects. However, it continued throughout the stretching movement and usually stopped just before the end of the displacement. No EMG activity was seen when the stretch was held at the end of the displacing movement. That is, there was no *static* stretch reflex. Thus, in this study, as in others (Rushworth, 1960; Burke *et al.*, 1970; Herman, 1970; Ashby & Burke, 1971; Burke *et al.*, 1972), spasticity was found to be an exclusively *dynamic* tonic stretch reflex. Other researchers have found otherwise (Powers *et al.*, 1989) (see 'Static tonic reflexes,' below). Some variation between patients was seen with faster rates of displacement producing shorter latency activity within the 61- to 107-ms 'normal' window in some and very slow velocities having much longer latencies (up to 400 ms) in others. The amount of reflex muscle contraction showed a positive linear correlation with the velocity of stretch, thus confirming that spasticity is velocity dependent (Burke *et al.*, 1970; Ashby & Burke, 1971; Burke *et al.*, 1972; Powers *et al.*, 1989). Hemiparetic patients without spasticity behaved similarly to the normal subjects.

The fact that a tonic stretch reflex is not present in normal subjects raises the question of whether it is an entirely new reflex arising after a UMN lesion or an increase in excitability of an existing, dormant one. If it is the latter, is the mechanism a decrease in threshold or an increase in gain? The case for each has been argued (Powers *et al.*, 1988, 1989; Thilmann *et al.*, 1991a) and it has even been suggested that stretch reflex gain in spastic ankles is at the high end of the normal range (Rack *et al.*, 1984). The absence of the reflex in normal subjects, even at rates as high as 500 degrees per second (Ashby & Burke, 1971), would suggest an implausibly high threshold (Thilmann *et al.*, 1991a). Against increased gain and in favor of a decreased threshold, both spastic patients and controls showed similar stretch reflex gains during active elbow flexion, a state assumed to eliminate threshold differences (Powers *et al.*, 1989). This and similar measures of the stretch reflex during voluntary contraction are not valid assessments of spasticity, however, which, by definition, requires the muscle to be at rest. Finally, arguments over the relative differences in stretch reflex gain between relaxed normal and spastic muscles may really be pointless given that such a reflex is not even present in normal subjects. As Thilmann *et al.* (1991a) point out, 'a qualitatively new reflex is present in the spastic subjects'.

Irrespective of whether the basic alteration is increased gain or decreased threshold, the common finding is that spasticity is due to hyperactive tonic stretch reflexes that are velocity sensitive. There is still a threshold velocity of displacement, however, as a slow movements will not elicit a reflex. Thilmann *et al.* (1991a) found this could be as low as 35 degrees per second in the biceps, while a higher threshold of 100 degrees per second has been found in the quadriceps (Burke *et al.*, 1970). The long latency of these reflexes, even accounting for delays due to mechanical factors, suggests a polysynaptic pathway. There is good evidence that Ia afferents from primary muscle spindles are linked by oligo- and polysynaptic pathways to their homonymous alpha motoneurons (Burke, 1988; Mailis & Ashby, 1990) and these remain the most likely mediator of tonic stretch reflexes. Group II afferents also have polysynaptic connections and may contribute to muscle stretch reflexes (see 'Group II polysynaptic excitatory pathways').

Tonic stretch reflexes (TSRs) are not only velocity dependent but also length dependent. In the lower limb, the TSR is less sensitive at longer lengths in the ankle plantarflexors (Meinders, 1996) and in the quadriceps (Burke *et al.*, 1970). In apparent contradiction, some researchers (He, 1998; Fleuren *et al.*, 2006) have found increased spasticity in the knee extensors when the rectus femoris was stretched. The explanation for this difference may be that the spasticity was compared between the sitting and supine positions. Although going from sitting to supine does lengthen the rectus femoris, it also stretches the

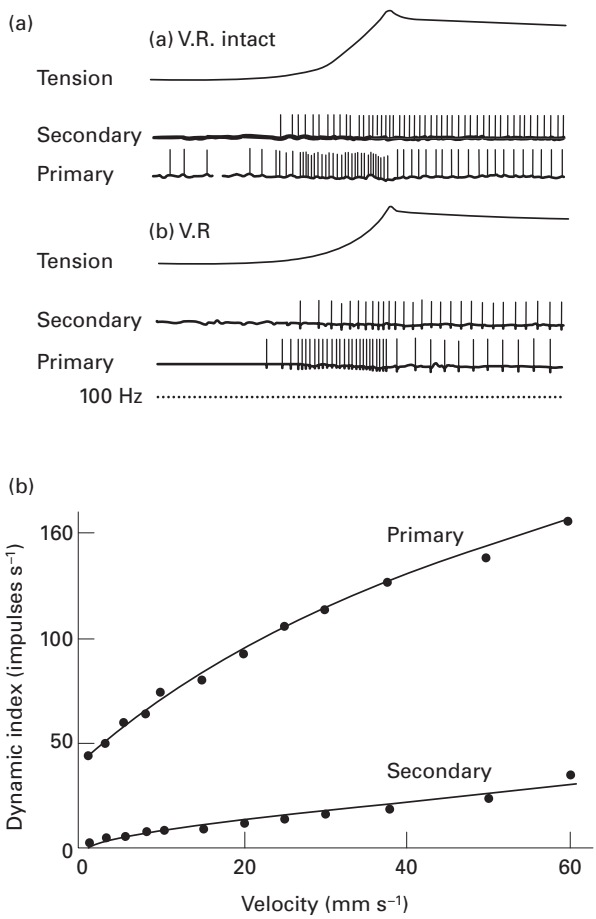

Figure 2.3. Velocity sensitivity of primary muscle spindle endings and relative insensitivity of secondary spindle endings. (a) Spindle afferent discharges with and without fusimotor drive (V. R. = ventral root). Note the dynamic sensitivity of the primary spindle endings during the course of the stretch. Note also that both spindle endings continue to discharge in the hold phase of the stretch, particularly the secondary spindle endings, indicating that both are sensitive to length changes as well as velocity. (b) Graphic representation of the velocity sensitivity of each spindle ending, expressed as the dynamic index. (From Matthews, 1972.)

iliopsoas muscle, which, as mentioned below (see 'Extensor reflexes and spasms'), tends to induce extensor reflexes in the quadriceps. This may also explain the reduction in hamstring spasticity that they observed in the supine position compared with sitting rather than shortening. There are also potential vestibulospinal and other supraspinal influences concerned with postural control influences that vary with posture to consider (He, 1998). In the upper limb, the effect of length on TSR sensitivity is the opposite. In finger flexors, tonic stretch reflexes are increased in the shorter position and reduced in the lengthened position (Li *et al.*, 2006). This study of stroke patients confirmed that spasticity is both velocity and length dependent, but it also found an interaction between the two. Velocity dependence was greater at longer lengths and length dependence was greater with faster stretches. These observations underline the need to consider not only velocity of stretch but also body position and muscle length when measuring spasticity, especially in research.

Clinical experience has shown that repeated stretching tends to reduce tone, although usually only for a short time, measured in hours. While some of this reduction is biomechanical (Nuyens *et al.*, 2002), reduced tonic stretch reflexes measured electromyographically have been observed in the knee extensors (Nuyens *et al.*, 2002) and elbow flexors (Schmit *et al.*, 2000), although with high variability (Schmit *et al.*, 2000). The explanation may be thixotropic changes in spindle sensitivity of habituation of central reflex pathways. These findings not only support the role of physical treatments in spasticity but indicate that spasticity measurement needs to take into consideration the number of stretches used to evaluate spasticity, as well as the factors of length, velocity and position already mentioned.

The velocity dependence of tonic stretch reflexes has been attributed to the fact that primary muscle spindles are velocity sensitive in animal models (Herman, 1970; Dietrichson, 1971, 1973; Rothwell, 1994) (Fig. 2.3). In cats, fusimotor drive increases the velocity sensitivity but fusimotor drive is not increased in human spasticity (Burke, 1983). This explanation has been challenged by results that show the velocity sensitivity of spasticity is quite weak and nonlinear (Powers *et al.*, 1989). An alternative explanation relies upon the dependence of the

motoneurone firing threshold upon the rate of change of the depolarizing current (Powers *et al.*, 1989). Houk and colleagues (1981) studied firing of primary (Ia) and secondary (group II) spindle afferents from the soleus of decerebrate cats. They discovered that firing of both afferent fibre types are length and velocity dependent, with an interaction between the two that mirrors the findings in human spastic subjects of Li *et al.* (2006) mentioned earlier: velocity dependence was greater at longer lengths and length dependence was greater with faster stretches. Recently, the length or positional dependence of primary muscle spindles in the wrist and finger extensors of normal humans has been confirmed (Cordo *et al.*, 2001).

The clasp-knife phenomenon

This well-known clinical sign has as its basis a hyperexcitable tonic stretch reflex. A fast passive movement of a joint in a relaxed limb, usually knee flexion or elbow extension, encounters a gradual buildup of resistance that opposes the movement momentarily before apparently suddenly melting away, allowing continuing stretch with relative ease (Fig. 2.4). The rapid buildup of resistance is spasticity, through the mechanisms already discussed. The apparently sudden decline in the stretch reflex was initially attributed to the sudden appearance of inhibition from the Golgi tendon organs (via Ib afferents), as a means to protect the muscle from dangerously high tension. It had been thought that these organs fire only at high muscle tension. However, it was later discovered that Golgi tendon organs actually have quite low tension thresholds (Houk & Henneman, 1966; cited in Rothwell, 1994). Furthermore, the inhibition of the stretch reflex extends well beyond the reduction in tension; Golgi tendon organs cease firing once the tension is relieved (Rothwell, 1994; Fig. 2.5). Finally, there is evidence of *reduced* Ib inhibitory activity in some cases of spasticity (see 'Ib Non-reciprocal inhibition'). It is unlikely then that Ib inhibitory activity from the Golgi tendon organs plays much of a role in the clasp-knife phenomenon (Rothwell, 1994).

The mechanism of the decline in stretch-reflex activity that gives rise to the apparently sudden release may be due to two factors. The first is the velocity sensitivity of the stretch reflex. The resistance produced by the stretch reflex slows the movement, which reduces the stimulus responsible for it to below threshold, the reflex contraction stops and the resistance declines. Burke (1988) believes that this is all that is required for the clasp-knife phenomenon in the biceps brachii but this reasoning does not explain why the continuing movement after the 'release' does not once again evoke a stretch reflex. The clasp-knife phenomenon is seen better in the quadriceps where the second factor also applies (Burke, 1988). Here, as well as in the ankle plantar flexors (Meinders *et al.*, 1996), the tonic stretch reflex seems not only velocity dependent but also length dependent, being less sensitive at longer lengths (Fig. 2.4). Thus, there is not only declining velocity during the movement but also increasing length. A critical point is reached where these two factors combine to reduce the effective stimulus to the stretch reflex, which suddenly ceases. Continuing movement does not again evoke a stretch reflex because the reflex is relatively insensitive at this longer length. While the resistance seems to suddenly melt away, the mechanism is really gradually declining stimulus (velocity) and stretch-reflex sensitivity (length). The length-dependent sensitivity of the stretch reflex appears to be due to length-dependent inhibition of the stretch reflex by a group of sensory fibres known as flexor reflex afferents (FRAs), which are discussed in more detail further on. In contrast to the quadriceps, stretch reflexes in the hamstrings are more sensitive at longer lengths (Fig. 2.4; Burke & Lance, 1973).

Static tonic stretch reflexes

As mentioned earlier, the stretch reflexes underlying spasticity have been regarded as dynamic, that is, present only when the joint is moving. Thilmann and colleagues (1991a) found that the stretch reflex usually declined towards the end of the movement as the velocity declined and if the muscle was held in stretch at this point, there was no EMG activity. Thus, it has been considered that there is no appreciable

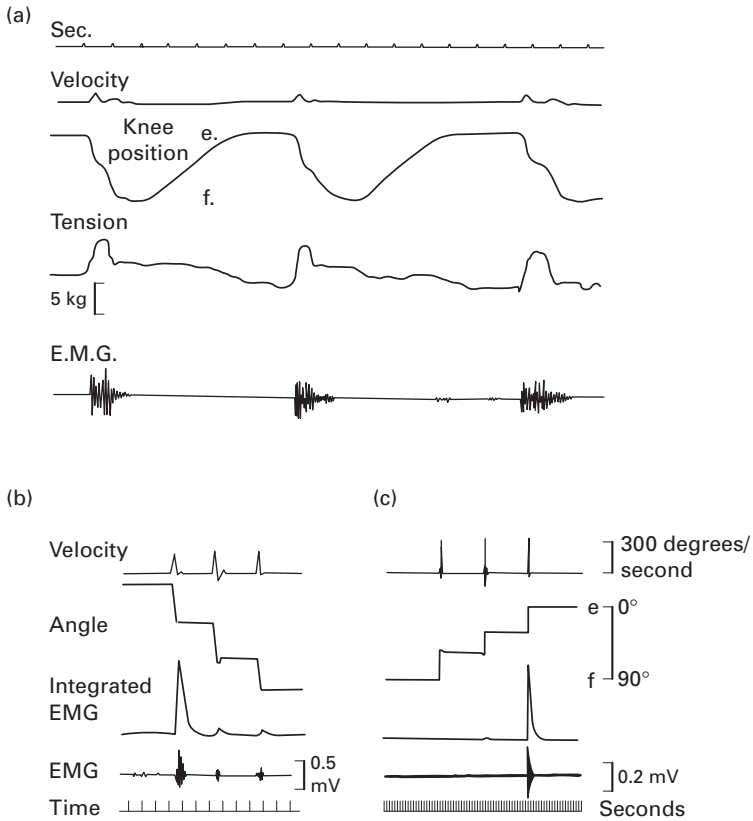

Figure 2.4. (a) The clasp-knife phenomenon at the knee. The subject is supine and the knee is passively flexed while surface electromyography (EMG) is recorded from the quadriceps and force exerted by the examiner's hand at the ankle (reflecting muscle tension). Passive flexion elicits a tonic stretch reflex, associated with rapid build-up of tension (resistance). This abrupted declines (clasp-knife phenomenon), coincident with the cessation of the tonic stretch reflex. (b) and (c) Length-dependent sensitivity of the tonic stretch reflex in the quadriceps (b) and the hamstrings (c). Muscle stretches are performed at increasing length of the muscle. In the quadriceps (b), the maximum reflex is elicited in the first step, with declining responses with increasing muscle length. The opposite is seen in the hamstrings (c), where a tonic stretch reflex is not elicited until the muscle is at nearly full stretch. (From Burke & Lance, 1973.)

static component to the tonic stretch reflex of spasticity.

However, several researchers have observed clear reflex activity in the maintained phase of a ramp-and-hold stretch of elbow flexors (Fig. 2.6) (Denny-Brown, 1966; Powers *et al.*, 1989; Sheean, 1998a). They suggested several methodological reasons why such reflex activity might have been missed in previous studies (Powers *et al.*, 1989). One obvious reason for its absence in the quadriceps might be length-dependent inhibition responsible in part for the clasp-knife phenomenon mentioned earlier. The situation may be truly different at the ankle, where static stretch reflexes have not been seen (Herman, 1970; Berardelli *et al.*, 1983; Hufschmidt & Mauritz, 1985).

The mechanism of static tonic stretch reflexes presumably involves receptors that are chiefly sensitive to muscle length and less to velocity. The primary muscle spindles (with Ia afferents) are sensitive to both but mainly to velocity (Rothwell, 1994). The secondary muscle spindles, via the slower

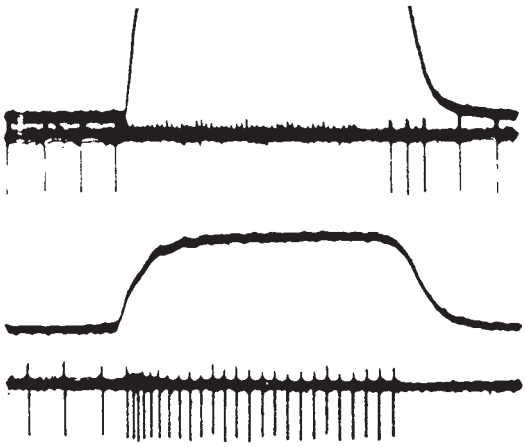

Figure 2.5. Demonstrating the sensitivity of Golgi tendon organs to small tensions. Two recordings from stimulation of motor axons to the soleus muscle of a cat. The upper trace of each recording represents the force in the tendon, and the lower trace the tendon organ Ib afferent discharge. The lower recording shows a vigorous discharge of the tendon organ, despite the weak contraction. The upper recording, from a stronger contraction, shows an initial discharge of Golgi tendon organ afferents, with subsequent cessation due to unloading of the receptor by contraction of neighbouring motor units. (From Houk & Henneman, 1967.)

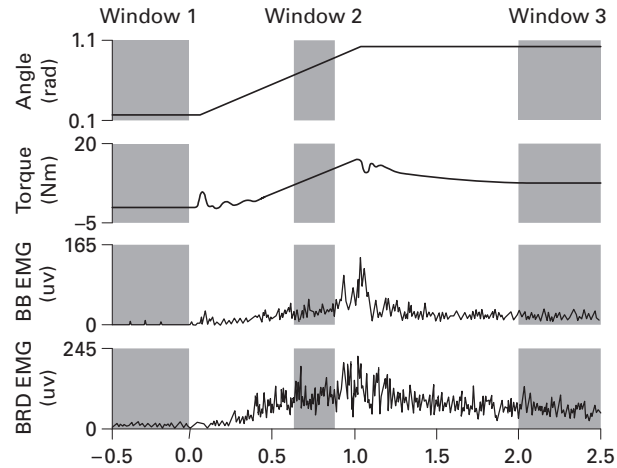

Figure 2.6. Static tonic stretch reflexes in the spastic biceps brachii (BB) and brachioradialis (BRD). Passive extension of the elbow (1 radian stretch at 1 radian/sec) elicits a tonic stretch reflex during the ramp portion of the stretch (dynamic tonic stretch reflex). The rectified surface EMG activity continues, especially in brachioradialis, during the ramp phase of the stretch after the movement has stopped (static tonic stretch reflex). (From Powers *et al.*, 1989.)

conducting group II afferents, maintain an increased firing level over baseline for as long as the muscle is held stretched and would be suitable candidates. Some evidence from comparative therapeutic and electrophysiological studies of baclofen and tizanidine in spinal cats suggests a role of group II afferents in spasticity (Skoog, 1996). Both agents are equally effective at reducing spasticity. Baclofen strongly depressed group I potentials but had inconsistent effects on group II potentials. In contrast, tizanidine strongly depressed the amplitude of monosynaptic field potentials in the spinal cord caused by group II afferents with little effect on group I potentials. Additionally, L-dopa, which depresses transmission from group II but not group I afferents, reduces spasticity, tendon hyperreflexia and clonus in humans with spinal cord injuries (Eriksson *et al.*, 1996). However, the depressed long-latency stretch reflexes of the upper limb in the UMN syndrome suggest a reduced effect of group II afferents. The discovery that group II afferents in the soleus of the decerebrate cat are both length and velocity dependent (Houk *et al.*, 1981) supports not only a role for these afferents in the static tonic stretch reflex but in the dynamic tonic stretch reflex (spasticity) as well.

Burke suggests that EMG activity continuing beyond the end of a movement must be due to some other stimulus, such as cutaneous stimulation (Burke, 1988). Therefore, this EMG activity in the hold phase may not be a reflex due to muscle stretch reflex. One possibility is a flexor reflex, mediated by flexor reflex afferents (see following discussion).

Tonic stretch reflexes during muscle activation

It is commonly held by clinicians that spasticity interferes with muscle function, a belief that

often leads to vigorous and unhelpful attempts to reduce tone. Spasticity, however, is defined by its presence in *relaxed*, not activated muscle. Setting aside semantics, the question is really, could hyperexcitable stretch reflexes impair function? If the tonic stretch reflex gain of activated spastic muscles were truly not increased, it would be hard to argue in favour of this. The situation is further complicated by secondary soft tissue changes that can increase tone, independent of stretch reflexes (see 'Nonreflex contributions to hypertonia').

In contrast with relaxed muscles, tonic stretch reflexes can be elicited in normal subjects while the muscle is voluntarily activated. Under these conditions, the tonic stretch reflex responses in elbow flexors between normal and spastic subjects are not significantly different (Lee *et al.*, 1987; Powers *et al.*, 1989; Burne *et al.*, 2005). This has been taken to indicate that the hyperexcitable tonic stretch reflex of spasticity is due to decreased threshold (see above) as, once threshold differences had been eliminated by voluntary activation, the stretch reflex gain was similar in the two groups. However, Nielsen (1972) had found that the stretch reflex gain of voluntarily activated spastic biceps muscles was fixed at a high level compared with normal subjects, in whom gain was strongly dependent upon the degree of voluntary activation. Given this, and the fact that the experimental paradigm is difficult to control (Noth, 1991), it is possible that differences in activated tonic stretch reflex gain between the two groups might have been missed.

A variation on this theme is the modulation of stretch reflexes during more complex movements such as gait. Short-latency stretch reflexes of soleus in normal subjects show substantial phase-dependent modulation during walking, probably through Ia presynaptic inhibition (Dietz *et al.*, 1990) (see 'Ia Presynaptic inhibition' on p. 40). That as much as 30% to 60% of the soleus EMG activity during the stance phase of walking is due to stretch reflexes (Yang *et al.*, 1991b) demonstrates their importance in normal gait. It has been argued that this impairment of stretch reflex modulation, because of disrupted supraspinal control (Fung & Barbeau, 1994), could contribute to the gait disorder in spasticity (Boorman *et al.*, 1992), by failure of the appropriate pattern of reflex suppression. In support of this idea, defective stretch reflex modulation in spastic subjects with multiple sclerosis has been reported (Sinkjaer *et al.*, 1996) and hyperactive soleus stretch reflexes during active dorsiflexion were found that impaired movement (Corcos *et al.*, 1986). Soleus (Yang & Whelan, 1993; Stein, 1995) and quadriceps (Dietz *et al.*, 1990) H reflexes are also normally modulated during gait and cycling (Boorman *et al.*, 1992) and impaired soleus H reflex modulation has also been found in spastic patients (Yang *et al.*, 1991a; Boorman *et al.*, 1992; Sinkjaer *et al.*, 1995). There was, however, a poor correlation between impaired soleus H-reflex modulation and the degree of walking difficulty in spastic patients with spinal cord lesions (Yang *et al.*, 1991a).

However, Ada *et al.* (1998) found that although abnormal tonic stretch reflexes were present at rest in the gastrocnemius of spastic subjects (post-stroke), the action tonic stretch reflexes present during simulated gait were no different to those of controls. They concluded that spasticity would not contribute to walking difficulties after stroke. Other researchers agree (Sinkjaer *et al.*, 1993) and add that nonreflex (soft tissue) hypertonia is more important in impairing ankle movement during walking (Dietz *et al.*, 1981; Dietz & Berger, 1983; Hufschmidt & Mauritz, 1985). The issue is clearly an important one. Attempts to reduce spasticity in order to improve function, especially gait, may be futile.

The physiological mechanisms underlying stretch reflex hyperexcitability

For a long time, the analogy was drawn between the stretch reflex hyperexcitability of the decerebrate cat and that of human spasticity. In the decerebrate cat, stretch reflexes are hyperexcitable because of increased fusimotor drive (via gamma motoneurones) to the muscle spindles making them more sensitive to stretch. Consequently, Ia afferent activity

is proportionately increased. A similar mechanism was assumed to be operating in human spasticity, but by the early 1980s it had become evident that fusimotor activity was not increased. The evidence for this conclusion was eloquently summarized and discussed by Burke (1983). Thus, if excessive proprioceptive afferent input was not the explanation, what could explain the enhanced reflex responses to normal afferent input? Could it be that the alpha motoneurones themselves are hyperexcitable, ready to overreact in response to the normal and appropriate afferent input? Or, given that the reflex circuits activated by the clinical stimuli (e.g. tendon tap, passive stretch) are complex, involving interneurones that are under strong supraspinal control, is it possible that either the gain of these circuits is increased or the threshold lowered?

The latter is the prevailing view, although it is difficult to investigate the possibility of hyperexcitable alpha motoneurones without using spinal reflexes, as discussed further on (see p. 47, 'Alpha motoneurone excitability'). Thus, the basis of stretch reflex hyperexcitability, which underlies the clinical signs of enhanced tendon reflexes and reflex irradiation, clonus and spasticity, is abnormal processing of proprioceptive information within the spinal cord. A similar mechanism operates in the exaggerated nociceptive and cutaneous reflexes, also an important component of the UMN syndrome. As has been mentioned, there has been some argument as to whether this abnormal processing arises from an increased gain or from a reduced threshold.

Nonreflex contributions to hypertonia: biomechanical factors

Contractures are a well known and feared complication of the UMN syndrome, reducing the range of motion of a joint. There has been a recent investigation of the relationship between the stretch reflex hyperexcitability of spasticity and contractures (O'Dwyer *et al.*, 1996), discussed later. However, contractures are not the only soft tissue changes to occur in the UMN syndrome. Muscles and tendons may become stiff and less compliant, resisting passive stretch and manifesting as increased tone. The passive range of motion might still remain normal if there is no fixed shortening or contracture. As we saw earlier, normal subjects do not exhibit stretch reflexes at normal rates of passive limb movement. Thus, it is the viscoelastic properties of the soft tissues alone that produce normal muscle tone. In other words, normal muscle tone is entirely biomechanical, with no neural contribution (Burke, 1988). Thus, there can be no real 'hypotonia' due to neurological disease (van der Meche & van Gijn, 1986; Burke, 1988). In the UMN syndrome, both neural and biomechanical factors may contribute to increased muscle tone.

This is an important concept, mainly because the treatment approaches to each type of hypertonia are different. Increased neural tone might respond to antispasticity medications or injections of botulinum toxin or phenol, whereas biomechanical tone would not. Increased biomechanical tone is best treated by physical measures, for example, passive stretching, splinting and serial casting.

The important role that soft tissue changes play in muscle tone and posture has been highlighted by Dietz and colleagues (1981) and confirmed by others (Hufschmidt & Mauritz, 1985; Thilmann *et al.*, 1991b; Sinkjaer *et al.*, 1993, 1996; Sinkjaer & Magnussen, 1994; Nielsen & Sinkjaer, 1996; Becher *et al.*, 1998). Plantar flexion of the ankle during gait is a common sequela of the UMN syndrome. It was generally assumed that this was produced by a combination of overactivity of the plantar flexors (referred to as spasticity) and underactivity of the ankle dorsiflexors. The latter would occur because of weakness from the UMN lesion and possibly reciprocal inhibition of these muscles by the presumed overactive plantarflexors. However, they found that despite the plantar-flexed ankle, the plantarflexors were actually underactive rather than overactive and that there was excessive activity in the dorsiflexors, presumably in an attempt to correct the posture (Fig. 2.7). The purpose of the research had been to investigate the suggestion that 'spasticity' played a role in the gait disturbance of the UMN syndrome, but it found, at

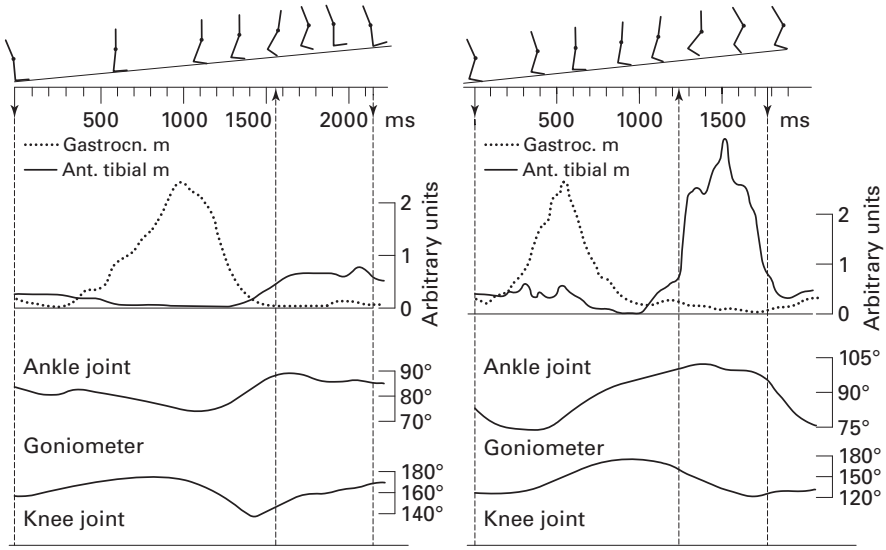

Figure 2.7. Electromyographic (EMG) activity (rectified and averaged) during walking of tibialis anterior (ant. tibial m) and gastrocnemius (gastrocn. m) of a normal subject (left side) and a spastic patient (right side). Verticle lines indicate lift-off and touch-down of the foot on the treadmill. Note that in the spastic subject, the foot remains plantarflexed during the swing phase, in the absence of significant EMG activity in gastrocnemius and despite greater than normal EMG activity in tibialis anterior. This indicates that the plantarflexed posture is not due to weakness of tibialis anterior, or to excessive contraction of gastrocnemius, either from stretch or co-contraction. Biomechanical factors in the triceps surae must be causing the resistance to ankle dorsiflexion. (From Dietz *et al.*, 1981.)

least at the ankle, that soft tissue changes were more important.

Similar experiments have been performed in the upper limb, correlating EMG activity of the elbow flexors, as a measure of stretch reflex hyperexcitability (spasticity), and resistance to passive movement, measured as torque (Lee *et al.*, 1987; Dietz *et al.*, 1991; Ibrahim *et al.*, 1993; O'Dwyer *et al.*, 1996). Higher-than-normal torque/EMG ratios indicate a significant soft tissue contribution to muscle hypertonia.

In clinical practice, it can be difficult to distinguish between neural and biomechanical hypertonia. Velocity-dependent hypertonia and the clasp-knife phenomenon would suggest a neural cause. Hypertonia with slow stretches would suggest reduced soft tissue compliance (Malouin *et al.*, 1997). The distinction often can be made with electromyography or, less practically, by examination under anesthesia. In many cases, both components are present (Sinkjaer *et al.*, 1996; Malouin *et al.*, 1997).

The conditions predisposing to reduced soft tissue compliance are probably the same as that of contracture formation, that is, prolonged immobilization of muscles and tendons at short length. This situation may arise because of spasticity (e.g. elbow flexors resisting straightening), spasms or poor positioning of weak muscles. Thus, neural hypertonia (spasticity) could result in secondary biomechanical hypertonia (Fig. 2.8). Such soft tissue changes can occur quite rapidly, as early as 2 months after stroke (O'Dwyer *et al.*, 1996; Malouin *et al.*, 1997). The stiffness could reside in either the passive connective tissue of the muscles, tendons and joints (reviewed in Herbert, 1988; Sinkjaer & Magnussen, 1994) or in the muscle fibres themselves, where histochemical changes resembling denervation have been found (Dietz *et al.*, 1986). Muscles immobilized at short length develop altered length–tension relationships that make them shorter and stiffer (Fig. 2.9) (see Herbert, 1988, or Foran *et al.*, 2005, for a review). The number of sarcomeres is also reduced in proportion

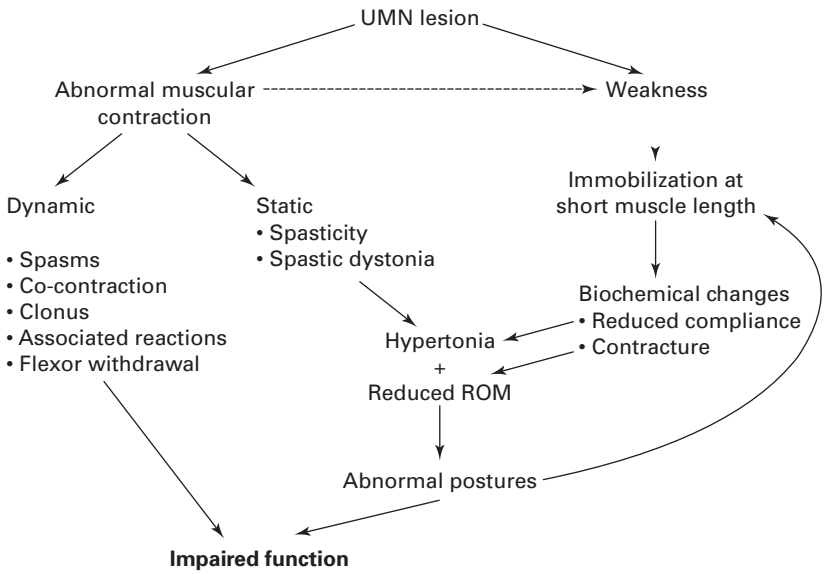

Figure 2.8. A model of the interaction between neural and biomechanical components of hypertonia in the upper motorneurone syndrome.

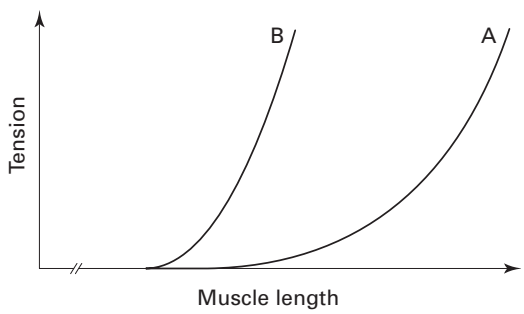

Figure 2.9. The effects of prolonged immobilization on muscle length and stiffness. Curve A is from a normal mouse soleus and curve B is from a soleus muscle immobilized in a shortened position for 3 weeks. The length of the muscle is naturally shorter but the length–tension curve is steeper indicating that it is also stiffer. (From Herbert, 1988, and adapted from Williams & Goldspink, 1978.)

to the reduced length, possibly in order to maintain optimal myofilament overlap. Chronic active muscle shortening – that is, actively contracting muscles – appears to accelerate the loss of sarcomeres. Thus, spasticity and the flexor and extensor spasms of the UMN syndrome can rapidly result in reduced soft tissue compliance and muscle shortening. Fortunately these changes are reversible if the muscle is lengthened, but timing is important; prolonged immobilization at short length can result in permanent shortening, or contractures.

It has been assumed that stretch hyperreflexia, spasticity, could result in prolonged muscle shortening, eventually leading to contracture. This assumption has provided an additional reason for treating spasticity in order to avoid this outcome (Brown, 1994). However, the relationship between spasticity and contracture has been challenged (O'Dwyer *et al.*, 1996). Contractures develop from prolonged muscle shortening, irrespective of whether there is active muscle contraction or not (O'Dwyer & Ada, 1996), and result in a reduced range of joint motion. They are frequently accompanied by increased muscle stiffness and therefore clinical hypertonia, which may also contribute to a reduced range of motion (O'Dwyer & Ada, 1996). However, fixed muscle shortening (i.e. contracture) can occur without hypertonia; there is a reduced range of joint motion but the tone within the available range of motion is normal. In a study of stroke patients, contracture

without spasticity was more common than with spasticity in elbow flexors (O'Dwyer *et al.*, 1996). These authors proposed that the muscle shortening produced by contracture may actually aggravate spasticity by shortening intrafusal as well as extrafusal fibres, thus activating them earlier in the stretch than usual. An additional hypothesis that this shortening might also make the spindles more sensitive to stretch (Vandervoot *et al.*, 1992) can be discounted for the same reasons as the increased fusimotor drive theory of spasticity (Burke, 1983).

One possible contribution to stiffness of the muscle fibres in spasticity is increased thixotropy. Thixotropy is a form of resistance to muscle stretch due to intrinsic stiffness of the muscle fibres resulting from cross-linking of actin and myosin filaments and is dependent upon the history of the movement (Walsh, 1992). Thixotropic stiffness has been reportedly increased in spasticity (Carey, 1990) but others have found it to be normal (Brown *et al.*, 1987). Thixotropy also affects intrafusal fibres (primary muscle spindles), altering their sensitivity to stretch (e.g. Hagbarth *et al.*, 1985), but this has yet to be studied in spasticity.

Nociceptive/cutaneous reflexes

Included in this category are the clinical phenomena of flexor spasms, extensor spasms and the extensor plantar response (Babinski sign). These are exteroceptive reflexes, defined as those mediated by nonproprioceptive afferents from skin, subcutaneous and other tissues that subserve the sensory modalities of touch, pressure, temperature and pain. The clasp-knife phenomenon is also discussed again here briefly.

Flexor withdrawal reflexes and flexor spasms

Flexor reflex afferents

In the cat, electrical stimulation of a group of sensory afferents arising from a variety of sources were found to have the effect of ipsilateral excitation of flexor and inhibition of extensor muscles (Rothwell, 1994). The result is a 'triple flexion' response of ankle dorsiflexion, knee flexion and hip flexion. Sensory afferents that evoke this flexion reflex are functionally defined as FRAs. These include afferents from secondary muscle spindles (group II), nonencapsulated muscle (group II, III and IV), joint mechanoreceptors and the skin (Fig. 2.10). Stimulation of FRAs exerts a weaker, opposite effect on the contralateral limb, with inhibition of flexors and excitation of extensors, resulting in limb extension (the crossed extensor reflex). One purpose of such a reflex would be to withdraw the limb from the stimulus (flexion) while supporting the animal on the other extended limb. FRAs have actions other than that described and may also be involved in the 'stepping generator' through their ipsilateral flexion/contralateral extension action (Rothwell, 1994).

FRA reflexes are polysynaptic and generally polysegmental, the latter suggesting involvement of the propriospinal pathways. The word 'flexor' implies that this is their only action but FRAs have access to alternative pathways with differing effects, including extensor facilitation and flexor inhibition (Burke, 1988). FRAs are under strong supraspinal control, both excitatory and inhibitory. The flexor reflex is facilitated in the spinal cat but suppressed in the midcollicular (decerebrate) cat (Rothwell, 1994). The supraspinal control presumably determines which of the available pathways are activated by the FRAs according to the particular task (Burke, 1988). The DRT is generally accepted to inhibit FRAs (Whitlock, 1990). However, flexor spasms were not produced by dorsolateral spinal lesions in cats involving the DRT (Taylor *et al.*, 1997). In another study though, a similar lesion enhanced spinal transmission from group II and III afferents (Cavallari & Pettersson, 1989). Inhibition also comes from the medial reticulospinal and vestibulospinal tracts (Brown, 1994). The effects of L-dopa and tizanidine indicate that the FRA activity is strongly suppressed by dopaminergic (Schomburg & Steffens, 1998) and noradrenergic (Delwaide & Pennisi, 1994) pathways, respectively.

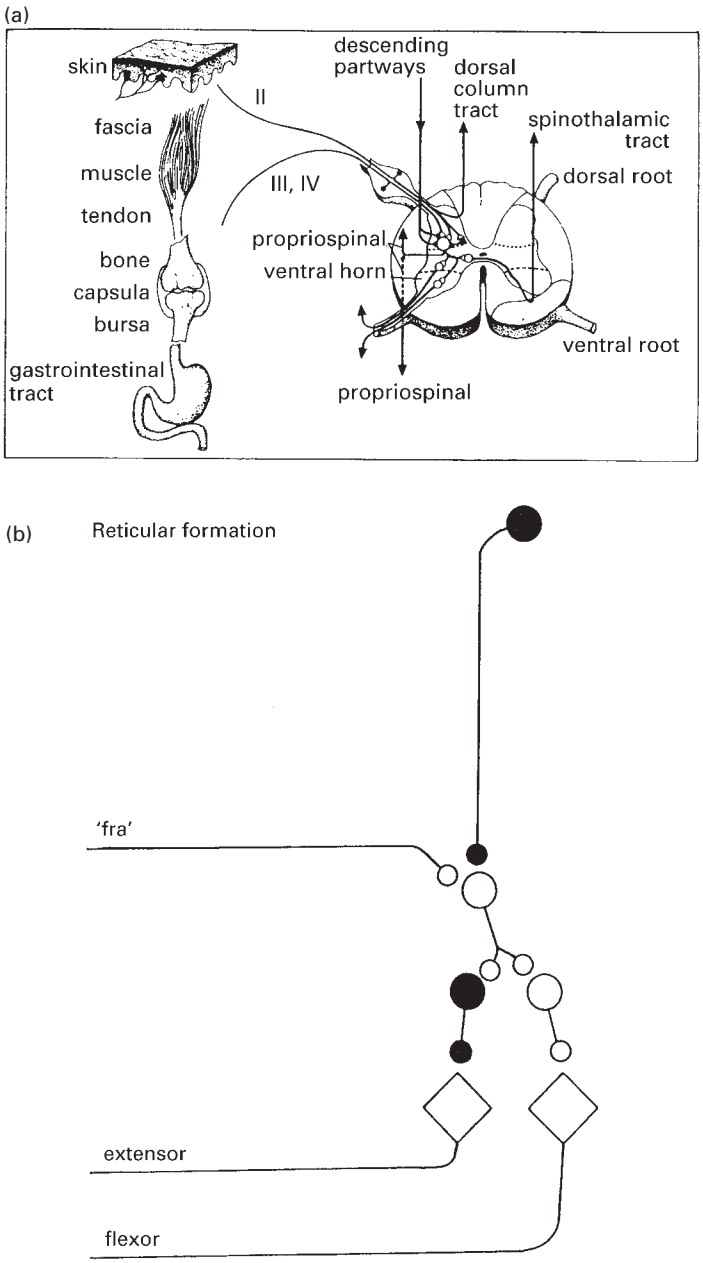

Figure 2.10. (a) Illustrating the multimodal (skin, muscle, joint) nature of the group II, III and IV fibres that comprise the flexor reflex afferents (FRAs) and some of their central connections. (b) FRAs converge on a polysynaptic spinal network that excites flexor and inhibits extensor motorneurones. The interneurones involved are inhibited by the dorsal reticulospinal tract (DRT) that arises in the pontomedullary reticular formation. Thus, afferent stimuli, both nociceptive and non-nociceptive, from a wide variety of sources, can excite FRAs and produce a flexor withdrawal reflex. In spasticity, these are exaggerated and manifest as flexor spasms. [(a) From Benecke *et al.*, 1987; (b) from Burke, 1988.]

The corticospinal and rubrospinal tracts facilitate FRAs (Burke, 1988). Evidence from animal studies suggests that serotonergic pathways facilitate flexor reflexes (Maj *et al.*, 1985). Supraspinal centres receive input from the FRAs via ascending tracts, including the spinocerebellar pathways. Such input keeps them apprised of the state of the spinal interneuronal networks and no doubt helps in their decision as to which of the FRA actions to facilitate. The quality of the peripheral stimulus may be important, too. Gentle pressure on the cat hindfoot produces an extension response (plantar flexion) whereas a noxious pinprick evokes a flexion response (dorsiflexion) (Rothwell, 1994). When facilitated in the spinal cat, less than noxious stimuli can elicit a flexion withdrawal response. FRAs are suppressed by opiates (Schomburg & Steffens, 1998). For a detailed review of flexor reflexes, see Sandrini *et al.* (2005).

Flexor withdrawal reflexes

Electrophysiologically, the flexor withdrawal reflex in the cat has two components (Rothwell, 1994). The short-latency component has a central delay of only a few milliseconds, while the delay for the long-latency component is 30 to 50 ms. The short-latency component appears to inhibit the later one.

Flexor withdrawal reflexes can be demonstrated in man by noxious stimulation of the foot. A 10- to 20-ms train of electrical stimuli delivered to the sole at low intensity produces a short-latency response in tibialis anterior at around 50 to 60 ms. At higher stimulus intensities, a later, stronger response appears at around 110 to 140 ms. It is this late component that dorsiflexes the foot and produces the withdrawal (Shahani & Young, 1971). The earlier response acts as a priming movement. At higher stimulus intensities, the latency of both components decreases (with larger reductions in the later component) and the amplitude and duration of the responses increases (Shahani & Cros, 1990). The latency of the late response would allow time for a cortical component, but the reflex persists in total spinal cord transection, indicating its spinal origin. The situation in man is therefore similar to that in the cat. The latency of these electrically evoked reflexes suggests they are mediated by group II afferents, which conduct at around 40 m/s, and not the very slowly conducting C fibres that conduct pain sensation (Rothwell, 1994). Others have suggested the group III afferents are responsible (Roby-Brami & Bussel, 1993). In the UMN syndrome, the early component disappears (Shahani & Young, 1980) while the late component is preserved but desynchronized (Meinck *et al.*, 1985).

Meinck and colleagues investigate this reflex in detail (Meinck *et al.*, 1985) (Fig. 2.11). Tibialis anterior had the lowest threshold of all the physiological leg flexors. Tonic activation of the muscles shortened the latency of both the early and late components and eliminated the threshold differences. This suggested supraspinal modulation of the reflex. Changing stimulus characteristics could also enhance the reflex. In the UMN syndrome, they found an impaired early component, a net increase in reflex activity, desynchronization, an abnormal sensitivity to facilitation, and irradiation to muscles not normally involved. Similar findings were found irrespective of the site of the UMN lesion, spinal cord, brainstem or cerebrum. On the other hand, Shahani and Young (1980) observed electrophysiological differences in the flexor withdrawal reflexes following spinal cord transection and cerebral hemisphere lesions.

Flexor reflexes in spastic subjects can also be elicited by ankle movement (Schmidt *et al.*, 2002) and knee extension (Wu *et al.*, 2006). In animals (Harris & Clarke, 2003) and in humans (Anderson *et al.*, 2004) with spinal cord lesions, the receptive field of the flexor reflex enlarges, indicating some degree of descending control over the reflex receptive fields. In humans, this expansion occurred into areas that would normally produce ankle plantar flexion when stimulated (Anderson *et al.*, 2004).

Flexor spasms

In the UMN syndrome, patients may suffer from spasms of the legs that resemble those of the flexor withdrawal reflex. These flexor spasms may

occur in response to a variety of sensory stimuli or apparently spontaneously. Common stimuli include nociceptive (bed sores) and nonnociceptive cutaneous stimuli, visceral stimuli such as bladder or bowel distension or bladder irritation (cystitis, in-dwelling catheters). Apparently spontaneous spasms are probably due to occult stimuli (Whitlock, 1990). It is likely that flexor spasms represent disinhibited and distorted flexor withdrawal reflexes. Differences in the occurrence of flexor spasms in partial spinal, complete spinal and cerebral lesions have been discussed earlier.

Flexor spasms are clearly separate from spasticity, as defined at the beginning of this chapter. However, they often accompany spasticity, especially in spinal cord lesions, and can be painful and debilitating.

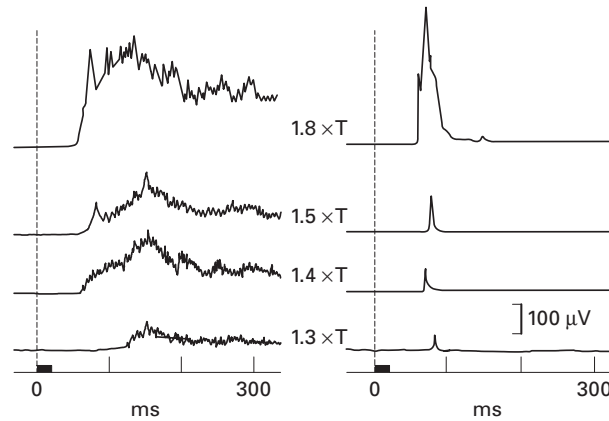

Figure 2.11. Tibialis anterior flexor withdrawal reflexes elicited in a spastic subject by medial plantar nerve stimulation. The hemiplegic side is shown on the left and the normal side on the right. As stimulus intensity is increased (expressed as a multiple of motor threshold, T), the amplitude of the reflex on both sides increases. The hemiplegic side shows an absence of the early phase until higher stimulus intensities and a prolonged late phase. Furthermore, the latency of the response from the hemiplegic side is highly dependent upon stimulus intensity, whereas the normal side is not. (From Meinck *et al.*, 1985.)

The extensor plantar response

The extensor plantar response, or Babinski sign, is discussed here following flexor spasms as it is really best considered a disinhibited flexion withdrawal reflex. Toe extension or dorsiflexion is regarded physiologically as flexion. In the spinal cat, the flexion withdrawal reflex includes dorsiflexion of the hallux in addition to the foot. Stroking the sole of an infant's foot also produces this response until the age of 1. Thereafter, this response is modified, so that the toes and ankle plantar flex while knee flexion and hip flexion are unchanged. This response still withdraws the stimulated part from the stimulus (sole) by arching the foot while maintaining contact with the ground through the toes. Such a modification is seen as an adaptation to the upright walking posture (Rothwell, 1994). In the upper motor neurone syndrome, the full flexion reflex returns with dorsiflexion of all the toes and the ankle. This is the only sign of the UMN syndrome that is unequivocally linked to the pyramidal tracts (Burke, 1988; Nathan, 1994; van Gijn, 1996).

However, Burke (1988) points out that the situation is actually quite complex. The plantar response is usually evoked by a stroke along the lateral border of the sole and over the ball of the foot, producing the normal response of toe plantar flexion. However, stimulation of the nearby base of the toes and pad of the hallux normally produces the opposite response of toe dorsiflexion. Cutaneous fields often overlap and the examiner could stray more towards this latter area. The normal plantar response would then be the product of two opposing reflexes, with the plantar-flexor reflex tending to dominate. However, should there be, in addition, contraction of the pretibial muscles (a frequent occurrence in anticipation of an unpleasant stroking of the sole), sufficient reciprocal inhibition could be produced to suppress the plantar-flexor muscles, leaving the dorsiflexor response unopposed and so the great toe dorsiflexes. The reflex response also depends upon the stimulus. Nonnociceptive sural nerve stimulation produces great toe plantar flexion, but nociceptive stimulation produces the full flexor withdrawal reflex, including dorsiflexion of the great toe.

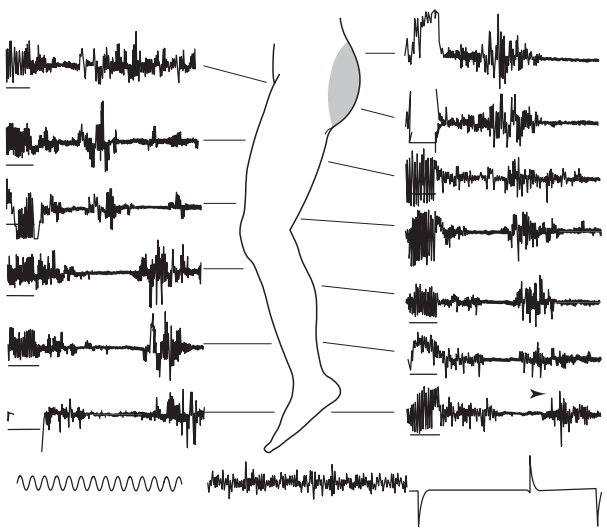

Figure 2.12. Extensor reflexes in the normal lower limb. Recordings from gluteus maximus performing a mild background contraction in response to noxious stimuli presented to the skin on different parts of the ventral and dorsal leg. Immediate strong contraction was produced by stimulation over the gluteal region, whereas most other areas produced a brief period of inhibition. (From Hagbarth, 1960.)

Thus, the direction of great toe movement when the plantar response is tested may depend upon the exact placement of the stimulus and its intensity and upon the degree of pretibial activation. Burke (1988) would view as definitely pathological an extensor plantar response from a nonnociceptive stimulus given to the midportion of the sole and would be suspicious of such a response to a nociceptive stimulus, particularly if accompanied by the typical 'triple flexion' response described earlier. Medical students are frequently under the misconception that the plantar stimulus should be painful. Furthermore, many neurologists examine with the patient sitting on the side of the bed, with the legs suspended. This can lead to a slight activation of pretibial muscles against gravity and a false-positive response.

An extensor plantar response is a flexion withdrawal response mediated by FRAs, which are facilitated by the pyramidal tracts (Lundberg & Voorhoeve, 1962). Somewhat paradoxically, the extensor plantar response is a firm sign of pyramidal tract injury, which would be expected to reduce FRA activity, not enhance it (Burke, 1988). The explanation lies in the complexity of the FRA circuits alluded to earlier, in which there may exist alternative pathways with opposing actions. The action of the pyramidal tracts on FRAs from the plantar surface is facilitation of a reflex of toe plantar flexion (physiological extension). Loss of this facilitation in a pyramidal lesion allows the alternative reflex pathway of great toe dorsiflexion to act unopposed. Despite being an exaggerated flexion reflex, the Babinski sign is not always associated with increases in other flexor reflex activity (van Gijn, 1978).

Extensor reflexes and spasms

In similar way to flexion withdrawal reflexes, nonnociceptive cutaneous stimulation in cats (Hagbarth, 1952) and man (Hagbarth, 1960; Kugelberg, 1962) can evoke extension responses in the stimulated limbs. Like flexion withdrawal reflexes, extension reflexes are protective, serving to move the area stimulated away from the stimulus. Whether a stimulus evokes a flexion or extension response is in part dependent upon the location of the stimulus. Extension responses in man may be evoked from cutaneous stimulation of such areas as the groin, buttock and posterior leg (Fig. 2.12). The 'crossed extension' component of a contralateral flexion withdrawal reflex is a form of extension reflex (see above). As already mentioned, flexion and extension reflexes are built into the spinal 'stepping generator' subserving locomotion.

Pathologically, extension responses occur in response to proprioceptive input from the hip: iliopsoas stretch (hip extension) induces hip flexion with knee extension and ankle plantarflexion in patients with spinal cord injury (Kuhn, 1950; Little, 1989; Schmidt & Benz, 2002). This matches clinical observation that going from the sitting to the supine position is a potent stimulator of extensor spasms (Kuhn, 1950). The positive support reaction, to be described,

is another extensor reflex and may be both proprioceptive and exteroceptive in nature.

Following complete spinal cord transection, patients often experience both flexor and extensor spasms, which is understandable, as both reflex pathways would be completely disinhibited by the loss of supraspinal control. Patients may, after several months, settle into a state of predominant extensor spasms (Hagbarth, 1960; Kugelberg, 1962), but paraplegia in flexion is also common. Perhaps the dominant posture is a matter of the net effect of the many afferent (exteroceptive and proprioceptive) inputs at the time. A bed sore on the heel or a urinary infection could transform paraplegia in extension into paraplegia in flexion. For reasons outlined earlier, partial spinal cord lesions tend to have fewer flexor spasms and take on a more dominant extensor tone (Barolat & Maiman, 1987).

Thus, both flexor and extensor spasms appear to be exaggerated manifestations of existing spinal reflexes (Burke, 1988) that exist for stance and locomotion. Often they are inappropriate and unwanted, but extensor spasms and an extensor posture could also be viewed as functionally advantageous by providing a rigid supporting limb for stance and gait.

Other UMN phenomena

Associated reactions

In the UMN syndrome, physical activity in one part of the body may be accompanied by unnecessary involuntary activity in another. A typical example would be the progressive elbow flexion seen in a patient with hemiparetic stroke during walking and is a familiar component of the 'hemiplegic posture'. Associated reactions can also occur with involuntary activity such as coughing, sneezing and yawning. Generally the part showing the associated reaction, the elbow flexors in the example given, are also affected by the UMN syndrome and usually display some degree of spasticity. The extent of the associated reaction seems to depend upon both the degree of motor effort (e.g. the effort of walking) and the degree of hypertonia in the limb showing the associated reaction. Thus, physiotherapists have used the associated reaction as a gauge of the patient's spasticity and overall motor function, and it has even been treated directly (Bobath, 1990). The phenomenon of associated reaction was first reported by Walshe in 1923 and has been described variously as 'released postural reactions deprived of voluntary control' (Walshe, 1923), 'synkinesia' (Bourbonnais, 1995) and 'stereotypic flexor synergy' (Bobath, 1990).

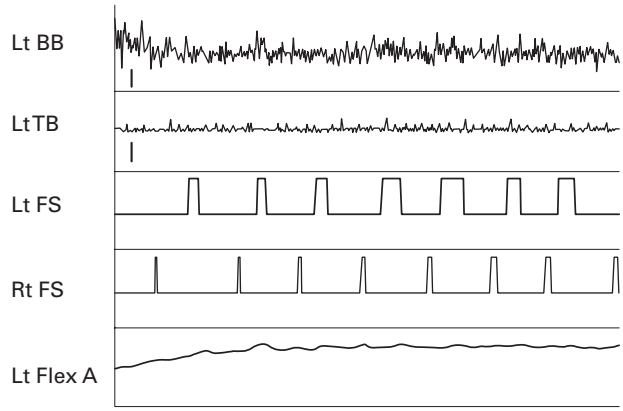

Figure 2.13. Associated reactions studied in the upper limb. A patient with a left hemiplegia exhibited progressive left elbow during gait with each successive step (time along the x-axis; total sweep about 54 seconds). Surface electromyography (EMG) was recorded from the left (Lt) biceps (BB) and triceps (TB) brachii. Traces labelled left (Lt) and right (Rt) FS represent successive footsteps. Flexion angle (Flex A) of the left elbow is shown in the bottom trace. Note increasing elbow flexion but a stable level of biceps EMG activity, indicating biomechanical factors in the elbow flexion. (From Dickstein *et al.*, 1996.)

Dickstein and colleagues (1996) have investigated the associated reaction of elbow flexion in hemiparetic subjects during walking. They found a rapid increase in elbow flexion during the first four steps and a gradual increase thereafter (Fig. 2.13). Confirming previous notions, the degree of elbow flexion correlated with the Ashworth score (Ashworth, 1964) of elbow flexor tone. However, there was a poor

correlation between the EMG activity of the elbow flexors and the degree of elbow flexion. They concluded that nonreflex soft tissue changes played an important role in this associated reaction.

Clearly though, there is also a neural component involving motoneurone activity. The mechanism of this is uncertain, but it is thought to be multifactorial (Dewald & Rymer, 1993). Dewald and Rymer (1993) concluded that enhanced flexion withdrawal reflexes probably do not play the primary role but that disturbed descending supraspinal commands may be involved. Their hypothesis is that unaffected bulbospinal motor pathways with more diffuse, polysegmental motoneurone connections may assume the role of the damaged UMN tracts in transmission of descending voluntary commands. These older bulbospinal pathways are less focussed than the pyramidal tracts. They have substantial connections to motoneurones of the axial and proximal limb musculature, which could result in the synergic patterns observed. Propriospinal pathways could also be involved. Compatible with the pattern of tone in the hemiparetic UMN syndrome, descending motor drive may favour flexors rather than extensors through increased excitability of flexor motoneurones and the interneurones of the flexor reflex pathways.

A further contributing factor could be vestibulospinal reflexes. Assumption of the upright posture, as in walking, enhances excitability of 'antigravity' motoneurones. Disinhibition of this pathway could generate sufficient descending motor drive to produce elbow flexion (and leg extension). Such a mechanism could contribute to the so-called hemiplegic posture, a form of spastic dystonia (Burke, 1988) (see 'Spastic dystonia' on p. 35). Alternatively, it could simply contribute to an increased excitability of the elbow flexor motoneurones, such that nonfocussed descending voluntary commands would favour these flexors.

Spastic co-contraction

Co-contraction refers to the simultaneous contraction of both agonist and antagonist muscles. In normal postnatal motor development, extensive co-contraction is a normal feature, associated with heteronymous, monosynaptic Ia projections from biceps to triceps and to regional synergists and antagonists (O'Sullivan *et al.*, 1998). Normally these connections become restricted to primary synergists in the 4 years of life (O'Sullivan *et al.*, 1998).

Controlled co-contraction thereafter is an important feature of normal motor function providing postural stability or fixation of a body part – for example, to stabilize the wrist when hitting a tennis ball. In these situations it is considered appropriate and functional and a manifestation of normal reciprocal innervation. Normal co-contraction is initiated and modulated as the movement demands. Co-contraction is dysfunctional when it is inappropriate or excessive and impairs agonist function, also making the agonist appear weaker than it is. Dysfunctional or pathological co-contraction is a common feature of dystonia and has been demonstrated more in cerebral palsy (Crenna, 1998) than in adult brain injury (O'Sullivan *et al.*, 1998). Furthermore, the contribution of pathological co-contraction in adult spasticity to impaired movement is controversial (Conrad *et al.*, 1985), with both protagonists (Yanagisawa & Tanaka, 1978; Corcos *et al.*, 1986; El-Abd, 1993) and antagonists (Mizrahi & Angel, 1979; Dietz *et al.*, 1981; Dietz & Berger, 1983; Fellows *et al.*, 1994; Davies *et al.*, 1996). This is particularly so for movements of the ankle, where some researchers believe that biomechanical factors may be more important (Dietz, 1981; Dietz & Berger, 1983; Becher *et al.*, 1998). These results have been challenged (Conrad *et al.*, 1985). The question of the existence and importance of co-contraction has therapeutic relevance; inappropriate antagonist contraction could be reduced focally by botulinum toxin injections (Sheean, 1998b) or phenol nerve blocks or by other antispasticity agents such as baclofen (Latash & Penn, 1996).

The pathophysiological substrate of co-contraction in dystonia is impairment of Ia reciprocal inhibition (Berardelli *et al.*, 1998) in the spinal cord. Normally, agonist Ia activity exerts an inhibitory effect on the antagonist motoneurones via an interneurone (see Fig. 2.19, p. 42). This activity

is influenced by supraspinal inputs (co-contraction is activated and deactivated at a cortical level (Humphrey & Reed, 1983) and by other segmental afferents (Delwaide & Olivier, 1987). Abnormalities of Ia reciprocal inhibition have been reported in spasticity and could contribute to co-contraction (Crone, 1994; Okuma *et al.*, 1996). Impaired spinal Ia reciprocal inhibition in dystonia probably arises from disordered supraspinal modulation and a similar mechanism in spasticity is probable. In spastic cerebral palsy the heteronymous Ia connections of infancy mentioned earlier are persistent, but this is not the case in adult hemiparesis due to stroke (O'Sullivan *et al.*, 1998). Some evidence suggests that impaired Ib reciprocal inhibition could contribute to co-contraction in the lower limb [see 'Ib Nonreciprocal (autogenic) inhibition' on p. 43]. Further discussion of reciprocal inhibition is presented below.

Co-contraction should be differentiated from a hyperactive stretch reflex in the antagonist muscle that is elicited by the lengthening produced by the agonist action. For example, active elbow extension by triceps will lengthen the biceps and may elicit a stretch response. This will appear as simultaneous contraction of both muscles but is fundamentally different to co-contraction produced by simultaneous motor drive to both muscles, a 'diffusion of descending commands' (Fellows *et al.*, 1994). Both situations could arise from similar pathophysiological mechanisms, however – that is, defects of Ia reciprocal inhibition (Delwaide & Olivier, 1987). The distinction could be made by isometric contraction of triceps that does not stretch biceps; the presence of biceps activity would indicate true co-contraction. One difficulty in interpreting isometric studies is the normal occurrence of co-contraction in isometric movements (Flanders & Cordo, 1987). Thus, in one study (Fellows *et al.*, 1994), there was no greater co-contraction of elbow flexors and extensors during isometric contractions in hemiparetic patients compared with normal controls.

Another indication that co-contraction is not a stretch reflex in an antagonist induced by agonist contraction is the appearance of antagonist contraction occurring simultaneously with or before contraction of the agonist (Fig. 2.14) during a non-isometric contraction. Finally, there are examples where the antagonist co-contraction overwhelms the agonist, producing the movement opposite of that intended (Fig. 2.15). A common clinical scenario is the patient with spastic finger flexors and weak extensors whose fingers flex more when he or she is trying to extend them.

Despite this, there is some indication that hyperactive stretch reflexes in an antagonist could interfere with movement. This is discussed further on, under 'The spastic movement disorder'.

Intact Ia reciprocal inhibition in the UMN syndrome may also cause problems. The ankle plantar flexors are frequently overactive and can inhibit the ankle dorsiflexors through preserved (Yanagisawa *et al.*, 1976) or even increased (Ashby & Wiens, 1989) Ia reciprocal inhibition, contributing to their apparent weakness and foot drop. Furthermore, local anaesthetic injections into the triceps surae to block afferent fibres led to increased strength of the ankle dorsiflexors (Yanagisawa & Tanaka, 1978). Dietz and colleagues (1981) have challenged this whole concept, however, finding minimal plantar-flexor EMG activity and *excessive* activation of ankle dorsiflexors during walking, despite a plantar-flexed posture and hypertonia at the ankle. They concluded that soft tissue changes were responsible, rather than neural causes.

Spastic dystonia

Dystonia is a condition characterized by 'sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures' (Fahn *et al.*, 1987). This definition usually refers to conditions arising from basal ganglia disorders. Patients suffering an UMN syndrome frequently adopt an abnormal posture, well known to most clinicians as the 'hemiplegic' or 'decorticate' posture. The hemiplegic posture involves flexion of the elbow, wrist and fingers with adduction of the shoulder and pronation of the forearm. The leg is extended at the hip and knee, plantar flexed and inverted at the ankle, with adduction of the hip. This may be loosely described

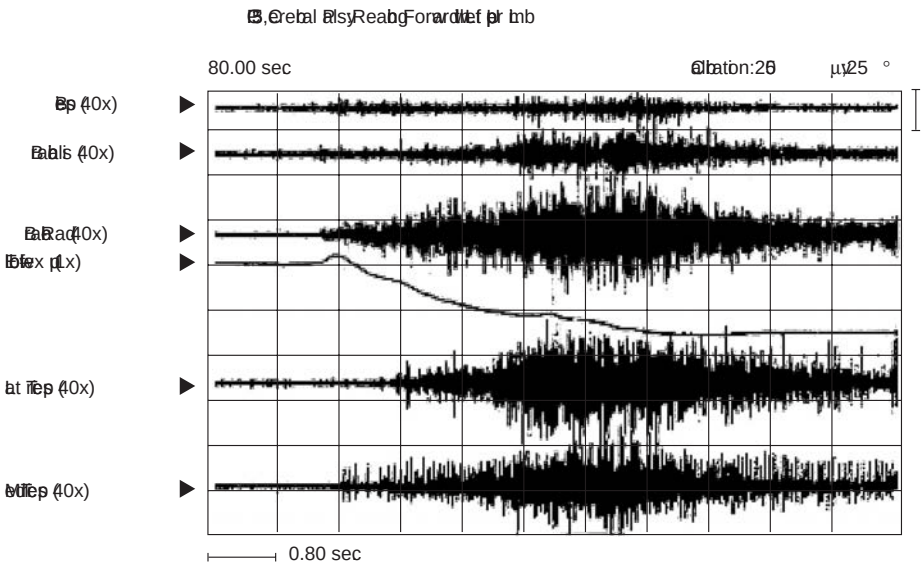

Figure 2.14. Co-contraction of elbow flexors and extensors during attempted extension. Note that EMG activity in the brachioradialis begins at the same time as the triceps, before any stretching of the elbow flexors has taken place indicating that this form of co-contraction is not a stretch reflex. (From Mayer & Herman, 2004.)

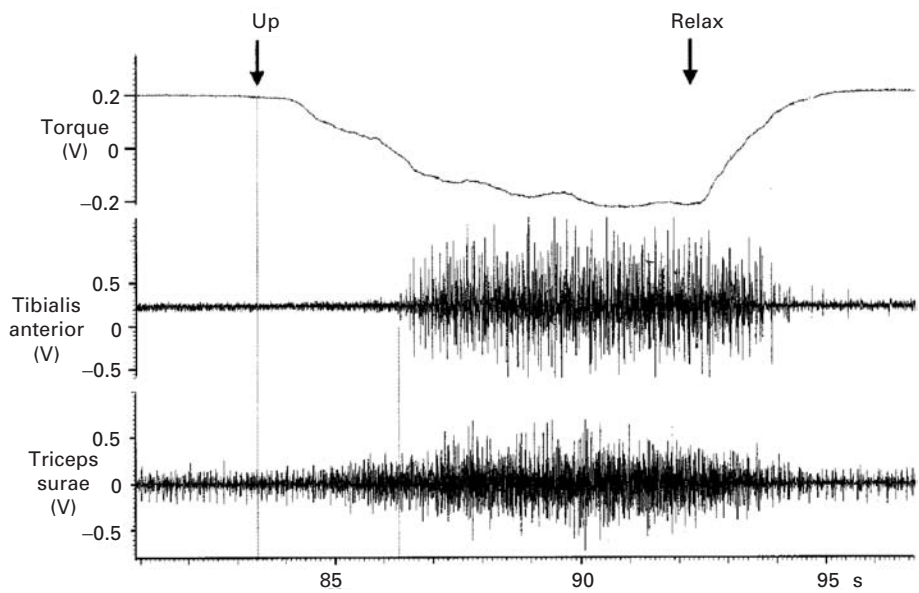

Figure 2.15. An attempt at isometric ankle dorsiflexion increases EMG activity in the ankle plantarflexors causing plantarflexion (downward torque). After a few seconds the ankle dorsiflexors are activated but are unable to overcome the ankle plantarflexors. The resting position was seated, with the hip flexed at 30 degrees and the ankle fixed at 90 degrees. The knee was fully straight, placing stretch on the gastrocnemius muscle, which probably accounts for the small amount of EMG activity in the triceps surae at rest. This shows a clear example of a misdirected descending command from dorsiflexors to plantarflexors – no stretch or other afferent input could account for this. (From Gracies, 2005.)

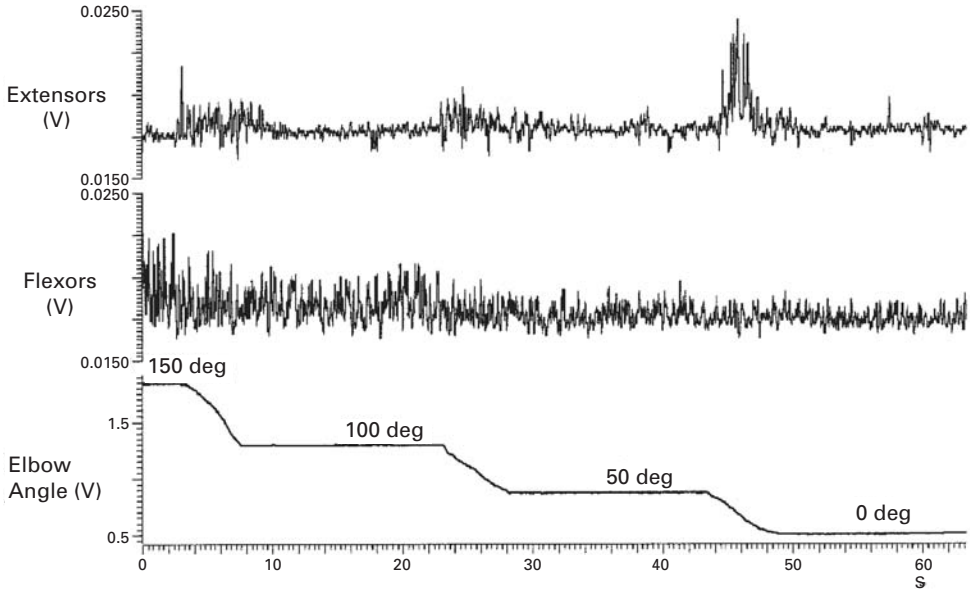

Figure 2.16. Spastic dystonia is sensitive to stretch. The figure shows the rectified EMG tracings of a hemiplegic patient. Initially, the elbow is highly flexed by the elbow flexor contraction. Stepwise extension by ramp and hold stretches were applied every 15 seconds at a rate of 10 degrees per second. Note that the EMG activity gradually decreases with each stretch. (From Gracies, 2005.)

as 'dystonia', but the term is confusing when used in the context of the UMN lesion and spasticity.

Although frequently accompanied by spasticity, the hemiplegic posture of spastic dystonia is fundamentally different. Spasticity is velocity dependent and mediated by hyperactive proprioceptive stretch reflexes. The continuous muscle contraction maintaining spastic dystonia is present without limb movement. Furthermore, it is not dependent upon afferent input from the limb, as it persists after dorsal root section (Denny-Brown, 1966). Although spastic dystonia is not dependent upon afferent input from the limb, it is affected by the degree of stretch placed on the muscle (Denny-Brown, 1966). For example, prolonged stretching can reduce spastic dystonia (Fig. 2.16), as every physiotherapist knows. The sensitivity of spasticity to stretch is well known and has already been described, including its diminuation with repeated stretching (see 'Tonic stretch reflexes' on p. 17). Spastic dystonia may arise from continuous supraspinal drive from areas disinhibited by the UMN lesion to the spinal motoneurones. In addition to stretch, spastic dystonia is altered by postural changes (Denny-Brown, 1966), presumably through vestibular mechanisms (Burke, 1988). The phenomenon of associated reactions (see above) indicates that the hemiplegic posture is also subject to other influences.

Another finding in patients with UMN syndrome is delayed relaxation after voluntary contraction caused by continued firing of motor units. Some consider this a form of spastic dystonia (Gracies, 2005). As discussed below, motoneuronal hyperexcitability, plateau potentials and repetitive firing could underliethis(see'Alpha motoneurone excitability' on p. 47).

Thus, unlike most of the other positive features of the UMN syndrome, the motor drive behind spastic dystonia is not a spinal reflex; it is *efferent* mediated rather than *afferent* mediated. This distinction

has important therapeutic implications. Spastic dystonia would not be expected to respond well to traditional antispastic therapies such as diazepam and baclofen, which suppress spinal reflex activity, or to dorsal rhizotomy, as Denny-Brown (1966) found. If plateau potentials are involved tizanidine might be effective, however (see 'Alpha motoneurone excitability'). Spastic dystonia should still respond to treatments that modify motor nerve or muscle activity, such as dantrolene, botulinum toxin, phenol injections and peripheral nerve section. It should be noted that some sustained abnormal postures in the UMN are reflex mediated, such as the continuous leg flexion of 'paraplegia in flexion' following total spinal cord section (already discussed). Soft tissue and joint pathology may also contribute to sustained abnormal postures.

Positive support reaction

This term is more commonly used by physiotherapists than physicians to describe a pattern of plantar flexion and inversion of the ankle of a patient with an UMN syndrome upon attempted weight bearing (Bobath, 1990). Others have termed this phenomenon the tonic ambulatory foot response (Manfredi *et al.*, 1975). There may be extension of the knee, producing a pattern of extensor thrust of the lower limb (Schomberg, 1990). A positive support reaction can be extremely debilitating and prevent standing and walking. It is presumed to be a reflex involving a proprioceptive stimulus elicited by stretch of the intrinsic foot muscles and an exteroceptive stimulus elicited by contact of the foot with the ground (Bobath, 1990). A similar physiological spinal extensor reflex exists in infants (Rothwell, 1994) and is normally suppressed. Analogous to the Babinski sign, this reflex is presumably disinhibited by the UMN lesion.

The supraspinal control of this reflex in humans is not known. However, a positive support reaction appeared in the cat following a lesion of the dorsolateral funiculus containing the (inhibitory) reticulospinal pathways, accompanied by spasticity (Taylor *et al.*, 1997).

Electrophysiological studies of spinal reflexes in spasticity

It is well established that spinal phasic and tonic stretch, flexor withdrawal and other reflexes are hyperexcitable in the UMN syndrome following interruption of the descending UMN pathways. However, the actual spinal circuitry responsible for the production of these effects is less well established. A number of the spinal reflex mechanisms involved in motor control, already mentioned, have been studied electrophysiologically in an attempt to understand the basis of the hyperexcitable proprioceptive reflexes and other phenomena of the UMN syndrome (Table 2.2). Most attention has been given to inhibitory mechanisms, with the expectation of finding decreased inhibition. However, excitatory mechanisms and the level of excitability of alpha motoneurones have also been examined. Flexor withdrawal reflexes, the basis of flexor spasms in the UMN syndrome, have already been discussed.

Spinal inhibitory mechanisms

The four main spinal inhibitory activities that have been studied are Ia presynaptic inhibition, Ia reciprocal inhibition, Ib nonreciprocal inhibition and Renshaw cell inhibition. Most techniques are based upon modulation of H reflexes, which are discussed briefly.

H reflexes

These were first discovered in the triceps surae by Hoffman in 1926, hence the name H reflex. Low-intensity electrical stimulation of the tibial nerve in the popliteal fossa elicits a reflex contraction of triceps surae without direct activation of the motor axons in the nerve (Fig. 2.17). By selecting appropriate stimulus parameters, the Ia afferents could be stimulated selectively. The latency of the reflex is around 30 ms. For a long time the H reflex was incorrectly thought to be equivalent to the tendon reflex (T reflex), except that the spindle is bypassed. It had considered that comparison of H- and

Table 2.2. The neurophysiology and neuropharmacology of spasticity

Spinal segmental activity	Electrophysiological test	Abnormality	Neurotransmitter	Medication effect
Ia Presynaptic inhibition	Vibratory inhibition of H reflex	Reduced	GABA(−)	Diazepam (+) baclofen (−) Tizanidine (+)
Ia Reciprocal inhibition	Conditioning of H reflex	Reduced	?Glycine (−)	Tizanidine (+)
Ib Nonreciprocal inhibition	Conditioning of H reflex	Reduced	Glycine (−)	Tizanidine (+)
Recurrent inhibition	Conditioning of H reflex	Increased and decreased		Baclofen (−)
Flexor withdrawal reflexes	Foot stimulation	Increased	Glutamate (+)	Tizanidine (−) baclofen(−) L-dopa (−)
Alpha motoneurone excitability	H_{max}/M_{max}	Increased	?	Tizanidine (−) baclofen(−)
	F wave amplitude	Increased	?	Tizanidine (−)
Other polysynaptic	H reflex recovery	Increased	EAAs	Diazepam (−) baclofen(+)
Ia excitatory	TVR	Decreased	EAA?	Diazepam(−) baclofen(−)
Group II excitatory	Long latency reflexes	Decreased and increased	EAA?	Tizanidine (−) L-dopa (−) Baclofen weak (−)

TVR: tonic vibration reflex; GABA: gamma-aminobutyric acid.

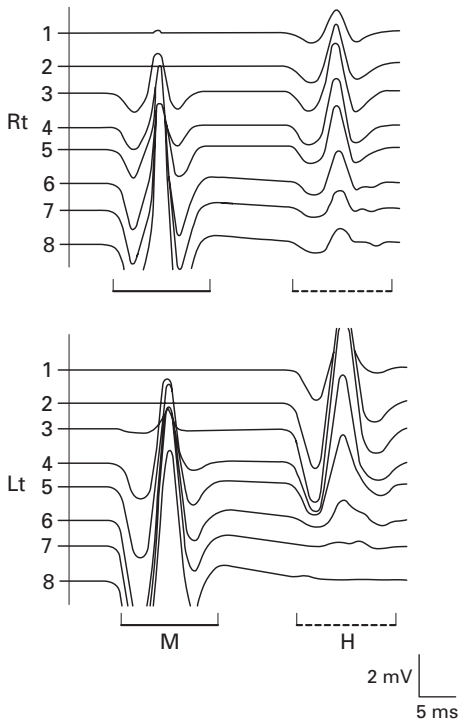

Figure 2.17. H reflexes elicited from the left and right soleus muscle of a normal subject by stimuli of increasing intensity delivered to the tibial nerve in the popliteal fossa. Note the appearance of the H reflex at around 30 ms latency before an M wave has appeared. Increasing stimulus intensity (from trace 1 to 8) results initially in an increased H-reflex amplitude, followed by a decline and replacement by an F wave. (From Kimura, 1989.)

T-reflex amplitudes would reflect muscle spindle sensitivity (and thus fusimotor drive) and that both are monosynaptic reflexes involving only Ia afferents. Burke (1985) has discussed this and several associated myths. H reflexes involve both oligo- and polysynaptic pathways (and thus interneurones) that are under supraspinal control as well as subject to other segmental influences. Thus, in addition to being a useful test in routine clinical neurophysiology, it is also a powerful tool in the study of spinal reflex pathways.

Ia Presynaptic inhibition

Collaterals of muscle spindle Ia afferents form axoaxonal synapse with the Ia afferent terminals and inhibit the release of neurotransmitter. This inhibitory activity is GABA-ergic and under supraspinal control. Presynaptic inhibition is important in normal motor control and exhibits task-dependent modulation by both CNS pattern generators and afferent feedback from the periphery (Stein, 1995). It is conceivable that reduction in presynaptic inhibition could result in increased tendon reflexes and possibly spasticity (Delwaide, 1993).

Muscle belly vibration, a potent stimulus of muscle spindle Ia afferents, elicits both excitatory and inhibitory responses. The excitatory response is contraction of the vibrated muscle, the tonic vibration reflex (see below), while tendon and H reflexes are inhibited (de Gail *et al.*, 1966) (Fig. 2.18). Vibratory inhibition of H reflexes is one of several methods available to evaluate presynaptic inhibition (Stein, 1995). Another is to examine the modulation of H or stretch reflexes during movement, thought to be effected via presynaptic. A third method is to study modulation of the soleus H reflex by a conditioning stimulus given to the ipsilateral femoral nerve (Nielsen *et al.*, 1995), which facilitates the reflex, or by a tap of the biceps femoris tendon, which inhibits the soleus H reflex: both act through presynaptic facilitation or inhibition of Ia afferents (Nielsen *et al.*, 1995).

Vibratory inhibition of H reflexes is reduced in spastic subjects (Burke & Ashby, 1972; Calancie *et al.*, 1993; Milanov, 1994) and task-dependent modulation is impaired (Schieppati *et al.*, 1985; Iles & Roberts, 1986; Yang *et al.*, 1991a; Boorman *et al.*, 1992; Toft *et al.*, 1993; Stein, 1995; Sinkjaer *et al.*, 1996). In spastic patients with multiple sclerosis, presynaptic facilitation by femoral nerve stimulation was increased and inhibition by biceps tendon tap was decreased (Nielsen *et al.*, 1995). Later, this same group would find that femoral nerve facilitation was decreased less in the spastic subjects at the onset of ankle dorsiflexion and increased less at the onset of ankle plantaflexion (Morita *et al.*,

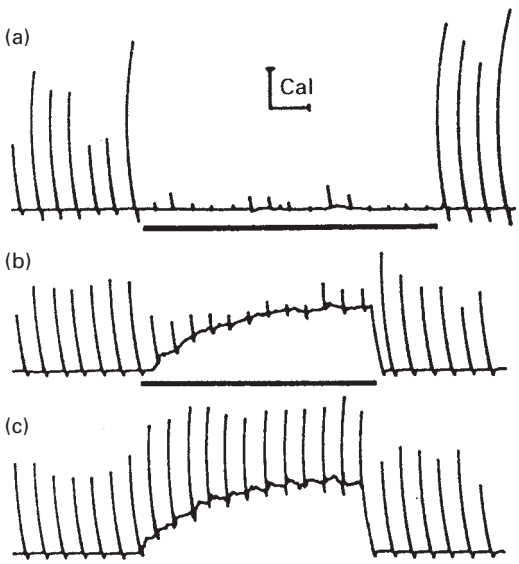

Figure 2.18. The tonic vibration reflex (TVR) and suppression of knee jerks by vibration in the human quadriceps. Knee jerks are elicited every 5 seconds and are depressed during the vibration of the muscle (black bar) both with (a) and without (b) the development of a TVR. In (c), the subject is mimicking a TVR with voluntary contraction but knee jerks are not inhibited. Vibration is a powerful stimulus of primary muscle spindle endings. This phenomenon illustrates the apparently paradoxical combination of simultaneous motorneurone excitation (TVR) and inhibition (knee-jerk suppression) by Ia afferent activity. Calibration: vertical 0.4 kg for (a), 0.6 kg for (b) and (c); horizontal 10 seconds. (From de Gail *et al.*, 1966.)

2001). There may be differences in presynaptic inhibition between spasticity of spinal and cerebral origins (Faist *et al.*, 1994). The effect of afferent feedback from the periphery on presynaptic inhibition is revealed by the prolonged reduction of vibratory inhibition and spasticity by transcutaneous electrical nerve stimulation (TENS) (Levin & Hui-Chan, 1992).

So, there is good evidence of impaired Ia presynaptic inhibition in spastic limbs, but is this major contributor to spasticity? Some weak correlation with the degree of spasticity measured clinically by the Ashworth scale (Ashworth, 1964) has been found by some (Harburn *et al.*, 1995), but not by others (Faist *et al.*, 1994). A better correlation exists between reduced presynaptic inhibition and tendon hyperreflexia (Delwaide & Pennisi, 1994). Yang *et al.* (1991a) found marked variability in the degree of impaired H-reflex modulation, a function of presynaptic inhibition, during walking among spastic spinal patients, and the degree of impaired modulation seemed poorly related to the severity of difficulty walking. Presynaptic inhibition is also reduced in Parkinson's disease (Roberts *et al.*, 1994; Hayashi *et al.*, 1997), a condition characterized by rigidity rather than spasticity; hence, additional factors must be operating to produce the spastic state.

Indirect evidence also suggests a role for impaired presynaptic inhibition in spasticity. Increased vibratory inhibition is a feature of 'spinal shock', suggesting increased presynaptic inhibition followed by spasticity and reduced presynaptic inhibition (Calancie *et al.*, 1993). The clinical antispastic effects of diazepam (Verrier *et al.*, 1975; Delwaide, 1985a), baclofen (Milanov, 1992), tizanidine (Milanov & Georgiev, 1994; Delwaide & Pennisi, 1994), clonidine (Nance *et al.*, 1989), TRH (Morin *et al.*, 1988) and TENS (Levin & Hui-Chan, 1992) are accompanied by improvements in measures of presynaptic inhibition. Because tizanidine reduces presynaptic inhibition (Delwaide & Pennisi, 1994; Milanov & Georgiev, 1994), clonus was expectedly reduced in one study (Delwaide & Pennisi, 1994), but tendon reflexes were unchanged in another (Milanov & Georgiev, 1994). This discrepancy casts some doubt upon the conclusion presented earlier that impaired presynaptic inhibition correlates better with tendon hyperreflexia than with muscle hypertonia.

The supraspinal control of presynaptic inhibition is unclear. Studies in humans using transcranial magnetic stimulation reveal conflicting results in the lower limb, indicating both facilitation (Meunier & Pierrot-Deseilligny, 1998) and depression (Valls-Sole *et al.*, 1994; Iles, 1996) of presynaptic inhibition by the corticospinal tracts. Vestibulospinal connections to interneurones mediating presynaptic inhibition are also known (Iles & Pisini, 1992) and might partly explain the modulation of presynaptic inhibition

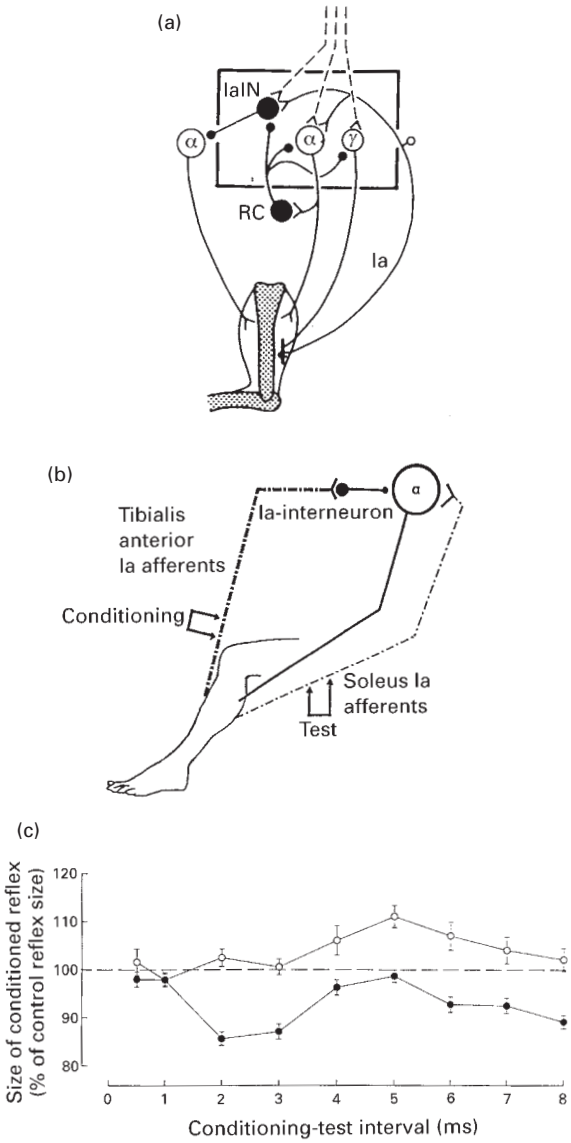

Figure 2.19. Reciprocal inhibition. (a) Illustrates the spinal circuitry of Ia reciprocal inhibition between agonist and antagonist muscles and the involvement of Renshaw cells and supraspinal connections. (b) Experimental technique for studying reciprocal inhibition in the lower limb. A conditioning shock is given to the peroneal nerve (from tibialis anterior) and the effect on the tibial nerve H reflex from soleus is observed for different time intervals between the two stimuli. (c) Responses in normal (closed circles) and spastic patients (open circles). The normal subjects demonstrate an early (1 to 4 ms), and a late period inhibition (6 to 8 ms) that is absent in spastic patients and replaced by facilitation. [(a) From Hultborn *et al.*, 1979; (b) and (c) from Crone *et al.*, 1994.]

with changes in body position; presynaptic inhibition is normally reduced when going from supine to standing (Mynark *et al.*, 1997). For a detailed review of presynaptic inhibition, see Rudomin and Schmidt (1999).

Ia Reciprocal inhibition

The Ia afferents of an agonist muscle inhibit, via Ia interneurones, the alpha motoneurones of its antagonist (Fig. 2.19). The Ia inhibitory interneurone receives both segmental (including Renshaw cells) and supraspinal afferents, including facilitation from corticospinal fibres (Delwaide, 1993). Ia reciprocal inhibition is readily studied in upper and lower limb muscles. One method (Fig. 2.19) involves threshold conditioning electrical stimuli that are applied to the nerve supplying antagonist muscles (e.g. peroneal nerve at the knee innervating ankle dorsiflexors) while observing the effect on the H reflex obtained from the agonists (ankle plantarflexors). Two main inhibitory effects are seen, distinguished by timing. The first is a short-latency, short-duration inhibition attributed to disynaptic mechanisms, and the second is a later, long-lasting inhibition attributed to presynaptic mechanisms.

Abnormalities have been reported in the early, disynaptic phase of inhibition in spasticity involving the lower (Crone *et al.*, 1994; Okuma *et al.*, 1996) and upper limbs (Nakashima *et al.*, 1989; Artieda *et al.*, 1991; Panizza *et al.*, 1995). Okuma and colleagues (1996) report reduced disynaptic inhibition by the ankle dorsiflexors on the plantarflexors in some hemiplegic patients with marked plantarflexor (extensor) spasticity, but they found normal results in others. Patients with only mild spasticity actually had *increased* inhibition and patients with improving spasticity studied serially showed increasing

inhibition. Crone and colleagues (1994) studied the lower limbs of patients with multiple sclerosis (MS) and found that most often the disynaptic phase of inhibition was abolished and in some cases replaced by a facilitatory phase of slightly longer latency (Fig. 2.19). Yaganisawa and Tanaka (1978) studied patients with both capsular and spinal lesions and also found impairment of reciprocal inhibition from ankle dorsiflexors to plantarflexors but preserved and strong reciprocal inhibition in the reverse direction. The late inhibitory phase is less well studied, but impairment has also been reported in human spasticity (Nakashima *et al.*, 1989; Artieda *et al.*, 1991; Panizza *et al.*, 1995) that is less well correlated with the presence of spasticity (Okuma *et al.*, 1996).

In contrast, Boorman and colleagues (1991) found weak inhibition of the soleus H reflexes in patients with spinal cord lesions that was not present in normal controls. Studies of cats subjected to spinal hemisection reveal *greater* facilitation of this reflex on the side of the lesion (Hultborn & Malmsten, 1983). Methodological factors may underlie the different results.

Impaired Ia reciprocal inhibition has been implicated in the abnormal co-contraction of the UMN syndrome. However, a potential criticism of the reflex studies cited so far is that they were performed at rest and therefore did not mimic the clinical situation where co-contraction occurs during voluntary movement. Boorman and colleagues (1996) studied 'natural reciprocal inhibition' by observing the inhibitory effect of voluntary ankle dorsiflexion on the soleus H reflex in spastic patients with incomplete spinal cord lesions. Reciprocal inhibition was impaired and correlated with the degree of co-contraction. Morita and colleagues (2001) found similar results in spastic MS patients and also that disynaptic Ia reciprocal inhibition failed to occur during active (isometric) dorsiflexion.

Thus, abnormalities of Ia reciprocal inhibition may contribute to co-contraction of agonist and antagonist muscle pairs and possibly impaired voluntary activation, but its role in the production of spasticity is unclear. This is partially so because spasticity is a sign elicited by passive stretch of muscles at rest so that the antagonist pair of the stretched muscle should be relaxed and therefore not providing any stimulus for reciprocal inhibition. Nonetheless, some correlation has been found between the degree of impaired reciprocal inhibition and the severity of clinical spasticity in the upper limbs (Panizza *et al.*, 1995).

Ib Nonreciprocal (autogenic) inhibition

Golgi tendon organs give rise to Ib afferents that project to inhibitory interneurones (Ib interneurones), which in turn exert an inhibitory effect on extensor and a facilitatory effect on flexor motoneurones (Delwaide, 1993). Like most spinal interneurones, the Ib interneurones receive input from descending spinal pathways as well as segmental afferents. The corticospinal tract may facilitate and the dorsal reticulospinal tract may inhibit this reflex activity (Fine *et al.*, 1998). Impaired Ib nonreciprocal inhibition contributes to extensor hypertonia decerebrate rigidity in the cat (Eccles & Lundberg, 1959); it was, therefore, postulated that it may play a similar role in the UMN syndrome in man.

A method to study Ib nonreciprocal inhibition was devised by Pierrot-Deseilligny (Pierrot-Deseilligny *et al.*, 1981). Stimulation of the medial gastrocnemius group I afferents inhibits the soleus H reflex, an effect thought to be mediated by Ib nonreciprocal inhibition (Fig. 2.20). Delwaide found that this inhibitory reflex activity was essentially absent on the hemiplegic side of spastic patients and replaced by facilitation (Fig. 2.20a and b) (Delwaide & Olivier, 1988). In contrast, Ib inhibition was found to be normal in patients with spinal cord lesions (Fig. 2.20c) (Downes *et al.*, 1995), suggesting there may be pathophysiological differences between spinal and cerebral spasticity.

The studies mentioned were performed at rest. Morita and colleagues (2006) studied Ib nonreciprocal inhibition in patients with spasticity from cervical myelopathy. At rest, there was no difference between the patients and the normal subjects. However, inhibition increased less in the patients during active tonic dorsiflexion (antagonist contraction)

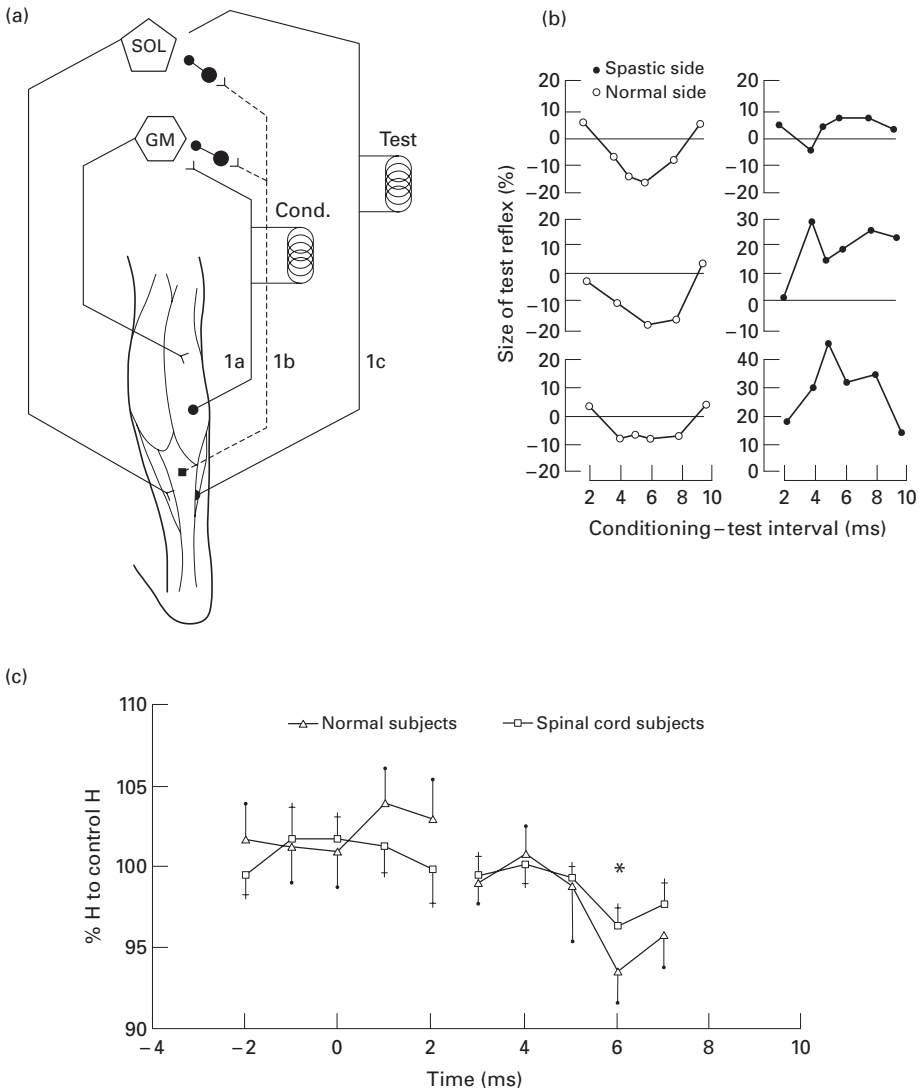

Figure 2.20. Ib Nonreciprocal inhibition. (a) Technique after Pierrot-Deseilligny *et al.* (1981). Conditioning stimulus given to the nerve to medial gastrocnemius (GM) and the test stimulus to the tibial nerve at varying interstimulus intervals, recording the H reflex from soleus (SOL). (b) The soleus H reflex in three hemiplegic subjects (normal side shown on left, spastic on right of diagram, average of 20 responses). The H reflex is modulated on the normal side with an initial period of facilitation followed by a period of inhibition. On the spastic hemiplegic side, there is little or no inhibition but rather facilitation. (c) In contrast, results of Ib nonreciprocal inhibition in the soleus H reflex of normal (diamond symbol) and spastic (square symbol) subjects with spinal cord lesions. The spastic subjects showed an impairment of inhibition at the six-test interval similar to that of normal controls. [(a) and (b) from Delwaide & Oliver, 1988; (c) from Downes et al., 1995.]

and in correlation with the severity of the spastic gait as measured by the timed 10-m walk.

Although this last study by Morita *et al.* (2006) indicates central impairment of the modulation of Ib inhibition during contraction, testing was performed with the subject seated. Ib inhibition is diminished during walking in normal human subjects, similar to the cat, where inhibition is replaced by excitation (Stephens & Yang, 1996). These changes with walking would serve to increase activity in the antigravity muscles. Ib inhibition during walking has not yet been investigated in spastic patients, but as Ib inhibition is already reduced at rest, further reduction during walking could account for the increased extensor activity observed. At the very least, the observations of Morita and colleagues (2006) suggest that impairment of Ib inhibition could contribute to spastic co-contraction.

Ib nonreciprocal inhibition is reduced by nociceptive discharges from muscle (Rossi *et al.*, 1997). This might explain why noxious limb lesions, like a painful in-grown toenail, sometimes produce increased extensor spasticity, rather than flexor spasms.

Interestingly, abnormalities of Ib nonreciprocal inhibition have also been observed in the rigidity syndromes of Parkinson's disease (Delwaide *et al.*, 1991) and progressive supranuclear palsy (Fine *et al.*, 1998). Despite good correlation between impaired Ib inhibition at rest and clinical hypertonia in the UMN syndrome (Delwaide & Pennisi, 1994), other factors must be operating, as there is no spasticity in these syndromes. There is some indirect evidence that the Ib inhibition interneurones are not glycinergic (Floeter *et al.*, 1996).

Recurrent (Renshaw) inhibition

Renshaw cells are spinal interneurones that are activated by a collateral of the alpha motoneurone axon. They inhibit not only the homologous motoneurone from which they receive the collateral (recurrent inhibition) but also its paired gamma motoneurone and the Ia inhibitory interneurones that mediate reciprocal inhibition of antagonist motoneurones (Fig. 2.21). Thus, Renshaw cells provide negative feedback on agonist motoneurones and facilitate (disinhibit) antagonist motoneurones. Similar to other spinal reflexes, Renshaw cell activity, or recurrent inhibition, may be studied electrophysiologically by an H-reflex conditioning technique (Bussel & Pierrot-Deseilligny, 1977). Like most spinal interneurones, Renshaw cell activity is influenced by descending motor pathways as demonstrated by changes in recurrent inhibition during voluntary or postural movements (Rossi *et al.*, 1992). The reticulospinal pathways may exert a tonic facilitatory effect and themselves receive branches from the corticospinal tracts (Mazzocchio & Rossi, 1997). There are also vestibular inputs (Rossi & Mazzocchio, 1988). The coerulospinal tracts have direct contacts onto Renshaw cells and inhibit recurrent inhibition (Fung *et al.*, 1988). Renshaw cells are thus important modulators of motoneurone excitability, and diminished recurrent inhibition could contribute to reflex hyperexcitability in the UMN syndrome. The modulation by vestibular input suggests a possible role in the changes in reflex activity associated with posture in the UMN syndrome.

It was therefore surprising to find *increased* recurrent inhibition at rest in chronic spinal cats (Hultborn & Malmsten, 1983). Recurrent inhibition is also increased in humans with spasticity from spinal lesions (Mazzocchio & Rossi, 1989; Shefner *et al.*, 1992) and there is some correlation with the degree of clinical spasticity (Shefner *et al.*, 1992). Patients showing improvement in spasticity were associated with decreases in recurrent inhibition towards normal (Shefner *et al.*, 1992). Interestingly, in one study, only those with hereditary spastic paraparesis and spinal cord transection showed reduced recurrent inhibition; two out of three patients with spastic paraparesis due to cord compression were normal (Mazzocchio & Rossi, 1989). Recurrent inhibition is reportedly normal at rest in hemiplegic patients (Katz & Pierrot-Deseilligny, 1982) but reduced in patients with amyotrophic lateral sclerosis (ALS) and spasticity (Fig. 2.21) (Raynor & Shefner, 1994). In the ALS patients, there was a correlation between impairment of recurrent inhibition and the Achilles tendon reflex. In a mixed group of spastic patients with spinal and cerebral lesions, recurrent inhibition

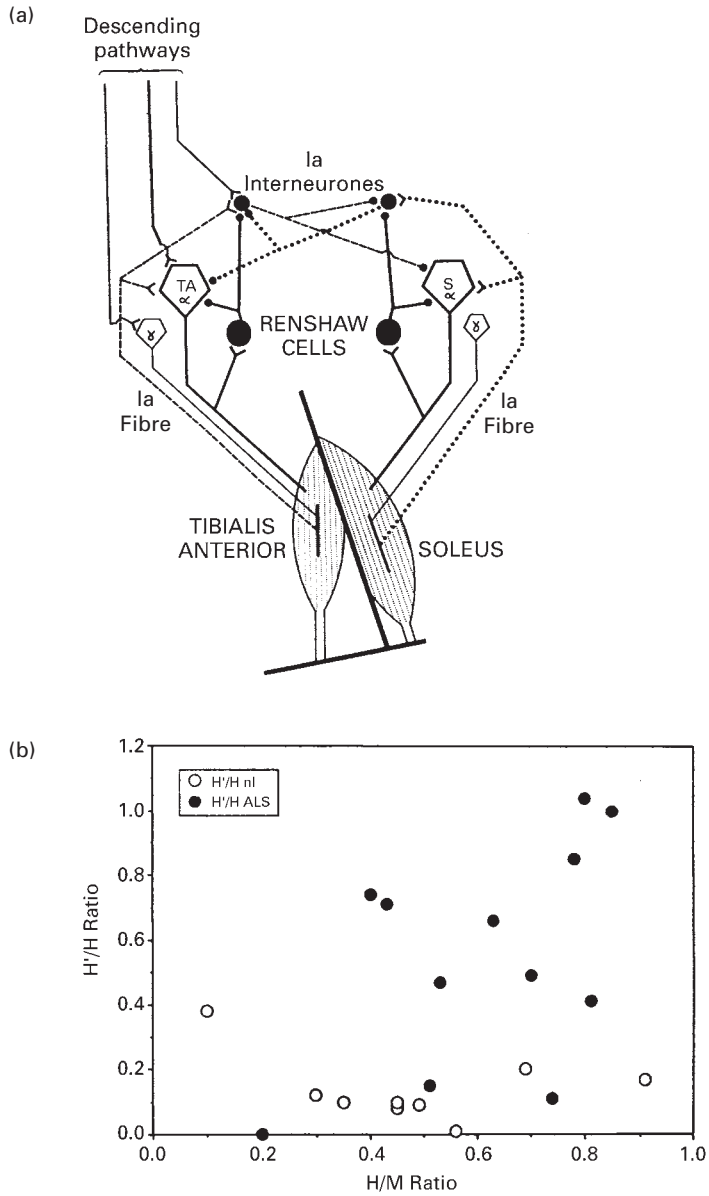

Figure 2.21. Renshaw cell recurrent inhibition. (a) Renshaw cells provide negative feedback on their alpha motorneurone partner and the Ia inhibitory interneurone mediating reciprocal inhibition of the antagonist muscle. (b) Recurrent inhibition studied in patients with amyotrophic lateral sclerosis (ALS)(closed circles) and spasticity and in normal (nl) subjects (open circles). Generally elevated H′/H ratios in the patient group indicates reduced recurrent inhibition. (From Raynor & Shefner, 1994.)

was found to be normal in half the patients and reduced or absent in the other half (Mazzocchio & Rossi, 1997). Thus, recurrent inhibition in the UMN syndrome is variable and again, the abnormalities of spinal physiology associated with spasticity may depend upon the type and location of the lesion causing the UMN syndrome.

Some of the spastic paraparetic patients studied by Mazzocchio and Rossi (1989) failed to modulate recurrent inhibition during voluntary contraction of soleus. This subgroup included subjects with both normal and reduced Renshaw cell activity at rest. Katz and Pierrot-Deseilligny (1982) also found impairment of the normal modulation during voluntary contraction but slightly increased recurrent inhibition at rest. This finding suggests that separate descending motor pathways may modulate recurrent inhibition at rest and during voluntary activity. Mentally retarded patients without spasticity but with rigidity or other movement disorders also showed failure of supraspinal modulation of recurrent inhibition (Rossi *et al.*, 1992). This could suggest that the descending motor pathways that were disordered in those subjects are different than those responsible for spasticity.

The role that abnormal recurrent inhibition plays in the hyperexcitability of stretch reflexes and production of spasticity is therefore uncertain. Disordered recurrent inhibition might, however, contribute to disturbed movement synergies seen in the UMN syndrome (Mazzocchio & Rossi, 1997). Disturbed Renshaw activity could also lead to dysfunction of other spinal reflex circuits. A lesion of the facilitatory reticulospinal tracts could make Renshaw cells less sensitive to other supraspinal influences, which could result in increased Ia reciprocal inhibition (Mazzocchio & Rossi, 1997). Generally though, Ia reciprocal inhibition is reduced in spasticity (see above).

Excitatory spinal activity

Alpha motoneurone excitability

If following an UMN lesion, the alpha motoneurones became intrinsically more excitable as a result of a change in their biophysical properties, their response to afferent stimuli might be greater. This could account for motor overactivity that characterises the positive features of the UMN syndrome, such as hyperexcitable spinal reflexes and the 'efferent' mediated phenomena.

Earlier studies of spinal cats had generally not supported this hypothesis (Delwaide, 1993). However, some work on motoneurone membrane properties has reinvigorated the idea. Alpha motoneurones have the property of bistability, the ability to fire stably at two different frequencies and to jump between the two states. Long-lasting periods of increased motoneurone excitability, called plateau potentials, are thought to be responsible for bistability and are generated by persistent inward currents (PICs) (Fig. 2.22). PICs are depolarizing currents generated by voltage-gated calcium and sodium channels that are long lasting (noninactivating). Most are generated in the dendrites of the motoneurones. Plateau potentials can produce a state of self-sustained repetitive firing of a motoneurone unless firing is blocked. Plateau potentials can be initiated and terminated by short-lasting synaptic excitation and inhibition respectively and are dependent upon activity in descending noradrenergic and serotonergic systems.

Plateau potentials have been recorded in chronic spinal cats (Eken *et al.*, 1989). The possible role of plateau potentials in spasticity has been discussed elsewhere (Nielsen & Hultborn, 1993; Heckman *et al.*, 2005) and are summarized here. Studies of rats with acute spinal cord lesions initially develop a state of spinal shock in which there is profound reduction of PICs and of motor neurone excitability resulting from loss of supraspinal monoaminergic input. Motorneurones lose the capacity to generate plateau potentials and for repetitive firing. After 1 month, the motorneurone recovers and is capable of generating large PICs, plateau potentials and repetitive firing, and is hyperexcitable. Responses to afferent input are exaggerated so that even low-threshold afferent inputs, especially cutaneous ones, are capable of triggering muscle spasms, in part because, after spinal injury, they generate unusually long pEPSPs (Li *et al.*, 2004). Ordinarily, these low-threshold

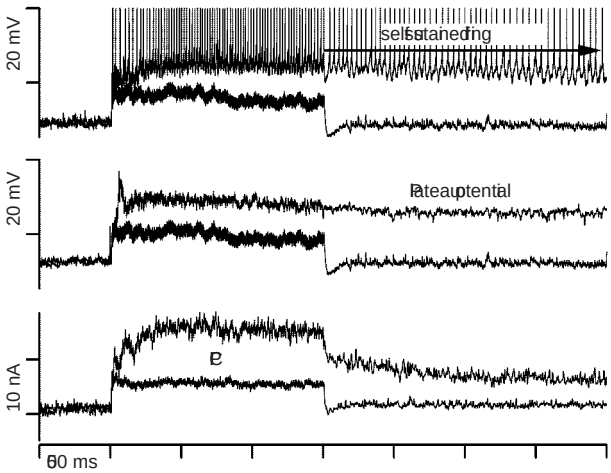

Figure 2.22. Persistent currents facilitated by descending monoaminergic inputs can generate plateau potentials and self-sustained firing in motorneurones. In each panel, the upper trace is taken while the cell is held hyperpolarized and indicates the time course of the applied synaptic input, and the lower trace is taken at more depolarized levels where the PIC can be activated (though shifted to line up with the upper trace). This ionotropic, monosynaptic excitatory input was generated by sustained activation of muscle spindle Ia afferents by tendon vibration. Lower panel: the synaptic input activates a strong persistent inward current (PIC) when the cell is voltage-clamped at a level where spikes are generated in unclamped conditions. Middel panel: In current clamp when spikes are blocked (here by intracellular injection of QX-314), the PIC generates a sustained plateau potential. Upper panel: When the cell is allowed to fire normally, the PIC drives self-sustained firing of the motorneurone. (From Heckman *et al.*, 2005.)

afferent inputs are too short to generate persistent inward currents. The spasms provoked can be terminated by blocking the PICs with hyperpolarization, which does not inhibit synaptic input, thus demonstrating that the PICs are the main cause of the prolonged spasms (Fig. 2.23), not the long duration pEPSPs, which is only the trigger. In this animal model of spasticity, baclofen blocks spinal reflexes but does so without effect on PICs, confirming that its action is presynaptic and suggesting that this model may

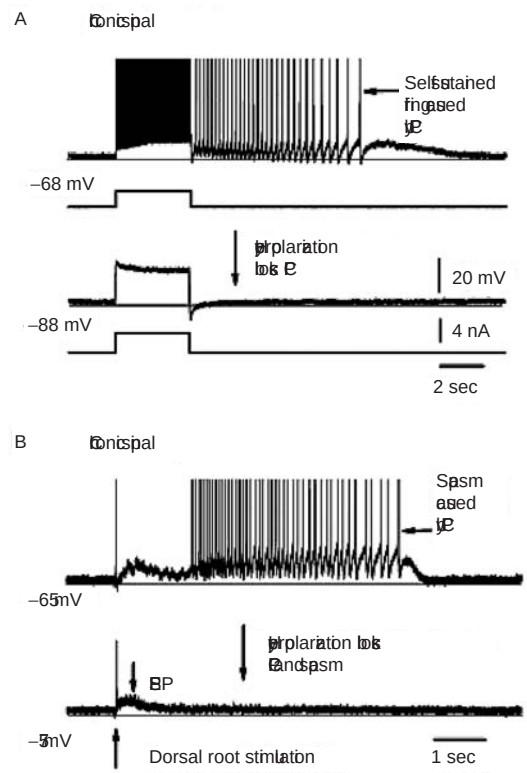

Figure 2.23. Self-sustained firing and spasm-like activity induced by PICs in a motorneurone of a chronic spinal rat. (A) Motorneurone in chronic spinal rat (2 months postinjury) with a plateau and self-sustained firing triggered by a short current injection. Hyperpolarization blocks the voltage-gated PICs and associated self-sustained firing (lower trace). (B) Dorsal root stimulation (2x threshold) evokes a long-lasting reflex discharge (spasm) in the same motorneurone. This many seconds long spasm is entirely produced by the PIC, because a block of the PIC with hyperpolarization (lower trace) reveals that the synaptic input to the motorneurone (EPSP) lasts for only half a second. (From Heckman *et al.*, 2005, adapted from Li *et al.*, 2004b.)

be a suitable one in which to study drugs destined to treat human spasticity (Li *et al.*, 2004).

It seems, therefore, that in this animal spinal model of spasticity, intrinsic motoneurone hyperexcitability may play a role in spasticity, deep tendon hyperreflexia, clonus and spasms. But PICs

and plateau potentials are difficult to study directly in humans. Some indirect evidence suggests that plateau potentials might exist in humans with spinal cord injury and contribute to muscle spasms (Nickolls *et al.*, 2004). The slow, low variability motor unit firing rate of muscle spasms in spinal cord spastic patients is compatible with motoneurone PICs (Gorassini, 1974). Recently, temporal summation that is reminiscent of the wind-up phenomenon observed in rat PICs has been observed in the tonic stretch reflexes of ankle plantar flexors in patients with spinal cord injury (Hornby, *et al.*, 2006).

The two main measures of alpha motoneurone excitability studied in humans are F-wave amplitudes and persistence, and H-reflex amplitudes (often expressed as a ratio of the maximum M wave, the Hmax/Mmax ratio). The F wave represents the recurrent discharge of a small percentage of the motoneurone pool activated antidromically by electrical stimulation of a motor nerve. The reproducibility of the H/M ratio has been demonstrated (Levin & Hui-Chan, 1993). Studies of both F waves (Schiller & Stalberg, 1978; Eisen & Odusote, 1979; Uncini *et al.*, 1990; Bischoff *et al.*, 1992; Milanov, 1994) and the Hmax/Mmax ratio (Shemesh *et al.*, 1977; Little & Halar, 1985; Ongerboer de Visser *et al.*, 1989; Koelman *et al.*, 1993) have indicated increased alpha motoneurone excitability in spasticity. However, these indirect means of evaluating alpha motoneurone excitability do not readily distinguish intrinsic motoneurone excitability and the effect of altered synaptic inputs (net increase in excitation) and the results are likely to reflect the latter (Delwaide, 1993; Milanov, 1994).

If PICs and plateau potentials do contribute to human spastic motor overactivity, medications that interfere with the monoaminergic input that is critical for their existence, such as noradrenergic (tizanidine) and serotinergic blockers, might be effective.

Excitatory interneurone hyperexcitability

Both Ia and group II afferents have excitatory polysynaptic connections to the alpha motoneurones that have been studied in spasticity (Delwaide & Olivier, 1987).

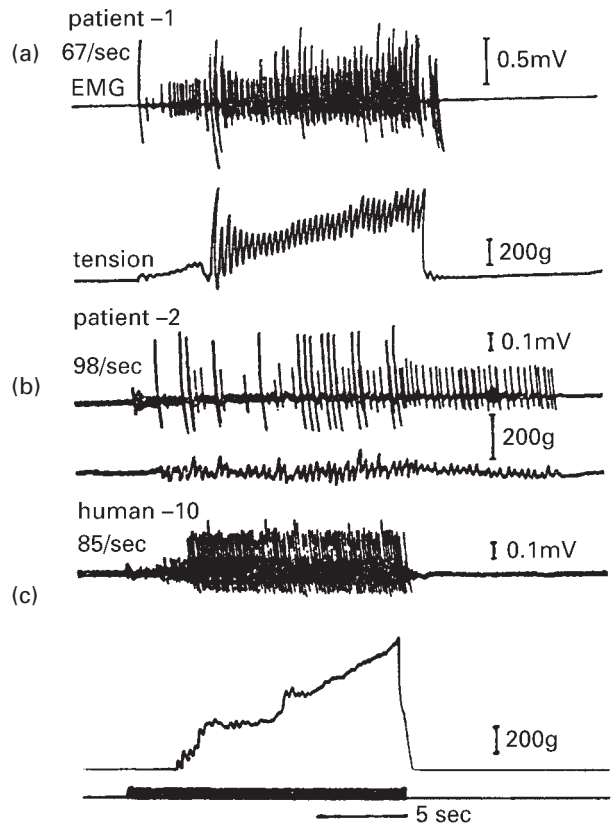

Figure 2.24. Tonic vibration reflexes (TVRs) in spasticity. Electromyographic (EMG) recorded from wire electrodes in the quadriceps muscles while force is measured during a period of vibration (black bar). (a) The well-preserved TVR of a spastic subject demonstrating vibratory clonus. (b) An impaired TVR in a spastic subject showing only vibratory clonus. (c) TVR of a normal subject, note no vibratory clonus. (From Kanda *et al.*, 1973.)

Ia Polysynaptic excitatory pathways

Sustained high-frequency vibration of a relaxed muscle produces a slowly rising contraction, known as a tonic vibration reflex (TVR), which gradually declines after the cessation of the vibration (Fig. 2.24) (Delwaide & Olivier, 1987). Vibration is a potent stimulus

of muscle spindles and the reflex is believed to involve polysynaptic Ia afferent pathways. This pathway receives supraspinal facilitation originating in the brainstem, based on its persistence in the decerebrate cat and abolition by cervical cord section (Matthews, 1972). The TVR is present in man but rather than being exaggerated, is impaired in spastic patients (Fig. 2.24b) (Hagbarth & Eklund, 1966; Kanda *et al.*, 1973; Dimitrijevic *et al.*, 1977). There may be superimposed vibratory clonus (Kanda *et al.*, 1973). It would seem then that the Ia polysynaptic excitatory pathways play no role in the production of spasticity. However, the TVR has some value in spasticity. The antispasticity agents diazepam (Verrier *et al.*, 1977) and baclofen (McLellan, 1973) suppress the TVR, which can therefore act as a nonspecific gauge of the effect of these medications on polysynaptic reflexes.

Group II polysynaptic excitatory pathways

The role of group II muscle spindle afferents, as one of the FRAs in the polysynaptic flexor withdrawal reflex, has already been mentioned. It had been assumed, therefore, that because the FRAs facilitate flexors and inhibit extensors, muscle spindle group II afferents would not be important in spasticity of the extensors. However, these afferents from the extensors were later discovered to excitatory (Matthews, 1972) and were postulated to contribute to the M2 phase of the stretch reflex (Matthews, 1984), also known as the long-latency stretch reflex. A small stretch applied to a tonically contracting muscle produces a short-latency response (SLR), a medium-latency response (MLR) and a longer-latency response (LLR). It has now been established that group II afferents contribute to the MLR (Nardone & Scieppati, 2005). In animal models (the decerebrate cat), group II spindle afferents appear to be involved in the enhanced extensor stretch reflexes (McGrath & Matthews, 1973; Kanda & Rymer, 1977; Pierrot-Deseilligny & Mazieres, 1985). Furthermore, group II afferents in the decerebrate cat demonstrate cat demonstrate both length- and velocity-dependent firing and the same interaction between the length and velocity that primary muscle spindles show (Houk *et al.*, 1981).

Thus, it is reasonable to suppose that group II afferents could play a role in the hyperexcitable dynamic stretch reflexes of human spasticity. As mentioned earlier, pharmacophysiological studies involving L-dopa (Erikkson *et al.*, 1996), tizanidine (Skoog, 1996) and, to a lesser extent, baclofen (Skoog, 1996) support the idea (see 'Static tonic stretch reflex' on p. 21). There is electrophysiological support as well. Nardone and Schieppati (2005) studied short and medium latency stretch reflexes from the soleus in standing, post-stroke hemiplegic patients, before and after applying vibration to the Achilles tendon. Before vibration, there were no differences between patients and controls. After vibration there was a dramatic increase in the MLR in patients but no change in the controls. The SLR increased in both groups, more so in the patients. Only the increase in the MLR correlated with hypertonia of the ankle plantar flexors, as measured by the modified Ashworth score. This provides a strong argument for the role of group II afferents in spasticity.

Group II afferents have also been studied by examining the effects of a conditioning stimulation of the common peroneal nerve on the quadriceps H reflex in patients with spastic hemiplegia. On their affected sides, patients demonstrated greater facilitation of both group I and group II components compared with their unaffected side and with controls (Marque *et al.*, 2001). There was no correlation with Ashworth scores. Later, this same group studying patients with spastic hemiplegia found that tizanidine, the alpha-2 noradrenergic agonist antispasticity drug, reduced the group II (and group I) facilitation of the quadriceps H reflex and decreased quadriceps spasticity (Maupas *et al.*, 2004). A trend towards correlation of the reduced group II facilitation and the spasticity was not significant.

Finally, some researchers report increased LLR amplitude and duration in the triceps surae, which correlates with the degree of clinical hypertonia (Berardelli *et al.*, 1983). On the other hand, others have found reduced long-latency reflexes in spastic

patients (Deuschl & Lucking, 1990) arguing against increased group II excitatory activity (Cody *et al.*, 1987). However, the LLR is a transcortical reflex (Deuschl & Lucking, 1990) and so reduced LLRs would not be surprising in spasticity caused by brain disease. Irrespective of the behaviour of LLRs in spasticity, there is a more fundamental disagreement over the importance of group II afferents in the LLR in man, with some claiming no role (Deuschl & Lucking, 1990).

In the first edition of this book, I concluded that the role of group II afferents in spasticity was controversial. The situation now is that there is much better evidence for this, suggesting that additional medications (beyond tizanidine and clonidine) aiming to reduce group II–mediated activity are worth pursuing.

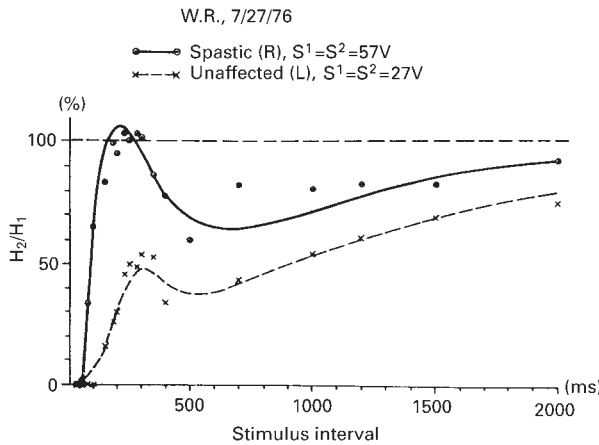

Figure 2.25. Soleus H-reflex recovery curves in a hemiplegic subject showing the normal and spastic sides. Note the general enhancement of the recovery curve on the spastic side. (From Sax & Johnson, 1980.)

H-reflex recovery curves

A soleus H-reflex recovery curve is produced by paired stimulation of the tibial nerve in the popliteal fossa. The amplitude of the second H reflex (H2) is compared with the first H reflex (H1) and the H2/H1 amplitude ratio plotted against interstimulus time interval (Fig. 2.25) (Sax & Johnson, 1980). The first stimulus is the conditioning stimulus and may be either weaker (subliminal or subthreshold) or equal to the second 'test' stimulus. As shown in Figure 2.25, following the conditioning stimulus there are periods of early suppression and facilitation, and a later period of suppression with a gradual recovery to normal. The H-reflex recovery involves polysynaptic pathways and has been used to investigate disorders of muscle tone, such as rigidity and spasticity, as a measure of polysynaptic influences on spinal motoneurone excitability (Kagamihara *et al.*, 1998). The facilitatory and inhibitory effects are probably mediated by circuits involving Ia afferents within the spinal cord, the facilitatory effects of which seem under supraspinal control, but not the inhibitory (Rossi *et al.*, 1988).

The results in human spasticity suggest facilitation of the recovery curve compared with normal subjects or the unaffected limb (Fig. 2.25) (Sax & Johnson, 1980; Koelman *et al.*, 1993; Panizza *et al.*, 1995). Some correlation with the severity of spasticity has been reported (Panizza *et al.*, 1995). However, the methodology of these studies has been criticized, making their results difficult to interpret and their value questionable (Ashby, 1980; Lance, 1980; Kagamihara *et al.*, 1998), and they have largely gone out of favour (Delwaide, 1985b). H-reflex recovery curves have featured in pharmacological studies of antispasticity agents (Delwaide *et al.*, 1980) with effective medications showing differing effects. As with other tests of spinal reflexes, similar abnormalities of the H-reflex recovery curve are also present in Parkinson's disease (Sax & Johnson, 1980) and dystonia (Koelman *et al.*, 1995).

Conclusion regarding spinal mechanisms in the UMN syndrome

Despite the wealth of research, clear correlation between individual spinal interneuronal circuits and the clinical features of the UMN syndrome are lacking except in the case of flexor spasms. The results

are plagued by inconsistencies in the basic finding of the presence or absence of abnormality between individual patients and between studies, particularly for recurrent inhibition. Furthermore, many of the abnormalities described are also found in patients with dystonia and Parkinson's disease, where spasticity, tendon hyperreflexia and flexor and extensor spasms are absent. Despite some association with existence of spasticity, the electrophysiological abnormalities described usually do not correlate with clinical measures of the degree of spasticity (Shemesh *et al.*, 1977; Cody *et al.*, 1987; Levin & Hui-Chan, 1993), raising doubt about their pathophysiological role in spasticity. An exception might be flexor withdrawal reflexes and flexor spasms, but in any case these are separate from spasticity (hyperactive tonic stretch reflexes). Hence, it is fair to say that no one test accurately reflects the basic pathophysiological substrate of spasticity, and it is quite probable that the condition is a heterogeneous one. Perhaps the strongest association exists between Ia presynaptic inhibition and tendon hyperreflexia.

Nonetheless, these electrophysiological tests often become more normal with antispastic medication, sometimes coincident with a reduction in clinical measures of spasticity (e.g. Mondrup & Pedersen, 1984; Macdonell *et al.*, 1989; Nance *et al.*, 1989; Delwaide & Pennisi, 1994; Maupas *et al.*, 2004), and sometimes not (Martinelli, 1990). For example, the H/M ratio, reciprocal Ia inhibition and recurrent inhibition were unchanged following protirelin tartrate (TRH-T) administration despite clear reduction in hypertonia and tendon hyperreflexia (Martinelli, 1990). Such a finding might lead to the conclusion that abnormalities of these spinal reflex activities in these patients (poststroke) were not important in the production of the clinical signs. As such, the spinal reflex changes may simply be epiphenomena. One potential problem when attempting to correlate electrophysiological findings with the clinical signs is that hypertonia may be due to both (neural) stretch hyperreflexia and biomechanical factors (Nielsen & Sinkjaer, 1996). Thus, a patient with minimal spasticity but marked hypertonia due to soft tissue changes may have only minimally abnormal spinal electrophysiological studies.

One beneficial product of these electrophysiological studies has been the ability to observe and quantify the effects of antispastic drugs. Effective drugs often have completely different electrophysiological effects despite similar clinical efficacy (Fig. 2.26) (Delwaide & Pennisi, 1994). Combined drug and electrophysiological studies may also help elucidate the pathophysiological mechanisms responsible for spasticity. It has even been suggested that the prescription of antispastic agents be based more scientifically upon the results electrophysiological tests, such as those outlined above (Delwaide & Pennisi, 1994) and could even provide a logical basis to combination drug therapy (Delwaide, 1985b).

Neuropharmacology of the UMN syndrome

This subject has been dealt with in other reviews (Noth, 1991; Young, 1994; Gracies *et al.*, 1997). However, from the foregoing discussion, the neurotransmitters GABA, glycine, noradrenaline, dopamine, serotonin and excitatory amino acids (glutamate) seem to play a role. Much of this information has come from observations of the clinical and electrophysiological effects of antispasticity agents, their agonists and antagonists. Caution must therefore be exercised before drawing the conclusion that these neurotransmitters are important in the production of spasticity and the other positive UMN features as opposed to their ability to ameliorate these signs.

The spastic movement disorder

The final discussion draws on some of the evidence already presented and concerns the role of spasticity in the disordered voluntary movement of the upper motor neurone syndrome. It should be emphasized that most of the disability of the UMN syndrome comes from the negative features, not the positive ones. Nonetheless, does spasticity interfere with voluntary movement? Is there a spastic movement

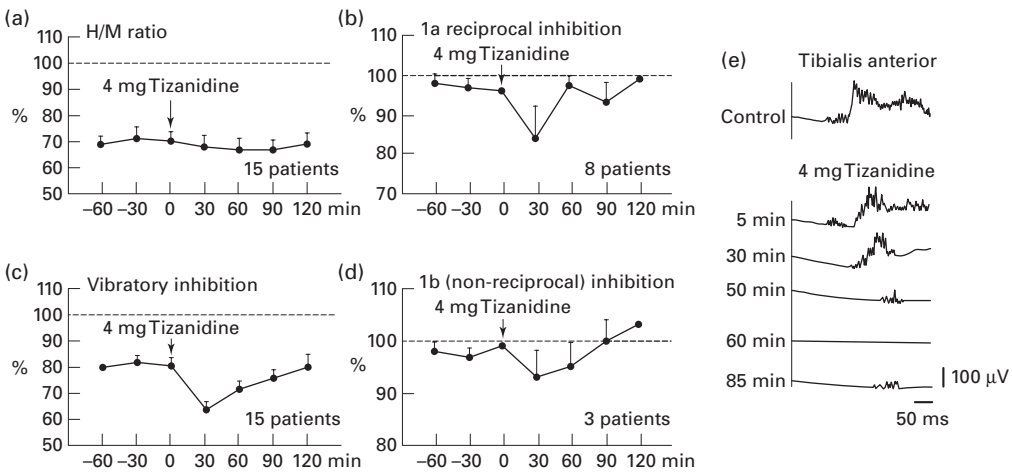

Figure 2.26. A battery of electrophysiological tests of spinal interneuronal pathways in spastic subjects before and after a single oral dose of tizanidine, 4 mg. Note an effect on Ia rediprocal inhibition (b), vibratory inhibition ((c), representing Ia presynaptic inhibition), Ib nonreciprocal inhibition (d) and flexor withdrawal reflexes from tibialis anterior elicited by sural nerve stimulation (e). The H/M ratio ((a), representing alpha motorneurone excitability) was unchanged. (From Delwaide & Pennisi, 1994.)

disorder? Anyone watching a child with diplegic cerebral palsy or a stiff-legged stroke patient walking would be tempted to think so. Similarly for the stroke patient trying to reach for an object who appears to be constrained from doing so by co-contraction of elbow flexors. The concept of the spastic movement disorder underlies attempts to improve active movement (and therefore active function) by reducing spasticity through physiotherapy, medications and surgery. The wisdom of doing so has been challenged, however (Landau, 1974, 1992, 1995, 2004; Dietz, 2003). Furthermore, some researchers have emphasized that soft tissue changes may be more restrictive to movement than muscle overactivity (see 'Nonreflex contributions to hypertonia: biomechanical factors' on p. 25). Others point out a lack of correlation between spasticity, whether measured clinically or electrophysiologically, and disability of movement, and suggest that the attention paid to spasticity in (stroke) rehabilitation far exceeds its clinical importance (Sommerfield *et al.*, 2004).

The discussion in the literature on this subject is muddled by differing uses of the word 'spasticity'. I propose the term 'spastic motor overactivity' to refer to a group of muscle overactivities that occur in the upper motor neurone syndrome. This group includes spasticity as defined by Lance (1980; see above), (spastic) co-contraction, spastic dystonia, flexor and extensor spasms, associated reactions and the positive support reaction. Thus, the question should be broader – does spastic motor overactivity interfere with movement? It would not be controversial to say that the occurrence of flexor and extensor spasms and the positive support reaction in the lower limb interferes with standing and walking. But does spasticity, spastic co-contraction or spastic dystonia cause a movement disorder and, by inference, can we improve movement by reducing it? From the earlier sections in this chapter, there is evidence suggesting that stretch reflex activity (spasticity) in antagonists and co-contraction of antagonists limits movement, even though not all researchers have found this. Spastic dystonia has not been studied much. Spasticity does not appear to exist in contracting agonists and in any case would not really interfere with movement.

One argument against treating spastic motor overactivity in the hopes of improving movement and

function seems to be based on its relative lack of importance in causing disability, particularly for complex movements (Landau, 2004), and that in the case of walking, it might actually be helpful (Dietz, 2003). Another concerns the treatment used – it is claimed that blanket suppression of all spinal reflex activity, including functionally useful polysynaptic reflexes, by drugs like baclofen, diazepam and tizanidine is unlikely to improve movement if motor control is impaired by exaggeration and lack of modulation of monosynaptic or disynaptic spinal reflexes (Dietz, 2003), which seems reasonable. Indeed, critics cite that there is no evidence that these drugs improve active movement (Landau, 2004). Unfortunately, this lack of improvement in active movement has been used to bolster the argument that spastic motor overactivity is not important in the movement disorder (Landau, 2004) – a flawed piece of logic that ignores that the treatment might be too heavy handed. An analgous argument might be that status epilepticus was not the cause of the patient's coma because (too) large doses of benzodiazepines or barbiturates did not wake the patient up even though the EEG showed that seizure had stopped. The situation for focal spasticity treatments, such as botulinum toxin and phenol, is not clear either (Sheean, 2001) but is more promising given their focal, targeted effects and lack of action centrally on spinal cord reflexes.

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3

The measurement of spasticity

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Introduction

Even today, although there are a number of validated techniques for the measurement of associated disability, the measurement of spasticity at the level of impairment is probably in its infancy. Because of the relative lack of treatment or therapy to reduce spasticity, there has been limited development of methods for its measurement. However, with the relatively recent advent of treatments for spasticity, such as botulinum toxin, there is now a considerable incentive to develop new methods.

One particular barrier to valid measurement relates to the need for a precise definition. The measurement of any physical phenomenon is impossible in the absence of a definition, and this is equally true in the case of spasticity. At the clinical level, there is almost certainly a wide variety of assumed definitions concerning stiffness and the lack or difficulty of movement. A relatively precise statement has been provided by Lance (1980), as follows: Spasticity, which is directly equated with spastic hypertonia, is a motor disorder that is '*characterised by a velocity dependent increase in the tonic stretch reflex (muscle tone) with exaggerated tendon reflexes, resulting from the hyper excitability of the stretch reflex, as one component of the upper motor neurone syndrome*' following a lesion at any level of the corticofugal pathways – cortex, internal capsule, brainstem or spinal cord (Burke, 1988). Furthermore, spastic hypertonia has also been described as the exaggeration of the spinal proprioceptive reflexes resulting from a loss of descending inhibitory control (Burke, 1988).

While these definitions would appear to be reasonably precise, there is a need to ask whether current clinical testing procedures are consistent with the model that underlies them and whether the model itself is sufficiently representative to allow reliable testing. Essentially, the neural contributions to increased tone[1] are likely to result from voluntary and involuntary (reflex) activation of the alpha motor neuron. The presence or absence of reflex activity is likely to be a function of muscle length, velocity of stretch, load on the tendon and threshold and gain in the reflex loops. It therefore appears that, at minimum, there are five variables that may account for the level of spasticity. This complexity is not adequately addressed by the definitions described above. The measurement challenge, therefore, is to develop a procedure which is broadly consistent with the clinical definition and perception of the impairment, but which is sensitive to the important variables. For instance, do the assessment procedures commonly in use always distinguish between spasticity, contracture or other abnormal tone such as the rigidity encountered in Parkinson's disease?

[1] The definition of tone is another moot point. There are two broad definitions of tone used in the literature: (a) resistance to an externally imposed movement and (b) the state of readiness (or background activity) in a resting muscle. In this chapter the former definition is used.

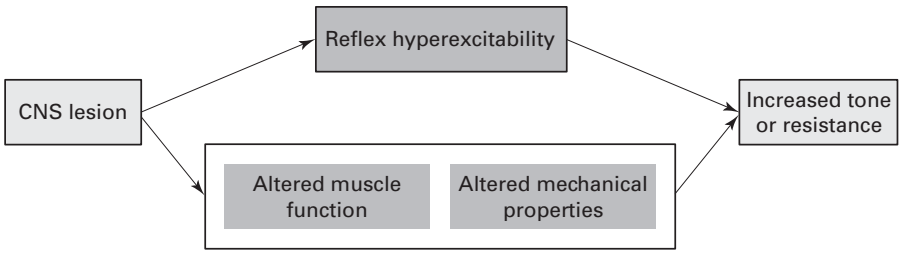

Figure 3.1. The major contributions to resistance to passive motion result from changes in both the reflex behaviour and in the passive mechanical properties of the muscle. It is important to note that, under certain circumstances, reflex activity can confounded by interactions between the cognitive system and the environment.

Approaches to measurement

Probably because of neurophysiological complexity and the lack of rigid definitions discussed above, there has been a variety of approaches to the measurement of spasticity. While the majority of clinicians probably rely on descriptive scales, there have been several attempts to use physical or biomechanical approaches. However, the common element of all these methods is that they are concerned with the quantification of resistance to passive motion, and it must be remembered that this can result from a combination of the neurophysiological effects together with biomechanical changes to the muscle(s), tendon(s) and capsule. The situation is summarized in Figure 3.1.

While the primary theme of this chapter is to consider methods for the measurement of the impairment associated with spasticity, it is important to note that techniques of both impairment and disability may be used clinically. While one particular approach to the measurement of disability, gait analysis, is discussed later, it is important to stress that the relationships between disability and spasticity are poorly understood and have yet to be fully explored.

Use of scales to measure spasticity

Requirements of measurement scales

Since most measurement of spasticity is performed using clinical scales, it is useful first to examine the properties of these instruments. A prerequisite for the use of any measurement scale is a knowledge of its performance characteristics and limitations, as these play a key part in interpreting the data and determining the appropriate method of statistical analysis. The key aspects of measurement scales are considered before going on to examine the attributes of instruments for the measurement of spasticity.

Level of measurement

There are four distinct levels of measurement that can be identified hierarchically as follows: nominal (categorical), ordinal, interval and ratio levels. These are described in Table 3.1 with examples.

The Ashworth scales

In the clinical setting, the most commonly used technique of measurement is the Ashworth scale (Ashworth, 1964), developed originally for the assessment of patients with multiple sclerosis. The Ashworth test is based upon the assessment of the resistance to passive stretch by the clinician who applies the movement. However, although this would appear to be broadly in conformity with the Lance definition, its reliability might be expected to depend upon the ability of the observer both to control the rate of stretch and to assess the resistance. However, despite its widespread use and further development (Bohannon & Smith, 1987), there are relatively few data available on the reliability of this scale. The

Table 3.1. The properties of scales

Type of scale	Mutually exclusive	Logical order	Scaled to perceived quantity	Intervals of equal length	True zero point
Nominal (e.g. type of stroke)	**x**				
Ordinal (e.g. strength measured on MRC scale)	**x**	**x**	**x**		
Interval (e.g. range of motion)	**x**	**x**	**x**	**x**	
Ratio (e.g. absolute strength)	**x**	**x**	**x**	**x**	**x**

Table 3.2. Definitions of the Ashworth and modified Ashworth scales

Score	Ashworth scale (Ashworth, 1964)	Modified Ashworth scale (Bohannon & Smith, 1987)
0	No increase in tone	No increase in muscle tone
1	Slight increase in tone giving a catch when the limb was moved in flexion or extension	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion (ROM) when the affected part(s) is moved in flexion or extension
1+		Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in tone but limb easily flexed	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in tone – passive movement difficult	Considerable increase in muscle tone passive, movement difficult
4	Limb rigid in flexion or extension	Affected part(s) rigid in flexion or extension

properties of these scales have been reviewed in detail by Pandyan and colleagues (Pandyan *et al.*, 1999) and the major points are outlined in Table 3.2.

Ashworth and modified Ashworth scales – level of measurement

Since the Ashworth scale does not measure the resistance to passive movement objectively, it cannot be treated as either a ratio or an interval level measure. The originator has proposed that the scale should be treated as an ordinal level measure of resistance to passive movement (Ashworth, 1964). Although it is not possible to give a clear guideline as to what would define a 'passive stretch', evidence suggests that velocities of greater than 10 degrees per second could trigger reflex activity, which in turn could contribute to an increase in the resistance to passive movement (Dewald & Given, 1994; Lamontagne *et al.*, 1998; Pandyan *et al.*, 2006). However, further investigation of this is almost certainly required.

The modified Ashworth scale, proposed by Bohannon and Smith (1987), contains an additional level of measurement (1+) and a revised definition of the lower end of the Ashworth scale. However, this modification may have introduced an ambiguity in the scale that reduces it to a nominal level

measure of resistance to passive movement. The reasons for this are the lack of clear clinical or biomechanical definitions for the terms 'catch' and 'release' and an assumption that 'catch and release' at end range of movement is the same as 'minimal resistance to passive movement'. In particular, the differentiation between grades 1 and 1+ depends upon the presence or absence of either 'release' or 'minimal resistance to passive movement at end range of movement', the latter of which is probably influenced by the viscoelastic properties. Since there is no published evidence supporting either an ordinal relationship between the grades 1 and 1+ or a relationship between the 'catch and release', 'minimal resistance to passive movement', 'increased resistance to passive movement', and spasticity, it is not possible to treat the modified Ashworth scale as an ordinal measure of resistance to passive movement.

Published data support the use of the original Ashworth scale as an ordinal level measure of resistance to passive movement. However, the modified Ashworth scale could be considered to be an ordinal level measure of resistance to passive movement if the ambiguity between the 1 and 1+ categories could be resolved.

Reliability of the Ashworth scales

Original Ashworth scale

Two studies have investigated the reliability of the original Ashworth scale (Lee *et al.*, 1989; Nuyens *et al.*, 1994), and a further four have studied the reliability of the modified Ashworth scale (Bohannon & Smith, 1987; Bodin & Morris, 1991; Sloan *et al.*, 1992; Allison *et al.*, 1996). One further study has compared the reliability of the two scales (Hass *et al.*, 1996). There appears to be conflicting evidence on the reliability of the Ashworth scales.

In the original paper, the Ashworth scale was used as one of several clinical observations to classify spasticity (Ashworth, 1964), although, surprisingly, this paper does not describe the exact testing protocol. Based on the Ashworth scale guidelines, Lee *et al.* (1989) investigated the inter- and intrarater reliability of spasticity measurement using a recoded and summated spasticity score. While it was not possible to draw any conclusions on the reliability of the Ashworth scale as a measure of spasticity in individual joints, there are important data analysis issues that need to be highlighted. If it is accepted that the Ashworth scale is not an interval or ratio level measurement of spasticity, then the use of parametric measures of intrarater reliability may be questioned. Similarly, the summing of individual joint scores to produce a summated Ashworth score is methodologically flawed.

Nuyens *et al.* (1994) investigated the interrater reliability of the Ashworth scale to measure spasticity in selected muscles of the lower limb, although it is not entirely clear how the authors differentiated between some muscle groups tested (e.g. m. soleus and m. gastrocnemius). Based on an initial assumption that it was an ordinal measure of spasticity, the authors supported the continued use of the Ashworth score as a clinical measure of spasticity. They also suggested that the inter-rater reliability of the scale when measuring spasticity in the lower limb may vary according to the muscle group being tested and concluded that the inter-rater reliability was better for the distal than the proximal muscle groups. In the same study, they summed the (nonparametric) Ashworth scores obtained from individual muscles to obtain a total score and showed that the median of these totals was similar for both assessors, even though the two raters often assessed spasticity differently. This latter finding highlights how the use of a summated score in intervention and reliability studies may mask any unreliability arising with the use of individual joint scores.

Modified Ashworth scale

Bohannon and Smith (1987), as well as being the originators, were the first to test the inter-rater reliability of the modified Ashworth scale. They concluded that the inter-rater reliability at the elbow was acceptable, but noted the possibility that the high degree of agreement may have been attributable to the interactions (mutual testing and discussions) between assessors. Bodin and Morris (1991) investigated the

inter-rater reliability of the scale for measuring wrist flexor spasticity and concluded that it was a reliable measure of wrist flexor spasticity when used by two trained testers. The authors were of the view that the good agreement was independent of interactions between assessors during the study period. Sloan *et al.* (1992) investigated the reliability of the scale in measuring spasticity of the elbow flexors and extensors and the knee flexors. Assuming an ordinal level of measurement, they concluded that the modified Ashworth scale was a reliable measure of spasticity at the elbow but not at the knee. The results from this study were similar in some respects to that of Bohannon and Smith (1987) and supported the conclusions that the modified Ashworth scale may have sufficient reliability to classify resistance to passive motion at the elbow.

Allison *et al.* (1996) investigated the intra- and inter-rater reliability of the modified Ashworth scale when measuring ankle plantar flexor spasticity and concluded, despite reservations, that it had sufficient reliability in measuring spasticity at the ankle in the clinical setting. The authors also highlighted some practical difficulties experienced when using the scale to classify spasticity in the ankle plantar flexors.

Comparison of the Ashworth and modified Ashworth scales

Hass *et al.* (1996) compared the inter-rater reliability of the Ashworth and the modified Ashworth scales achieved by two assessors grading spasticity in the lower limbs of 30 subjects with spinal cord injury. Using the Cohen's κ to test for the inter-rater reliability, they concluded that both scales should be used with extreme caution since the inter-rater reliability in classifying spasticity in the lower limb was poor. They also showed that inter-rater reliability was better for the original Ashworth scale.

It could be argued that by adding an extra level of classification to increase the sensitivity, Bohannon and Smith (1987) had also increased the probability of errors occurring in the modified Ashworth scale. In addition, as pointed out earlier, there is a certain degree of ambiguity between the grades 1 and 1+ in the modified Ashworth (Kumar *et al.*, 2006). The lower reliability observed when using the modified Ashworth scale to grade spasticity could be explained by the above two factors.

Ashworth scales – conclusions and recommendations

Based on the published evidence, the Ashworth scale and the modified Ashworth scale can be regarded as ordinal and nominal level measures of resistance to passive movement, respectively. These scales are unable to reliably differentiate changes in resistance to passive movement between the grades 0, 1, 1+ and 2. However, they may only be regarded as measures of spasticity if the velocity of passive joint movement is consistent, the joint range of movement is not compromised and in the absence of pathologies which may cause other forms of increased tone such as rigidity. The use of parametric procedures such as a recoded and/or summated Ashworth score in the place of individual joint (or muscle) scores is not recommended, since two individuals who rate resistance to passive movement quiet differently can produce similar summated scores.

Some further key points which arise are as follows:

1. Although the use of the frequency distributions, median and interquartile ranges (mean and standard deviation/confidence intervals) may be used in descriptive studies, it is appropriate only to use categorical/nonparametric data analysis techniques in reliability and intervention studies (Chatfield & Collins, 1980; Bland, 1995; Agresti, 1996).
2. In any clinical trials, it is essential that the investigators apply the scales as described in the source publications (Ashworth, 1964; Bohannon & Smith, 1987) and are not tempted to introduce intermediate levels (e.g. spasticity grades of 2.5) (Agresti, 1996).
3. Given the uncertainty surrounding the inter-rater reliability of these scales, it is advisable that a

single assessor is used in all clinical trials. If this is not possible (e.g. multicentre studies), then it is suggested that the consistency between assessors be tested before the actual trial.

4. While an implicit assumption in the original scales is that the resistance to passive movement is tested through the full range of passive movement (except grade 4), this may not always be possible in clinical practice (Kumar *et al.*, 2006). Although many investigators provide information related to passive range of movement, few provide a measure of the starting position of the limb or an indication of whether the subject experienced pain during the assessment of spasticity. It should be remembered that reflex excitability may be influenced by the resting length of the limb and pain (Burka, 1988; Rymer & Katz, 1994; Rothwell, 1994). Thus, it is recommended that in future studies, information on the passive range of movement, the resting limb posture before stretch, and pain during the stretch be recorded.
5. Many authors use repeated cycles of passive stretching prior to grading spasticity. It is also important to realize that the viscoelastic contributions to the resistance to passive movement are likely to decrease with repeated cycles of stretching (Pandyan, 1997) while the changes in the tone-related components will need to be considered indeterministic (i.e. it could either increase, reduce or remain unchanged and will depend on many extraneous factors). It is therefore essential that repeated movements be kept to a minimum and the guidelines described by Nuyens *et al.* (1994) would be recommended in future clinical trials.
6. Environmental and postural considerations are also likely to be important. For instance, measurements should always be carried out in a room of the same temperature on each occasion, and the posture of the subject should be kept the same at each measurement occasion.
7. It would appear that the modified Ashworth scale, when compared with the original Ashworth scale, has lower reliability when used to classify resistance to passive movement at the lower limb (Sloan *et al.*, 1992; Nuyens *et al.*, 1994; Hass *et al.*, 1996). It is possible that the difference arises from the modified Ashworth scale having an additional level classification (Kumar *et al.*, 2006). In addition, the loss of reliability in the lower limb may be attributable to difficulties in perceiving reflex-mediated stiffness when moving the heavier shank and foot segments.

Further work is now required to examine both the validity and the reliability of both the Ashworth and modified Ashworth scales thoroughly, particularly as there may be an increase in their clinical use with the advent of more therapeutic interventions focussed at reducing spasticity.

The Tardieu method of assessment

Following the original research of Tardieu and colleagues (1954) in the early 1950s, a new scale for classifying spasticity based was developed by Held and Pierrot-Deseilligny (1969). This scale has since been translated to English and undergone substantial modifications. Under currently published guidelines, for classifying spasticity using the Tardieu method (Held *et al.*, 1969; Gracies, 2001), the assessor is required initially to apply two sequential stretches to the limb segment, as follows:

- A slow stretch using a velocity below which the stretch reflex cannot be elicited.
- A fast stretch, which, depending on the limb segment under test, could either be (1) the natural drop of the limb segment under gravity (in a way similar to the Wartenberg approach described in the following section) or (2) passively stretched at a rate faster than the rate of the natural drop of the limb segment under gravity.

Spasticity is then classified using the quality of the muscle reaction (*X*) (Table 3.3) and the angle at which this muscle reaction occurred (*Y*).

The use of two velocities for quantifying the muscle reaction makes this method of measurement consistent with the Lance definition (Lance, 1980). Although the original methods described by Tardieu

Table 3.3. The guideline for classifying the quality of the muscle reactions (X) when using the Tardieu scale

Grade	Quality of the muscle reaction
0	No resistance throughout the course of the passive movement
1	Slight resistance throughout the course of the passive movement, with no clear catch at precise angle
2	Clear catch at precise angle, interrupting the passive movement, followed by release
3	Fatiguable clonus (<10 seconds when maintaining pressure) occurring at precise angle
4	Infatiguable clonus (>10 seconds when maintaining pressure) occurring at precise angle

and colleagues (1954) involved quantitative measurements of displacement, velocity and muscle activity, there is insufficient data to establish the validity of the currently used versions of this scale (Haugh *et al.*, 2006).

Tardieu method of assessment – level of measurement

The Tardieu method of assessment provides a composite measure of spasticity. The quality of the muscle reaction (*X*) is a categorical level of measurement and therefore can primarily used for classification purposes only (Held & Pierrot-Deseilligny, 1969; Gracies, 2001; Haugh *et al.*, 2006; Morris, 2006). However, whether one can use this as a classification of spasticity remains open to debate (Haugh *et al.*, 2006). The angle of the muscle reaction (*Y*) can be considered to be an interval or ordinal level of measurement depending on method used to measure the angle. If instrumented measures are used, it will be possible to obtain an interval level of measurement; if visual estimation methods are used, it will be possible to get an ordinal level of measurement.

Reliability of the Tardieu method of assessment

There are two elements to be considered when exploring the reliability of the Tardieu scale. There is a need to first ensure that it is possible to reliably apply the perturbations as prescribed by the proponents of the scale. The evidence to date suggests that this is not possible, even when the limb is allowed to fall naturally under the influence of gravity.

Research on the reliability of describing the quality of the muscle reaction and the angle of the muscle reaction is patchy. There is more focus on the angle of the muscle reaction as opposed to the quality of the muscle reaction. A recent review has concluded that there is insufficient evidence to draw any meaningful conclusions on the reliability of the Tardieu method of assessment (Haugh *et al.*, 2006). It is essential that any future study of reliability should incorporate methods to monitor both the velocity of any externally imposed perturbation and the muscle activity to ensure that there is no reflex activation when the limb segment is perturbed using the slow stretch and that the velocity during the fast movement is consistent. Evidence from existing studies would suggest that the muscle response to an externally imposed perturbation can significantly vary with even very small changes in velocity (Dewald & Given, 1994; Pandyan *et al.*, 2006).

The Tardieu method of assessment – conclusions and recommendations

The Tardieu scale is capable of providing a method of classifying features of the upper motor neuron syndrome if a consistent perturbation protocols are utilized. The guidance given by the original developers of the scale should be followed (Held & Pierrot-Deseilligny, 1969; Gracies, 2001; Morris, 2006). These are as follows:

1. Start the perturbation with the limb placed where the muscle to be tested is in its least stretched position.
2. Assessment should take place at 'the same time of day, with the same body position and a constant position of other limb segments' (upper limb tests performed with the patient in sitting and lower limb tests in supine).

Biomechanical approaches

Since the usual definition of spasticity concerns the relationship between velocity of passive stretch and resistance to motion, it is logical to investigate biomechanical approaches to quantification. For instance, techniques have been developed to use a motor-powered system to apply the motion and measure the resistance in a controlled manner.

Wartenberg test

The procedure that has received the most attention is the pendulum test, originally proposed by Wartenberg (1951), in which the knee is released from full extension and the leg allowed to swing until motion ceases. In his original paper, Wartenberg observed that in the normal healthy subject the leg would swing approximately six times after release and proposed a test for the assessment of spasticity involving the counting the number of swings before the limb comes to rest. This procedure was further examined by the Bajd and Vodovnik (1984), who attached a goniometer to the knee and recorded the movements at the joint after release. They then proposed a relaxation index, based on the rate of decay of oscillation, as a measure of spasticity. However, despite quite extensive technical development, they did not validate the technique in clinical practice. While, superficially, this test should provide a measure of spasticity according to the Lance definition, it must be remembered that the reflex system is complex with a number of important variables. In order to study this, He and Norling (1997) have performed a mathematical modelling study of the test taking into account both the thresholds and the gain in the reflex arc together with the nonlinear force production properties of muscle. This study highlights the complex behaviour of reflexes during the experiment and the difficulties of making a simple interpretation; in particular, it demonstrates how this complexity can lead to patterns of movement which are distinctly different from those of a simple damped pendulum.

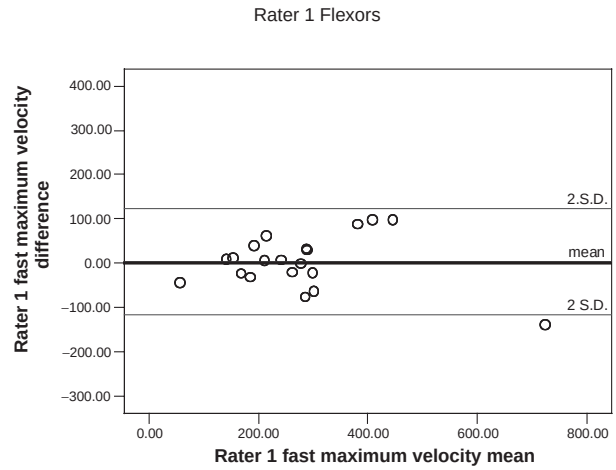

Figure 3.2. Bland and Altman plot of intra-rater reliability of fast maximum velocity measures 1 and 2. This graph demonstrates that the maximum velocity of the externally imposed perturbation varies considerably when a limb segment is allowed to fall under the influence of gravity twice. Data were collected when a single assessor was taking measurements from 10 patients with upper motor neurone lesions.

From the practical clinical viewpoint, Leslie and colleagues (1922) have examined the relationship between measurements of spasticity in patients with multiple sclerosis made on the Ashworth scale and those obtained from the Wartenberg test. They established that the two methods appear to assess similar features of muscle function but that there were significant changes in the relaxation index within a single Ashworth grade, suggesting that the pendulum test is a rather more sensitive measure of spasticity. Katz and colleagues (1969) have reported the use of this test and have suggested that it is an acceptable clinical measure that corresponds to the clinical perception of spasticity.

While the Wartenberg pendulum test can be used in cases of relatively mild spasticity, it is likely to be unsuitable for the commonly occurring clinical situations in which spasticity prevents true oscillation of the limb (in engineering terms, when the viscous damping attributable to spasticity is near to or greater than critical). In this situation there is a

need for a technique that does not rely upon the measurement of damped oscillations but provides a soundly based physical measurement. Duckworth and Jordan (1995) performed a preliminary study in which they used a 'myometer' (a single-axis force transducer) to measure resistance to motion. While the technique probably does not conform with the definition of spasticity, early results were encouraging from the point of view of reliability. Lamontagne and colleagues (1998) used a similar technique and found it reliable for the measurement of non-reflex components of resistance to passive motion. More recent work has resulted in the development of a variety of simple systems that can be used for the measurement of stiffness about the wrist (Agresti, 1996; Pandyan *et al.*, 1997), elbow (Pandyan *et al.*, 2001) and ankle (van der Salm *et al.*, 2005). The reliability of these systems has been thoroughly investigated and errors of measurement have been reported. Therefore, more efforts should now be taken to incorporate objective measurements into routine clinical practice.

Powered systems

The need to study the relationship between joint motion and resistance has led to a number of projects using powered biomechanical systems for the measurement of spasticity. Before going on to describe these systems, it is useful to highlight the important biomechanical parameters which can, potentially, be studied. In biomechanical terms, a joint and muscle exhibiting spasticity can be regarded as a system exhibiting both elastic (recoverable) and viscous (energy-absorbing) behaviour. These two aspects are illustrated in Figure 3.3 showing a *hysteresis loop*, which is the relationship between the displacement and moment measured at a joint being moved in cyclical flexion and extension. Essentially two quantities can be measured from this graph. While the average gradient is a measure of the elastic behaviour, the area within the curve represents the energy absorbed and therefore the viscous behaviour. Jones *et al.* (1992) used a powered device to move the joint in a known manner and showed that it could provide useful measurements.

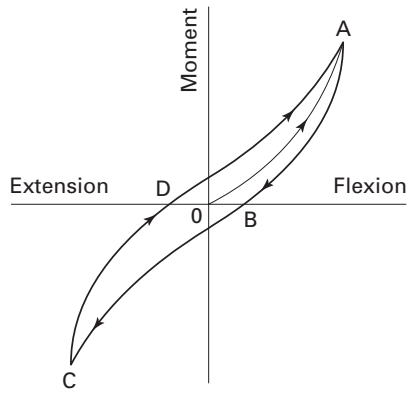

Figure 3.3. An idealized hysteresis loop obtained from cyclical movement of a joint affected by spasticity. Two key variables may be measured from this graph: the mean slope, which represents elastic stiffness, and the area within the loop, which represents hysteresis effects associated with spasticity.

However, while they demonstrated the ability to measure joint stiffness and hysteresis, there are no further data on clinical validation of the system. Katz and Rymer (1989) have demonstrated a powered system for the measurement of stiffness at the wrist but concluded that this was probably not a useful measure of spasticity. They have suggested, in particular, that an increase in stiffness may be related more to contracture than spasticity and have proposed, instead, that it may be more appropriate to measure joint torque at some specified joint angle. In later studies, Given and Rymer (1995) have demonstrated that while there are changes in the hysteresis elements of torque angle curves at the wrist, the elastic stiffness appears unchanged. Becher and colleagues (1998) have followed a similar approach and have used a powered system to investigate the resistance of lower Iimb muscles and the associated EMG signals while applying sinusoidal motion at the ankle. In this preliminary study, they were able to detect differences in stiffness between the impaired and unimpaired sides of patients with hemiplegia and were able to demonstrate that muscle stiffness remained unchanged after local anaesthesia. Lehmann and colleagues (1989) have used a similar technique and demonstrated an analytical method to separate passive from reflex responses. However,

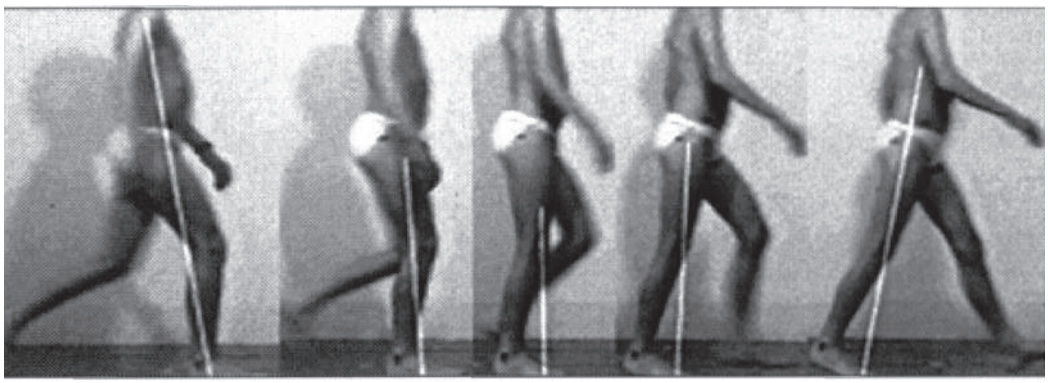

Figure 3.4. An illustration of the relationship between the ground reaction-force vector (seen as a white line) and the hip, knee and ankle during normal gait. Note how the vector passes close to the knee and hip, signifying a low turning moment.

the method has not been validated in the clinic. All of these studies demonstrate that, while powered systems highlight important changes in muscle function, the interpretation of the data is difficult and certainly not at a level for routine clinical use.

Interesting studies have been performed by Walsh (1996), who, using a low-inertia electrical drive to apply powered oscillation at the wrist, was able to demonstrate some novel phenomena. In particular, he showed that, after the application of a number of cycles of movement, the resistance to motion would be reduced and that a larger amplitude oscillation could be sustained. This situation was maintained for as long as the movement was applied but the joint returned to its previous state after a resting period. This phenomenon is not fully explained but may be due to some change in muscle and, possibly, reflex behaviour. This interesting work has not been repeated by other workers nor has it led to any clinically useful method of measurement. However, this effect or reducing resistance after prolonged excitation may be of importance when designing research studies. In a related study (Lakie *et al.*, 1988), the same research group has used this powered system to assess spasticity in patients with hemiplegia. While they established that both resonant frequency and damping were increased in these patients, they did not propose a measurement of spasticity as such.

Clearly, the application of powered systems allows detailed studies of the relationship between resistance to motion and kinematic variables. However, while such systems may be powerful research tools, the techniques are almost certainly too complex for regular clinical use.

Indirect biomechanical approaches – gait analysis

While, so far we have looked at the measurement of spasticity at the impairment level, there is also a need to consider measurements of disability such as gait analysis. There can be little doubt that gait disorders result from spasticity but the exact relationships would seem to be far from clear. Probably the best way to examine this link is to consider the changes in external loading of the hip, knee and ankle during gait and, in particular, to look at the moments at the joints. The moment at a joint, which may be considered as the turning effect of the ground reaction force, is determined by the magnitude of that force and the distance of the force vector from the joint in question. While such biomechanical measurements require relatively sophisticated measurement equipment, the video vector technique, pioneered by the Orthotics Research and Locomotor Assessment Unit (ORLAU) in Oswestry, allows a rapid visualization of these joint moments. Figure 3.4 illustrates the visual

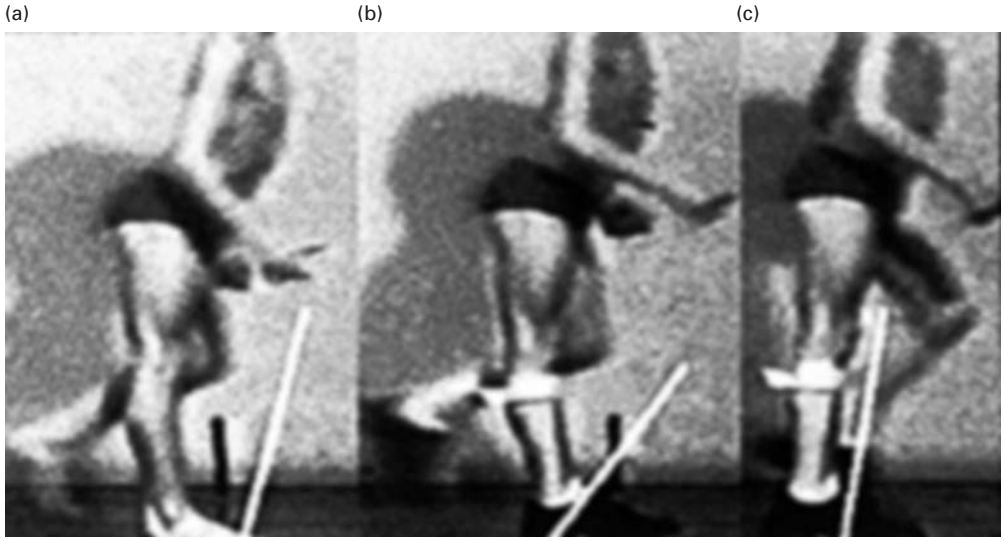

Figure 3.5. In these illustrations, the relationship between the ground reaction force vector and the hip and knee during pathological gait can be clearly seen. In (1) the large distance between the vector and the knee is shown; in (2), although the vector now originates at the heel, it is still at a large distance from the knee. In (3), the use of a "tuned" orthosis aligns the vector more closely with the knee and so reduces the effects of spasticity.

output of the system, in which the ground reaction force vector, shown as a white line, can be seen superimposed upon the image of the subject. It will be seen in this illustration of normal walking that the distance between the vector and the centres of hip and knee is relatively small. This indicates that the moment of the force and, therefore, the activity of the associated muscles about these joints is small. In contrast, Figure 3.5 shows the equivalent output for a child with cerebral palsy in which the large distance between the vector and the hip and knee is clearly visible (Butler *et al.*, 1992). In this situation there must be greatly increased muscle activity to resist these moments. It is also interesting to note how the position of the vector is changed according to the orthotic treatment, indicating that the effects of the spasticity within the gait cycle may be changed by provision of an orthosis. However, it must be stressed that, while this technique demonstrates the excessive and poorly synchronized muscle activity that may be associated with spasticity, this situation does not correspond directly with the definition of spasticity. This last point is of particular importance and highlights the need for further research investigating the exact relationships between spasticity and these phenomena.

Neurophysiological approaches to measurement

As spasticity results from altered conduction in the reflex pathways (see Chapter 2), there have been numerous attempts to quantify it by investigating the abnormalities in the reflex pathways (i.e. altered presynaptic inhibition and reciprocal inhibition, excitability in the Ia afferent pathway and increased α-motor neurone excitability). The three common techniques that have been used for clinical quantification are spasticity tendon jerks, H-reflex studies, and F-wave studies.

Tendon jerks

The most commonly used method to illustrate a spinal reflex is the tendon jerk that is obtained by a rapid (but small) stretch of a muscle. The ensuing response is reported primarily to involve the monosynaptic pathway, although it has also

been suggested that this action could be influenced by oligosynaptic pathways (Rothwell, 1994; Pierrot-Deseilligny & Burke, 2005). It has been reported that tendon jerks are more readily elicited in people with spasticity, i.e. they can be elicited with smaller levels of stimuli than normal, and the response to these stimuli has a higher amplitude and is more diffuse – that is, it can involve muscles which were not originally stimulated). Therefore, it has been hypothesised that the tendon jerk can be a quantifiable measure of spasticity. However, it is important to note that increase in tendon jerk is not exclusive to spasticity. Furthermore, whether the increase in the tendon jerk response is related to increased gain, decreased threshold or a combination of both needs to be resolved.

H Reflexes

The H reflex is a long-latency reflex obtained by electrically stimulating a mixed nerve submaximally. The muscle response that follows results from conduction via the Ia afferent pathways. Although these reflexes are thought of as being primarily monosynaptic, there is evidence that oligosynaptic reflex pathways could also be involved (Rothwell, 1994; Pierrot-Deseilligny & Burke, 2005). (N. B.: The H-reflex response is independent of the muscle spindle activity). The H-reflex has be used to study both excitability in the Ia afferent pathways and abnormalities in presynaptic and reciprocal inhibition, in spasticity (Burke *et al.*, 1983; Panizza *et al.*, 1990, 1995; Harburn *et al.*, 1992; Katz *et al.*, 1992; Rothwell, 1994; Pierrot-Deseilligny & Burke, 2005). Despite the reported ease of conducting these tests, there can be a varied outcome. This is reported to result from variations in stimulus intensity, the resting posture of the limb, the ability of a subject to relax or the neck and vestibular reflexes, and would suggest that the results should be treated with caution (Ketz & Rymer, 1989; Katz, 1994; Pierrot-Deseilligny & Burke, 2005; Voerman *et al.*, 2005). In order to normalize for this variability, the H-reflex response has been expressed as a percentage of the M-response (i.e. the stimulus of a muscle to supramaximal stimulation). It should be noted that when using this ratio, there is an assumption that the presynaptic component in the reflex response is fixed. While there are reports that H/M ratios are increased in spasticity, it has also been demonstrated that the ratios did not decrease following treatment of spasticity (Matthews, 1966). It has also been reported that the correlation between H/M ratios and the severity of spastic hyperreflexia was poor (Matthews, 1966; Katz *et al.*, 1992; Voerman *et al.*, 2005). There have been attempts to use the influence of vibration on the H reflex. Since, in normal subjects, the vibration of muscle inhibits H-reflex activity, it has been hypothesised that, in spastic limbs, this inhibition should be reduced. However, more work is needed to develop this as a clinically usable technique to quantify spasticity (Rothwell, 1994; Pierrot-Deseilligny & Burke, 2005; Voerman *et al.*, 2005).

F waves

F waves are obtained by the supramaximal stimulation of a mixed nerve and have been used as a measure of α-motor neurone excitability. Unlike H reflexes, the F wave does not result from stimulation of a sensory nerve but from the antidormic stimulation of the α-motor neurone. Furthermore, unlike the H reflex that shows an inverse relationship with the M wave, the F wave, which follows the M wave, shows no correlation with M-wave amplitudes. In addition, the amplitude of the F-wave is much smaller than that of the H reflex (Rothwell, 1994; Pierrot-Deseilligny & Burke, 2005; Voerman *et al.*, 2005). Although the F wave provides a more stable signal which is less influenced by resting posture and the ability of a subject to relax, the average F-wave response from repeated tests is often used because of variations in latency and amplitude. It has been demonstrated that spastic subjects show increased F-wave amplitudes, suggesting increased motor neuronal excitability (Eigen & Odusote, 1979; Voerman *et al.*, 2005). However, more work is still required to develop this technique as a reliable clinical measure of spasticity.

The primary problem with existing electrophysiological methods to quantify spasticity appears to

be the poor correlation with the other clinical techniques. The fact that the most commonly used clinical scales to quantify spasticity have been shown not to be an exclusive measure of spasticity adds further to this confusion. In conclusion, although there are many tests available to measure spasticity the clinical usefulness of many of these techniques still remains unproven and further work will be required to prove their validity, reliability and clinical applicability.

Overall conclusions

The measurement of any variable depends upon an adequate definition. In the case of spasticity, it appears that the complexity of any comprehensive definition (Pandyan *et al.*, 2005) makes direct clinical measurement very difficult. While the Lance definition provides a useful basis for measurement and appears to have a biomechanical interpretation, the complex behaviour of the reflex arcs and the wide variations in pathology, probably make a single universal definition impossible (Pandyan *et al.*, 2005). As a direct result, a universal measurement system may also be impossible to achieve (Burridge *et al.*, 2005). It is almost certainly this background which has confounded attempts to produce reliable instruments.

The evidence to date would suggest that existing clinical scale cannot provide a measure of spasticity. Although biomechanical approaches to measurement are attractive, there are real problems in producing systems which are universally applicable and which can be used in the clinical setting. However, the simplest of these methods, the Wartenberg pendulum test, is attractive in that it provides a simple method of measurement based on relatively well-defined biomechanical principles. It is believed that this is worthy of further investigation. Finally, while gait analysis provides much useful data on the disability of patients with spasticity, it cannot be regarded as a measure of the actual impairment. The neurophysiological protocols are capable of directly measuring aspects of spasticity. However, most of these tests are cumbersome to carry out in routine clinical practice and show a high degree of variability. It is unfortunate that the neurophysiological tests have primarily been deemed as insufficient measures as they have not corresponded to unvalidated clinical scales. To redress this balance substantially more fundamental research will be required. Significant technological advances in the field of computing has resulted in the development of novel hybrid methods of measurement (i.e. a combination of simultaneous biomechanical and neurophysiological protocols) (Pandyan *et al.*, 2005, 2006). Using these methods it is now possible to explore the phenomenon of spasticity more comprehensively. However, more research and development is required to make these devices clinically relevant (Burridge *et al.*, 2005).

It is believed, therefore, that the Ashworth and possibly the modified Ashworth scales and the Tardieu method of assessment will continue to be used in the clinic. If this is the case, then it is essential that the limitations highlighted in this chapter are recognised and that the recommended testing guidelines are followed.

Acknowledgements

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4

Physiotherapy management of spasticity

Roslyn N. Boyd and Louise Ada

In the past, much of the controversy about the management of spasticity has been due to a lack of commonly accepted definitions of the disorder, the difficulty in measuring spasticity as well as the changing nature of the motor activity limitations with growth and maturation. There was also a paucity of data to validate clinical practice. However, there is now a growing body of evidence on which to base clinical practice. While many disciplines are involved in the management of spasticity, physiotherapists have a unique role in applying their understanding of the biomechanics of movement to the analysis of motor activity limitations and their knowledge of motor learning principles to reduce activity limitations. The emphasis of this chapter is on improving muscle performance in order to enable activity rather than preparing the patient for function by affecting abnormal reflex activity. In addition, we discuss the physiotherapist's goal in using orthoses and the role of physiotherapists in pharmacological and surgical interventions. Clinical applications for children with cerebral palsy and adults after stroke are highlighted because these individuals are the largest groups with brain damage.

What is spasticity?

Spasticity is one of the impairments affecting function following brain damage. It is typical to consider the impairments associated with the upper motor neurone syndrome as either positive or negative. Negative impairments are those features that have been lost following brain damage (e.g. loss of strength and dexterity), whereas positive impairments are those features which are additional (e.g. spasticity and abnormal postures) (Jackson, 1958; Landau, 1980; Burke, 1988).

The most widely used definition of spasticity comes from a consensus statement resulting from a conference in 1980 and describes it as 'a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperreflexia of the stretch reflex as one component of the upper motor neuron syndrome' (Lance, 1980, p. 485). This puts the problem clearly in the realm of an abnormality of the reflex system. It is common for clinicians to argue for a broader definition of spasticity, often inclusive of the whole upper motor neurone syndrome, rather than viewing spasticity as one feature of the syndrome. Recently, a new definition has been put forward but this definition has not yet been tested or widely adopted (Pandyan *et al.*, 2005). However, the proposed definition is problematic, since it does not include one of the main features of spasticity – its velocity-dependent nature. This feature assists the clinician in differentiating spasticity from other confounding impairments such as contracture. We argue that it is important to accept Lance's relatively narrow but clear physiological definition and this is in line with the definitions of spasticity, dystonia and rigidity agreed on by the North American Taskforce (Sanger *et al.*, 2003) (Table 4.1).

Increasingly, the independence of the positive and negative features has been recognized (e.g. Burke,

Table 4.1.

Term	Definition
Spasticity	A motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperreflexia of the stretch reflex as one component of the upper motor neurone syndrome (Lance, 1980, p. 485).
Hyperreflexia	A greater than normal reflex response (e.g. the presence of reflex responses when a relaxed muscle is stretched at the speed of normal movement).
Tone	The resistance felt when moving a limb passively through range due to inertia and the compliance of the tissues.
Hypertonia	A greater than normal resistance felt when moving a limb passively through range.
Dystonia	A movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures or both (Sanger *et al.*, 2003).
Overactivity	Excessive muscle activity for the requirements of the task.
Passive stiffness	The force required to lengthen a muscle at rest (i.e. the slope of the force-displacement curve).
Active stiffness	The force required to lengthen a muscle, which is active (i.e. the slope of the active force-displacement curve).
Impairment	Loss of body function or problem in body structure (WHO, 2001).
Activity limitation	Difficulty in execution of a task or action (WHO, 2001).
Participation restriction	Problems experienced in involvement in life situations in a societal role (WHO, 2001).

1988). Viewing the positive and negative impairments as separate features of the syndrome will affect assessment and management procedures. For example, it is important to initially differentiate the relative contributions of the impairments so that intervention specific to the problem can be instituted. Grouping all impairments seen following an upper motor neurone lesion under one category, as a spastic 'syndrome' does not help this process.

How important a determinant of activity limitations is spasticity?

If spasticity is only one of several impairments following brain damage, physiotherapists need to clarify how spasticity affects the ability to move. Historically, spasticity was seen as the major determinant of activity limitations. However, Landau (1974) questioned this assumption, and a variety of experiments have since supported his position. First, experiments eliminating spasticity in specific muscles after stroke (McLellan, 1977) and in children with cerebral palsy (Nathan, 1969; Neilson & McCaughey, 1982) did not result in improved performance of that particular muscle. Second, studies examining the relation between spasticity and muscle performance found no correlation between them (Sahrmann & Norton, 1977; O'Dwyer *et al.*, 1996). These experimental findings resulted in dexterity being viewed as a separate impairment rather than the result of spasticity. However, these findings are often misinterpreted as suggesting that spasticity either does not exist or is never a problem. Severe spasticity will obviously limit everyday activities and restrict participation in society. Rather, the implication of these findings is that reducing spasticity will not automatically improve function and the abnormal negative features require specific training.

Experiments on the nature of the abnormality of the stretch reflex after brain damage may help us to understand how spasticity can contribute to

activity limitations. Clinically, the picture of spasticity is one of increased resistance to passive movement of a relaxed muscle caused by abnormal reflex activity. There is an assumption that this abnormal reflex activity will be exaggerated when the person attempts to move. However, there is growing evidence that, rather than the picture of a small reflex abnormality under relaxed conditions being exaggerated under active conditions, the reflex is not modulated. That is, the reflex responses do not get larger under active conditions. Lack of modulation of the reflex has been found when studying phasic stretch reflexes (Ibrahim *et al.*, 1993) as well as polysynaptic, tonic stretch reflexes (Ada *et al.*, 1998; Ibrahim *et al.*, 1993). This paints a picture, not of an abnormal 'out-of-control' reflex but of a reflex that is not being modulated. Normally, the reflex is modulated up and down according to the requirements of the task. In the presence of spasticity, the reflex is 'on' regardless of conditions. Perhaps the amount the reflex is 'on' is the determining factor as to whether spasticity interferes with movement control. A person with an abnormal stretch reflex that is 'on' a small amount will register as spastic when measured clinically but the reflex response may not increase with movement, thereby not interfering with function. This suggests that patients who are measured as mildly to moderately spastic under passive conditions are not necessarily hampered by this spasticity during function. On the other hand, if the reflex is always 'on' a large amount, even if the response does not increase with effort, it will interfere with movement. That is, moderate to severe spasticity may contribute to activity limitations by causing excessive muscle contraction which resists lengthening of the affected muscle during everyday actions.

Confusion between spasticity and other impairments

The difficulty in assessing the contribution of different impairments to activity limitations makes it possible for other impairments to be mislabeled as spasticity. One of the major confusions is between the neural and peripheral causes of hypertonia, a term often used interchangeably with spasticity. 'Hypertonia' refers to the excessive resistance, which may be felt when the limb of a brain-damaged person is moved passively. The resistance felt when a normal limb is moved slowly through range is the result of the inertia of the limb and the compliance of the soft tissues (Katz & Rymer, 1989). Normally, there is no contribution from reflex activity – that is, the muscles are electrically silent (Burke, 1983). The increase in resistance often felt after brain damage is usually assumed to be the result of hyperreflexia – that is, it is a neural problem, in line with Lance's definition. However, the increased resistance may be the result of a peripheral problem, such as the increase in stiffness often associated with contracture. Animal studies into the muscle biology of contracture have revealed that contracture is associated with an increase in muscle stiffness due to a remodeling of the connective tissue (e.g. Goldspink & Williams, 1990). Furthermore, the ability of a muscle with contracture to produce an increase in the resistance to passive movement in humans has been verified. O'Dwyer *et al.* (1996) found that muscle stiffness can be associated with muscle contracture, even in the absence of hyperreflexia. The confusion is further reinforced because the one of the most common clinical measures of hypertonia – the Ashworth scale – does not differentiate between neural and peripheral causes of hypertonia. It is important, however, for physiotherapists to be able to differentiate between these two causes of hypertonia because the intervention for muscle contracture is different than that for spasticity. Figure 4.1 illustrates figuratively two possible mechanisms of hypertonia.

Another possible confusion between motor impairments is that between spasticity and voluntary muscle overactivity. When the person with spasticity activates a muscle, thereby stretching the muscle spindle and exciting the hyperactive stretch reflex, this in turn causes the muscle to contract excessively relative to the original neural input. While spasticity is undoubtedly one cause of overactivity exhibited by people with brain damage, another may be lack of skill. Unskilled performance

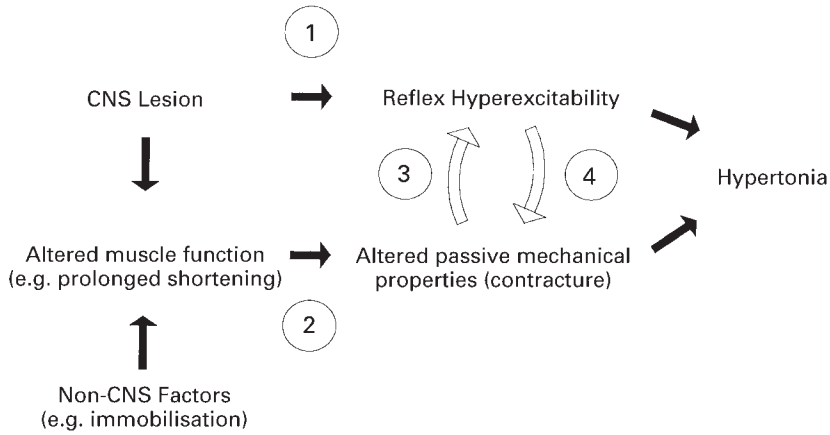


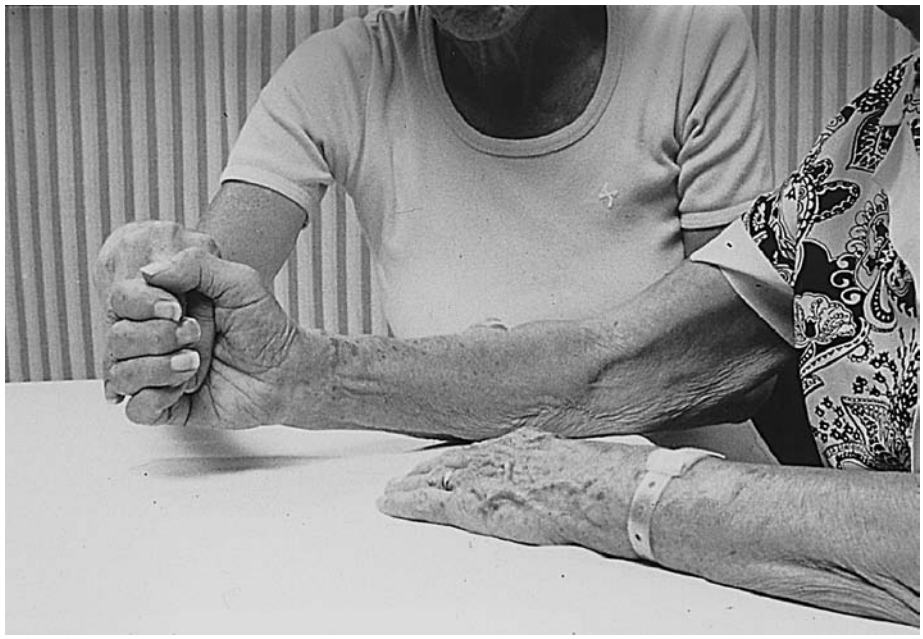
Figure 4.1. Two possible mechanisms of hypertonia following an upper motor neurone lesion. The solid arrows indicate well-established mechanisms, while the open arrows indicate more hypothetical mechanisms. (With permission from O'Dwyer & Ada 1996.)

is usually accompanied by excessive, unnecessary muscle activity (Basmajian, 1977; Basmajian & Blumenstein, 1980). Several studies have demonstrated that an increase in skill is accompanied by a decrease in muscle activity (Payton & Kelley, 1972; Payton, 1974; Hobart *et al.*, 1975). It may be that some of the motor behavior that clinicians have viewed as spastic is the result of lack of skill. For example, Figure 4.2 illustrates an attempt by a person after stroke to lift a glass off the table, but instead of the wrist radially deviating, the elbow flexes. Behavior such as this is often attributed to biceps spasticity. However, overactivity in the biceps in this case is unlikely to be the result of spasticity since, following feedback about performance, the patient successfully lifts his or her hand without any accompanying elbow flexion. In a recent study (Canning *et al.*, 2000), adults following chronic stroke demonstrated excessive, unnecessary activity during the performance of a task which was correlated with poor performance but not with spasticity. Yet more confusion exists between spasticity and other neurological impairments such as dystonia and rigidity. It is important to differentiate these impairments from each other since this will have implications for assessment and intervention. This has been made easier recently by the consensus definitions put forward by the North American Taskforce (Sanger *et al.*, 2003) (Table 4.1).

Effect of pathology and maturation on spasticity

The operational definitions and relative importance of spasticity are confounded by the issue of how spasticity affects growth and maturation in children with spastic-type cerebral palsy. It is a common clinical observation that muscle growth does not keep pace with bone growth in young children with cerebral palsy (Rang, 1990). It is assumed that decreased longitudinal growth of the muscle is caused by overactivity due to spasticity. Animal models of spasticity have demonstrated the lack of longitudinal growth of the muscle relative to bone (Ziv *et al.*, 1984). Furthermore, normal longitudinal muscle growth has been restored following intramuscular injections of Botulinum toxin A (BoNT-A) to reduce spasticiy, thereby allowing full muscle excursion (Cosgrove & Graham, 1994). Human studies have supported the notion that the muscle normally grows in response to full muscle excursion (Koning *et al.*, 1987).

(a)



(b)

Figure 4.2. (a) When this woman was asked to lift her hand off the table, she flexed her elbow. (b) However, when she understood that elbow flexion should not take place, with practise, she lifted her hand by bending at the wrist only. (With permission from Carr *et al.*, 1995.)

In addition, how muscles respond to casting to lengthen muscles may vary with age. Animal studies have shown that the response of young muscle to immobilization in a lengthened position differs to that of older muscle (Tardieu *et al.*, 1977a). The young muscle initially responds in a similar way to adult muscle by the addition of sarcomeres. However, no further addition of sarcomeres but a relative lengthening of the muscle tendon in the young animal follows this. Although there should be some caution in extrapolating evidence from the animal literature to clinical practice, these findings may explain the tendency for an overlengthened calf muscle tendon and short gastrosoleus muscle belly frequently seen after growth periods and after extended periods of serial casting in children with cerebral palsy. Recent ultrasound data support the shortness of the reduced fibre diameter in certain muscles (medial gastrocnemius) rather than reduced fibre length (Shortland *et al.*, 2002), which explains the differences in muscle architecture of children with cerebral palsy before and after surgery (Shortland *et al.*, 2004).

There can be an appreciable difference in the peripheral components of hypertonia in a young child with cerebral palsy (1 to 4 years) compared with adolescents who have undergone their second growth spurt. Clinically, younger children tend to demonstrate overactivity, which leads to reduced muscle excursion, while adolescents are more likely to demonstrate contracture and weakness. In addition, the development of contracture in certain muscle groups may be faster according to the motor distribution. In children with hemiplegia due to cerebral palsy, it is often the calf muscles before the hamstring muscles which develop reduced excursion whereas in children with diplegia it is often the hamstring and adductor muscles before the calf muscles (Boyd & Graham, 1997). The concept of the *biological clock* ticking faster in children with cerebral palsy in certain muscles according to motor type and aetiology has been proposed (Boyd & Graham, 1997). On the other hand, there may be a mechanical explanation. The child with cerebral palsy who spends most of his or her time sitting and crawling is likely to have shorter hamstring muscles. Prediction of which muscles are 'at risk' of shortening from observation of common patterns of overactivity and increased muscle stiffness will help in the prevention of muscle contracture.

The relative contribution of the positive and negative features in adults and children appears to differ due to the health condition. In stroke, problems of weakness and dexterity are more apparent (Carr *et al.*, 1995). In young children with cerebral palsy, the positive features of velocity-dependent hyperreflexia and inappropriate muscle overactivity lead to reduced muscle excursion and eventual contracture (Rang, 1990; Cosgrove *et al.*, 1994). By adolescence, weakness and muscle contracture may become greater problems.

Assessment of spasticity

An important component of the clinical management of brain damage is careful assessment of the contribution of various impairments to activity limitations. Unfortunately, this is not an easy task. Spasticity is most commonly measured clinically by either grading the response of the tendon jerk while the subject is relaxed (where an increased response is reported as hyperreflexia) and/or grading the resistance to passive movement while the subject is relaxed (where increased resistance is reported as hypertonia, e.g. Ashworth, 1964). Spasticity is most commonly measured in the laboratory by moving the joint (mechanically or manually), either by repeated oscillation (sinusoidal movement) or by a single ramp movement and quantifying the EMG activity in response to stretch (e.g. Neilson & Lance, 1978; O'Dwyer *et al.*, 1996b) and/or quantifying the resistance to movement (e.g. Gottlieb *et al.*, 1978; Rack *et al.*, 1984; Hufschmidt & Mauritz, 1985; Lehmann *et al.*, 1989; Corry *et al.*, 1997).

The difficulty is that both the clinical and laboratory measures of resistance to movement do not differentiate whether the cause of the hypertonia is neural or peripheral. The most valid measure of spasticity is the use of EMG during passive stretch of a muscle because the presence of stretch-evoked muscle activity is the only way of ascertaining a neural component. However, this is not a feasible

technique for clinical use. In one study, no relation was found between clinically measured phasic stretch reflexes (tendon jerks) and laboratory measured tonic stretch reflexes (Vattanasilp & Ada, 1999). The lack of relationship between these two tests of reflex activity can be explained by the fact that they are measuring different components of the stretch reflex response. The tendon jerk excites a phasic, monosynaptic component of the stretch reflex in response to a rapid stimulus. In contrast, sinusoidal stretch in which the input is ongoing excites a tonic, polysynaptic component of the stretch reflex. Fellows *et al.* (1993) have previously pointed out that the tendon jerk has limitations in providing a complete picture of the pathological changes in reflex responses following stroke.

While the Ashworth scale has been shown to adequately measure resistance (Vattanasilp & Ada, 1999), it measures both the neural and peripheral contributions to resistance without differentiating their individual contributions. However, the Tardieu scale (Tardieu *et al.*, 1954, 1957; Held & Pierrot-Deseilligny, 1969; Gracies *et al.*, 2000) appears on the face of it to be better at identifying a neural component (Scholtes *et al.*, 2006). By moving the limb at different velocities, the response to stretch can be more easily gauged since the stretch reflex responds differentially to velocity. A recent study (Patrick & Ada, 2006) indicates that the Tardieu scale is able to identify the presence of spasticity after stroke more effectively than the Ashworth scale in both an upper and lower limb muscle. Not only was the Tardieu scale able to identify the presence of spasticity, but it was also able to differentiate it from the presence of contracture. The velocity-dependent nature of the stretch reflex means that contracture can be measured under conditions in which hyperreflexia will be minimized. For example, by moving the limb slowly so as not to excite hyperexcitable reflexes and holding the muscle in a lengthened position for a while so as to dampen the reflex response, an accurate picture of muscle length can be gained. In order to increase reliability of the Tardieu scale, Boyd and Graham (1999) proposed standardized positions and velocities under which the catch angle of muscles should be tested in children with cerebral palsy (Fig. 4.3). Studies of inter-rater reliability of the modified Tardieu scale show acceptable reliability in the lower limb in children with cerebral palsy (Fosang *et al.*, 2003), yet Mackey *et al.* (2004) reported poorer reliability in the upper limb in children with hemiplegia. Mackey highlighted the difficulties in standardizing the velocity at which the limb is moved and the difficulties in defining the angle of catch range (Mackey *et al.*, 2004). These differences in reliability highlight the technical difficulties in standardizing a clinical measure in the presence of varying limb pathology in the upper and lower limbs in children with cerebral palsy. Nevertheless, the angle of response in the lower limb has been found to be more useful in detecting changes in spasticity after intervention in children with cerebral palsy (Lespargot *et al.*, 1994; Boyd & Graham, 1999; Love *et al.*, 2001).

In contrast, reliability has been reported as poor to moderate in severely brain-damaged adults (Mehrholz *et al.*, 2005). Patrick and Ada (2006) found that the level of muscle response to stretch was more valid than the angle in adults after stroke. At this stage, the Tardieu scale appears to be a useful tool, which is better than the Ashworth scale, particularly at differentiating spasticity from contracture.

Clinically, the most important measurement for physiotherapists is at the level of activity limitations – that is, the level at which impairments affect the everyday life of the person with brain damage. Spasticity is just one of the impairments which affects function. The clinician needs to carefully assess the relative contribution of the individual impairments and how they impact on activity limitations. In summary, in the clinic, muscle contracture and function can be assessed, and it is possible to gain some insight into the contribution of spasticity versus contracture to increased muscle stiffness.

Intervention

There is very little evidence of the efficacy of physiotherapy interventions directed specifically at reducing or eliminating spasticity to guide clinical practice. The little evidence from randomized controlled

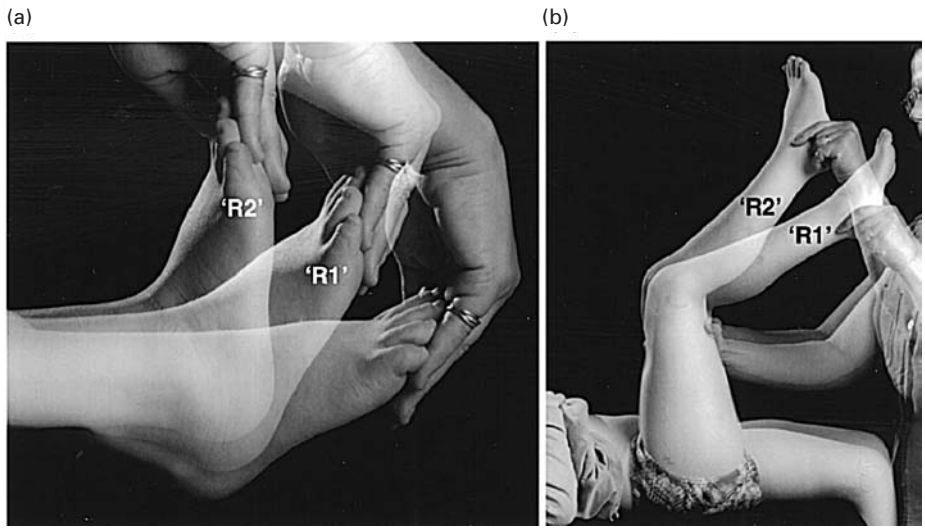


Figure 4.3. Modified Tardieu scale used in children with spastic-type cerebral palsy. (a) Ankle being moved into dorsiflexion and (b) knee being moved into extension. R1 represents the angle of muscle response (catch) as the joint is moved at the fastest velocity possible (Tardieu V3). R2 represents the angle of muscle response (end range) at the slowest velocity possible (Tardieu V1). The difference between R1 and R2 will indicate the relative contribution of spasticity versus contracture. A large difference between R1 and R2 indicates more spasticity whereas a small difference indicates more contracture. The difference between R1 and R2 can be used over time as a measure of impairment in clinical trials and to predict potential response to spasticity management.

trials or systematic reviews that exist is for an immediate effect of short-term interventions. For example, Gracies *et al.* (2000) applied dynamic lycra splints for 3 hours to the arms of people after stroke and found an immediate reduction in spasticity. Likewise, Agerionoti *et al.* (1990) vibrated the antagonist muscle and produced a reduction in spasticity of the agonist muscle after stroke. Currently there is no evidence to support a reduction in spasticity in children with cerebral palsy with physiotherapy (Butler & Darrah, 2001; Lannin *et al.*, 2006). Because of this paucity of information, clinicians need to identify the contribution of spasticity to activity limitations in order to plan effective management. For example, in adults, spasticity early after stroke has been found to contribute to contracture (Ada *et al.*, 2006). On the other hand, in children with cerebral palsy, the impairments of overactivity, inappropriate muscle force, adaptive soft tissue changes due to overactivity and imbalances with growth are most evident in younger children, whereas weakness and adaptive soft tissue changes due to non-use may become increasingly evident in the teenage years. Intervention needs to include training the patient to control muscles for specific tasks while eliminating unnecessary muscle activity during motor performance as well as maintaining soft tissue extensibility. It may be necessary to apply pharmacological treatment to dampen overactivity and reduce muscle stiffness, or if contracture already exists, to lengthen muscles by serial casting followed by training in these lengthened ranges (Boyd & Graham, 1997). If the lack of soft tissue extensibility is mostly contracture and/or bony deformity it may be appropriate to collaborate in surgical programs which will restore biomechanical alignment and balance the soft tissue contractures (Gage, 1994; Gough *et al.*, 2004). Where appropriate, orthoses may enable more practice to be carried out with appropriate biomechanical alignment. All these options must be accompanied by

motor training to control muscles for specific tasks while eliminating unnecessary muscle activity during motor performance.

Elimination of unnecessary activity

In the past, it was common for therapists to avoid instructing the patient to contract any potentially spastic muscles (Bobath, 1990). One of the difficulties with this strategy is that all muscle activity not appropriate to an action is considered spastic. Avoiding encouraging muscle activity due to apprehension that it will cause spasticity has been challenged by recent studies showing that, after a strength-training program, spasticity was not increased compared to the control (Winchester *et al.*, 1983; Dickstein *et al.*, 1986; Heckmann *et al.*, 1997; Powell *et al.*, 1999; Teixeira-Salmela *et al.*, 1999; Stein *et al.*, 2004; Taylor *et al.*, 2005). Not only have spastic muscles been found to be weak in cerebral palsy (Wiley & Damiano, 1998) but strength training has also shown improvements in function with no mention of an increase in spasticity (Damiano *et al.*, 1995; MacPhail & Kramer, 1995). In fact, strength training in children with cerebral palsy has been shown to be as effective in improving function as a selective dorsal rhizotomy plus strength training (McLaughlin *et al.*, 2002). It is important to aggressively train muscles which are important for everyday function (e.g. the calf muscles even if they are considered to be a common site of spasticity). Learning to control muscles eccentrically during task performance may be particularly useful as it involves the patient learning to decrease muscle activity. For example, the calf muscles work eccentrically during stance phase to control the movement of the shank forward over the fixed foot as the hip extends and then concentrically at push-off. These eccentric contractions can be practised by placing the forefoot on a wedge and lowering the body weight (Fig. 4.4a). For push-off the patient practises plantarflexion in step stance with the hip and knee extended and the ankle initially dorsiflexed (Fig. 4.4b). By learning to control calf muscle activity in these positions, the risk of developing overactivity and/or muscle contracture in these muscles is reduced.

In young children, such training is often more difficult to perform and tasks need to be adapted to account for lack of motivation and poor concentration by use of a suitable reward system. In training calf muscles in their lengthened range, the emphasis may be on walking up slopes, stair climbing and reaching in inclined standing with the hip and knee extended and the feet dorsiflexed under the body to ensure maximal lengthening. Increased amounts of appropriate practice can be achieved by the use of an ankle foot orthosis (Morris, 2002; Autti-Ramo, 2006) tuned with a wedge to correctly align the ground reaction force with the knee joint and ensure appropriate control of the calf muscle in gait. This training can progress to less constrained conditions by use of high-topped boots which encourage dorsiflexion, thereby enabling achievement of heel strike at initial contact, while still allowing control of forward progression of the tibia during midstance.

Training of appropriate muscles

Excessive, inappropriate muscle force can be a manifestation of spasticity or lack of skill. Either way, it is important to emphasize the correct application of muscle force during the performance of tasks. Practice may, therefore, need to be modified to allow the patient to participate without using unnecessary muscle activity. For example, during standing up from a seat, the greatest extensor torque is required at thighs off and this is larger the lower the chair (Burdett *et al.*, 1985). When standing up from a normal height chair is outside the realm of possibilities for a patient, the attempt may produce excessive weight shift to the intact side so that the knee extensor effort in the affected side causes the foot to move forward (often labeled as spasticity) rather than the trunk moving forward over a fixed foot. If the task is modified so that the patient practises standing up from a higher than normal chair, the extensor torque requirements are reduced and may enable more optimal practice. The patient will be able to keep more weight on the affected foot, thereby avoiding

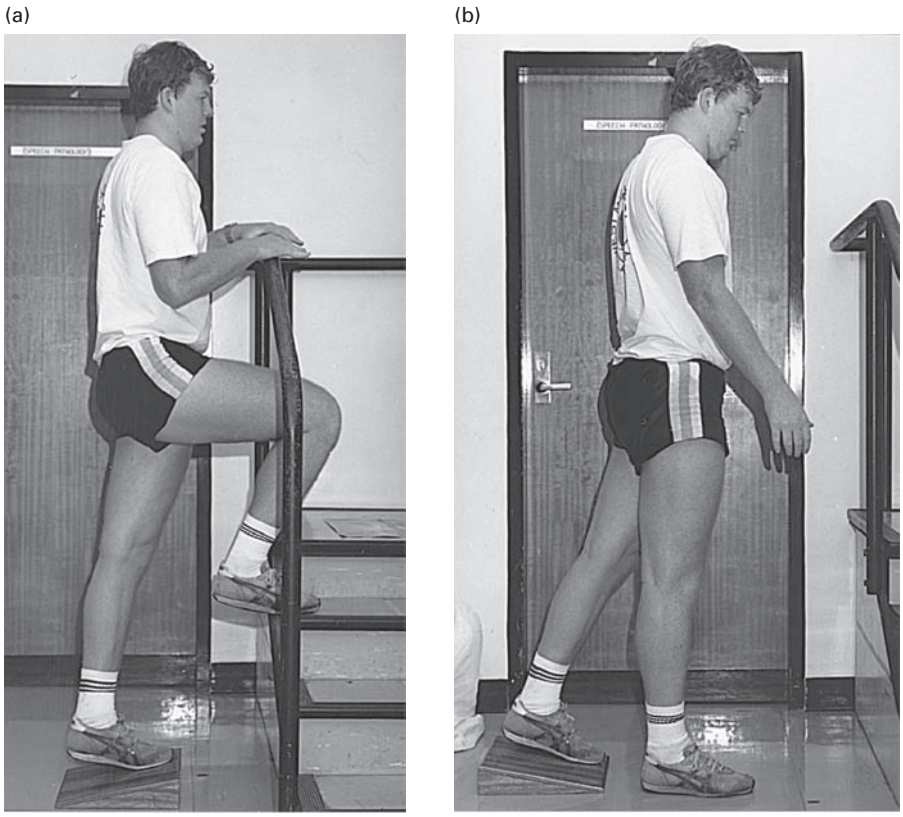


Figure 4.4. (a) By standing with the ball of one foot on a wedge and raising and lowering himself, this patient practises controlling his plantar flexors eccentrically and concentrically in a lengthened range. (b) He practises plantarflexing during the last part of push-off by shifting his weight forward with his hip and knee in extension.

the adaptive responses seen when standing up from a normal-height chair (Carr & Shepherd, 2003).

In children, it is more difficult for the physiotherapist to train the appropriate use of force in a motor task. There needs to be a greater emphasis on adaptation of the environment as well as use of auditory and visual cues to modify emerging motor behaviors. In grasping an object, they frequently use too much force so it may be appropriate to train drinking from a cup by grasping a 'squashy' plastic cup or to use Plasticine to make animal shapes, where appropriate force will be needed to produce the correct shapes. Different textures may be needed to reduce excessive force such as the adult task of holding a soft tomato without deformation and then progression of the task by cutting the tomato with a knife with the other hand.

In young children and adults with hemiplegia, there can be a strong tendency for non-use of the affected limb or more frequently the lack of skill in that limb means it is rarely used except in bimanual tasks. Constraint-induced movement therapy has been shown to be effective in overcoming this problem in adults (Hakkennes & Keating, 2005). In children with hemiplegia, there is growing evidence for a modified approach (Taub *et al.*, 2004; Eliasson *et al.*, 2005; Gordon *et al.*, 2005; Charles *et al.*, 2006; Hoare *et al.*, 2006). Manual restraint of the unaffected limb can be unacceptable to children, so placing the arm inside the clothing, placing objects out of reach of

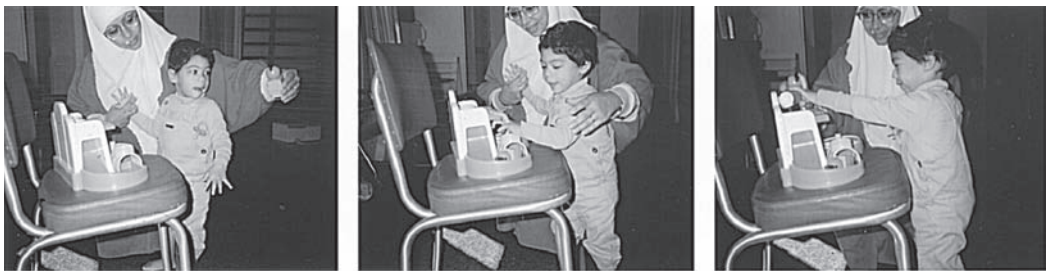


Figure 4.5. A young boy with left hemiplegia has his unaffected arm restrained by his mother during training of reaching and manipulation. The task is designed so that attainment of the goal (dropping the toy through the slot) is only achieved by appropriate manipulation of the toy.

the unaffected arm or use of that arm for support of the body can all be effective (Fig. 4.5). Training tasks for young children need to be motivating, so that successful completion of the task will give positive feedback and knowledge of results.

Prevention of adaptive soft tissue changes

Diligent prevention of muscle contracture is important, not only because full muscle length is necessary for optimal function but because of the relation between spasticity and contracture (Ada *et al.*, 2006). Both the immobility that is a major consequence of adult brain damage and the overactivity that is prevalent in children with brain damage may lead to increased muscle stiffness and contracture. Muscle length should be maintained, preferably through active training but where necessary by passive methods.

Muscles at risk of shortening should be trained in a lengthened part of range so that the voluntary contraction of the muscle and its antagonist can be practised. For example, in adults following stroke, muscles around the shoulder that are particularly at risk of shortening when muscle activity is poor are the internal rotators and horizontal adductors. By side lying with the shoulder in 90 degrees of abduction and the arm rotated to face the wall while moving the arm in small excursions from this position, these muscles are being lengthened and required to contract eccentrically (Fig. 4.6). Once some control over agonist and antagonist muscle groups in different ranges around the joint has been regained, the risk of developing contracture is diminished.

In young children with cerebral palsy, the greater issue is overactivity leading to increased muscle stiffness and reduced muscle excursion rather that inactivity leading to soft tissue adaptations. However, this relative contribution of overactivity and adaptive changes in inactive or weak muscle changes in adolescence. It is important for the clinician to predict in which muscles overactivity will lead to increased muscle stiffness (such as the adductor and medial hamstring muscles which result in scissoring postures in standing and stepping). If reduced muscle excursion continues, lateral displacement of the hip may occur. It will be useful to encourage abducted postures and training of reciprocal leg movements in an abducted position (e.g. riding a bike with adapted foot plates). Frequently overactivity of the adductor muscles occurs during a large portion of the day, so it may be appropriate to utilize functional bracing which still allows sitting, stepping, sit to stand and crawling in an abducted range (such as the variable hip abduction orthosis) (Fig. 4.7).

It is necessary to determine the relative contribution of muscle overactivity and length to alignment. For example, it is common for children with cerebral palsy to stand up on their toes (in equinus) with their knees flexed due to hamstring contracture and/or quadriceps weakness. A biomechanical approach to assessment analysis needs to differentiate whether the plantarflexed posture of the ankles is ‘true equinus’ (due to predominantly

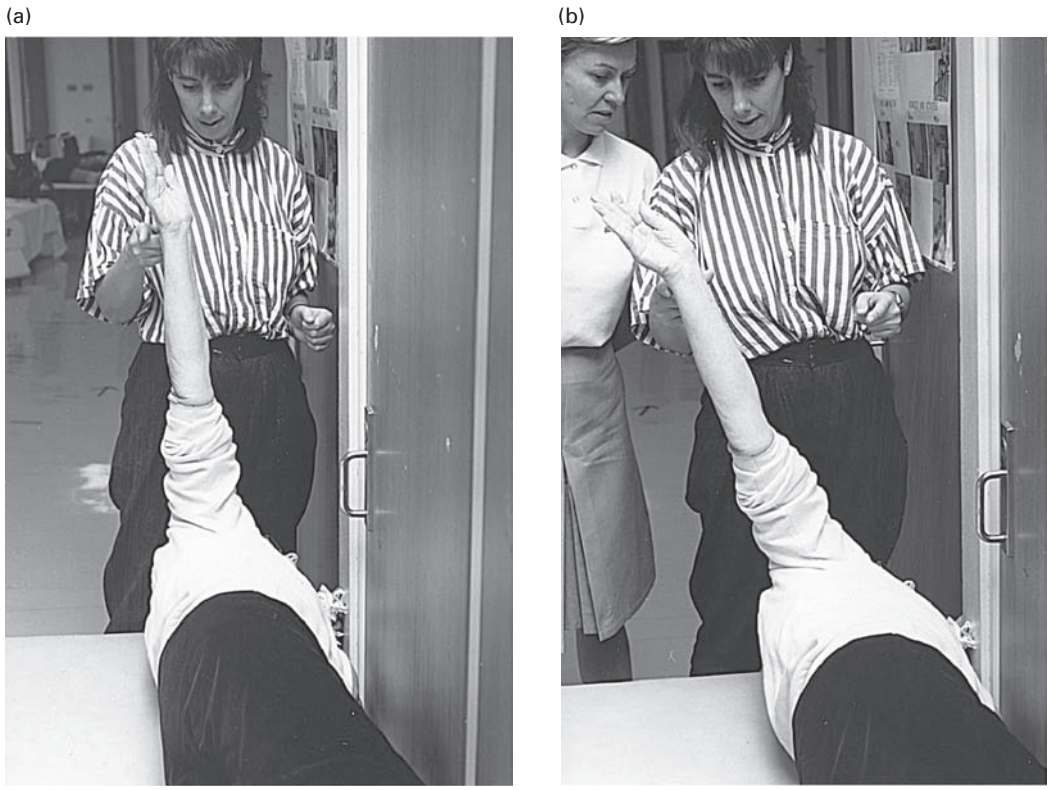


Figure 4.6. (a) By lying on her side with her arm facing the wall, the patient's muscles at risk of developing contracture (such as the horizontal adductors and internal rotators) are in a lengthened range. (b) The patient can then practise using her weak shoulder muscles in a relatively gravity eliminated position by making small excursions from this position.

an overactive calf muscle) or whether it is 'apparent equinus' flexed knee position (due predominantly hamstring overactivity) (Boyd & Graham, 1999). In apparent equinus, management needs to focus on training the hamstrings in the lengthened position as well as training the weak quadriceps using, e.g. squat to stand maneuvers. For example, Damiano *et al.* (1995) demonstrated the effectiveness of a quadriceps strengthening program in improving crouch gait. If calf muscle length is adequate, then techniques to lengthen the calf muscles alone would be ineffective.

Where patients are immobilized due to either paralysis following stroke, severe overactivity due to cerebral palsy and/or unconsciousness following head injury, muscle length may have to be maintained using passive methods. The most important principle is to keep the muscle at risk of shortening in a lengthened position for some time. Sustained periods of lengthening may be achieved by using sandbags to weight a limb and keep it in one position as well as gaiters or splints to control limb position. Positioning to lengthen multiarticular muscles needs to take into account the position of all the joints that the muscle crosses (e.g. lengthening the hamstrings requires hip flexion as well as knee extension).

In severe cases of children with bilateral cerebral palsy, maintaining muscle length will require sustained positioning using special seating, standing frames and supportive mobility devices in positions that will allow functional training of the upper limbs.

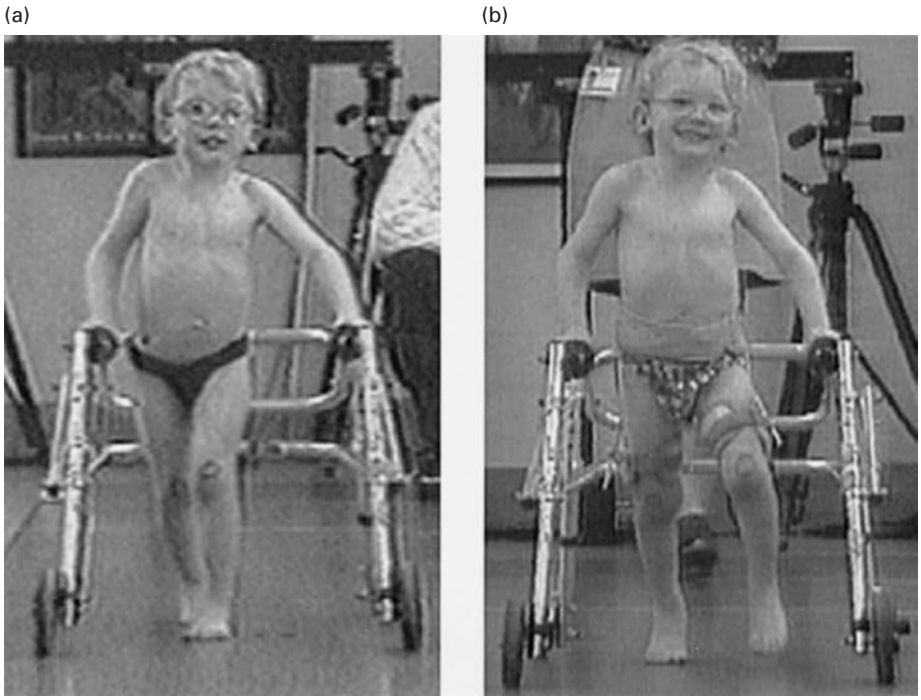


Figure 4.7. (a) A young boy with spastic-type diplegia usually walks with a scissoring posture of the lower limbs. (b) Use of a variable hip abduction orthosis puts the adductors in a lengthened position during walking.

It may be necessary to focus on training motor behaviors such as standing and stepping and bypassing others such as crawling as certain important muscles which tend to shorten with growth may not be utilized in their lengthened range in crawling. This is the case when the hamstring muscles shorten in children with cerebral palsy who predominantly crawl, sit between their heels and who therefore find full knee extension for standing and stepping more difficult.

There is some evidence that serial casting, the most extreme form of positioning available to the physiotherapist, is effective in lengthening muscles which have already shortened in adult brain injury (Mortenson & Eng, 2003). Interestingly, in a recent randomized trial of adults with traumatic brain injury, Verplancke *et al.* (2005) showed that the addition of botulinum toxin A did not result in any greater gains in range of motion than casting alone, probably because botulinum toxin A would not be expected to have an effect on contracture. The emphasis on casting techniques should be upon short periods of casting with frequent changes to serially lengthen the muscle because extended periods of casting may lead to weakness and stiffness.

In children with cerebral palsy there is good evidence to support the effectiveness of intramuscular injections of botulinum toxin A compared to placebo for equinus gait in presence of spasticity (Boyd & Hays, 2001). There is some evidence to support the effectiveness of BoNT-A provided prior to casting for a combination of spasticity and contracture in the gastrocnemius (Boyd *et al.*, 2001; Delsoorvere *et al.*, 2001; Bottos *et al.*, 2003; Ackmann *et al.*, 2005) but not in combination in the presence of contracture (Kay *et al.*, 2004). There is some evidence for casting alone in the lower limb for equinus gait in the presence

of contracture (Cottalorda *et al.*, 2000) but there are no randomized trials of casting alone compared to therapy.

Pharmacological and surgical options

There are many pharmacological and surgical options available in the management of spasticity, which may be focal or general, reversible or permanent in action (Boyd & Graham, 1997). Several other chapters in this book address these options in detail, so our emphasis here is upon the physiotherapist's role in patient selection, evaluation of outcome and, most importantly, motor training to achieve maximum benefit.

In pharmacological management, the physiotherapist's role is to identify the relative contribution of the positive impairments such as spasticity, muscle stiffness and muscle contracture, and the negative impairments such as weakness and poor selective control so that a total program can be planned which is aimed at the individual impairments. In assessing suitability of patients for pharmacological agents, it is important to recognize the expected action of the agent on the motor impairments, and choose appropriate tools to evaluate impairments (e.g. it is important to determine whether efficacy in the target muscle group has been established). For example, botulinum toxin A can be expected to reduce spasticity but has been shown not to be useful in reducing contracture when used as an addition to casting in adult brain-injured people (Verplancke *et al.*, 2005). This illustrates the importance of a clinical measure that differentiates spasticity from contracture such as the Tardieu scale.

There have been systematic reviews and more recent randomized trials evaluating the outcome of botulinum toxin A in the upper limb of cerebral palsy children in comparison to other upper limb treatment options (Boyd & Hays, 2001); with and without varying intensities of upper limb training (Wasiak *et al.*, 2004; Speth *et al.*, 2005; Lowe *et al.*, 2006). There are improvements at the level of impairment established (Wasiak *et al.*, 2004) and activity limitation (Boyd *et al.*, 2004; Lowe *et al.*, 2006) but no additional benefit for participation and health-related quality of life over task-specific training alone (Boyd *et al.*, 2004). In the lower limb there is good evidence for a treatment effect compared to placebo injections in equinus gait (Ade-Hall & Moore, 1999; Boyd & Hays, 2001) but variable evidence to support improvements in activity limitation (Love *et al.*, 2001; Reddihough *et al.*, 2002). These data have been sufficient to support the additional use of BoNT-A for equinus management in terms of costs and consequences (Houltram *et al.*, 2001).

An initial intramuscular injection BoNT-A to address overactive or stiff muscles may need to be followed by short periods of serial casting to address any residual muscle contracture (Boyd *et al.*, 1999; Desloovere *et al.*, 2001). A training program is essential to address any negative features of incoordination and weakness, which may be evident. Management may require suitable orthoses that are geared to providing the appropriate biomechanical alignment outside training sessions. For example, improvement in gait is not always seen following BoNT-A injection alone. Active training and use of orthoses for carryover has been shown to be essential in achieving improved motor performance (Boyd & Graham, 1997; Morris, 2002). In some cases, these interventions have enabled carryover of effects of BoNT-A injections well beyond the estimated 6 months pharmocological response (Boyd *et al.*, 1999; Boyd *et al.*, 2000) (Fig. 4.8).

There is evidence that BoNT-A decreases spasticity in adults with severe spasticity after stroke and makes caring for the individual easier (Van Kuijk *et al.*, 2002). Similarly, intrathecal baclofen decreases spasticity and improves caregiving although significant adverse effects such as infection and technical failure of the pump have been reported (Creedon *et al.*, 1997; Meythaler *et al.*, 2001; Steinbok & O'Donnell, 2000). The physiotherapist's role in these situations is to optimize the outcome by maintaining the gain in range of motion that allows easier handling of the patient.

Where spasticity is generalized and persistent, surgical procedures such as selective dorsal rhizotomy (SDR) have been proposed. Results from three

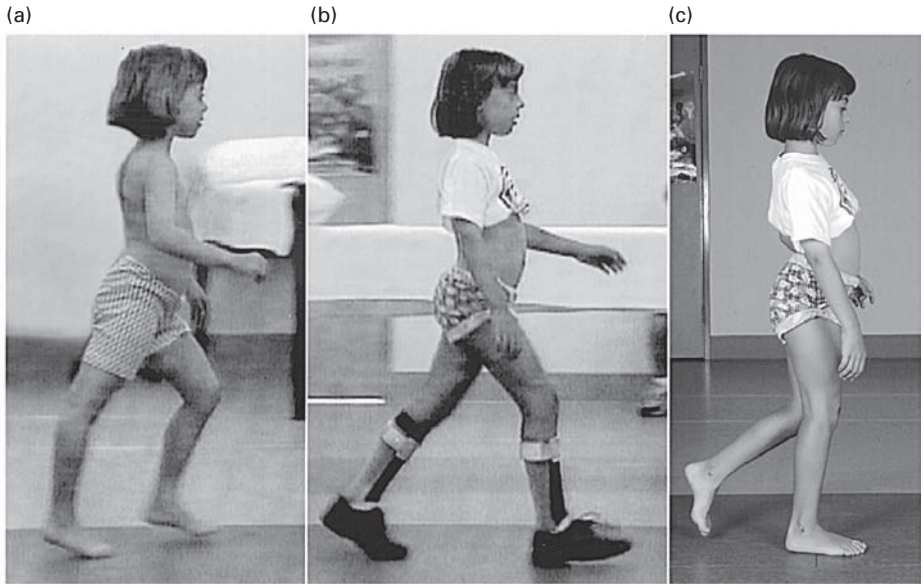


Figure 4.8. (a) A girl with spastic-type diplegia walks with an overactive plantar flexion–knee extension couple due to overactivity of the calf muscles. (b) Following intramuscular injection of BoNT-A, a fixed ankle-foot orthosis is used to provide the appropriate biomechanical conditions to train knee control during gait. (c) Thirteen months later, adequate length of the calf muscles has been maintained and good control without the orthosis has been achieved.

randomised controlled trials appear variable (Lin, 1998; McLaughlin *et al.*, 2002). McLaughlin (1997) compared a strengthening program with SDR plus strengthening and showed no difference between the groups in terms of gross motor function. SDR aimed at managing spasticity may have been inappropriate as weakness rather than hyperreflexia may have been the main problem (Guiliani, 1991). These findings illustrate the importance of patient selection for SDR and training the negative features of brain damage, such as strength, as well as attending to the positive features (Dodd *et al.*, 2002; Taylor *et al.*, 2005).

In children with cerebral palsy where muscle contracture and poor biomechanical alignment has become severe, a program of single-event multilevel surgery (SEMLS) (Boyd & Graham, 1997) may be appropriate as opposed to multiple surgical events at single levels ('the birthday syndrome') (Rang, 1990; Gage, 1994; Gough *et al.*, 2004). SEMLS should only be undertaken after the initial growth period and when gait performance has plateaued around 7 to 10 years of age. An effective program of management of muscle overactivity (with BoNT-A) and motor training is used to delay SEMLS to after gait maturation (Boyd & Graham, 1997). The outcome from SEMLS will not be optimal if overactivity continues to cause reduced muscle excursion and interfere with motor function. This surgical approach of restoring bony lever arm alignment and balancing soft tissues in one occasion of treatment needs to be followed by an active training and strengthening program. Children may be taller and straighter following SEMLS but not necessarily more effective in motor performance. The physiotherapist must train control of lengthened and transferred muscles in the context of motor tasks (e.g. stepping up and down, sit to stand), using objective assessment of gait to prescribe appropriate ankle foot orthoses and gait aids. They should continue to suggest training programs to build confidence, stamina, gait independence and participation in activities of daily living and sport.

Conclusion

Effective intervention for the activity limitations associated with adults with stroke and children with cerebral palsy requires careful assessment of the contributing impairments – not only spasticity but also contracture, weakness and loss of dexterity. In this chapter, we have presented an evidence-based model of clinical intervention for both adults and children with spasticity following brain damage. Strategies presented are increasingly focused on improving activity rather than solely reducing impairments. Examples have taken into account the modifications necessary to cope with growth, maturation and motor learning in children.

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5

Seating and positioning

Craig A. Kirkwood and Geoff I. Bardsley

Introduction

Spasticity causes seating challenges for a wide variety of people with disabilities: from children with cerebral palsy, young adults with head injuries, middle-aged people with multiple sclerosis (MS) and older persons who have suffered cerebrovascular accidents (CVAs) and use wheelchairs.

The nature of spasticity is complex and controversial, as discussed elsewhere in this volume. Clinical characteristics described as constituting spasticity and that influence seating include increased muscle tone, hyperactive stretch reflexes, changes in muscle structure and function and abnormal activity caused by posture (e.g. tonic neck and labyrinthine reflexes) (Ford, 1986; Shepherd, 1995).

Spasticity, in itself, is not necessarily a problem and may assist in maintaining a seated posture. This is in contrast to hypotonia, where providing seated support in a functional position is often very difficult. However, there are three key problems that spasticity can cause to the person in a seated position:

1. Postural instability
2. Reduced upper limb function
3. Joint contractures

Correct positioning of the person can assist in reducing these problems (Zollars, 1993). Addressing one of the areas has a largely beneficial effect on the others, so there is little trade-off in strategies to tackle these problems. Barnes (1993) states: 'positioning of the individual is the most important element in the management of spasticity' (see also Vaughan & Bhakta, 1995).

Appropriate seating should be seen as adjunct to the other approaches discussed in this book which may have greater precedence with increasing severity of spasticity (e.g. pharmacological, surgical) (Richardson & Thompson, 1999). This is important to note, as there are often expectations that correct seating will tackle all problems an individual has resulting from spasticity when other methods have been unsuccessful.

As Barnes (1993) notes, the management of spasticity requires a team approach with the involvement of 'nurses, physiotherapists, physicians, occupational therapists, orthotists and wheelchair specialists' in addition to the patient and their carers. This multidisciplinary approach should be regarded as 'best practice' as often the various health professionals seek to tackle spasticity with little knowledge of what the others are doing.

Although this chapter is mainly concerned with the seated aspect of positioning, particularly for those who spend long periods in a wheelchair, it is important to remember that people also spend many hours lying down, and correct positioning during this period is equally important (Scrutton, 1971, 1978; Todd, 1974; Bell & Watson, 1985; Nelham *et al.*, 1992). While the same principles in terms of positioning and design considerations apply, it is also important that, over a 24-hour period, a variety of positions be used to move joints through their range of motion (ROM)

and prevent soft tissues from becoming contracted in a 'seated' position.

Clinical assessment

Detailed assessment is essential so that a full picture of the patient's problems relating to spasticity is drawn up in order that clear, specific and realistic objectives can be agreed on by all those present and a detailed prescription produced to achieve the objectives.

Assessing the patient with spasticity for seating may involve four procedures to assist in determining the effect of the spasticity:

1. History taking. Soliciting information of the particular problems that occur with increased tone and factors which exacerbate tone and produce associated reactions. This background information is particularly important, as the clinical situation itself can have a significant effect on the patient's presentation (Harburn & Potter, 1993), and he or she may also have recently had medication to control spasticity – particularly if traveling a distance to an appointment. It may be useful for video to be used to unobtrusively monitor the patient in particular situations where there is a problem – as in feeding.
2. Examination on plinth in supine. While determining range of joint motion, account can be taken of resistance to motion and variation according to speed of movement.
3. Support in seated posture. While the patient is well supported in a seated posture (by one or more staff), account can be taken of tone in body (by those supporting) and changes to apparent range of motion in lower limbs, as it is often found that in patients with very high tone, hip flexion in supine is extremely difficult; but when seated with support, there is a reduction in tone, allowing true level of contractures to be assessed. As sitting balance is affected by the level of spasticity (Yang *et al.*, 1996) it may be useful to grade this – as by using the Chailey scale (Green & Nelham, 1991).
4. While supported in a seating simulator. Account can be taken for functional ability (e.g. to lift cup and drink) and the simulator can be adjusted to check for variations in function.

Principles of seating and positioning

The basic philosophy of seating is the same for all patients: 'that the body should be maintained in a balanced, symmetrical and stable posture that is both comfortable and maximizes function' (Barnes, 1993). It is the nature of spasticity to produce postures that are unbalanced, nonsymmetrical and unstable with the result that the patient is uncomfortable and there is impairment of functional ability.

The following are ten principles which should be considered in seeking to achieve an 'optimum' seated position for those with spasticity. They explore the diverse range of factors which relate positioning and spasticity and which may affect postural stability, function and the development of contractures.

Sustained muscle stretch

The key principle in reducing spastic contraction is the same as that applied in physiotherapy – sustained muscle stretch, that is, working against the spastic muscle (Bobath, 1977). Stretching reduces spasticity directly in the muscle being stretched by depressing the muscle spindle (Kaplan, 1962). It also reduces the possibility of contractures (Harburn & Potter, 1993; Bakheit, 1996). It has also been demonstrated that such a reduction of spasticity may also permit greater use of the upper limbs (Nwaobi, 1987a).

As such, correct positioning in seating is consistent with a physiotherapy program that emphasizes the importance of daily ROM exercises and static muscle stretch to prevent contracture and reduce spasticity (Little & Massagli, 1993). Odeen (1981) reported increased ROM and decreased activation of the antagonist in voluntary abduction by using a mechanical leg abductor for 30-minute treatment sessions.

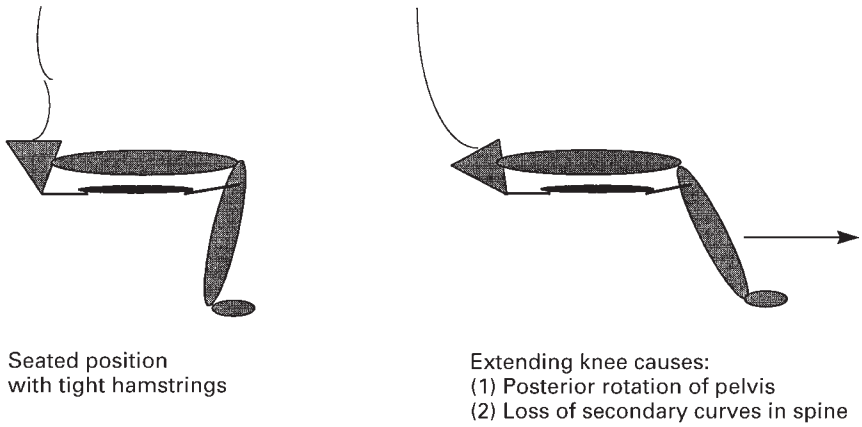

Figure 5.1. Effect of hamstring stretch on seated posture.

As well as reducing spasticity, sustained muscle stretch helps to prevent contractures which is important because of pain they can produce and the difficulty of treating (Botte *et al.*, 1988). The muscle contracture itself may potentiate the stretch reflex (O'Dwyer *et al.*, 1996) causing further problems with spasticity.

When applying a muscle stretch using seating support elements, the same principle as serial casting (Brunner *et al.*, 1996) can be utilized, whereby gains in comfortable ROM at a joint can be consolidated and increased by providing progressively greater stretch. This implies that the seating must be monitored and frequently reviewed to build on gains and address failures.

One possible exception to this principle, when applied to the seated posture, is stretching of the hamstrings. This is because they extend over two joints; therefore, in the common case where there is knee flexion produced by spasticity, extending the knee also acts to posteriorly rotate the pelvis (Zollars, 1996) and has tendency to pull the person out of the wheelchair and produce a kyphtoic spinal posture (see Fig. 5.1). In order for a hamstring stretch to be effective, the pelvis must be firmly secured both anteriorly and posteriorly to prevent movement, and in practice this is difficult to achieve.

The link between hip flexion and hand function is controversial. No relationship was reported by Seeger *et al.* (1984), but Nwaobi *et al.* (1986) reported that 90 degrees gave better function compared to 50, 70 and 110 degrees.

Using standing (e.g. tilt table) for load bearing (Odeen & Knutsson, 1981; Tremblay *et al.*, 1990) has been successful in producing a muscle stretch that reduced spasticity. This position has other benefits, such as bladder drainage and increasing bone density for those who spend long periods sitting.

Maintenance of hip integrity

A common problem encountered in seating children with cerebral palsy is hip subluxation and dislocation. Kalen and Bleck (1985) identify the primary aetiology and therefore the primary focus of treatment to be adductor and iliopsoas spasticity and contracture.

It has been noted from X-rays that the acetabulum of the adducted hip does not develop normally, with increasing subluxation and eventual dislocation of the hip (Fulford & Brown, 1976). Howard *et al.* (1985) found from examining the X-rays of hips of patients with cerebral palsy that 79% of bilateral hemiplegics had abnormal hips; the majority of these were

nonwalkers and the others required a frame or rollator. Young *et al.* (1998) found that of patients determined to have spastic quadriplegia, 25% had hip dislocation and 63% subluxation. This reinforces the need to address hip status, particularly among children with more involved cerebral palsy.

In addition to the pain that can be caused to the patient by compromised hips (Bagg *et al.*, 1993), there is then an asymmetry in the interface between the patients' pelvis and hips and the seated surface, thus producing an asymmetric pelvis and consequent postural scoliosis, which may become less flexible with time. There is also an increased risk of pressure sore problems on the more heavily loaded side of the pelvis.

Helping to maintain hip joint integrity is therefore an important part of seating in wheelchairs. Problems are particularly likely in patients with adductor spasticity. When the distal end of the femur is pulled to the midline, this tends to pull the femoral head away from the socket, therefore compounding the lack of normal weight bearing in promoting acetabular development. Scrutton (1991) emphasizes the need for correct positioning and the experience of standing for those under 4 years of age, as this is when such problems begin to develop.

A common, related problem is 'windsweeping', where there is an abduction contracture of one hip and an adduction contracture of the contralateral hip, with subluxation or dislocation (Lonstein & Beck, 1986). This is often related to pelvic obliquity and scoliosis, thus presenting a significant seating problem (Young *et al.*, 1998). As Young *et al.* state: 'those with asymmetry of tone and severe spasticity seem to be at the greatest risk for dislocation, with a windswept hip deformity toward the opposite side'.

Tight, and eventually contracted adductors with consequent dislocated hips cause serious toileting problems (Cornell, 1995) and represent a common indication for surgery, together with the impossibility of relocating the hip joint by soft tissue operations alone (Samilson *et al.*, 1967). As Spencer (1999) emphasizes, the complexity of surgery, the problem of postoperative pain for the child and great difficulty in treating a painful dislocation in young adults are strong indicators for the close monitoring and conservative management of hips in children with cerebral palsy.

This problem needs to be addressed primarily by abducting the hips. In seating, it is important that sufficient abduction is used to produce the required muscle stretch and maintain the integrity of the femoral head/acetabulum interface. Many pommels that are commonly used in cushions are relatively narrow in width and therefore serve mainly to prevent contact between the thighs, thus limiting adduction without producing abduction. This may be general practise because a pommel wide enough to produce an abducted hip position would have poor cosmesis and may be impractical when skirts are worn.

An alternative option is the use of a hip abduction orthosis (Bower, 1990) to maintain the relationship between the femurs and pelvis combined with use of a seating system. Another is to use a seating orthosis combing spinal jacket and abduction orthosis (Carlson & Winter, 1978), which gives better control of hip position.

An approach commonly used in seating that addresses the problem of windsweeping is the application of a knee block (Scrutton, 1978; Green & Nelham, 1991). Figure 5.2 illustrates the application of forces to produce a corrected position. The knee block works by applying a derotational force along the femur of the abducted hip and an abducting force to the adducting hip together with stabilization of the pelvis. It is critical that a knee block be adjusted and used correctly if it is to be effective and that hip integrity is established on the side that the derotational force is applied.

Proper positioning following hip surgery is also crucial in order to maximize its benefits (Scrutton, 1989). It is vital, therefore, particularly when casts are removed, that the hips be positioned correctly when the patient is seated in the wheelchair in order to consolidate gains made by surgery.

Trunk orientation

Appropriate orientation of the trunk in space is an important consideration in any seating system. As a

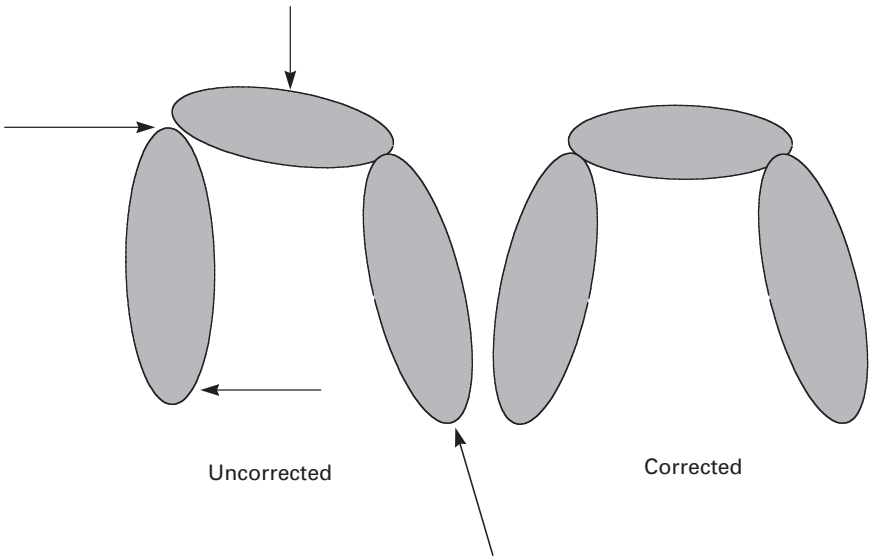

Figure 5.2. Application of forces to correct windswept deformity and establish hip integrity.

number of patients present with anterior trunk postural stability problems, it is often tempting to use a seated orientation that is tilted back to increase use of the back rest and utilize the effects of gravity to locate the patient against the back rest, therefore reducing the need for activation of postural support muscles.

Research with able-bodied people has shown that sitting against a more reclined back rest reduced activation of the back extensor (Andersson *et al.*, 1974, 1975). This finding, however, cannot be transferred to those with spasticity, where factors such as labyrinthine responses and a feeling of disorientation and falling (Green *et al.*, 1992) can have a significant effect.

It has been shown that muscle activity and movement time of upper limbs increased in children with cerebral palsy when a back rest reclined from the upright was used (Nwaobi & Trefler, 1985; Nwaobi, 1987a).

Nwaobi (1986) looked at twelve children with cerebral palsy (spastic diplegia, mild to moderate) who were tested in an upright and 30 degrees tilted back position. There was a marked and statistically significant ($p \leq 0.05$) increase in activity of back extensors when tilted back (the hip adductors and ankle plantar flexors showed small increases in mean value, but this was not statistically significant).

The variability of such studies was shown when Nwaobi *et al.* (1983) looked at eleven children with cerebral palsy in seven combinations of seat and back rest inclination. This study showed that the mean EMG increased with a rearward inclined back rest, but not significantly ($p = 0.05$) so; there was a marked and significant change with the back rest inclined forward by 15 degrees.

Tilting someone back also reduces their ability to interact with their environment and decreases social stimulation and visual awareness. While a compromise may be considered in a device with variable tilt, it is important that the way such a device is used be discussed with the patient's caregivers, so that it is tilted back only when appropriate (e.g. if the user falls asleep).

Restraint of arm movement

It may be appropriate in certain situations that unwanted arm movement is restrained to help reduce tone and associated reactions and produce functional gains.

Restraint of nondominant arm

A request that is often by made by patients presenting with athetosis is that the nondominant arm be restrained in order to gain better control of the dominant arm (e.g. for use of a joystick on a powered wheelchair). Sometimes this effect has been achieved by the patients themselves, wedging their nondominant arm within the wheelchair/seating system to restrict its movement.

A single case study by Nwaobi (1987b) showed a marked reduction in deltoid activity in the restrained arm and some reduction in the nonrestrained arm. It was also found that quadriceps activity in both legs reduced notably, showing that there was no overflow to distal segments caused by the restraint and, in fact, that there is a generalized reduction in tone.

Restraint of both arms

Where both arms are nonfunctional and athetosis is a problem, it may be appropriate to restrain both arms to achieve functional gains with, for example, chin control of an electric wheelchair.

Trefler (1986) found, in a study of fourteen children with athetoid cerebral palsy using arm-restraint trays, that they were perceived by the parents and teachers as providing more function and comfort and that they were generally well received by the children.

Postural stabilization

The importance of an integrated approach to postural stabilization has been examined by Myhr and von Wendt (1990, 1991, 1993) and Myhr (1994). These studies have explored a 'functional sitting position' which has the following as key elements:

1. Symmetrical fixation of pelvis with firm posterior support and hip belt anchored under seat
2. Abduction orthosis
3. Placement of the line of gravity of the upper body anterior to the axis of rotation of the ischial tuberosities

The seated position also incorporates a tray to assist upper body support as a result of (3) and free positioning of the feet (which tend to move backward).

It was found that this stabilization of position produced improved postural control and upper limb function by reducing pathological movements and spasticity.

Reduction of unnecessary upper limb activity

In past years it was standard practise to prescribe occupant-propelled wheelchairs, often with one-arm drive, to patients with hemiparesis during their rehabilitation to encourage physical activity and promote independence. However, it was often noted that the effort involved in propelling the wheelchair increased tone and associated reactions in such patients (Ashburn & Lynch, 1988) because of the general principle that associated reactions are caused by forceful movements in other parts of the body (De Wald, 1987). Therefore, this was undermining the efforts of physiotherapists to reduce spasticity.

Cornell (1991) looked at ten subjects with hemiparesis undergoing rehabilitation. Both attendant and occupant propulsion were used on a test track with photographs being taken before during and after the test run. The photographs were independently assessed to indicate the level of spasticity by body position. In general the level of spasticity increased, often markedly, with occupant propulsion, whereas in general there was little difference with attendant propulsion.

Dvir *et al.* (1996) after examining the relationship between graded effort and associated reactions, concluded: 'This study indicates that there is a direct relationship between levels of effort induced in the nonplegic forearm and the associated reactions elicited in the plegic forearm of post-stroke patients'.

For this reason, it may often be more appropriate to use a powered wheelchair, at least initially, so that independence can be gained without producing associated reactions and an increase in spasticity. Although, as Ashburn and Lynch (1988) comment, there is a danger in becoming dependent on the

wheelchair with resulting disuse of motor skills, pain, stiffness and difficulties in extending lower limbs together with the difficulty of taking a wheelchair away from a patient once issued.

In addition it should be noted that Blower *et al.* (1995) found that wheelchair propulsion ability at 3 weeks poststroke was 'the most accurate guide to walking potential that has been reported to date'.

The same rationale means that any unnecessary activity involving significant exertion whether in the upper limbs or lower limbs (e.g. propelling by foot paddling) should be avoided (Bobath, 1977); therefore, activities should be constructed to minimize exertion and thereby avoid increasing spasticity.

Although there are those (Blower, 1988) who feel that the benefits of independent manual wheelchair use outweigh any disadvantages accruing from an increase in spasticity, the benefits of independence and morale are equally true of using a powered chair and perhaps more so, as they give a greater range of travel and leave the users less fatigued to perform activities on arrival at their destinations.

The use of manual and powered chairs and encouraging walking therefore requires careful judgement to balance the relative advantages and disadvantages in the early rehabilitation of stroke patients. All patients with spasticity using manual chairs should therefore be monitored for adverse effects.

Reduction of noxious stimuli

The provision of seated postural support must also take account of the fact that it is not only external, physical factors altering position that influence the level of spasticity but also the patient's mental state and perceptions, which have an important mediating effect. So, for example, biofeedback can be utilized to control the stretch reflex gain. O'Dwyer, Neilson and Nash (1994) found that after a training programme involving feedback of the gain of the tonic stretch reflex, that the stretch reflex gain was significantly reduced in all subjects.

Katz (1988), Barnes (1993) and Bakheit (1996) have highlighted the importance of avoiding noxious stimuli, involving prompt treating of urinary tract complications, preventing pressure sores and contractures and proper bowel and bladder management. In the context of providing seated support, noxious stimuli can arise from factors such as discomfort from long periods of sitting (insufficient pressure relief), excessive pressure being applied to maintain seated posture and inappropriate seating causing pain (e.g. pressure from wheelchair back rest tubes).

An important aim therefore is that the seating system should be comfortable, in all aspects, for a reasonable sitting duration coupled with the recognition that changes in seated position and device are important throughout the day. Therefore an armchair for relaxation should offer equally as appropriate support as the wheelchair.

It is of particular importance to take account of variations in the patient's state during the day (e.g. tiredness, reduced tone after pharmacological intervention) so that the seat gives the required support for these states. Patients may sit well in a clinic when highly stimulated to maintain posture and when no upper limb activities are being performed. However, in everyday situations, they may find their activities limited by, for example, fear of imbalance when using the upper limbs, giving rise to an increase in tone because of the perceived problem – just as fear of falling increases spasticity in ambulant hemiplegic patients (Bobath, 1977). The placebo effect of a clinic should not be underestimated (Bishop, 1977), although a clinic event may also give rise to anxiety and worsening of spasticity. The user's perception of postural security and comfort is as important as the 'actual' support and pressure distribution provided.

Factors such as the importance of outdoor clothing to maintain temperature (Shirado *et al.*, 1995) also deserve consideration.

Alternative postures

Variation in posture is important to maintain joint mobility, reduce the effects of sustained application

of pressure and provide different types of stimulation.

It is important not to be constrained by standard ideas of what constitutes a seated posture, particularly for those who have impaired walking ability. Other aspects of seating have been explored in relation to reductions in spasticity and improved posture and function.

Horseback riding

In addition to the static aspects of sitting, the dynamics of sitting are emphasized in horseback riding (Bertoti, 1988; Heine, 1997), where a combination of sitting posture with legs held in flexion, abduction and external rotation together with the movement of the horse are believed to help reduce spasticity. Quint and Toomey (1998) used a horse-riding simulator and reported increased pelvic mobility after use indicating that the hip abduction and rhythmical movement may reduce spasticity.

SAM system

The SAM system, where a saddle seat system is used, was developed by Pope *et al.* (1988). They conclude that 'indications exist which suggest that the control of spasm is more a function of trunk posture relative to the supporting base than of the degree of hip flexion'.

Standing

Noronka *et al.* (1989) report no difference in upper limb function between sitting and prone standing. However, Odeen and Knutsson (1981) reported significant reductions in spasticity with paraplegic patients who engaged in weight bearing by using a tilt table and thus stretched their calf muscles. Similairly, Tremblay *et al.* (1990) found significant reductions in spasticity in twenty-two children with spastic cerebral palsy also standing with feet dorsiflexed on a tilt table.

Positioning in the seat

A well-designed seating system is only as good as the accuracy within which the person is positioned. A particular difficulty frequently encountered is that an appropriately prescribed seating system is not used correctly and therefore has reduced effectiveness.

Typically, when a patient is hoisted, to transfer into a seat, there is an increase in tone, often producing hip extension or knee flexion, so that when the patient is positioned on the seat, he or she is not in the correct position (Scrutton, 1966). Time needs to be taken to allow the tone to reduce and to move affected joints slowly to allow a repositioning in the seat.

This is very important, as patients who have been incorrectly positioned are frequently encountered, and the same level of care should be applied to instruction of use of the system in practise as to the original prescription. This particularly applies to removable items, such as knee blocks, which can easily be misused. It should also be considered to what extent restraining straps and belts require to be adjustable, as inappropriate slackening can reduce the effectiveness of the entire seating system.

Position of tasks

While it is important to reduce upper limb effort, it is of equal importance to consider the placement of even minimal effort tasks relative to the wheelchair user. The task should not be orientated so that the patient has to move out of the supported position. In the context of ergonomics a sloping work surface has been found to a have a significant impact on upper body posture (Bridger, 1988) and Bendix (1987) states 'The influence on posture from [angle of desk surface] is greater than that of optimizing the chair'.

Seat design and spasticity

Implementation of the preceding principles in a seating system requires careful consideration of the seat design.

Strength and durability

Support surfaces providing resistance to muscle contraction or providing muscle stretch require to be relatively noncompressible, so that they will not yield under the often very high forces produced during extensor thrust. The strength of materials is important for resistance to instantaneous force. They must be able to resist the highest force produced and the materials must be fatigue resistant, so as to withstand repeated extensor thrusts over a long period. The effects of such fatigue problems should not be underestimated. In clinical practice at Dundee, one patient has been able to fracture double upright aluminium tubes used to strengthen the back rest of a custom-moulded seat. In this regard it is important to note that strengthening one part of a seating system (e.g. seat to resist hip extension) will result in forces being transferred elsewhere (e.g. to the back rest).

Alternatively, experience in Vancouver, Canada, has shown that the use of 'dynamic seating', which is flexible enough to permit movement, can prolong the life of seating systems for people with very strong extensor patterns (Cooper *et al.*, 2001).

Pressure reduction

While structures require strength and fatigue endurance to apply muscle strength and resist spastic muscle action, the surfaces through which the forces are applied should not produce excessively high pressures. Therefore, area of contact between these surfaces and body part should be maximized. This could either involve contouring the support system or having layer of more compliant material on top (padding) to increase area of support as force is applied.

Where extensor spasticity is a problem, it is important, in seat cushions, where a thick layer of foam, gel or an air-filled system is often used for pressure redistribution. The same principle of using a firm, contoured (either preformed or shaped to the individual) surface with a thin layer of foam/gel, etc., will provide resistance to movement while giving the required redistribution of pressure.

As discomfort can itself increase spasticity, as a noxious stimulus, good pressure distribution is a prerequisite of the seating system.

Shear forces

As the movements produced by spasticity also tend to produce high shear forces at the body/seat interface, which also contribute significantly to pressure sores, it is important to inhibit movement as well as spread loads. Secure location of the person in the seat is a significant step towards reducing the potential for skin breakdown.

Restraining movement – safety aspects

As some patients combine strong muscle contractions with osteoporosis, consideration has to be given to the safety of restricting motion of some body segments. This is of particular clinical relevance where a patient has strong extensor thrust at hips and knees and will therefore be seated on a form cushion with a belt restricting motion of the pelvis. With these elements restrained, the remaining body part that moves is the lower leg as the knee extends. Restricting the motion by foot straps can result in sufficient force to fracture the leg.

Adjustability

Being able to alter a seating system to address changes in the patient's presentation is important, whether during the early phases of rehabilitation, or through the neurodevelopmental maturity of a child or disease progression (Nelham *et al.*, 1988).

There are, however, disadvantages in adjustable systems:

- They may be knocked out of adjustment accidentally (e.g. when transferring to car boot).
- They may move out of adjustment by forces applied by patient.
- They may be adjusted by those not trained to do so.

- With 'infinite' adjustments, recording the setup configuration is very difficult.

The situation in which the system is to be used will assist in evaluating whether the benefits outweigh the disadvantages.

Evaluating success of seating systems

In any system that claims to reduce spasticity and thereby promote good seated posture, reduction in joint contractures and improvement in upper limb function, it is important that such claims are validated.

Nwaobi (1983) cautions against using upper limb function as a measure of the success of spasticity reduction interventions. After reviewing the literature, he concludes that 'basic neural deficits, such as prolonged EMG summation time required for voluntary movement and decreased firing frequency of motor units, may be significant factors in limiting voluntary movement in patients with UMN lesions'.

Measuring spasticity is difficult (Katz & Roger, 1989), not least in view of the debate of the nature of spasticity. Pierson (1997) proposes that a battery of tools may be the best approach to take.

Much of the research in the area of positioning and spasticity, cited in this chapter, is based on small samples from a single case, with few using more than twelve subjects. The difficulty in research is compounded by the nonhomogeneous nature of the subject's presentation and the wide variations that occur within an individual.

As Harburn and Potter (1993) note: 'Until the time arrives when spasticity can be sensitively, validly, and reliably measured, it will be difficult to measure the efficacy of treatment approaches designed to reduce spasticity. . . . Rather, use of the treatment or treatment approaches that the clinician believes to be efficacious are appropriate'.

What is certainly apparent is that the deformities seen in patients who could not easily be seated in a former generation and were largely nursed in bed are not seen in recent times in those who have had appropriate seating provided from an early age.

Medhat *et al.* (1986) reported for 11 patients: 32% improvement in spasticity, 86% comfortable, 87% reported being well positioned and 35% improved in learning abilities.

Work is progressing to develop methods for quantifying posture with the aim of gathering evidence on the effects of seating on the progression of deformity. For example, an International Standards Organisation working group (ISO TC173 SC1 WG11) has developed a standard that defines reference axis system along with reference points on the body and seating system to quantify the postural configuration of the seat and its occupant (International Standards Organisation, 2006).

Choosing seating systems

Having considered the principles of appropriate seating for those with spasticity and design considerations of the seat providing the support, there is then the question of which seating system to use, particularly as facilities to produce custom-made seating are often limited.

A great variety of commercial seating systems are available. It would be inappropriate to discuss particular examples to the neglect of others – also, the process of continual development means that a particular disadvantage in a system may be rectified in the latest model. However the principles, design considerations and above examples should provide significant guidance in evaluating the usefulness of a particular commercial system. A variety of types of systems is summarized in Bardsley (1993).

Braus and Dieter (1993) highlight the importance of correctly setting up an adjustable wheelchair and, based on a small sample, report that a correctly adjusted wheelchair results in a decrease in spasticity compared with a standard (nonadjustable) wheelchair.

Anderson and Anderson (1986) describe the construction of a seat for neonates and infants to help promote normal posture while reducing extensor tone. The seat positions the child 'with hips flexed to a greater than 90^{o} angle, hips abducted to a greater

than 20º angle, body and head well supported, and shoulders well protracted'. The position is designed to reduce extensor tone. The seat consists of a rigid plastic exterior with positioning pieces of firm foam and is covered with lambs' wool. The seat thus combines the design features of firm support to resist movement while giving a soft and warm interface. The authors report that 'agitated behaviour and irritability decrease when the infant is in the seat, probably because the discomfort of the extensor pattern, which leaves the infant out of control, is decreased'.

Custom-moulded plastic seating (Nelham, 1975; Ring *et al.*, 1978; Trefler *et al.*, 1978; Bardsley, 1984; Medhat & Redford, 1985) has been used extensively, particularly for those with severe cerebral palsy who often have joint contractures and spinal deformity. This type of seating provides intimately contoured support to maintain position and is firm and strong, thus resisting spastic muscle contraction. Many users of this type of system would in former years have been regarded as 'unseatable' and therefore left in postures where further contractures often developed.

An alternative to individually contoured seating, which often has a relatively fixed configuration, is to provide a highly adjustable system that can be tailored to suit the user's needs. Barnes (1993) highlights the need for seats to have a variety of adjustments and supports including 'foot straps, knee blocks, adductor pommels, lumbar supports, lateral trunk supports, and head and neck support systems'. It is important both that such seats are configured correctly and also that the configuration is not adjusted except following clinical review of needs.

One approach that seeks to maximize the adjustability and provide all the relevant components for positioning young children utilizes a car seat–style plastic shell into which firm foam pads can be velcroed in the desired configuration (Bardsley, 1993). It also includes foot support with straps and an adjustable pommel.

Over recent years there has been interest in the use of what is termed 'dynamic seating'. This involves building flexibility into the seating system which permits postural movement usually at the hips. It has the benefit of avoiding discomfort from being supported in one posture. This approach can be very useful for people with very strong extensor patterns, who can frequently break systems through the strength and frequency of their movements. The seat permits the movements to take place and returns the occupant to the preferred resting position when they relax. It absorbs the energy of the movement and therefore prolongs the life of the seating system (Cooper *et al.*, 2001).

Consideration should also be given to the need for transportation in a vehicle, especially if it requires to be folded and/or dismantled. While there are a growing number of wheelchair-accessible vehicles, a large number of wheelchairs are still transported in the boot of a car. As seating systems and their chasses increase in support offered and adjustability, so inevitably the weight rises and the ability to store them in a small space decreases. Alternatively, the system may be used within the vehicle and therefore will require to be designed and tested to resist crash forces, and will need appropriate harnessing and clamping. It is important that this be taken into account in prescription of a system.

Conclusion

Carefully designed, correctly used seating is indispensable in managing the spasticity of the seated individual. Appropriate seating not only produces immediate functional benefits but also serves to limit the development of contractures.

This review has highlighted the wide extent of work in this area, although much of it is either subjective or based on small sample studies.

It is important that research, although difficult to carry out, continue in this field in order that the findings described may be fully validated and the relative effectiveness of each strategy compared. In this regard the choice of appropriate outcome measures in measuring the benefit obtained for an intervention is an area of current activity (Pierson, 1997; Richardson & Thompson, 1999).

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6

Orthoses, splints and casts

Paul T. Charlton and Duncan W. N. Ferguson

Introduction

As defined by the International Standards Organization, 'An orthosis is an external device used to modify the structural or functional characteristics of the neuromuscular system'. This definition encompasses all other devices referred to as splints, braces and casts. Although not so well defined, it is common practice for clinicians to refer to orthoses as those external devices provided by an orthotist, while splints are commonly recognized as orthoses made of low-temperature plastics or fabric by therapists other than orthotists. Nonremovable orthoses made of plaster or casting tape are referred to as casts.

The use of orthoses (in all their forms) for adults presenting with spasticity has been controversial (ACPIN, 1988), and use varies from centre to centre depending on the treatment regime used by the therapist. However, in pediatrics, their use is more widely accepted, partially due to the work of Meadows (1984) in the early 1980s and those therapists using the Conductive Education techniques promoted by the Peto Institute.

In adult neurology, treatment is often based on the Bobath concept of normal movement (Bobath, 1980), which for many years frowned on the use of splinting because of the obvious impingement on the ability to perform normal movement.

Normal movement is the ultimate goal in neurorehabilitation. However, to expect all patients with a neurological deficit to make a full recovery is not realistic. It must be accepted that, despite our best efforts, at some stage recovery will plateau and the remaining deficit may require mechanical management to allow the person optimum function. This factor must be a consideration when the need for an orthosis is assessed and highlights the need for regular review, at which time thought can be given to the true aim of intervention: rehabilitation or management. It is now generally accepted that there can be a place for orthoses following proper assessment and selection.

The aim of orthotic intervention should be, where it is achievable, to realign the limb segments as near as possible to the normal position in the hope that normal posture will occur through recruitment of the appropriate muscle groups. It should also be recognized that orthotic intervention is only one of the options in neurological rehabilitation and that the aims of treatment and intervention must fit with those of the rest of the multidisciplinary team, communication with whom is another vital part of the assessment. It is this understanding that is crucial to correct orthotic assessment and provision.

It should be recognized that while most orthoses are designed for their biomechanical effect, there is always a sensory element to their use. It may be that some simple orthoses change movement or presentation on that basis. There is considerable ongoing work on the effect and mechanism of Lycra orthoses, with some centres using them widely as full body suits or specific limb garments for various presentations. At present the mechanism and criteria on how these work and could be used is unclear, but use continues with some claiming considerable success.

Orthotic aims

The fundamental aim of providing an orthosis may be to help and improve recovery or to manage remaining deficits. Often there are choices in how to intervene, depending on the prognosis, potential for change and input of other therapies. Where provision of an orthosis is part of the treatment regime, it should be recognized that one device may not provide for the patient's requirements throughout their rehabilitation and, as with other interventions, its use will require monitoring and adjusting as changes occur.

The aim of any orthosis should be clearly identified at the assessment stage. The most common aims are outlined below.

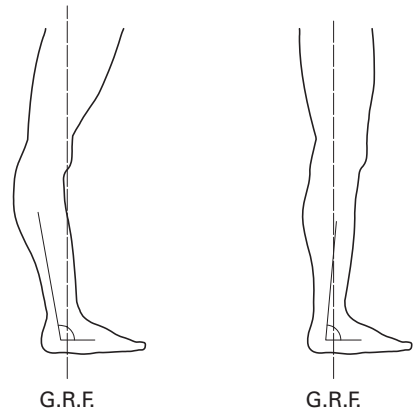

Figure 6.1. Line of ground reaction force and ankle in normal subject compared to one with a hyperextended knee.

Reduce or inhibit an abnormal pattern by positioning

Holding an ankle in slight dorsiflexion can inhibit the onset of an extensor pattern and is often achieved by the use of an ankle-foot orthosis (AFO). Gross trunk extension can be managed by holding the hip in flexion and inducing a lumbar lordosis, as with special seating or a sitting brace often used in children. These devices must be sufficiently rigid to prevent movement beyond the desired position. Another example is the use of dynamic insoles and AFOs to reduce tone as described by Hylton (Hylton & Allan, 1997).

Prevent abnormal movement

By splinting in a position of maximum function with a rigid device even if the spasticity can not be inhibited then the abnormal movement caused by it may be prevented. This should be undertaken with care, as the forces generated can be considerable.

Promote normal alignment and movement

In many patients it is possible to fine-tune the positioning in either sitting or standing such that the alignment of the body segments is as close as possible to the recognized normal. In standing, this can be achieved with some accuracy with the use of gait analysis, which allows alignment with reference to the ground reaction force (Stallard, 1987). The effect of this is to place the body in optimum position to recruit normal movement and prevent compensatory movements. The most common example of this is the hemiplegic patient with an extensor pattern who typically presents with a plantar-flexed ankle, hyperextended knee and flexed hip and trunk. By fixing the ankle in slight dorsiflexion, it is possible to push the knee anteriorly, which then encourages the patient to extend the hip and trunk to maintain balance. Ideally a force platform with ground reaction force visualization is used and the ankle angle is altered until the ground reaction force is just posterior to the knee centre (Stallard, 1987) (Fig. 6.1).

This is a well-documented technique with cerebral palsy children but is equally effective with hemiplegic adults (Butler *et al.*, 1997).

Preventing contractures and maintaining or increasing joint ranges

There is now evidence that contractures are a common sequel to neurological damage, and the

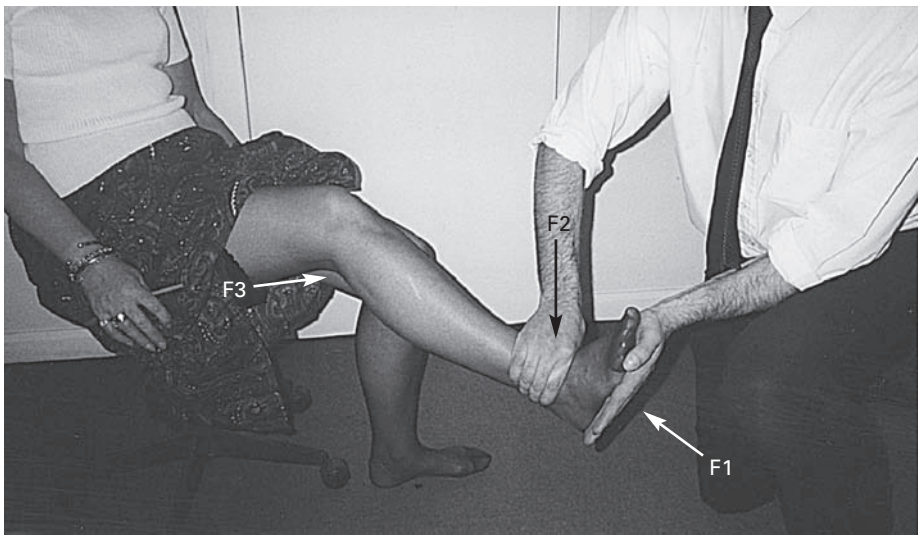

Figure 6.2. Correction of a plantar-flexed ankle and the forces (F1, F2, F3) applied.

importance of prevention is recognized. A greater understanding of the response of muscle to changes in length and position has led to improved orthotic management. However, there is much to understand about the role of orthoses for the prevention or alleviation of contractures. For example, we do not know how long the device needs to be in place during a 24-hour period in order to be effective.

Targeted motor learning

Butler and Major (1992) have strong evidence to suggest that an effective method of learning is to immobilize joints caudally until sufficient control is gained proximally and then removing support at the next level until control is gained there. This is mainly geared towards the cerebral palsy child and starts with head control and works down each spinal level. The same logic is applicable to the lower limbs. It is difficult to work on improving hip control if there is little control of the knee supporting it. There is increasing recognition and understanding of the influence of mechanical alignment on postural muscle recruitment and postural tone (Shumway-Cook, 2001).

Biomechanics and materials

A good understanding of this subject is essential to appreciate fully the forces involved and their influence on the design of orthoses. Those interested may find the 'Further Reading' list at the end of this chapter useful.

Any external device must provide force to have an effect, and an important consideration of applying an orthosis is how and where to apply these forces and make them as tolerable and effective as possible. One of the main skills of the orthotist is to identify, minimize and optimize the forces and pressures generated at the patient orthosis interface. To do this, knowledge of basic mechanics is important. In particular, it is useful to note that most orthoses use the application of a set of three forces to produce the required effect; this is usefully illustrated by considering the correction of a plantar-flexed ankle.

To correct a flaccid foot (Fig. 6.2) would merely require the application of a force under the forefoot. However, if the patients' ankle were tight or demonstrating clonus, then the orthotist should place one hand over the top of the ankle and one hand would be positioned to provide a better push on the base. If

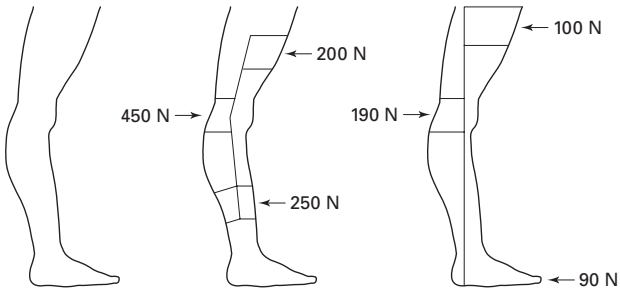

Figure 6.3. Forces applied to control a hyperextending knee and the effect of increasing lever length.

the foot is very tight or there is a strong extensor pattern, then there is a danger that you might push hard enough to tip the whole patient backwards. This is because it is possible to overcome the frictional force of the patient on the chair as indicated by force. An indication of how mechanics can influence orthotic design is shown in the diagrams depicting the forces involved in correcting a hyperextended knee. It can be clearly seen how an increase in the overall length of the orthosis can lead to reductions in the applied forces, since the turning effect (moment) applied at the knee is determined by both the magnitude of the forces and the distance between them (Fig. 6.3).

It is for this reason that a Swedish knee brace is likely to be uncomfortable and a long leg device may be the only practical orthotic solution for quadriceps spasticity.

The ability of an orthosis to manage spasticity will depend on how the spasticity presents. There is a need to be aware of any counter forces, which may have pressure and skin care repercussions. The ability of the patient to tolerate the required forces necessary to achieve the aim of the device is of ultimate importance. It may be that, at review, a decision is made that the forces required are intolerable. In such a case the patient may be considered for other forms of spasticity management such as injection, pharmaceutical or surgical intervention as well as or instead of the orthosis.

Plastic or metal orthosis?

While it is not within the remit of this chapter to explore the varieties and limitations of available materials, it is worth explaining a commonly asked question.

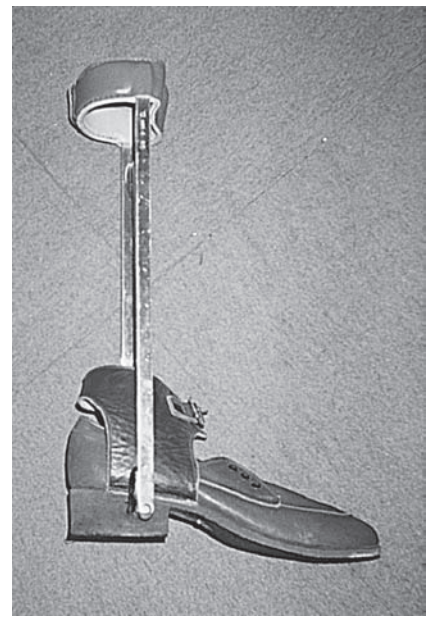

Figure 6.4. Distortion of a shoe with metal ankle-foot orthosis and T-strap by plantar flexion.

It is often assumed that because metal is a stronger material, that metal orthoses are stronger and therefore more effective than plastic orthoses at withstanding high forces. In fact, often the opposite is true because of the method by which the orthoses acts upon the limb. The benefit of the plastic orthosis is that it can be moulded to the patient and so apply loads in precisely determined positions and frequently over a large area. The metal orthosis, on the other hand, usually depends on the patient's shoe being an integral part of the orthosis. This may lead to failures both in the fixing of the orthosis to the shoe (the socket) and the shoe itself deforming. It may also depend on some of the forces being applied by leather straps under the influence of the patient or carer. Metal orthoses are undoubtedly heavier than plastic orthoses, but often the weight is as much due to the shoe socket as the calliper itself. In addition, the shoe may require reinforcing to prevent distortion from the forces applied which may further increase weight (Fig. 6.4).

Obviously any increase in weight is a disadvantage especially where there is a combination of weakness and spasticity as, for example, in multiple sclerosis.

Assessment

An orthotic assessment should ideally be performed by an orthotist and the treating therapist preferably with experience in orthotics. The team should then explore the history, current treatment and likely prognosis in order to define the aims of the orthosis.

Consideration of the prognosis is important and will help determine the practicality of an aggressive approach. For example, a young patient 6 weeks poststroke presenting with a hemiplegia would hopefully recover sufficient motor control to attain a reasonable gait. The orthotic aim in such a case may well be to provide realignment to a degree that may challenge stability to ensure that compensatory positions are not recruited in favour of 'normal' activity, as it becomes available. In practise this may be a rigid AFO set in dorsiflexion to prevent knee hyperextension, even if tone in the quadriceps is not quite sufficient to maintain stability for any length of time. In an older patient, several years poststroke, the orthotic aim may well be purely to maintain stability or prevent pain.

Understanding is increasing of how orthoses can help to manage ground reaction force throughout the gait cycle and provide dynamic stretch at both calf and hip towards terminal stance by use of a rigid AFO. Meadows (2004) and Owens (2004) have demonstrated in detail how this can be further enhanced by shoe design and modification.

It is worth noting that, depending on resources and the patient and therapist commitment, it is sometimes possible to change and improve quite established gait patterns (Butler *et al.*, 1997; Baker & Charlton, 2004). It is in these instances that the simulation of the effect of an orthosis, before proceeding to a definitive one, is extremely useful and gives some indication as to the possible outcome.

When examining the patient, consideration should be given to joint range, muscle tone in rest and during activity, force required holding a position, skin condition, sensory loss and oedema. If the use of a device seems a possibility, consideration should be given to the effect on other joints, the patient's function and the need for other intervention such as spasticity management, stretching regime or physiotherapy for gait re-education prior to or after supply.

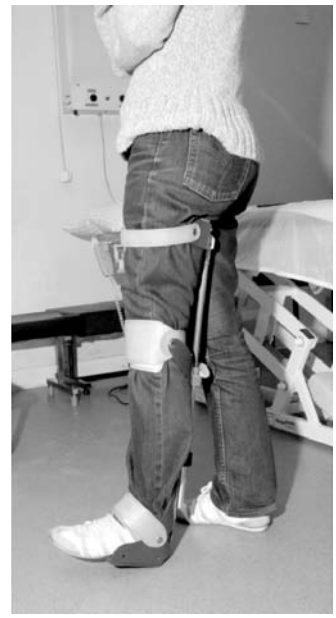

Figure 6.5. Lower extremity telescopic orthosis (LETHOR) for assessment or treatment.

To assist in making these decisions, it is extremely useful to simulate the effect of the orthosis either by bandaging the limb in the desired position or by adapting an existing orthosis. Even a brief glimpse as to how the patient may perform in a definitive orthosis will avoid unnecessary work. Prediction of functional effect is difficult without such a trial. Assessment tools may be stock orthoses or discarded bespoke orthoses. In particular, it is useful to have an assessment knee-ankle-foot orthosis which may allow the patient to experience full knee extension (Fig. 6.5).

The opportunity to apply a firm dorsiflexion bandage is also useful to simulate the effect of an AFO to limit plantarflexion. Common findings during assessment include:

- Weak hip flexors when the initial assumption was that lack of ankle dorsiflexion was the cause of poor foot clearance.
- Quiet zones. It is not uncommon with diplegic cerebral palsy children and some poststroke hemiplegic people with extensor tone to find a range of ankle dorsiflexion where the spasticity can not be induced. In such patients the orthosis is made to limit movement to within that quiet zone (Meadows, 1984).
- Rigidity. The force can be so strong that it cannot be opposed tolerably and orthotic management may be limited to accommodation and stability.
- 'Positive support' is a term commonly used by physiotherapists to describe the onset of spasticity in response to loading the foot. In such cases a dynamic insole can be used to accommodate the contours and dynamic arches of the foot to help this settle, this can be incorporated into an AFO (Small, 1995).
- It is our experience that a mechanism exists whereby a patient will tend towards an abnormal pattern of either flexion or extension in anticipation of having to bear weight on the side over which he or she does not have full control. This confidence factor, we believe, is demonstrated by patients who present with an abnormal pattern yet can improve considerably by the provision of a relatively simple device such as an ankle stirrup. We know that the ankle stirrup does not apply the appropriate forces to control the limb but believe that because it gives the wearer greater confidence, he or she does not recruit the abnormal activity in trying to improve stability.
- Shunting has been described as the situation where the control of spasticity at one joint leads to its increase at another, usually the next, joint (Edwards, 1998). This is commonly seen in patients with spastic diplegia where the control of ankle position may result in increased knee flexion or internal hip rotation. In such a case, orthotic intervention may be contraindicated.
- Severe spasticity can often generate sufficient force either to overcome the orthosis or to endanger tissue breakdown at the patient orthosis interface. If orthoses are used, this can be in conjunction with botulinum toxin injections which can reduce the force generated. Even with other management techniques it is often accepted that the orthosis will not fully correct the affected joint; for instance, with the inverting ankle the orthosis is used to minimize damage to the joint. Because of the dangers of pressure, it is common to use the more tolerable correction of a padded leather T strap and metal AFO than the less forgiving correction of a close-fitting plastic orthosis. The added benefit of the metal AFO and T strap is that the degree of correction can be controlled by the length and tension of the strap. There are those who would argue that with severe spasticity, the presence of an orthosis encourages the muscle to pull against it and therefore reinforce the pattern, although there appears to be little evidence to support this.
- Assessment can also give the orthotist an idea of the forces involved and thus help to determine the type of orthoses required.

Once a specific presentation has been identified then it is worth exploring the underlying cause. An example of this is knee hyperextension, a common presentation in hemiplegia. The underlying mechanical cause of this can be:

- Inability to get the heel to the ground due to tightness of the tendo Achilles tendon
- Hamstring weakness
- Quadriceps weakness
- Quadriceps spasticity
- Weak hip extensors

The simplest method of preventing knee hyperextension is the Swedish knee brace, which, although not an effective definitive orthosis, is a very effective assessment tool. Often when the knee is controlled, ankle control is lost and it becomes apparent that the knee is a secondary problem to lack of range or control at the ankle. There is also benefit in using this orthosis as a therapy tool as by preventing knee hyperextension then a far more effective stretch of the tendon Achilles is achieved on weight bearing (Fig. 6.6).

A successful assessment does not necessarily result in the supply of an orthosis, although often

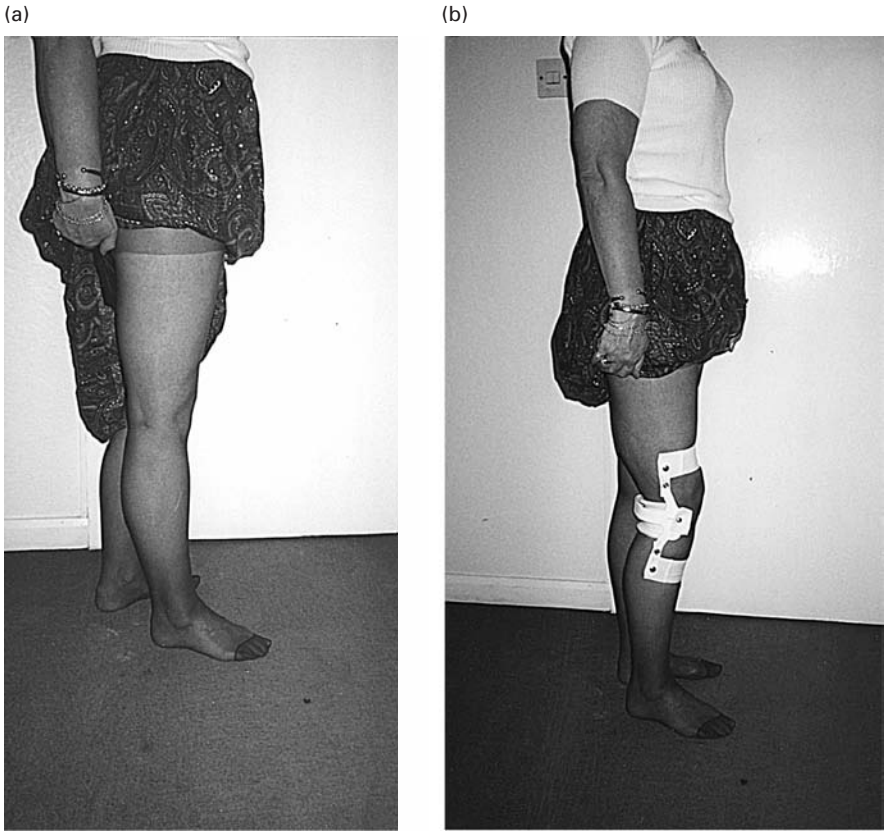

Figure 6.6. Use of a Swedish knee brace to prevent hyperextension and increase stretch on Achilles tendon.

the process of assessment will have other benefits, such as highlighting and clarifying where problems lie and consequently where treatment can be more specifically targeted.

Having identified deficits in motor control, joint range and other physical factors, it is important to assess sensory and perceptual loss. We can now make a decision on the aims and objectives of the orthosis and identify which orthosis to provide. This decision may be influenced by a number of factors such as oedema, sensation, pressure tolerance or patient acceptance.

If the aim involves using the orthosis unsupervised on a daily basis, it is essential that individual acceptance is fully addressed. If the person refuses to wear the orthosis, then supply is pointless. Acceptance is helped greatly if the patient or carer is made fully aware of the aims of the orthosis, shown the potential benefits and warned, at an early stage, of any practical implications such as difficulty with footwear.

As with so many other forms of treatment, the final prescription may well be a compromise between the ideal, the practical and the acceptable. The most successful prescription is that which has been made with the full involvement of the person and his or her carers.

Casting

There are several advantages of the use of casting versus providing a definitive orthoses, such as cost and

availability. In addition, the freedom to change the position easily and accurately and the fact that the cast may not be removable means that the limb has time to settle and accommodate to its new position. This will hopefully make the joint more amenable to a further stretch to a new position. By totally encasing the limb, any corrective forces are spread over a maximum area, therefore reducing pressure. Consequently serial casting has been found to be extremely effective in stretching out contractures (Zander & Healy, 1992), often with the final cast being bivalved and used as a removable splint to maintain the new range acquired. When a spastic limb has been enclosed in a cast, it will often be found less active and therefore more likely to tolerate an orthosis. Full-length leg plaster back slabs are now commonly applied to the early neurological insult. This will minimize knee flexion and hamstring contraction but also allow for early weight bearing, which will give effective stretch to the Achilles tendon.

The use of plasters is also a useful prelude to a definitive orthosis, both for early application and for assessment. The development of modern casting materials and the availability of casting courses for therapists have meant that the ability to apply good casting technique is accessible in most hospitals and centres. It is still essential that skill be used to ensure a smooth patient–cast interface and that the distally exposed limb be monitored for any signs of problems beneath the plaster, such as swelling, discoloration or temperature changes, which may indicate pressure problems and necessitate cast removal. Clear guidelines exist for the application of casts, and it is important that these be adhered to (ACPIN, 1998).

Timing of orthotic intervention

In order to minimize contractures, it is generally recognized that early aggressive intervention is essential. However, the timing of intervention for rehabilitation of normal movement is not quite so well defined. Common sense may dictate that the earlier the patient can experience 'normal' positioning and alignment the better, although evidence for early intervention is lacking. It is important that optimum foot position and alignment be achieved before attempts are made to achieve free standing and walking. It is undesirable to teach normal hip and knee movement when there is insufficient ankle dorsiflexion to attain heel strike. This is practically impossible for the patient, as without adopting some form of compensatory strategy, there is a risk of tripping over the slightest obstacle. Failure to use an orthosis in this situation will lead to a higher energy cost or an unsafe gait.

When to wear an orthosis

This will depend on the aim of the orthosis and needs of the patient. An orthosis, if designed to realign the skeleton in a patient early in their rehabilitation, may require more motor control than the patient is capable of, and the aim may be to use the orthosis only within therapy to work on developing recruitment. Patients progressing in their rehabilitation may be able to demonstrate good control without an orthosis when they are concentrating in a controlled environment, but they may lose that ability in performing functional tasks elsewhere. In this case the orthosis may be worn between therapy sessions but removed for therapy to try and develop independent control. Some patients demonstrate good control most of the time but may lose control and alignment when fatigued as in the case of many MS patients. These patients often use an orthosis selectively when they wish to walk longer distances or when they anticipate problems with their mobility. This should be considered and discussed at the assessment stage.

Orthotics in paediatric management

As one might expect, there are special considerations in dealing with children with spasticity. The absence of normal muscle tone on an immature skeleton can lead to considerable complications. Around the

hip joint, for example, it is believed that spasticity can lead to malformation of the acetabulum and recurrent or permanent dislocation. A dislocated hip, as well as causing pain, can lead to problems with seating and secondary spinal scoliosis. It is not uncommon for major orthopaedic intervention to be required to resolve these problems. Orthotic intervention can help as positioning hips in maximum abduction ensures maximum containment of the femoral head and optimizes development of the acetabulum.

Types of orthoses

Classification

A system has been developed whereby orthoses are classified and named by reference to the parts of the body over which they pass (Harris, 1973). For example, an orthosis around the ankle is called an ankle-AFO and a full leg calliper is termed a knee-ankle-foot orthosis (KAFO). This classification is useful but does not describe the function, construction or aim of the orthosis.

Footwear and adaptations to shoes

An extensor pattern of the lower limb is often accompanied by spasticity in the toe flexors. This leads to clawing, causing pain on the tops of the toes from pressure from the shoe and on the tips of the toes from bearing weight on them. This or any pain tends to increase tone and further compound the problems. Fabrication of a silicone orthosis under the toes to lift the tips from the ground can relieve this pain and help reduce overactivity. Patients with mild spasticity may benefit from careful selection of footwear. A common occurrence is overactivity in the ankle inverters and long toe flexors, which presents as lateral instability of the ankle and clawing of the toes. Shoes with a strong heel stiffener but soft deep forepart are frequently sufficient to resolve or manage these problems. Preferably the shoe should have a broad heel to increase stability, but if this is not available, conventional shoes can be modified to have a broader heel and a light tilt can be added to provide further stability. Insoles may be added to conventional shoes to achieve increased stability, an improved base of support, stretch on the plantar fascia or redistribution of pressure. The height of heel may be altered to accommodate loss of range of the Achilles tendon and achieve a heel strike and knee alignment. It should be realized, however, that this is at the expense of stretching and that, once a heel raise has been used, there may be a loss of range, which cannot be recovered. Tightness of the Achilles tendon can also lead to a compensatory collapse of the medial arch of the foot. It is common for the midfoot to evert and dorsiflex in order to achieve heel contact with the ground.

Ankle-foot orthoses

The most commonly recognized AFO is probably that which gives some control to ankle plantar dorsiflexion. It should however be recognized that AFOs also include orthoses that control mediolateral movement such as the Aircast and Malleolock (Fig. 6.7) as well as various soft orthoses that may offer compression or limitations of movement by strapping.

AFOs that help the ankle to maintain a dorsiflexed position are not useful in the management of spasticity, as the force of the spastic muscle can override it and render it ineffective. Static or limited-motion orthoses include callipers with range-of-movement adjustments, of which there are many types. As mentioned earlier, it is important that the foot be well fixed in the shoe and that the shoe not distort. While it is common to use the high-strength resilient material Ortholen for many AFOs, this is to be avoided with spasticity, where rigidity is essential.

Yates (1968) examined the concept of the AFO made of polypropylene, and some fundamental flaws were noted when it was applied to spasticity management. The AFOs were contoured to allow for the shoe pitch, which placed the ankle in a plantarflexed position. As the spasticity increased, the centre of gravity moved back and the heel elevated out

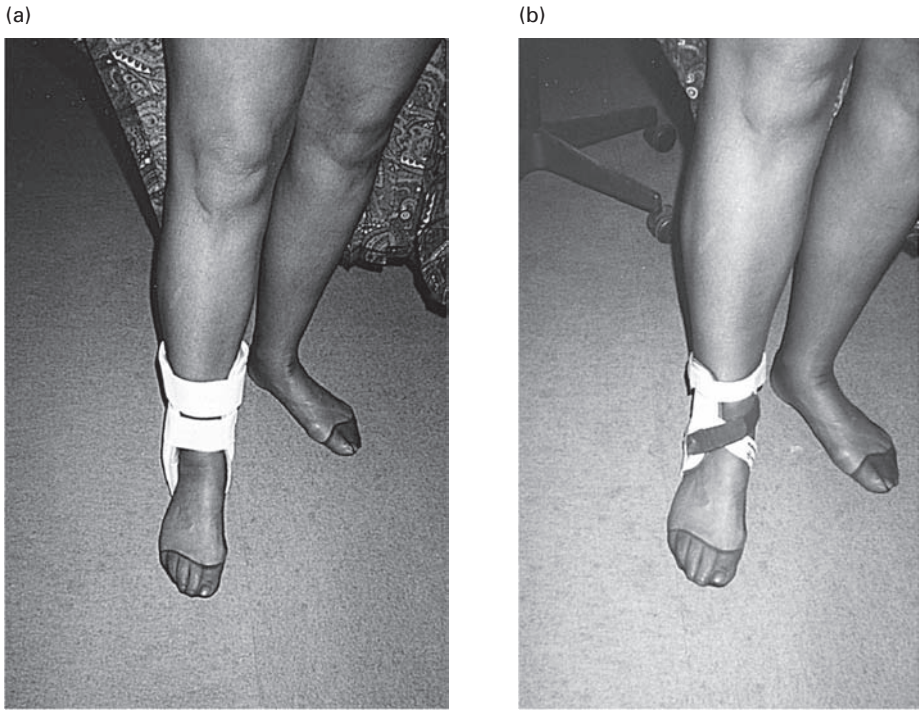

Figure 6.7. (a) Aircast ankle stirrup and (b) Malleolock ankle brace.

of the orthosis because the shoe was unable to apply sufficient force to hold the foot. This, combined with plantar flexion for the pitch of the shoe, can lead to contracture of the calf muscles. The trim line behind the metatarsal head sometimes simulated a plantar grasp reaction, thus increasing the level of spasticity.

Meadows (1984) endorsed the casting of AFOs at 90 degrees with a stretch encouraged on the Achilles tendon from a fitted heel strap, which bisected the foot and leg at 45 degrees (Fig. 6.8). This encourages better control of the hindfoot. The additional use of a sole wedge or rocker made the flow of mobility more fluent from heel strike to toe-off by maintaining a superior leg-over-foot position controlled by the proper application of forces around the knee through the walking cycle. The study went on to show that there was a reduction in tone, the necessity for surgery was less and long-term complications of scarring and a shortened spastic muscle were diminished.

Types of ankle-foot orthoses

Dynamic insoles and dynamic ankle-foot orthoses (DAFOs)

Much publicity was given to these by the work of Hylton (Hylton, 1989; Hylton & Allan, 1997), who advocated the use of a footplate or insole that was manufactured accurately to reinforce all of the dynamic arches of the foot, including the lateral arch (Fig. 6.9). As well as aggressively supporting these arches, she also advocated building up and supporting the toes, other than the great toe. An insole made to this specification cradles the calcaneum and metatarsal heads, providing an optimum weight-bearing surface, which is most likely to allow the foot to settle. This footplate was used as a basis for a dynamic AFO, which, unlike other AFOs, extends only just proximal to the malleoli, offering ankle alignment without addressing plantar dorsiflexion. The material used is thin malleable plastic and the aim of the orthosis

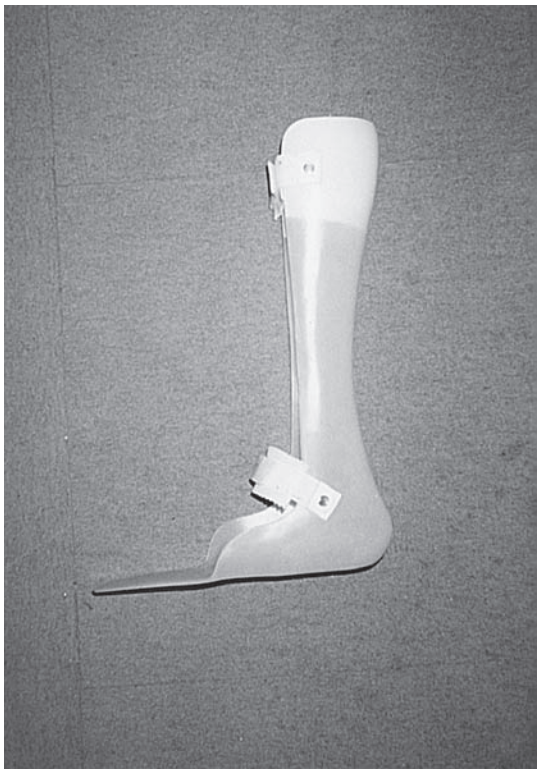

Figure 6.8. Polypropylene ankle-foot orthosis with full foot piece and 45-degree ankle strap.

is to have a tone-reducing effect such that normal movement may be recruited. Often the ability of the patient to recruit dorsiflexion is absent. The footplate, however, is a useful adjunct to a conventional AFO in helping an overactive foot to settle.

Hinged ankle-foot orthoses

A rigid polypropylene AFO may be cut at the ankle joint axis and a hinge introduced (Fig. 6.10). A posterior stop may provide the desired resistance to plantar flexion while allowing a range of dorsiflexion. This is especially useful for those patients who have a quality of gait that allows walking over uneven ground and also makes simple tasks such as getting from sit to stand and negotiating stairs much easier. Care must be taken at the assessment stage, as some patients have a deficit that may benefit from some restriction to dorsiflexion (e.g. those prone to a flexed gait). By providing adjustable plantarflexion, the position can be altered to fine-tune the orthosis.

Figure 6.9. Dynamic ankle-foot orthosis.

Ground-reaction ankle-foot orthoses

This variation (Fig. 6.11) of a rigid AFO is aimed at resisting dorsiflexion and therefore limits progression of the tibia over the foot during stance phase. This is sometimes useful in those patients presenting with a crouch gait. The anterior load-bearing surface requiring a posterior opening ensures correct application of forces. More recently the principle of the ground-reaction AFO has been adopted into standard static AFOs with a more robust and padded calf strap, as the pressure from polypropylene on the anterior aspect of the tibia can be uncomfortable.

Knee orthoses and knee-ankle-foot orthoses

The principal aim of the knee orthosis is to prevent knee hyperextension in extensor tone and flexion in flexor tone. However, as previously mentioned, they are often too short to provide sufficient leverage

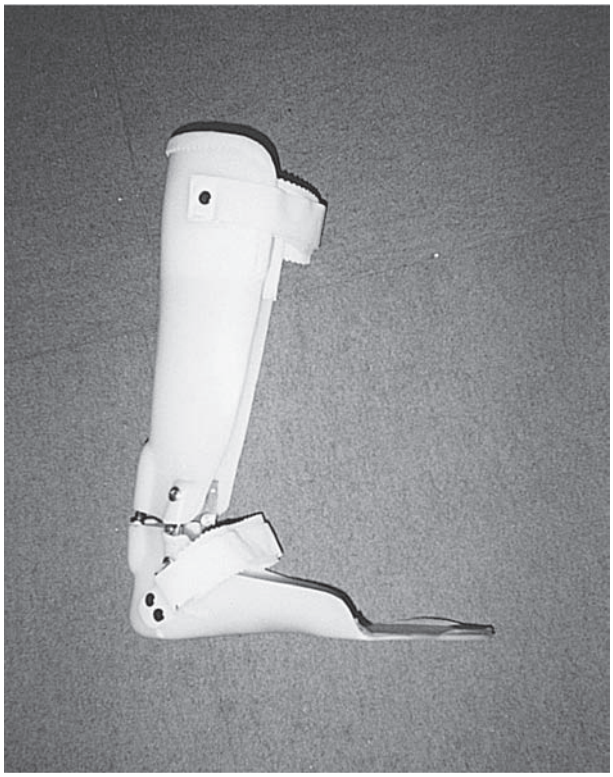

Figure 6.10. Hinged ankle-foot orthosis with adjustable-screw plantar flexion stop.

Figure 6.11. Ground-reaction ankle-foot orthosis.

to control the effect of spasticity about the joint. In either case, the joint should be realigned as near as possible to the normal standing position (Fig. 6.12). In the case of spasticity of the hamstrings the forces involved are considerable and may make automatic knee joints unreliable and therefore dangerous. The traditional manual knee locks are probably more appropriate to allow flexion for sitting.

A relatively new development is the intelligent knee jointed KAFO, of which there are various designs, allowing for stability in stance and free flexion in swing phase of gait (Fig. 6.13). A very new advancement of this technology is an assessment and training KAFO that allows the therapist to switch the KAFO from free knee to knee, stabilizing at any knee angle or stage of the gait cycle. While expensive, it would seem appropriate for one unit to remain permanently at a rehabilitation unit as a training device rather than a definitive orthosis.

Hip and hip-knee-ankle-foot orthoses (HKAFOs)
Hip orthoses, sometimes known as sitting braces, can assist in postural control to help with windswept, scissoring and sacral sitting positions. This may be instead of or along with special seating. As mentioned earlier, hip position can play an important part in hip containment and development. The more complex orthoses, such as the Parawalker (Butler & Major, 1987) and reciprocal gait orthosis (Douglas & Solomonow, 1987) developed for paraplegics, both require relatively smooth symmetrical hip action and probably preclude all but the mildest of spasticity. 'Twisters' are functional hip orthoses that control internal rotation during gait; they can be most effective and are most commonly used in children with diplegia.

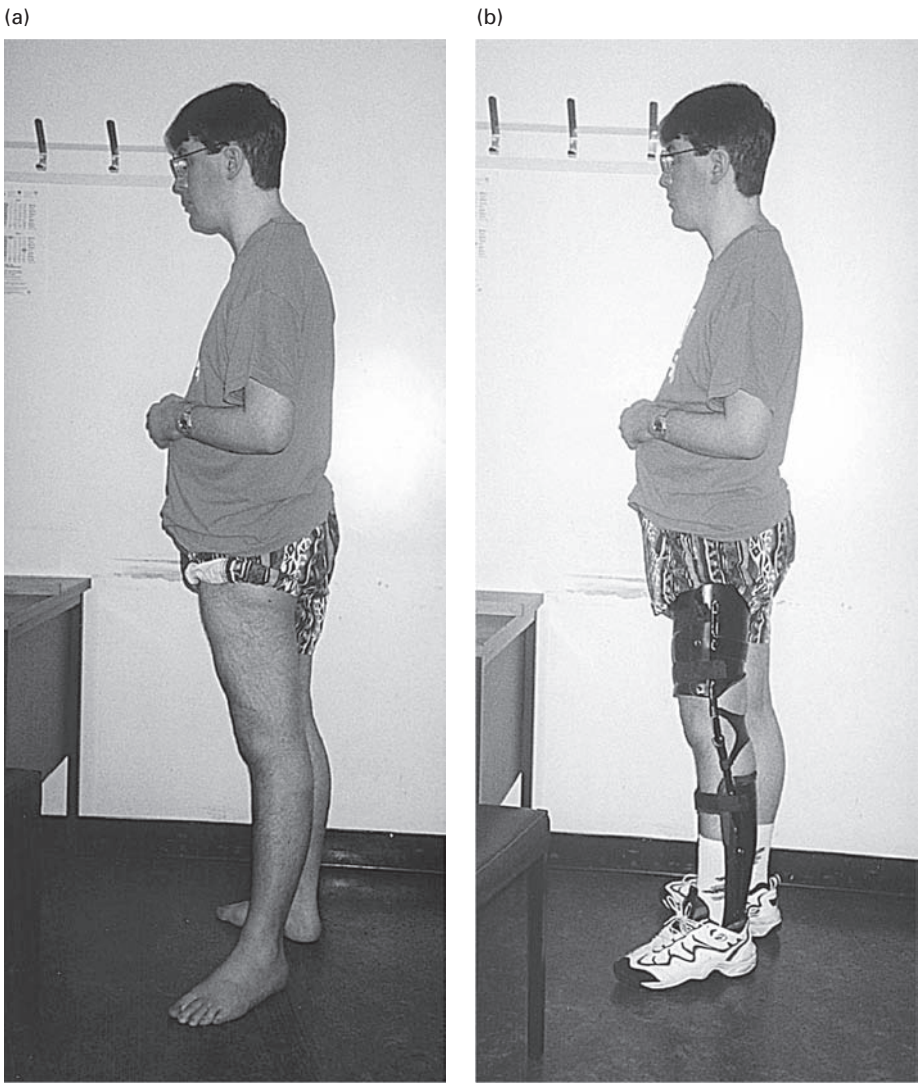

Figure 6.12. Knee-ankle-foot orthoses with hyperextension stop showing patient realignment.

Cervical orthoses and the cervical spine

Spasticity can affect the control of the head and neck. Some control may be provided by an intimately fitted collar (Fig. 6.13), either moulded directly to the patient or made to a plaster cast. Care must be taken regarding pressure, as sometimes the forces generated are considerable. Sometimes the combination of a collar and the use botulinum toxin injections may lead to the best success. Occasionally the extensors of the cervical spine are affected, making fitting a collar extremely hazardous, as the counterpressure is on the throat. This problem can be overcome by extending the orthosis down over the front of the clavicle and under the arm. By fastening around the back, this creates a three-point pressure with the

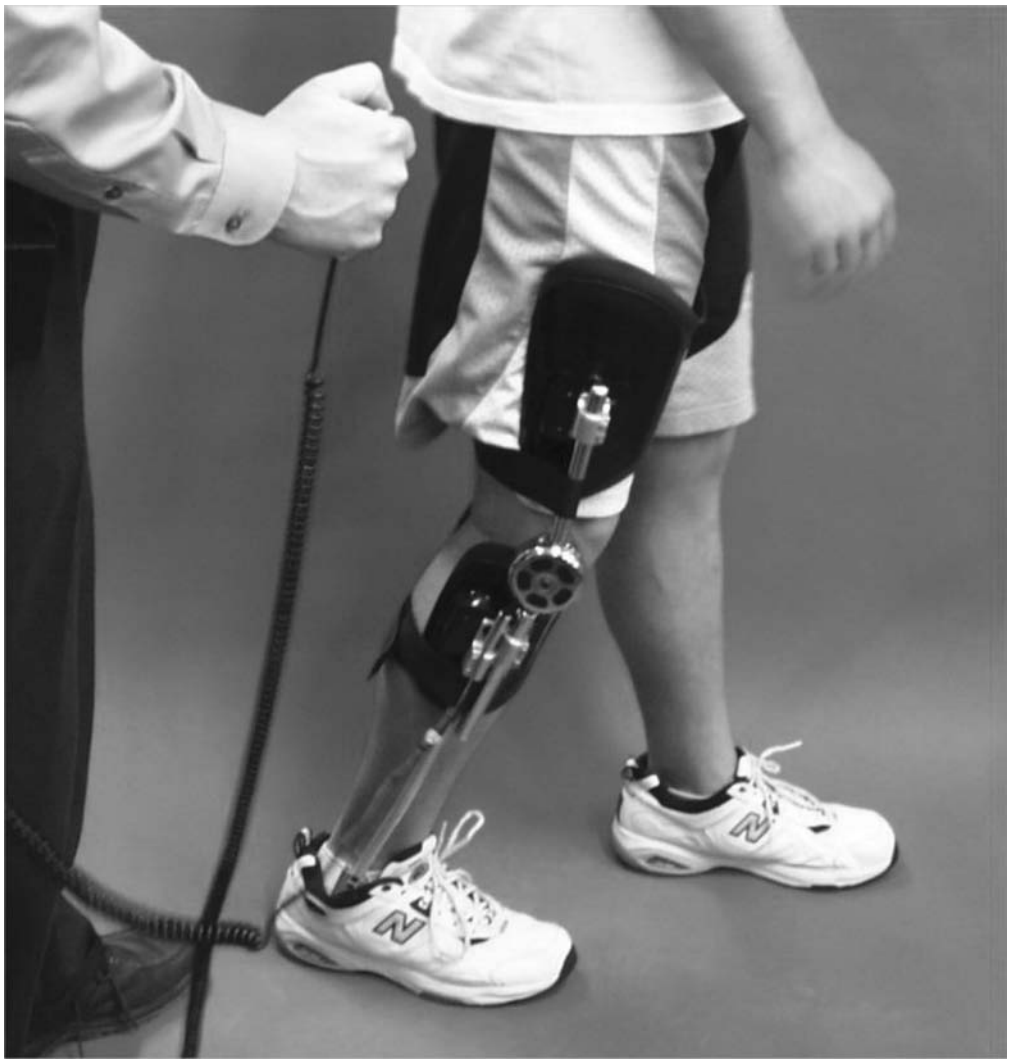

Figure 6.13. 2 Becker intelligent knee assessment KAFO.

back, the back of the head and the front of the clavicle. Although this is cumbersome and some may feel impractical, it may have uses for helping with specific tasks such as eating.

The hemiplegic shoulder

Management of the hemiplegic shoulder is a source of frustration for patients and clinicians, and the cause of the problems is not always clear. Sometimes it appears to be due mainly to subluxation, while at other times tightness due to spasticity in the rotator cuff is the cause. The shoulder is often painful but, in addition, laxity and subluxation makes it prone to injury in handling. These problems can be exacerbated if the upper limb is oedematous and heavy, leading to misalignment of the whole trunk. The complexity of these interactions has been

demonstrated by Price *et al.* (1999) in studying the variations in scapular motion in these patients.

Orthotic intervention, although common, is not usually satisfactory. The biomechanical aim is to reduce subluxation by unloading the shoulder joint by suspending the humerus in a cuff on a figure-of-eight bandage about the opposite shoulder. However, if subluxation is due to spasticity of downward-acting muscles, as seems possible, then this strategy is unlikely to be successful.

In orthoses designed to prevent subluxation, a cylindrical cuff around the soft tissue of the upper arm is used to apply the necessary force. However, this is rarely successful, since the humerus tends to slide through the cuff (Carus *et al.*, 1993). Attempts to prevent this by increasing the cuff pressure can impede circulation, causing discomfort under the axilla. However, it is surprising how frequently the subcuff is still used despite its limitations. Among users, it is commonly accepted that it can give confidence to the wearer and remind carers of the problem at the shoulder. A mechanically more effective device consists of a broad strap over the effected shoulder extending to a cuff just distal to the elbow. This provides a fulcrum about which the weight of the forearm and hand; acting down, therefore, produces an upward vertical force to the humerus that may reduce subluxation (Cool, 1989). However, this device does depend on some flexion of the elbow that is not always desirable, as it may reinforce the typical flexor pattern, which is often best avoided. Patients who present with reduced tone in the shoulder girdle and heavy arm, as described earlier, often benefit from strapping the arm to the body in a way as to distribute its weight evenly and minimize the effect of pulling down. An effective orthosis for this is similar to a half jacket, which spreads the load evenly. This is sometimes known as a Dr. Berrhill jacket (Fig. 6.14).

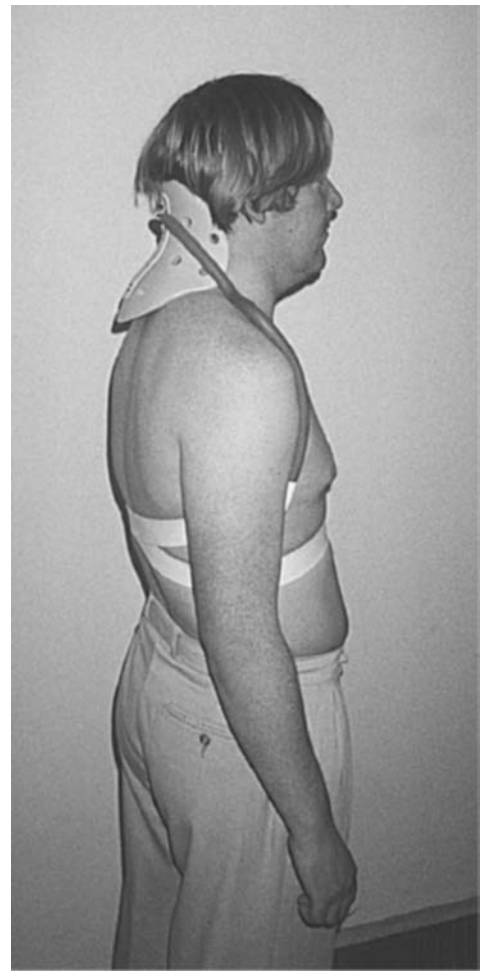

Figure 6.14. Collar.

The hand and wrist

The fine movements of the hand and fingers make it difficult to apply any orthosis without interfering with function. Orthotic intervention for the spastic hand is therefore aimed at maintaining muscle length and trying to inhibit spasticity. This second claim is unclear and not defined well in the literature. It is possible that tone is inhibited by applying a splint to the dorsal aspect of the wrist. Mechanically the most effective stretch can be applied by an orthosis applied to the volar aspect of the hand, with straps over the wrist and MCP joints to stretch the spastic flexor groups. As with other orthoses, this should be reviewed and alternatives tried if not successful. Often these orthoses are made of low-temperature thermoplastics, which, while easy to

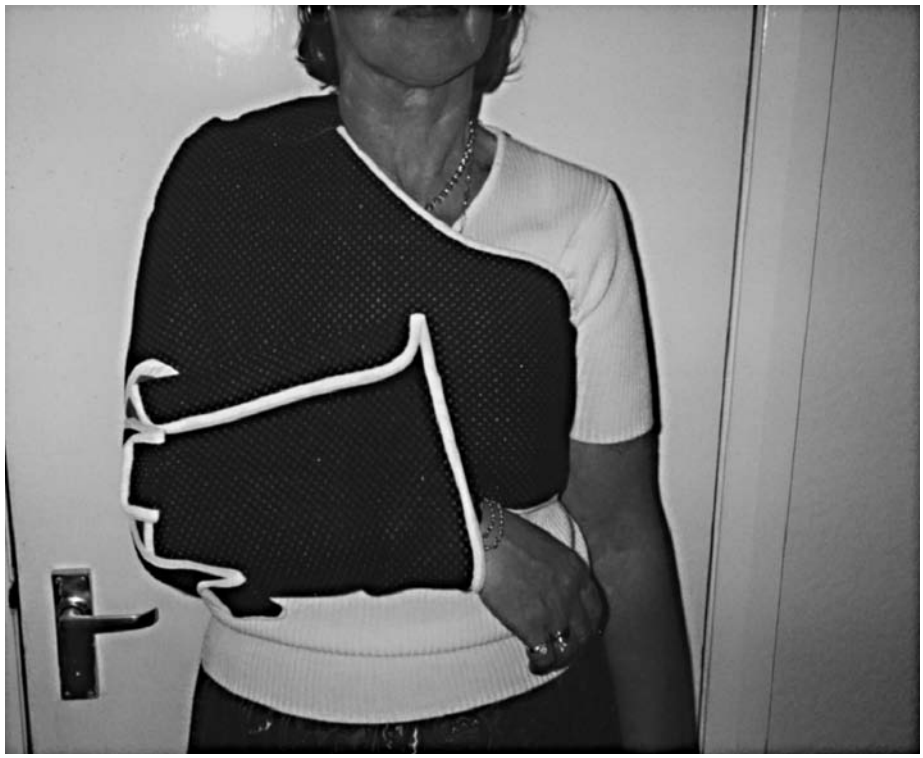

Figure 6.15. Dr. Berrhill jacket.

mould and adjust to achieve an accurate fit, have limited strength and durability. For patients using such orthoses, long term, it can be beneficial to use a low-temperature orthosis as a template for a high-temperature, more durable orthosis. An added benefit is that the higher-temperature (polypropylene) orthosis is more rigid and will give a more effective stretch, whereas the lower-temperature orthoses often buckle under the force of the spastic muscle. An important consideration is hygiene. If the hand is allowed to stay flexed for a prolonged period, it may become impossible to open it sufficiently to clean it and trim fingernails. In such cases of neglect, it has been necessary to insert rods of gradually increasingly diameter to open the hand.

The list of available orthoses continues to grow. New designs are being developed and existing ones are always being customized to cater for the needs of individual patients. The important point is that the orthosis should meet the function of the prescription that is derived from careful assessment and discussion with the patient, carers and treating staff.

Functional electrical stimulation (FES)

This method of stimulating a peripheral nerve to induce a muscle contraction is now being used in some centres as an orthotic intervention. One surface electrode is placed over the appropriate motor nerve and the other over the muscle to be stimulated; the current between these electrodes induces activation of that nerve and a subsequent muscle contraction. However, this is obviously limited to those nerves and muscles that lie superficially. The technique is particularly well tested in the management

of foot drop (Taylor & Burridge, 1999) and well recorded in use on the upper limb. While having an obvious role as an alternative to conventional orthotic management, it may often have particular benefits as a training technique in early rehabilitation following neurological insult, as it allows the patient to experience muscle contraction, which may be useful in the learning process. FES may also be useful in building up muscle bulk to help soft tissue integrity, as in gluteal muscles for sitting or for strengthening weak muscles. Current research is studying the effect of FES on the antagonist to stretch contractures in combination with orthoses.

Future developments

Gait analysis is undoubtedly becoming more clinically accessible; with the development of mobile units, it may be possible to make this more routinely available for the fine tuning of orthoses.

Advances are also being made in lighter, stronger materials, which may make orthoses less obtrusive and more acceptable. Silicone is now used in the construction of orthoses, but care should be taken, as it may be too flexible to oppose the forces generated in the presence of spasticity.

The International Society of Prosthetics and Orthotics International Consensus Conference on the Orthotic Management of Stroke (2004) recommended that orthoses could, and should, be considered in rehabilitation. They also strongly recommended more rigorous research in this field, and it is hoped that this may lead to evidence-based practise of extending the benefits of orthoses more effectively to more patients.

Conclusion

Orthoses can be highly effective tools in the management of spasticity. However, accurate and careful assessment, prescription and follow-up are required for the best results, and thus a trained orthotist is an invaluable member of the spasticity team. Rather than looking for the 'tone-inhibiting orthosis', one must consider what factors influence the presentation. Clinicians with experience know that there are some presentations that may respond only to radical, aggressive denervation and that orthoses are unlikely to succeed. Other presentations are due to movement, stability or alignment, which orthoses can address if selected appropriately.

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7

Pharmacological management of spasticity

Anthony B. Ward and Sajida Javaid

Introduction

The management of spasticity requires a multiprofessional approach and is based on addressing the troublesome effects of the increased tone. Nursing staff have a considerable role in this context along with physiotherapists, occupational therapists, speech and language therapists and doctors. The essential treatment of spasticity is physical. Even when pharmacological agents are used, physical treatment strategies should be in place and pharmacological interventions should be regarded as adjunctive rather than as substitutes for physical management (Ward *et al.*, 1997).

Spasticity may not be harmful, particularly in early rehabilitation after an injury to the brain or spinal cord, where it may be utilized to improve functioning. For example, a spastic leg with minimal motor control may be a useful prop after a stroke to allow a stand pivot transfer and weight bearing. Treatment should be clearly set within the context of goals for rehabilitation (Ward *et al.*, 1997). Even in patients who develop this impairment without much disability, treatment goals should be documented and agreed on with the patient and carers. Spasticity is not a condition that needs treatment in its own right and, indeed, medication may sometimes result in systemic side effects producing greater impairment. There are several situations in which spasticity reduction would serve no valid functional goal. For example, a patient with severe spasticity and poor selective motor control but whose spasticity is not painful and not interfering with care or positioning may not experience any improvement after tone reduction.

Oral antispastic medications have been long thought as "non-invasive treatment" in contrast with treatment by injections or surgical interventions. However this is a misconception and inappropriate, as all the systemic medications described in this chapter are chemical ligands to numerous receptors in the central nervous system. They may therefore alter or depress higher circuitry other than motor functions, e.g. cognition, alertness, mood, personality, etc. Unfortunately, these neurological side effects are insidious and may thus be poorly recognized in routine practice.

An important consideration, therefore, when selecting an antispastic agent, is the concept of passive versus active function. Passive function represents functions performed by the therapist or caregiver and mainly requires flexibility and looseness or, in other words, passive range of movement of the limbs to accomplish daily activities. Active function, on the other hand, is performed by the patient himself or herself and requires an active range of movement, strength, concentration, attention, alertness and even positive mood. It is therefore important for the physician to recognize this and prioritize between these two when prescribing drug treatment, as most of these are likely to prove deleterious for active function due to generalized weakness, sedation, hypotension, depression, etc.

Finally, careful attention should be paid routinely to diminishing noxious and external stimuli before pharmacological treatment for spasticity

Table 7.1. Peripheral causes of aggravated muscle over activity

External stimuli	Internal stimuli
Tight clothing Tight bandages, orthoses, etc. Kinked/blocked catheters Condom drainage appliances	Constipation, especially colonic faecal loading Infection and abscesses Urinary retention and infections Pressure sores Heterotopic ossification Fractures/dislocations

is considered (Katz, 1988), as afferent stimulation (e.g. flexor reflex afferents) rather than stretch receptors may result in muscle over activity. These are described in Table 7.1.

This chapter, therefore, discusses oral agents and their place in overall management strategies. Descriptions of other treatments may be found elsewhere in this textbook.

Goals of treatment

It is essential to have a clear goal and expected outcome prior to deciding the best course of treatment. Oral medication should be started only if generalized spasticity interferes with some level of activity (e.g. positioning, care or comfort) and if treatment is likely to ameliorate this interference (see Table 7.2).

Management strategy

Spasticity treatment is worthwhile if there is impairment of the patient's function or the carer's ability to care. Initially, treatment will be physical, as already discussed, and thereafter will be indicated through treatment shown in the Table 7.2. Treatment choices are usually quite straightforward, but occasionally patient will seek treatment for their body image and self-esteem rather than purely their physical functioning. Over time, chronic spasticity leads to rheological changes within the muscles, which lead, in turn, to shortening and eventually contracture of myocytes (Rack, 1966) and tendon shortening and eventually limb deformity (Katz & Rymer, 1989). This is seen most commonly in antigravity muscles and is described in Chapter 2.

Table 7.2. Goals of pharmacological treatment of spasticity

Control of symptoms	Reduction in pain and frequency of spasm
Functional improvement	Improvement in mobility and dexterity, preservation of sexual function, improvement in range of joint movement and facilitation of therapy and orthotic fit
Aesthetic	Improvement in position of limb/body
Carer's burden	Reduced burden of care with hygiene, etc.
Prevention of complications	Prevention of joint contractures and hence delay of corrective surgery

A management strategy is thus required. Pharmacological treatment may be initiated through oral antispastic agents. By and large, baclofen is the most commonly used agent, but is it really indicated for spasticity of spinal origin (Pedersen *et al.*, 1974). Dantrolene sodium is regarded as more effective in cerebral spasticity, although its cognitive side effects do limit its desirability in traumatic brain injury (Monster, 1974). For patients with mild spasticity, these drugs are quite effective, but success becomes more limited as the spasticity worsens. Because of the small therapeutic window between clinical effect and toxicity, patients frequently find that getting an effect from the drug involves intolerable side effects. Clinicians must be therefore aware of risk/benefit ratio when considering systemic agents. Other treatments are available to complement these traditional therapies (Penn *et al.*, 1984; Das & Park, 1989), such as botulinum toxin for focal problems of spasticity and nerve and neuromuscular junction blockade with phenol and alcohol either alone or

in combination with botulinum toxin (Liversedge, 1960). Neurosurgery is less commonly undertaken in the UK and surgical techniques are mainly confined to orthopaedic procedures like tendon lengthening and soft tissue release. These are addressed elsewhere in this volume.

Patient types

Spasticity should be actively treated when it is causing harm. Oral agents are generally given to people with widespread spasticity rather than when it is a localized problem. However, treatment is part of the rehabilitation process and its aim should fit into those of the overall rehabilitation objectives. Clear goals must therefore be communicated to the patient in order to ensure the right expectations (Wade, 1988). Their side effects should be explained, particularly as they may cause drowsiness, and there may thus be difficulties in patients with cognitive deficits. This impairment is one of the main reasons why their use has been limited in rehabilitation of patients with severe disabilities. Generally speaking, these drugs are introduced in small doses and the dose increased to a point where there is an optimal clinical effect. The dose should therefore be titrated against the side effect. If the later is too troublesome, then the drug should be stopped or reduced. In this situation, combination treatment needs to be considered.

The goals for patients may differ depending on their particular skills and the expected responses to treatment may alter accordingly. The spasticity management of someone with residual functioning will be quite different to that of a nonfunctioning patient (e.g. ambulation), whose cognitive abilities may also be quite impaired. If the aim is to get the patient to walk or to be dextrous, then a drug regimen that allows safety will be necessary, where drugs to achieve a better posture in a wheelchair may have different characteristics. Sometimes spasticity may require treatment not for the disabled person but to assist the carer. Reducing spasticity to allow perineal hygiene, to ease dressing and to seat a patient comfortably in chair or wheelchair decreases the burden on the carer, and this may be the primary treatment aim (Young & Delwaide, 1981; Ward, 2002).

Combination treatment

Most oral antispastic agents can be used in combination with each other. The only reason for this is to improve the clinical effect and lessen the incidence of side effects, as it is ideally better to use one drug on its own. Combinations of baclofen with dantrolene sodium or benzodiazepines are probably the commonest, but these are more likely to affect higher cerebral functioning. More importantly, though, they can be used with newer treatments, such as botulinum toxin, phenol and intrathecal baclofen. Studies are under way to demonstrate this point.

Outcome measures

Wherever any treatment is used for spasticity, it is important to measure the effect of the intervention. Outcome measures have thus to be developed for easy use and to justify specific effect of the antispastic treatment. This applies to all forms of treatment, including physical therapy. These are discussed in more detail elsewhere, but measures should try to be as specific as possible in order to identify the individual patient's needs. They should thus be tied in with the overall goals of treatment and goal attainment should also be included. Because antispastic agents are used for generalized spasticity, there is a greater chance of seeing a change in general physical functioning than with other more focal agents. Sadly this is not usually the case, but testing along the lines of the ICF can be helpful. Examples of impairment testing include the motricity index (Demeurisse *et al.*, 1980) and stride length (Ward, 1999), of activity timed walking test (Bradstater *et al.*, 1983), the nine-hole peg test (Mathiowetz *et al.*, 1985) and of participation and quality of life include the Nottingham Health Profile (Hunt *et al.*, 1980) and Short Form 36 Questionnaire (Ware, 1993). Many of these tests are quite sensitive for function in patients with progressive disability, such as multiple sclerosis, where they give an indication not

Table 7.3. Tone intensity scale

Name	Description	Reference
Modified Ashworth	Ordinal scale of tone intensity 0–5	Bohannon & Smith, 1986
Oswestry scale of grading	Ordinal scale of stage and distribution of tone and quality of isolated movements	Goff, 1976
Degree of adductor muscle tone	Ordinal rating of hip adductors	Snow, 1990

Table 7.4. Spasm frequency scale

Name	Description	Reference
Pen spasm frequency score	Ordinal scale of frequency of leg spasm per hour	Penn, 1989
Spasm frequency score	Ordinal ranking of spasm frequency per day	Snow, 1990

Table 7.5. Activities of daily living/hygiene scale

Name	Description	Reference
Barthel ADL index	Subset of Barthel index	Mahoney & Barthel, 1965

Table 7.6. Upper extremity dexterity and strength testing

Name	Description	Reference
Grasp dynamometer testing	Objective instrument to measure grasp in pounds	Trombly & Scottad, 1977
The nine-hole peg test	Simple and time-efficient measure of finger dexterity	Kellor & Frost, 1971

Table 7.7. Clinical gait scores

Name	Description	Reference
Timed ambulation	Temporal distance gait measure	Holden & Gill, 1984
Ambulation index	Ordinal scale of ambulation distance, speed and level of assistance needed	Hauser, Dawson, Lehrich, Beal, & Kevy, 1983
Functional ambulation classification	Nominal scale of ambulation dependence/independence grading amount of assistance needed	Holden & Gill, 1984

only of the patient's ability to ambulate but also of his or her well-being. No one scale is superior as a measure of every aspect of spasticity and resultant functional change associated with the use of antispastic agents. As a result, the planned outcome measures must be selected with a specific purpose in mind. While the use of only one scale may be justified in some clinical situations, more meaningful results will almost always be obtained by using several different well-chosen scales; some of them are discussed briefly below (Tables 7.3 to 7.11). See also Chapter 3.

Table 7.8. Goniometry

Name	Description	Reference
The clinical measure of joint motion	Instrumental measure of range of movement	Greene & Heckman, 1994

Table 7.9. Pain assessment scale

Name	Description	Reference
Visual analogue scale	Patient self-rating of pain intensity on 10-point scale ranging from no pain to extremely intense pain	Gracey & McGrath, 1978
Brace-wear measure	Ordinal scale of orthotic fit	Pierson & Kartz, 1996

Table 7.10. Global scales of disability

Name	Description	Reference
Functional independence measure (FIM)	Ordinal scale of function in multiple areas including feeding, grooming, bathing, dressing, toileting, transfers, locomotion, comprehension, expression, social interaction and problem solving	Buffalo, New York, 1993

Table 7.11. Patient/caregiver assessment/quality of life measures

Name	Description	Reference
SF-36 health survey	36-Item patient report regarding patient's perception of health and physical limitations, subscores are weighted in an interval style	SF-36 health survey, 1992
Caregiver dependency scale	Patients report regarding the amount of caregiver assistance required on a typical day	Environmental status scale, National MS Society, 1985
Northwick Park care dependency scale	To assess dependency of patients in a rehabilitation setting in terms of impact on nursing staff time	Turner-Stokes *et al.*, 1990

Specific treatments

Oral antispastic agents are usually indicated in patients with diffuse or regional muscle spasticity rather than localized muscle spasticity. Despite the large number of drugs that have been reported to influence muscle tone, very few have been found useful in clinical practice. The commonly used antispastic drugs are baclofen, benzodiazepines, dantrolene sodium and tizanidine. The drugs can be used alone as monotherapy or in combination to reduce the spasticity effectively. Cannabis has been widely discussed, but there is no evidence that it has a sustained effect as an antispastic drug (CAMS Study).

Baclofen

Baclofen is a structural analogue of gamma-aminobutyric acid (GABA), which is one of the main inhibitory neurotransmitters in the central nervous

Table 7.12. Efficacy of antispastic agents in specific patient population

Antispasticity medication	MS	SCI	Stroke	TBI	CP	Side effects
Dantrolene	+	+	++		+	Muscle weakness, hepatotoxicity
Baclofen(oral)	++	+	+/−			Sedation, difficult seizure control
Tizanidine	++	+	+			Dryness of mouth, liver dysfunction
Diazepam	+	+	+/−		+	Sedation
Clonazepam	+?					Sedation

+ The antispastic efficacy and tolerance have been established in a double-blind study.
++ The antispastic efficacy and tolerance of the drug have been demonstrated to be greater than the one of the standard drugs in double-blind comparative studies.
+/− The overall improvement was mitigated in the double-blind trials mainly because of intolerable side effects.
+? Open-label trials have been promising but no double-blind studies have been conducted.
An empty box means that the drug has not been investigated to our knowledge in the condition indicated.
MS=multiple sclerosis; SCI=spinal cord injury; TBI=traumatic brain injury; CP=cerebral palsy.

system. Chemically, baclofen has the structure of beta-chlorphenyl-gamma-aminobutyric acid and is available as an approved drug in its racemic mixture with about equal content of the two enantomeres D-baclofen and L-baclofen. Laboratory studies have shown that L-baclofen is the active enantiomer (Olpe *et al.*, 1978; Johnston *et al.*, 1980) and D-baclofen antagonizes the action of L-baclofen (Sawynok & Dickson, 1985; Fromm & Terrence, 1987).

Mechanism of action

Baclofen binds to the bicuculline-insensitive GABA-B receptors (Price *et al.*, 1984; Hwang & Wilcox, 1989), which are primarily located presynaptically at the Ia sensory afferent neurones or the interneurones (Price *et al.*, 1987) and some are also located postsynaptically at the motor neurones (Wang & Dun, 1990). Upon binding the GABA-B receptor sites, the calcium influx through high-voltage–activated channels in the membrane of group Ia presynaptic terminals is inhibited and the release of endogenous excitatory neurotransmitters such as glutamate and aspartate are suppressed (Hill & Bowery, 1981; Davidoff, 1991; Curtis *et al.*, 1997). The postsynaptic GABA-B receptor–mediated inhibition is likely to occur by activating potassium channels through a membrane-delimited pathway and also through a second-messenger pathway involving arachidonic acid (Misgeld *et al.*, 1995). It also inhibits gamma motor neurone activity and reduces intrafusal spindle muscle sensitivity. The net result in inhibition of both monosynaptic and polysynaptic reflexes. In addition, animal studies have suggested that baclofen also has anti-nociceptive and analgesic properties, possibly by reducing the release of substance P from nociceptive afferent nerve terminals (Henry, 1980).

Pharmacokinetics

Baclofen can be administered both by mouth and by intrathecal injection. After oral administration, it is rapidly and completely absorbed from the gastrointestinal tract, with peak plasma levels occurring 1 to 2 hours after administration. Its plasma half-life is approximately 3.5 hours (range 2 to 6.8 hours). The serum protein-binding rate is approximately 30%, and 70% to 80% of baclofen is excreted unchanged through the kidneys within 72 hours. A small proportion (about 10%) is metabolized in the liver (Faigle & Keberle, 1992). It can cross the placenta, and only a small amount crosses the blood–brain barrier (Pedersen *et al.*, 1974).

Clinical efficacy

Baclofen has been used as an antispastic drug for over 30 years. The majority of clinical trials in several

countries generally involve patients with multiple sclerosis and spinal cord lesions and have proven that baclofen is effective in reducing spasticity and sudden painful flexor spasms (Pinto *et al.*, 1972; Duncan *et al.*, 1976; Feldman *et al.*, 1978). However, most of the studies fail to demonstrate improvement of mobility and activities of daily living (From & Heltberg, 1975).

In a double-blind crossover trial of baclofen and placebo in 23 patients (18 with multiple sclerosis and 5 with spinal cord lesions), Hudgson and Weihtman (1971) reported a reduction in spasticity and baclofen was well tolerated. In 1976, Duncan *et al.* (1976) performed a double-blind, crossover study on 22 patients with spinal cord lesions and found that baclofen was significantly effective in reducing spasticity and reflex spasms of the legs and urinary bladder and was well tolerated. The larger multicentre, double-blind, placebo-controlled trial in 106 patients with spasticity secondary to multiple sclerosis also confirmed that baclofen was effective in relieving symptoms of spasticity such as flexor spasms, clonus, pain, stiffness, resistance to passive movement of joints and tendon stretch reflex (Sachais *et al.*, 1977).

In three comparative studies (Ketlaer & Kneeler, 1972; Cartlidge *et al.*, 1974; From & Heltberg, 1975), baclofen was found to be significantly more effective than diazepam in reducing spasticity secondary to multiple sclerosis, with considerably less daytime sedation. In a double crossover study (Roussan *et al.*, 1987) of baclofen versus diazepam in 13 patients (7 with multiple sclerosis and 6 with spinal cord injury), both drugs produced similar improvement of spasticity, but side effects, especially excessive daytime sedation, were more common in those treated with diazepam. This study again showed the long-term efficacy and safety of baclofen therapy without evidence of drug tolerance, even after many years.

There have been few studies investigating the effect of baclofen in treatment of spasticity of cerebral origin, and the results described suggest a more limited benefit that achieved among patients with multiple sclerosis and spinal cord lesions (Whyte & Robinson, 1990).

Dosage and administration

The recommended oral dosage ranges from 40 to 100 mg daily. In adults, the dosage begins with 5 mg orally two to three times daily and is gradually titrated to achieve an optimal clinical response with minimal side effects. If the dosage is too high or has been increased too rapidly, side effects may occur, especially in patients who are immobile or elderly. Although the manufacturer's maximum recommended oral dosage is 100 mg daily, many patients with multiple sclerosis have received higher doses, which were found to be well tolerated (Pinto *et al.*, 1972; Smith *et al.*, 1991). If the therapeutic effects are not evident in 6 weeks, it may not benefit the patient to continue with the therapy.

Elderly patients are more susceptible to side effects and small initial dose increments under careful supervision are advised. In children, dosages in the range of 0. 75 to 2.5 mg/kg body weight should be used, and the treatment usually initiates with 2.5 mg four times daily, with gradual increments at approximately 3-day intervals until a therapeutic response is achieved.

Side effects

There is low incidence of side effects, and these usually occur upon initial treatment with large doses or in the treatment of patients with spasticity of cerebral origin and of the elderly (Aisen *et al.*, 1993). These adverse effects rarely require withdrawal of medication and are frequently mild and transient. Modifying the dosage may lessen or eliminate the side effects. Sometimes it may be difficult to distinguish between drug-induced undesirable effects and those caused by the underlying diseases being treated.

Mild gastrointestinal disturbances such as a dry mouth, nausea, vomiting, constipation or diarrhoea have been reported. Drowsiness and daytime sedation may occur especially at the initiation of treatment. Other reported neurological effects are lassitude, exhaustion, lightheadedness, ataxia, confusion, dizziness, headache, insomnia, myalgia, muscle weakness, euphoria, hallucinations,

nightmares, depression and dyskinesia (Hattab, 1980; Wakefield, 1986; Ryan & Blumenthal, 1993). Baclofen may interfere with attention and memory in elderly patients and patients following acquired brain injury. In patients with epilepsy, seizure control may be lost during treatment with baclofen due to lower convulsion threshold. Sudden withdrawal of baclofen may lead to seizures, hallucinations, visual disturbances, anxiety, confusion, psychosis (Terrence & Fromm, 1981; Rivas *et al.*, 1993) and, as a rebound phenomenon, temporary aggravation of spasticity. Baclofen might precipitate bronchoconstriction in susceptible individuals. There was a report of baclofen-induced bronchoconstriction in an asthmatic patient taking baclofen on two separate occasions (Dicpinigaitis *et al.*, 1993). Another asymptomatic patient with a history of exercise-induced dyspnoea and wheezing displayed bronchial hyper-responsiveness to inhaled methacholine only after taking a single dose of baclofen (Dicpinigaitis *et al.*, 1993). Paradoxically, increased spasticity as a contradictory response to the medication has been reported in patients with spasticity of cerebral origin (Knutsson *et al.*, 1974).

Benzodiazepines

The antispastic effect of benzodiazepines is mediated via the GABA receptor, which consists of a GABA recognition site, a benzodiazepine binding site and a chloride ion channel (Davidoff, 1985). Among benzodiazepines, diazepam is the earliest antispastic medication used in widespread clinical practice, and other benzodiazepine analogues, such as chlorazepate, clonazepam and tetrazepam, have been shown to reduce muscle spasticity effectively.

Mechanism of action

The pharmacological and antispastic effects of benzodiazepines are thought to be mediated by a functionally coupled benzodiazepine-GABA receptor chloride ionophore complex (Olsen, 1987; Costa & Guidotti, 1997). Biochemical studies indicated that benzodiazepines enhance the efficacy of GABA binding to GABA receptors in rat (Guidotti *et al.*, 1978; Skerritt *et al.*, 1982; Skerritt & Johnston, 1983). Activation of GABA recognition site initiates the opening of the chloride ion channel and the resulting increase in chloride conductance is responsible for the inhibitory postsynaptic effect of GABA. The benzodiazepines exert their antispastic action through facilitation of the postsynaptic effects of GABA, resulting in an increase in presynaptic inhibition at spinal and supraspinal sites and then a reduction of mono- and polysynaptic reflexes at the spinal level (Schlosser, 1971; Polc *et al.*, 1974; Schwartz *et al.*, 1983).

Diazepam

Diazepam is a long-acting benzodiazepine and has been used widely as an antispastic drug for over 30 years.

Pharmacokinetics

Diazepam is well absorbed after oral administration, reaching a peak blood level in 1 to 2 hours. It is metabolized in liver to achieve the metabolites N-desmethyl-diazepam and oxazepam. Excretion is through the kidneys in the form of conjugated oxazepam and temazepam. Diazepam is 98% protein bound, and its half-life varies from 20 to 50 hours while that of desmethyl-diazepam ranges up to 100 hours, depending on the patient's age and liver function. It crosses the placenta and is secreted into breast milk. Diazepam is highly lipid soluble and readily crosses the blood–brain barrier.

Clinical efficacy

Diazepam has been used most extensively in patients with muscle spasticity resulting from spinal cord lesions; its effectiveness has been demonstrated in these conditions in two double-blind crossover trials (Wilson & McKechine, 1966; Corbett *et al.*, 1972). Whether it is more effective in patients with complete or incomplete spinal cord lesions remains controversial (Cook & Nathan, 1967; Verrier *et al.*, 1977). In children with cerebral palsy, diazepam has also been shown to be effective not only for spasticity but also

for athetosis (March, 1965; Engle, 1966). Diazepam is generally unsuitable in patients with acquired brain injury because of its effects on attention and memory (Kendall, 1964).

Diazepam was marginally less efficacious than baclofen in reducing the symptoms of spasticity in the three comparative studies (Ketlaer & Ketelaer, 1972; Cartlidge *et al.*, 1974; Fromm & Heltberg, 1975). In a double–blind, crossover study (Roussau *et al.*, 1987), however, both drugs were shown to be equally effective in reducing spasticity in patients with multiple sclerosis and spinal cord injury. Nevertheless, daytime sedation was much more common with diazepam, and clinicians and patients preferred baclofen in most of the studies.

Dosage and administration

Treatment with oral diazepam usually initiates with 2 mg twice daily; it is then slowly titrated at 2-mg increments up to a maximum dose of 40 to 60 mg per day in divided doses. In children, the dosage ranges from 0.12 to 0.8 mg/kg in divided doses.

Side effects

Common adverse effects related to central nervous system depression include drowsiness, sedation, unsteadiness and ataxia. The elderly are particularly sensitive to these centrally acting depressant effects and may experience confusion, especially if organic brain changes are present. Diazepam can suppress arousal, reduce motor coordination and impair intellect, attention and memory (Kendall, 1964; Cocchiarella *et al.*, 1967). Other rare adverse effects are headache, vertigo, visual disturbances, hypotension, gastrointestinal upsets, urinary retention, changes in libido and skin rashes. The physiological dependence potential is low, but this increases when high doses are used, especially when given over longer periods. This is seen particularly in patients with marked personality disorders. Withdrawal symptoms such as depression, anxiety, nervousness, agitation, irritability, restlessness, tremor, muscle fasciculation and twitching, rebound insomnia, sweating, nausea and diarrhoea have been reported following abrupt cessation or rapid tapering of treatment with diazepam.

Other benzodiazepines

Clonazepam, which is commonly used in epilepsy, has been compared with baclofen as an antispastic efficacy in patients mostly of multiple sclerosis (Cendrowski *et al.*, 1977) and was found to be as effective as diazepam but less tolerated due to adverse effects such as sedation, confusion and fatigue, resulting in more frequent discontinuation of the drug. It is used mainly for suppression of nocturnal painful spasms. Clorazepate, a benzodiazepam analogue, has been shown in a double-blind study to be effective in reducing phasic stretch reflexes in patients with stroke and multiple sclerosis (Lossius *et al.*, 1985). Ketazolam, a benzodiazepine derivative, has been shown to be effective and slightly less sedating than diazepam in a double-blind, randomized, crossover study of 50 patients with spasticity of various causes (Basmajan *et al.*, 1984). Terazepam, another benzodiazepine derivative, was reported to reduce the tonic stretch reflexes in patients with spasticity without effect on muscle strength (Milanov, 1992).

Dantrolene sodium

Dantrolene sodium, 1-[(5-nitrophenyl) furfurylidene] amino hydantoin sodium hydrate, is a hydantoin derative and is the only drug in clinical use for spasticity that produces relaxation of contracted skeletal muscle by affecting the contractile response at a site beyond the neuromuscular junction.

Mechanism of action

Dantrolene sodium acts peripherally on muscle fibers, where it is thought to suppress the release of calcium ions from the sacroplasmic reticulum, thereby producing a dissociation of excitation-contraction coupling and diminishing the force of muscle contraction (Ellis & Carpenter, 1974; Putney & Bianchi, 1974; Hainaut & Desmedt, 1975;

Pinder *et al.*, 1977; Ward *et al.*, 1986). In animal studies, the muscle-relaxant effect is seen in both fast-contracting and slow-contracting muscle fibres, but it is more pronounced in fast-contracting fibres (Browman, 1979; Leslie & Part, 1981b; Jami *et al.*, 1983). In addition, dantrolene exerts its greatest effect on contractile responses at the lower frequency of motor unit firing in the particular muscle length. These findings suggest that the clinical effects of dantrolene will depend on a balance between the frequency of motor unit firing in the particular muscle and the type of muscle fibre firing in that muscle. Dantrolene also affects both extrafusal and intrafusal muscle fibre contraction in the muscle spindles (Monster *et al.*, 1974; Petite *et al.*, 1980; Leslie & Part, 1981a), which indicates that its antispastic effect is partly due to alteration in muscle spindle sensitivity.

Pharmacokinetics

After oral administration, approximately 70% of dantrolene sodium is absorbed through the small intestine and the majority is metabolized into 5-hydroxydantrolene in the liver. It is then excreted in the urine and bile, with 15% to 25% in unchanged form in the urine. After an oral dose of 100 mg, the peak blood concentration of the free acid, dantrolene, occurs in 3 to 6 hours and of its active metabolite occurs in 4 to 8 hours. The half-life of dantrolene sodium is approximately 15 hours after oral administration and about 12 hours after intravenous administration (Herman *et al.*, 1972; Ward *et al.*, 1986). It is lipophilic and crosses the placenta and blood–brain barrier well.

Clinical efficacy

Most of the placebo-controlled trials have demonstrated that dantrolene is superior to placebo in adults and children with spasticity from various conditions, as evidenced by muscle and reflex responses to mechanical and electrical stimulation and by clinical assessment of disability and activities of daily living (Pinder *et al.*, 1977). Although dantrolene is generally preferred for spasticity resulting from supraspinal lesions such as stroke, traumatic brain injury or cerebral palsy, this common belief remains controversial. Some workers have suggested that stroke patients are more likely to improve with dantrolene (Chyatta *et al.*, 1971; Ketel & Kolb, 1984), whereas others have found that it did not clinically produce alteration in muscle tone or a change in functional outcome in patients with hemispheric stroke when dantrolene was commenced within 8 weeks of onset of stroke (Katrak *et al.*, 1992). It was reported that patients with spinal cord injury also responded well to dantrolene (Pinder *et al.*, 1977). It is somewhat less effective in patients with multiple sclerosis (Gelenberg & Poskanzer, 1973; Tolosa *et al.*, 1975). In four placebo-controlled clinical trials, dantrolene sodium was found to be an effective antispastic agent in children with cerebral palsy (Haslam *et al.*, 1976) in three comparative studies (Glass & Hannah, 1974; Nogen, 1976; Schmidt *et al.*, 1976). There was no significant difference between dantrolene and diazepam in terms of reduction in spasticity, clonus and hyper-reflexia, but dantrolene was significantly better in its side-effect profile.

Dosage and administration

The manufacturer's maximum recommended daily oral dosage in adults is 400 mg. The initial dosage is 25 mg per day; this may be gradually increased to 100 mg four times a day. The dosage should be titrated against clinical improvement, and the lowest dose compatible with optimal response is recommended. However, clinical responses are not clearly related to dose and may reach a plateau at a dosage of 100 mg per day (Meyeler *et al.*, 1981). If no clinical benefit is derived from administration of dantrolene after 6 weeks, it should be discontinued. In some of the clinical studies, higher than the recommended dosage of 400 mg per day was used. In children, the dose begins at 0.5 mg twice daily and the dosage and frequency are increased until the maximum clinical response is achieved (British National Formulary, March 2000). The maximum dosage in children is 3 mg/kg four times daily but not more than 100 mg four times daily.

Side effects

Dantrolene commonly causes transient drowsiness, dizziness, weakness, general malaise, fatigue and diarrhoea at the start of therapy, but these are generally mild. Other side effects include central nervous system disturbance, anorexia, nausea, vomiting and skin rash. Muscle weakness may be the principal limiting side effect in ambulant patients, particularly in those with multiple sclerosis, and it could be hazardous in patients with pre-existing bulbar or respiratory muscle weakness (Pinder *et al.*, 1977). Dantrolene has caused transient abnormalities in liver function, with symptomatic hepatitis in 0.35% to 0.5% and fatal, idiosyncratic hepatitis in 0.1% to 0.2% (Utili *et al.*, 1977; Wilkinson *et al.*, 1979). The reactions occur at all doses but are more frequent in patients taking over 400 mg per day. The risk of hepatic toxicity is greatest in women over 35 years of age with concomitant medication such as oestrogen. Hence, liver function should be checked periodically during dantrolene therapy. Pleuropericardial reaction to treatment with dantrolene for 2 to 3 months has been reported, and all four patients studied developed peripheral blood eosinophilia (Petusevsky *et al.*, 1979; Miller & Haas, 1984).

Central alpha-2 adrenergic receptor agonists

Clonidine and tizanidine are imidazoline derivatives that affect central alpha-2 adrenergic receptors and their antispastic effect may be related to restoration or enhancement of noradrenergic presynaptic inhibitory descending pathway. Clonidine has been used as an antihypertensive since the early 1970s and tizanidine has only been licensed as an antispastic drug in the UK for more than 7 years, although it has been used in other European Union countries for a longer time.

Mechanism of action

The mechanism of action of clonidine is not fully understood, but it probably acts at multiple levels as a selective alpha-2 adrenergic receptor agonist in the brain, the brainstem and substantia gelatinosa and intermediolateral cell columns of the dorsal spinal cord (Unnerstall *et al.*, 1984). Other suggested mechanisms of action include suppression of alpha motor neurone excitability, enhancement of alpha-2–mediated presynaptic inhibitation of sensory afferents and suppression of polysynaptic reflexes (Naftchi, 1982; Tremblay & Bedard, 1986; Schomburg & Steffens, 1988). Recent work suggests that clonidine's antinociceptive activity seems to be exerted either at the spinal and/or supraspinal level with the involvement of alpha-1 adrenergic, alpha-2 adrenergic and opioid receptors (Sierralta *et al.*, 1996).

The precise mechanism of action of tizanidine is not clearly understood, but it has been postulated that its effects are mainly related to its central alpha-2 adrenergic agonist properties (Coward, 1994) and also its probable effect on imidazoline receptor sites (Sayers *et al.*, 1980; Muramatsu & Kigoshi, 1992). Tizanidine acts presynaptically at the spinal level on the release of excitatory amino acids – i.e. glutamate and aspartate of interneurones (Davies, 1982; Davies *et al.*, 1983). Another study has reported evidence for a possible depressant effect of tizanidine on the polysynaptic excitation of interneurones by postsynaptic reduction in the effectiveness of the release of excitatory amino acids (Curtis *et al.*, 1983). In addition to direct action at spinal level, its supraspinal effect may also involve an alpha-2 adrenergic receptor–mediated influences on the descending, facilitatory coeruleospinal pathways (Foote *et al.*, 1983; Chen *et al.*, 1987; Palmeri & Weisendanger, 1990). Recently Delwaide and Pennisi (1994) postulated that tizanidine reinforces presynaptic inhibition and may reduce flexor reflexes.

Clonidine

Pharmacokinetics

Clonidine is well absorbed from the gastrointestinal tract and its peak plasma concentrations are achieved 3 to 5 hours after oral administration. Its half-life is approximately 23 hours and it is metabolized in the liver; about 20% is excreted in the faeces. About 65% is exerted in the urine, partly unchanged.

Clinical efficacy

There are few clinical trials with clonidine as an antispastic agent and no double-blind placebo-controlled studies have been published. Two open-label trials have found clonidine to be effective objectively and subjectively in reducing spasticity in patients with spinal cord lesions (Nance *et al.*, 1985; Maynard, 1986). It has been shown to be an effective therapeutic agent in the management of spasticity in conjunction with baclofen in patients with spinal cord injury (Donovan *et al.*, 1988). In a single-blind study of six spinal cord injury patients comparing clonidine with diazepam and placebo, clonidine reduced spasticity, both subjectively and objectively, in terms of vibratory inhibition of the H reflex (Nance *et al.*, 1989). In another comparative clinical trial, clonidine had a similar antispastic efficacy to baclofen and cyproheptadine in the spinal cord–injured patients (Nance, 1994). In the single case report, a patient who developed spasticity after brainstem infarct responded rapidly to clonidine (Sandford *et al.*, 1988), and in a case series report, it was suggested that clonidine may also be useful in the management of spasticity associated with various forms of brain injury (Dall *et al.*, 1996). One study suggested that it may be helpful in reducing spasticity in patients with multiple sclerosis who fail to respond to baclofen and diazepam (Kahn & Olek, 1995). In addition to an oral form, the transdermal clonidine patch has also been shown to have efficiency in the treatment of spinal spasticity, with the advantage of fewer systemic side effects (Weingarden & Belen, 1992; Yablon & Sipski, 1993). Clearly, double-blind placebo-controlled trials are needed to confirm and establish the efficiency of clonidine in the management of spasticity.

Tizanidine

Pharmacokinetics

Tizanidine is rapidly absorbed from the gastrointestinal tract after a single oral dose, reaching peak plasma concentration in 0.75 to 2 hours. The half-life ranges from 2.1 to 4.2 hours. It is extensively metabolized in the liver via oxidation, and less than 3% of the administered dose is exerted in the urine unchanged. About 20% of the administered dose is exerted in the faeces and 53% to 66% in the urine as three main metabolites.

Clinical efficacy

A number of randomized, double-blind, placebo-controlled studies involving 544 patients have clearly demonstrated a beneficial effect of tizanidine in spasticity related to multiple sclerosis and in spinal cord–injured patients, but no definite functional improvements were observed (Lapierre *et al.*, 1987; Nance *et al.*, 1994; Smith *et al.*, 1994; United Kingdom Tizanidine Trial Group, 1994). Several double-blind, randomized, comparative trials have shown that tizanidine has a similar efficacy to baclofen in patients with multiple sclerosis or with spinal cord pathology (Hassan & McLellan, 1980; Smolenski *et al.*, 1981; Newman *et al.*, 1982; Stein *et al.*, 1987; Bass *et al.*, Eyssette *et al.*, 1988; Hoogstraten *et al.*, 1988; Pagano *et al.*, 1988; Medici *et al.*, 1989). It has also been compared to diazepam in a multicentre, double-blind trial in patients with spasticity associated with hemiplegia resulting from stroke and traumatic brain injury (Bes *et al.*, 1988). It had a similar clinical efficacy but showed a significantly better walking distance in the tizanidine treatment group. Most of these studies also showed objective improvement or preservation of muscle strength to a similar or greater extent in tizanidine group compared with those receiving baclofen or diazepam. Tizanidine also had a favourable adverse effects profile, although sedation was prominent side effect (Wagstaff & Bryson, 1997).

Dosage and administration

The most effective dose of tizanidine should be determined for each patient; a titration period of 2 to 4 weeks appears adequate to ascertain the optimal therapeutic dosage. Tizanidine therapy is usually initiated with 2 mg twice daily and increased in 4-mg increments every 4 to 7 days to a maximum 36 mg per day divided into three or four doses. At higher dosages, patients may experience sedation within an

hour of administration, which can be prevented by giving the drug in divided doses.

Side effects

Common side effects reported in clinical trials are dryness of mouth, drowsiness, somnolence, insomnia, dizziness, postural hypotension and muscle weakness. Side effects are dose related and often improve or resolve with a decrease in dosage. Other adverse effects are visual hallucinations and abnormalities of liver function (Wallace, 1994). Clinically significant increases in liver enzymes occurred in 5% to 7% of patients, resolving with the withdrawal of tizanidine. An incident of fatal acute fulminant hepatitis has been reported in a patient who was treated with tizanidine and oxazepam for about 2 months (Rustemovic *et al.*, 1994). Another type of serious tizanidine-induced hepatic injury was reported in patients who received tizanidine for several months together with baclofen, diazepam, flurazepam and diclofenac (De Graaf *et al.*, 1996). Measurement of liver function is recommended before initiation of tizanidine and then regularly after a month of treatment.

Cannabis

Cannabis has been widely used for several hundred years as an intoxicant or an herbal medicine. Delta-9-tetrahydroccabinol (THC) is the major active ingredient and is 1 of 66 cannaboid constitutes of *Cannabis sativa* (Ross & Elsohlt, 1995). Pure THC is now available as dronabinol (Marinol) or as synthetic cannaboid, nabilone (Cesament). There have been anecdotal reports of muscle-relaxant effects of smoking marijuana in spinal cord–injured patients with spasticity (Dunn & Davies, 1974; Malec *et al.*, 1982). In a double-blind trial of oral THC (either 5 or 10 mg of THC, or placebo) in 9 patients with spasticity related to multiple sclerosis, there was a reduction in pain and spasticity scores (Petro & Ellenberger, 1981). In another double-blind, placebo-controlled, crossover clinical trial of delta-9-THC in 13 patients with spasticity due to multiple sclerosis, there was significant improvement in subjective ratings of spasticity at the dosage greater than 7.5 mg of THC (Ungerleider *et al.*, 1987). Clifford (1987) reported that THC improved motor co-ordination in 2 out of 8 multiple sclerosis patients who were severely disabled with tremor and ataxia, and a case report suggests that THC has benefits for patients with spasticity related to multiple sclerosis (Meinck *et al.*, 1989). However, a double-blind, randomized, placebo-controlled study of the effect of smoking marijuana in patients with multiple sclerosis showed that posture and balance deteriorated owing to the treatment (Greenberg *et al.*, 1994), and similar findings were shown in normal volunteers (Kiplinger *et al.*, 1971). The CAMS study in 2003 (Zajicek *et al.*, 2003) did not show any beneficial objective improvement on the Ashworth scale, although there was some improvement in mobility and subjective improvement in pain associated with spasticity.

Recently, Sativex has appeared on the market and is the first cannabis-based medicine to undergo conventional clinical development and be approved as prescription medicine. It is not yet licenced in the UK but is in the midst of the licensing process and already has a licence for use in Canada for the indication of neuropathic pain. It is an oromucosal spray that allows flexible, individualized dosing. Patients self-titrate their overall dose and pattern of dosing according to their response to and tolerance of the medicine. This usually results in the administration of approximately 8 to 12 sprays per day. Each spray delivers tetrahydrocannabinol 2.7 mg and cannabidiol 2.5 mg, giving an approximate average dose of tetrahydrocannabinol of 22 to 32 mg per day and cannabidiol 20 to 30 mg per day (Barnes, 2006).

Development has concentrated on the treatment of symptoms of multiple sclerosis, notably spasticity and neuropathic pain, as well as the treatment of neuropathic pain of other aetiologies. There have been positive results in placebo-controlled trials in the use of Sativex as add-on therapy. It seems to be both efficacious and well tolerated. A recent publication by Wade and colleagues (2006) confirmed the long-term use of Sativex in the treatment of spasticity and concluded that it was both safe and effective and that its actions were maintained in the long term

(an average of 434 days in this study). The side-effect profile indicated the long-term safety of the product. However, the precise place of Sativex in the management of spasticity awaits larger and longer-term studies.

Gabapentin

In recent years there have been a few studies regarding the efficacy of gabapentin for the management of spasticity. There is significant evidence of the efficacy of gabapentin as an antiepileptic agent as well as an agent for the management of neuropathic pain. The early studies were conducted in the late 1990s. One of the first double-blind, placebo-controlled, crossover studies was conducted by Mueller and colleagues (Mueller *et al.*, 1997). This study showed that a dose of 400 mg orally three times a day of gabapentin significantly reduced spasticity as measured by the Ashworth scale and other outcome measures when compared to placebo. A further study was conducted by Cutter and colleagues in 2000 (Cutter *et al.*, 2000). This was a prospective, double-blind, placebo-controlled, crossover study and demonstrated the efficacy of 900 mg of gabapentin orally three times a day or placebo over a 6-day period. They found a statistically significant reduction in spasticity both by self-report scales and by the use of the modified Ashworth scale. They concluded that gabapentin reduced the impairment of spasticity when compared to placebo but had the advantage of not having the side effects typical with other oral antispasticity agents, such as worsening of concentration and fatigue. Gabapentin also has the additional advantage of having neuralgic analgesic properties and thus may be a useful choice in the management of spasticity associated with significant levels of pain. It is usually well tolerated but the typical antispastic dosage of between 2 700 to 3 600 mg per day is at the upper end of the suggested dose range for the compound; thus, some side effects typical of the anticonvulsant drugs can be expected. (Formica *et al.*, 2005). Recently pregabalin (Lyrica) has been released as another anticonvulsant analgesic drug, and we await with interest studies of its efficacy in spasticity. It may be better tolerated than gabapentin, but no double-blind studies have yet been conducted for a spasticity indication.

Conclusion

Oral antispastic agents are first-line treatment for the pharmacological management of generalized spasticity following physical therapy. There are now a number of useful agents, but their small therapeutic range make them ineffective in some patients before side effects occur. However, they are essentially safe in most patients, and those with milder forms of spasticity generally tolerate them well. They are best used along with physical measures to reduce tone in the limbs and trunk and can be employed in combination with other therapeutic agents. A good understanding of their uses, side effects and limitations is essential in rehabilitation of patients with neurological disorders producing significant spasticity, and it is necessary for patients and their carers to take on realistic expectations of their place in the overall management of the condition. As more drugs become available and as more becomes known about spasticity, health professionals will become more skilled in utilizing different regimens. Spasticity management is a team responsibility designed to address the needs of the disabled individuals and the carer. The place of oral antispastic agents has been well established.

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8

Chemical neurolysis in the management of muscle spasticity

A. Magid O. Bakheit

Introduction

Destruction of peripheral nerves with chemical substances such as phenol and alcohol solutions (chemical neurolysis) was introduced as a novel therapeutic modality in the 1930s, but it became a popular method of treatment of severe, intractable pain associated with cancer in the mid-1950s (Maher, 1955; Brown, 1958). A few years later peripheral nerve blocks with local anaesthetics and neurolytic agents were found to be effective in the management of muscle spasticity and neurogenic bladder disorders and more recently they have also been used to predict the outcome of certain surgical procedures such as selective dorsal rhizotomy.

An important therapeutic use of peripheral nerve and intrathecal blocks is in the treatment of severe or intractable pain (e.g. pain associated with cancer and with trigeminal and postherpetic neuralgia). Complete symptomatic relief is achieved in more than 70% of patients with chronic pain due to neurogenic causes or ischaemia (Hatangdi & Boas, 1975). Nerve blocks have also been shown to be valuable in the management of bladder dysfunction due to spinal cord injury or disease. The selective chemical denervation of S3 sacral segment in patients with a hyperactive detrusor muscle increases bladder capacity and reduces the uninhibited contractions. Continence is usually achieved in these patients without sphincter disturbances or sexual dysfunction (Torrens, 1974; Rockswold & Bradley, 1977). In addition, chemical neurolysis has proved to be an effective intervention in the management of severe upper and lower limb muscle spasticity. In most patients it relieves the muscle spasticity without significantly affecting the strength of the voluntary muscle contraction (Brown, 1958; Khalili & Betts, 1967). This confers chemical neurolysis a major advantage over treatment with oral antispasticity drugs.

Chemical neurolysis can be achieved with peripheral nerve blocks, motor point (intramuscular) injections and the intrathecal administration of alcohol or phenol. These procedures are generally safe, effective and relatively easy to perform. They are preferred to oral antispasticity drugs which often cause systemic adverse effects and are nonselective in their action, thus affecting spastic and nonspastic muscles. The latter adverse effect may lead to functional loss. In a study by Katrak and colleagues (1992) of patients recovering from stroke, dantrolene reduced muscle strength in the unaffected extremities without significantly reducing muscle tone or improving function in the spastic limbs. Another disadvantage of systemic antispasticity drugs is that their effectiveness diminishes with prolonged use due to pharmacological tolerance. Tolerance to these drugs usually develops after a few weeks or months of treatment and progressive dosage increments are often required to maintain the initial therapeutic response.

Chemical neurolysis is only one of many methods of treatment of muscle spasticity and the best clinical outcomes are achieved when it is utilized as part of an overall management strategy. Factors that precipitate or aggravate muscle spasticity, such as urinary tract infections and faecal impaction, should

be identified and treated. Empirical clinical experience also suggests that an intensive physiotherapy programme enhances the beneficial effect of nerve blocks and motor point injections. In some cases it is more useful to combine chemical neurolysis with serial splinting of the spastic limb, the application of plaster casts or the use of an orthosis.

The effect of neurolytic agents is usually irreversible and their use should, therefore, only be considered when a clear treatment goal has been identified. There is a large variation in the way muscle spasticity affects patients depending on the site and chronicity of the upper motor neurone lesion, its underlying cause, the degree of neural recovery and the way the nervous system compensates for the functional loss. Frequently spasticity is functionally useful and an individualized approach to the management of this symptom is, therefore, essential.

Indications for treatment

Severe chronic muscle spasticity often causes constant gnawing pain. In addition, it is frequently associated with muscle spasms which occur spontaneously or when the patient attempts to move. In severe cases the spasms may even be precipitated by external stimuli, such as a sudden noise. Spasms of the hip flexors, extensors or adductors may be accompanied by involuntary bladder emptying and occasionally faecal incontinence. Other effects of severe muscle spasticity include impaired motor function and the development of deformities and fixed contractures. Generally, treatment of spasticity is indicated to alleviate distressing symptoms such as pain or muscle spasms, to improve motor function, to facilitate activities of daily living (e.g. washing and dressing, urethral catheterization or perineal hygiene) or to prevent or reduce the complications often associated with muscle hypertonia (e.g. fixed contractures or difficulties in maintaining a comfortable position in bed or chair).

There is no research evidence at present to show which patients are most likely to benefit from nerve blocks and motor point injections. However, given the fact that the beneficial effect of these procedures usually lasts for several months and that good results cannot be relied upon after two or three injections (Bakheit *et al.*, 1996a), it is likely that the technique is most helpful for those whose spasticity may be troublesome in the medium rather than the long term. This would include patients recovering from severe head injury or a recent relapse of multiple sclerosis in whom spasticity is so severe that splinting or the application of plaster casts is impracticable because of the risk of soft tissue damage. Another group of patients who are likely to benefit from chemical neurolysis are those in whom spasticity is preventing the acquisition of new motor skills, such as children with cerebral palsy establishing increased independence in walking. A third group is subjects who are likely to require future surgical treatment for the complications of spasticity, such as the control of pain, the relief of muscle spasms or the surgical release of contractures, but in whom there are clinical or technical advantages in delaying such surgery.

Indications for medial popliteal nerve blocks

Medial popliteal nerve blocks and motor point injections of the gastrosoleus muscle group are indicated in cases of severe dynamic foot equinus (i.e. ankle plantar flexion that is not due to a fixed contracture), especially if resistant to serial casting or preventing the effective use of an ankle-foot orthoses. In these circumstances the foot equinus usually prevents the correct placement of the patient's foot in stance and causes insufficient clearance of the foot from the ground in the swing phase of the gait cycle, thus rendering the patient's gait unsafe. Another indication for medial popliteal nerve blocks is when sustained ankle clonus interferes with motor function or causes discomfort to the patient (e.g. if it prevents comfortable placement of the foot on the wheelchair footplate). They are also useful, as a diagnostic test, in the management of distal foot deformities in children with cerebral palsy. For example, by reducing the muscle imbalance in the lower limb a medial popliteal nerve block provides valuable information regarding the choice of the surgical procedure for

the treatment of secondary foot deformities such as hallux valgus or metatarsal subluxations (Carpenter, 1983).

Indications for obturator nerve blocks

The main indications for obturator nerve blocks in ambulatory patients is 'scissoring gait'. In nonambulatory patients this treatment may be considered when severe spasticity of the hip adductors prevents easy urethral catheterization, washing and cleaning the perineal area and seating or positioning in bed. Occasionally, obturator nerve blocks are used to prevent the development of, or to promote the healing of, skin pressure sores on the medial aspect of the knees.

Obturator nerve blocks have also been used in the management of dislocation and subluxation of the hip joint. This complication occurs in 25% of patients with severe spastic cerebral palsy and is often associated with severe pain. Treatment is usually effective in pain relief probably due to reduced stretching of the joint capsule and less friction of the femoral head against the periosteum of the acetabulum (Trainer *et al.*, 1986).

Nerve blocks for upper limb muscle spasticity

In the upper limbs, chemical neurolysis seldom improves motor function and is mainly indicated to facilitate activities of daily living. For example, the improved elbow extension following a successful musculocutaneous nerve block often makes putting on and removing upper body garments easier and in some cases also increases the patient's reach with the paretic hand. Reduction of spasticity of the finger flexors is sometimes necessary to facilitate hand hygiene and to prevent skin laceration in the palm of a claw hand. Percutaneous phenol nerve blocks are often successful in these cases but the procedure involves a higher risk than when it is used for lower limb spasticity. This is because the median and ulnar nerves run in close proximity to the blood vessels of the upper limb and an attempt to infiltrate these nerves with the neurolytic agent may result in vascular damage. Furthermore, both nerves contain sensory fibres and the sensory loss following neurolysis may cause loss or deterioration of hand function and increase the risk of burns and injury. The use of botulinum toxin is probably more appropriate than alcohol or phenol for the management of upper limb spasticity.

The diagnostic use of nerve blocks

Diagnostic nerve blocks with local anaesthetics are sometimes necessary to assess the risk/benefit ratio of chemical neurolysis. Although the effect of local anaesthetics is not identical to that of phenol and alcohol, their use often yields clinically valuable information. Bupivacaine is best suited for this purpose, as its effect lasts 7 to 8 hours when given in a dose of 1 mg/kg body weight (0.5% Marcain contains 5.28 mg/ml of bupivacaine Hcl).

Diagnostic nerve blocks may be used to predict the effects of chemical neurolysis on motor function (e.g. when severe spasticity of the wrist and finger flexors is causing functional difficulties but the patient still has some voluntary muscle strength in the affected hand). They may also be used to assess the effects of sensory loss on the patients' functional ability when injections of mixed sensory-motor nerves are being considered. Diagnostic nerve blocks have also been found valuable in predicting the functional outcome of surgical procedures for spasticity, such as selective dorsal rhizotomy, and in the management of foot dystonia (Bakheit *et al.*, 1996b).

The pharmacological properties of neurolytic agents

Phenol (a benzene derivative of carbolic acid) and ethyl alcohol are the drugs most commonly used for peripheral nerve and intrathecal blocks. Other agents, such as cresol and chlorocresol, may also be used. Although phenol and alcohol were initially thought to reduce muscle tone by the selective inhibition of gamma efferent pathways, their mode of action was subsequently shown to be due to a local

anaesthetic and neurolytic effect. The local anaesthetic effect is immediate and transient. As with conventional local anaesthetics, nerve conduction is initially blocked in the small fibres within the nerve trunk (i.e. sympathetic and sensory fibres) and then in the large motor axons. Braun *et al.* (1973) attributed this selective effect of dilute solutions of phenol or alcohol to the fact that fibres with a small diameter have more relative surface contact area for a given volume of nerve tissue than large alpha fibres. Typically, recovery of nerve conduction occurs in the reverse order. The neurolytic properties of alcohol and phenol account for their more lasting clinical effect.

Neurolytic agents in high concentration penetrate the nerve tissue and coagulate protein. The application of phenol or alcohol solutions causes nerve tissue destruction, which is proportional to the concentration and volume of fluid injected. Interestingly, the myelin sheath is more susceptible than the axons to this neurolytic injury. The pathological changes resulting from chemical neurolysis occur in a predictable sequence. Histological changes consisting of a marked inflammatory reaction in the nerve tissue occur within hours of the application of the neurolytic agent (Nathan *et al.*, 1965). These are followed in a few days by Wallerian degeneration that is maximal 2 weeks after the injection. In the event of severe damage the nerve fibres are often replaced by fibrous tissue. Finally, within a few weeks of the injection evidence of partial nerve regeneration, mainly by collateral sprouting, is usually evident; and by the 14th week regeneration is almost complete (Burkell & McPhee, 1970). The neurolytic effect is nonselective and involves myelinated and nonmyelinated nerve fibres. Very high concentrations of neurolytic agents; for example, 15% phenol in saline or 10% phenol in iophendylate (Myodil) may also cause localized vasculitis, tissue infarction and arachnoiditis (Baxter & Schacherl, 1962).

Phenol is soluble in water, glycerine and other organic solvents. Aqueous phenol is suitable for peripheral nerve blocks and motor point injections, whereas phenol in glycerine is preferred for intrathecal block. Phenol in glycerine has a higher specific gravity (i.e. heavier) than cerebrospinal fluid. This allows the solution to be easily manipulated around the desired nerve roots by the appropriate careful positioning of the patient. Interestingly, chlorocresol in glycerine (1: 50) is thought to be a better agent than phenol for the management of pain in cancer patients. It was claimed to provide a more reliable symptomatic relief, presumably because it acts partly by diffusion and spreads to a greater length of the nerve root. Aqueous solutions of phenol have been shown to have a more potent neurolytic effect than phenol in glycerine.

Procedure of peripheral nerve blocks

Nerve blocks

Chemical neurolysis is most frequently used for blocks of the medial popliteal, the obturator, the sciatic and the musculocutaneous nerve of the arm. Nerve blocks are usually carried out percutaneously as described below. However, occasionally 'open' blocks of the motor branches of mixed sensory-motor nerves are performed. Following the surgical exposure of the nerve, the motor division is identified with an electrical stimulator and 2 to 5 ml of the neurolytic agent are injected in a 2-cm segment of the nerve beneath the neural sheath. The most effective site of block depends on the course of the nerve in the limb and where it divides to innervate the muscles being considered for treatment.

An essential prerequisite for the success of peripheral percutaneous nerve blocks is the accurate placement of the injection. This can be achieved easily with an electrical stimulator utilizing a Teflon-coated needle electrode as a probe. Alternatively, a standard Venflon connected to the cathode of the stimulator could be used. The electrode wire is wrapped around the needle shaft at the top and the plastic sheath is replaced to ensure that the needle is insulated except at the tip. Although some clinicians use anatomical landmarks as the guide for needle placement, this method is often inadequate and is associated with up to 40% treatment failure (Ferrer-Brechner &

Brechner, 1976). Nerve blocks require full cooperation from the patient, and the frequent discomfort that occurs afterwards means that children might require a light general anaesthetic.

Medial popliteal nerve block

The medial popliteal (tibial) nerve is a continuation of the sciatic nerve. It runs in the middle of the popliteal fossa, where it gives off branches to the two heads of the gastrocnemius from its proximal portion approximately 1 cm above the head of the fibula. Each of these divisions gives off three to five terminal branches in the proximal fifth of the muscle. The middle and distal branches enter deep into the muscle and supply the main muscle mass and the distal third, respectively. The branches to the soleus, popliteus and tibialis posterior muscles arise more distally. Further branches below the popliteal fossa innervate the flexor digitorum longus and flexor hallucis longus muscles. The terminal branches innervate the toe flexors and the small muscles of the foot.

The medial popliteal nerve may be blocked at the apex of the popliteal fossa or 2 to 3 cm lower, at the level of the popliteal crease (Fig. 8.1). However, injection placement in the latter site is thought to be less effective than a more proximal block (Felsenthal, 1974). This is presumably because the nerve fibres are more dispersed distally. It is easier to do medial popliteal nerve blocks with the patient lying prone. Alternatively, the procedure could be performed with the patient lying on his or her side and the limb held in full extension by an assistant to prevent flexion withdrawal. The location of the medial popliteal nerve behind the knee can be easily identified at the level of the tibial epicondyles with an electrical stimulator, initially using surface electrodes delivering 5- to 50-volt pulses of 0.1-msec duration. The skin is then cleansed with iodine solution and infiltrated with 1% lignocaine. The needle probe is then introduced and manoeuvred in the tissue using stimulus pulses of decreasing strength until a contraction of the spastic muscles supplied by the nerve is obtained in response to 0.5-mA electrical pulse with a stimulus duration of 0.05 to 0.1 msec. Between 3 and 5 ml of 4.5% phenol in water or 50% ethyl alcohol is then injected over 3 to 4 minutes. Slowly the position of the needle tip is readjusted in each plane to ensure that the twitch had been fully suppressed. If a new site is found during this manoeuvre a further 1 to 2 ml of phenol should be injected. Ankle clonus is immediately abolished or significantly attenuated with a successful medial popliteal nerve block.

Obturator nerve blocks

The obturator nerve passes through the obturator foramen into the thigh in the upper medial part of the femoral triangle. (The femoral triangle is formed by the lateral border of the adductor longus, the sartorius muscle and the inguinal ligament.) The nerve emerges about 2 cm below the inguinal ligament and just lateral to the origin of the tendon of the adductor longus muscle (Fig. 8.2). It then immediately divides into an anterior (superficial) and posterior (deep) branches. It is a predominantly motor nerve and supplies the hip adductors. It also gives off branches to the hip and knee joints and a cutaneous branch to a small skin area on the medial aspect of the middle of the thigh. In one third of subjects there is an accessory obturator nerve which emerges from the pelvis above the superior pubic ramus and joins the anterior branch of the main trunk approximately 4 to 5 cm below the inguinal ligament.

Localization of the obturator nerve is made with the patient supine and both legs slightly abducted. The tendon of the adductor longus muscle is usually easily palpable in patients with hip adductor spasticity. The femoral artery is approximately 2 cm lateral to the obturator nerve and femoral pulsation is another useful landmark. Stimulation of the nerve may initially be carried out using a surface probe and then a needle electrode as described in the above section and is confirmed when a significant contraction of the adductor muscles is seen. Following injection of the anterior branch the needle is inserted 2 cm deeper and perpendicular to the coronal plane to block the posterior branch. A total of 4 to 5 ml of phenol or alcohol equally divided between the two sites is usually sufficient.

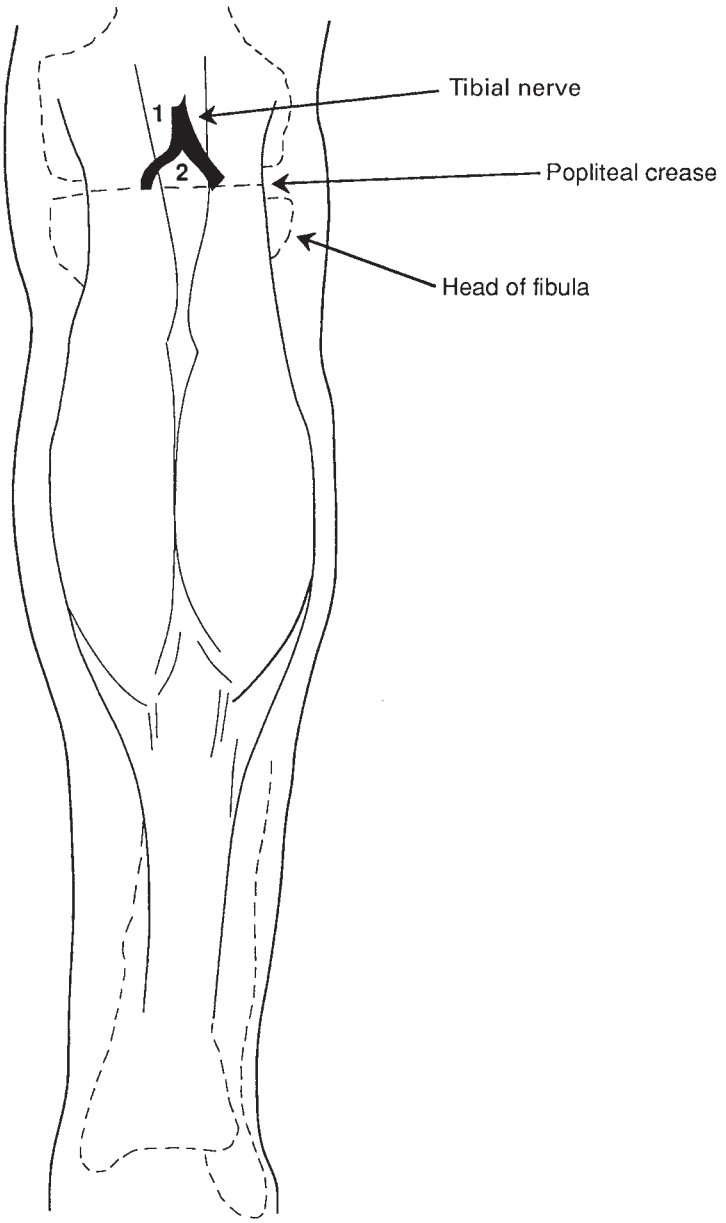

Figure 8.1. Medial popliteal nerve block at the apex of the popliteal fossa (1) is more effective than a nerve block at the level of the popliteal crease (2).

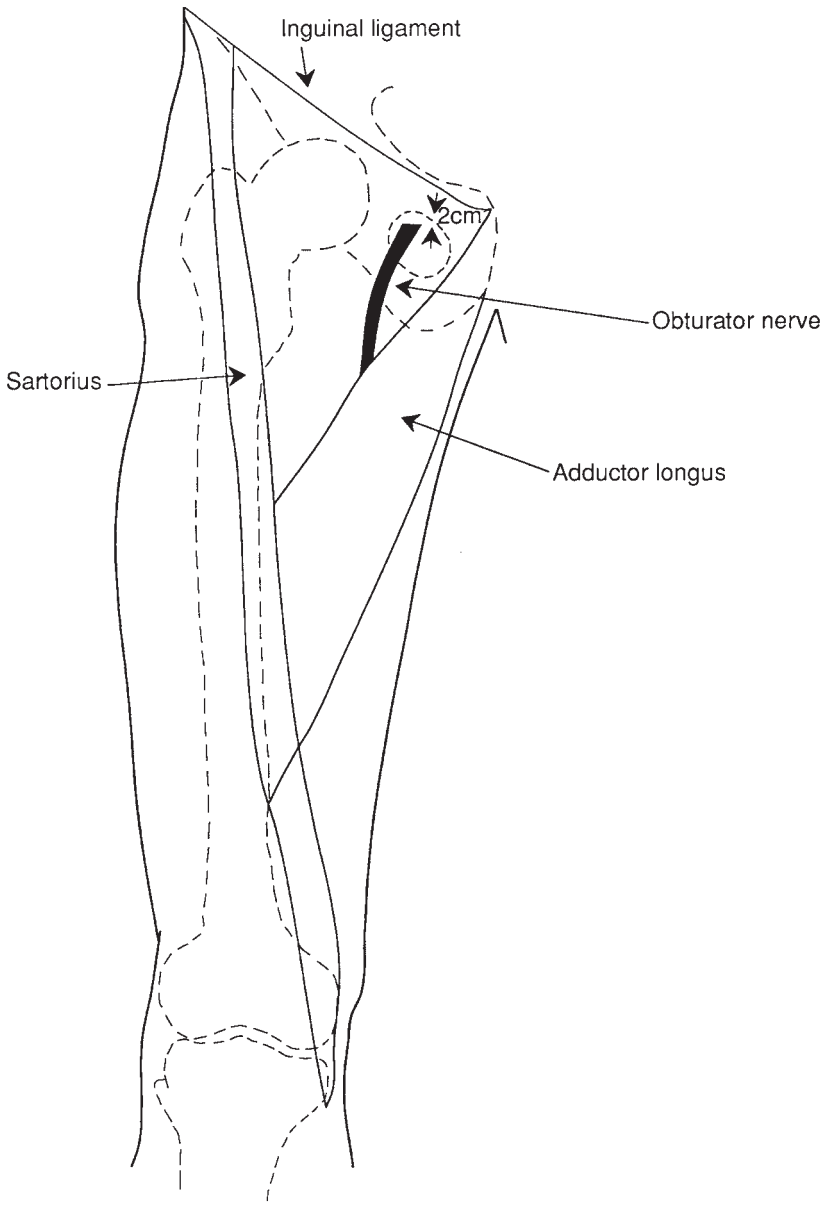

Figure 8.2. A diagram showing the exit of the obturator nerve in the upper medial part of the femoral triangle, approximately 2 cm below the inguinal ligament.

The obturator nerve can be blocked in the pelvis before it divides, but this procedure is technically difficult in patients with spasticity of the hip flexors and/or adductors. This difficulty arises because the needle has to pass through the obturator foramen into the pelvis in a direction parallel to the trunk.

Sciatic nerve block

The sciatic nerve exits the pelvis through the sciatic foramen and runs between the greater trochanter and the ischeal tuberosity. The nerve gives off branches to the hamstring muscles before it divides, usually at the level of mid thigh, into the tibial (medial popliteal) and common peroneal nerves.

Sciatic nerve fibres to the hamstrings converge at the level of the gluteal fold (Felsenthal, 1974) and are easily localized with a nerve stimulator in the middle of a line joining the greater trochanter and the ischeal tuberosity. Sciatic nerve blocks are indicated for the relief of knee flexors spasticity.

Block of the musculo-cutaneous nerve of the arm

This nerve is a continuation of the lateral cord of the brachial plexus. It innervates the biceps brachii, brachialis and coracobrachialis muscles and the skin of the lateral aspect of the forearm. With the patient supine and the upper limb abducted to 90 degrees and externally rotated the nerve can be easily identified with an electrical nerve stimulator in the proximal third of the medial aspect of the arm. At this level the nerve runs in the groove formed by the biceps brachii and the short head of the brachialis muscles. Musculocutaneous nerve blocks may be used alone, but a better response is usually obtained if combined with motor point injections of the brachioradialis muscle (Keenan *et al.*, 1990).

Lumbar spinal nerve blocks

Multiple paravertebral lumbar spinal nerve blocks have been reported to reduce hip flexor spasticity for a period of 4 to 10 months in most cases (Meelhuysen *et al.*, 1968). For an optimal therapeutic response the nerves of L2, L3 and L4 ipsilateral to the flexed hip need to be injected in a single treatment session.

The spinal nerves are blocked close to their point of exit from the vertebral foramina as follows. With the patient lying on his or her side and the spine flexed, the spinal nerve is localised in the appropriate intervertebral space 4 cm lateral to the midline. A useful surface landmark is the iliac crest, which corresponds to L4–L5 intervertebral space. The needle (which also acts as the stimulating electrode) is introduced perpendicular to the skin to a depth of 5 cm and then manipulated medially and downwards until responses from the iliacus and psoas major muscles are observed. Good clinical results may be obtained by injecting as little as 0.2 ml of 5% aqueous phenol per each site.

Motor point injections

Clinical experience suggests that nerve blocks are more effective than motor point injections. The effect of motor point injections is usually incomplete and is of shorter duration in most cases. Nevertheless, because the technique of motor point injections is simple, inexpensive, and does not require special equipment, this procedure still has a place in the management of muscle spasticity, especially when the appropriate equipment or expertise is not available or the financial cost of treatment is an important consideration.

The motor points of a muscle is the area of arborization of the motor nerve terminals and clustering of the motor end plates. These generally correspond to the sites used for placement of electrodes for conventional electromyography (EMG). Motor point blocks may be performed without EMG guidance using anatomical surface landmarks. A general rule of thumb is that the motor points of limb muscles lie in the muscle belly, halfway between the muscle origin and its point of insertion (Brash, 1955).

A modification of motor point injections known as the intramuscular alcohol (or phenol) wash is to infiltrate multiple sites in the muscle belly with the neurolytic agent, which renders the accurate localization of the motor points unnecessary (Carpenter

& Seitz, 1980). The beneficial effect of intramuscular alcohol wash is usually 1 to 4 weeks.

Motor point injections of the gastrosoleus muscles

Effective motor point blocks can be achieved by directly injecting the two heads of the gastrocnemius muscle just below the popliteal crease. By contrast, an intramuscular alcohol or phenol wash of the gastrocnemius muscles is carried out as follows. The visible bulk of the calf muscle is divided into four equal parts and 2 to 4 ml of the neurolytic agent is infiltrated into the centre of each quadrant. The dose depends on the patient's age, muscle size and the desired effect on muscle tone. The soleus muscle is injected through the same points as those in the distal two quadrants of the gastrocnemius but the needle is passed deeper and directed medially towards the axis of the limb in order to penetrate the muscle bulk.

Motor point injections of the hip adductors

It is easier to identify each of the three hip adductor muscles with the patient supine and both legs slightly abducted. The adductor brevis runs diagonally from the inferior pubic ramus to the lesser trochanter of the femur below the adductor longus. All the motor points of this muscle are concentrated in the proximal and middle thirds (Brash, 1955).

In more than 80% of subjects the neurovascular hilum of the adductor longus is found in the proximal two thirds of the muscle (Brash, 1955). This roughly corresponds to the motor points of the adductor brevis and in adults lies approximately 7 to 8 cm below the pubic tubercle (which can be located by palpating the tendon of the adductor longus). Infiltration of the motor points of both muscles can, therefore, be achieved through insertion of the needle at this point. After injecting 3 to 4 ml of the neurolytic agent into the muscle belly of the adductor longus the needle should be advanced to a depth of 4 to 5 cm to reach the adductor brevis where a further 3 to 4 ml of the drug is released.

The adductor magnus receives nerve supply mostly from the deep division of the obturator nerve by a variable number of branches which enter the muscle in the proximal and middle thirds. This area lies halfway between the site of the muscle origin and its insertion (i.e. the pubic tubercle and the medial femoral epicondyle, respectively). This is the optimal site for the motor point injection. However, if the patient can tolerate a second injection, the treatment effect is often enhanced by the additional infiltration of the proximal third of the muscle. The superficial placement of the injection may result in the denervation of the gracilis muscle (which, in addition to thigh adduction, rotates the tibia medially).

A simpler technique of intramuscular neurolysis of the hip adductors is to infiltrate each of the four quadrants of the muscle bulk in the upper third of the medial aspect of the thigh with the neurolytic agent (Carpenter & Seitz, 1980). Up to 20 ml of alcohol may be required for a good response. However, this method is less likely to be as effective as the motor point injection of individual muscles.

Motor point blocks of the hip flexors

The main hip flexor is the psoas major muscle. The fibres of this muscle arise from T12 and L1–L5 vertebrae and converge as they descend into the pelvis. The muscle tendon passes beneath the inguinal ligament to its site of insertion on the lesser trochanter of the femur. Adjacent to the anterior surface of the psoas major lie the kidney, ureters, renal vessels, the common and external iliac artery and vein. Consequently infiltration of the psoas major with alcohol or phenol can result in damage to the aforementioned retroperitoneal structures. Furthermore, rectal, vesical and sexual dysfunction following this procedure may result from damage of sympathetic and parasympathetic nerve fibres. However, these risks are reduced if the procedure is carried out under ultrasound monitoring (Koyama *et al.*, 1992). With the patient in the lateral position, the inferior pole of the kidney and the psoas muscle are identified from

the back with the ultrasound probe at the level of L1–L4. The thickness and width of the muscle are then determined. The block is made in the medial part of the muscle near the vertebral body avoiding the lumbar and femoral arteries.

The therapeutic effects of chemical neurolysis

A number of factors contribute to the motor functional disability associated with long-standing upper motor neurone lesions. Although muscle spasticity may interfere with motor function, abnormalities of the descending neural control and reorganization of the reflex activity at the spinal segmental level, as well as changes in the contractile and viscoelastic properties of muscle fibres are also important in the pathogenesis of the poor motor performance in these patients. This explains some of the variability of the clinical response to chemical neurolysis.

The long-term clinical effect of nerve blocks with phenol or alcohol on spasticity is usually evident with the onset of denervation approximately 2 weeks after the injection. However, an immediate transient effect due to the anaesthetic properties of these agents may be observed. The patient develops hypotonia of the appropriate muscle group and reduced resistance to passive muscle stretch. The corresponding deep tendon reflexes are diminished or abolished and impairment or loss of skin sensation occurs with neurolysis of mixed sensory-motor nerves. Painful dysaesthesiae may also develop. In most cases the voluntary muscle strength is not affected presumably because of a compensatory increase in the recruitment of motor units. (The force generated by a muscle partially depends on the number of motor units recruited.) An immediate increase in motor function following nerve blocks has been reported in some patients with residual muscle strength and in a few cases active movements which were not present before the block were observed (Copp *et al.*, 1970).

The optimal concentration and dosage of the neurolytic agents

Chemical neurolysis is most effective when spasticity is the main cause of the functional disability; the clinical effect of treatment depends on the concentration and the volume of the injected neurolytic agent. Functional gains are also more likely to occur in patients who had selective motor control, i.e. the ability to move part of the limb at will, before treatment (Braun *et al.*, 1973). Spasticity may be functionally beneficial (e.g. when a primitive extensor pattern is utilized for ambulation). In these circumstances partial nerve blocks may be desirable, and it is often necessary to "titrate" the dose of the neurolytic agent in order not to abolish the useful effect of spasticity.

Various concentrations and dosage schedules of aqueous phenol have been used for peripheral nerve blocks. Generally, the effect of phenol when used in concentrations less than 4.5% seems to be modest and short lived. This clinical observation is consistent with laboratory evidence. Even at 1% concentration, phenol resulted in degeneration of nerve fibres in experimental animals; but this neurolytic effect was considerably less than that of 5% and 7.5% phenol (Nathan *et al.*, 1965).

No prospective comparative clinical studies of the effectiveness of the different concentration of neurolytic agents have been carried out to date. In a retrospective study, Bakheit *et al.* (1996a) have found that 4.5% aqueous phenol was more effective than the 3% solution for obturator and medial popliteal nerve blocks. Using a functional assessment scale based on predetermined treatment goals that have been identified for each patient, the results of 56 nerve blocks in 28 patients were evaluated over a follow up period of up to 18 months. The treatment goals were achieved in 89% of those treated with 4.5% phenol compared to 18% of those who received the drug in 3% concentration. The duration of effect was also shorter with 3% phenol.

Tardieu and colleagues (1968) attempted to establish the optimal concentration of ethyl alcohol for

peripheral nerve blocks. They found that the stepwise increase in the concentration of alcohol up to 45% progressively increased the effectiveness of the injection of a given volume of fluid but that no additional benefit resulted from further increases in concentration. Generally the effect of 50% alcohol in peripheral nerve blocks is comparable to that of 4.5% phenol in water (Bakheit *et al.*, 1996a).

In a study of 36 patients who received a total of 50 nerve blocks with 2 to 3 ml of 5% phenol, improvement in muscle tone by two or three grades on the Ashworth scale was achieved in just over half the patients at 1 month; this effect was still maintained at 2 months in only two thirds of the respondents (Gunduz *et al.*, 1992). By contrast, when an average of 3.2 ml of 6.7% phenol (range 1 to 6 ml) were given per medial popliteal nerve block, good results were obtained in all of the 92 nerve blocks performed, and only 22 of them (37.2%) were repeated during a mean follow up period of 16.8 months (Petrillo & Knoploch, 1988). In most patients the beneficial effects of treatment last 3 to 4 months. The effectiveness of the injection often diminishes when the procedure is repeated more than two or three times, presumably because of fibrous tissue formation in the vicinity of the nerve (Bakheit *et al.*, 1996a).

Complications of peripheral nerve blocks

Chemical neurolysis of peripheral nerves is generally safe and effective when it is carried out by a physician experienced in the procedure. By far the commonest complication is treatment failure. This is usually due to poor localization of the nerve, inadequate dose or concentration of the neurolytic agent or the presence of heterotopic ossification of the muscle being treated.

Complications directly resulting from the injection technique, such as soft tissue injury, are rare. Occasionally, intramuscular haematomas due to vascular injury complicate motor point blocks. There is also a small risk of damage to blood vessels with the neurolytic agents. This has occasionally led to the development of ischaemic gangrene of the upper limb. Surgical exploration and the direct injection of phenol or alcohol into the motor branches of mixed peripheral nerves in the upper limbs has been suggested to safeguard against this complication. However, the use of botulinum toxin injections is a preferred alternative treatment for upper limb spasticity. Infection at the site of the injection is very rare probably because of the antiseptic properties of the neurolytic agents. Nerve blocks of mixed sensory motor nerves often result in severe impairment of skin sensation and increase the risk of burns and injury. Some patients also develop painful dysaesthesiae, but these are often transient. Interestingly, phenol is less likely than alcohol to cause dysaesthesiae when used for neurolysis of mixed sensory-motor nerves. Occasionally, a paroxysmal lancinating pain similar to that of trigeminal neuralgia develops in the area of the nerve block, but it usually resolves spontaneously in 7 to 10 days.

Lumbar paravertebral nerve blocks are also safe. In one series of 12 patients who received a total of 31 treatments (Meeluysen *et al.*, 1968) the only complication reported was constipation and faecal impaction in one subject.

Following motor point blocks, pain at the injection site and a transient burning sensation may develop, but these are usually uncommon. However, in some cases they may last up to 3 months or more. Treatment with transcutaneous electrical stimulation and/or tricyclic antidepressants is usually effective; however, in severe cases refractory to these measures, a further nerve block or even neurectomy may be necessary (Braun *et al.*, 1973). Some patients develop transient local hyperaemia and tenderness lasting 1 or 2 days. Contrary to common belief, local tissue necrosis with subsequent fibrous tissue formation does not seem to occur frequently. In a study by Carpenter and Seitz (1980) of patients treated with 50% alcohol in doses of 2 to 6 ml, no fibrosis was found on muscle biopsy 4 to 6 weeks after the motor point injections.

Intrathecal block

Administration of phenol or alcohol into the intrathecal subarachnoid space is generally reserved for severe symptomatic cases of lower limb spasticity refractory to other methods of treatment. It may result in serious morbidity and should be avoided in subjects with a reasonable bladder and bowel control and in ambulatory patients. Intrathecal blocks are most useful for the treatment of intractable painful muscle spasticity in paraplegic or tetraplegic patients who have no realistic prospects of functional recovery, no skin sensation in the lower half of the body and no control over their bowel and bladder function.

Procedure of intrathecal block

Either phenol in glycerine or alcohol may be used for intrathecal block, but phenol is preferred. Phenol in glycerine is heavier than CSF (its specific gravity is 1.25 compared to 1.007 for CSF) and it is therefore easier to manoeuvre around the desired nerve roots by the careful positioning of the patient and tilting of the table. However, a disadvantage of the high viscosity is that phenol in glycerine is difficult to inject into the subarachnoid space; this can be overcome by warming the phenol slightly before its administration. Phenol is administered into the subarachnoid space using a standard lumber puncture (LP) technique in the space between the L1–L2 or L2–L3 vertebrae. The LP is performed with the patient sitting up or in the lateral position. When the procedure is carried out with the patient in the lateral position, the nerve roots to be treated should be lower most. It is sometimes necessary to carry out the procedure under radiographic control, as severe muscle spasticity may be associated with deformity of the spine and distortion of the anatomical surface landmarks which are commonly used to determine the site of the lumbar puncture. The use of an X-ray contrast medium to enable tracking of the spread of phenol in the subarachnoid space and nerve roots is usually unnecessary, except when the function of some nerve roots needs to be preserved (e.g. the sacral nerve roots in patients with normal bowel function). It is advisable that a test injection with 0.5 ml of a local anaesthetic is given to ensure the correct placement of the needle in the subarachnoid space. The patient usually reports tingling or skin sensory loss in the distribution of the blocked nerve root within 40 seconds of a successful injection.

Positioning of the patient for the lumbar intrathecal block is critical. Once the LP needle has been placed into the subarachnoid space and *before phenol is injected* the upper half of the patient's body should be at 45 degrees or more from the horizontal to prevent the solution from running towards the head or into nerve roots higher than those intended for treatment. This position should be maintained for at least 15 minutes (and preferably for 1 or 2 hours) after the administration of phenol is completed (Morikawa *et al.*, 1966). Phenol is injected in small increments and the skin sensation, muscle tone and reflexes in the lower limbs are checked periodically. Impairment of skin sensation, reduction in the muscle tone and loss of the tendon reflexes suggests that a sufficient dose of phenol has been administered. The patient is then rocked gently forwards and backwards to allow the phenol to gravitate into all the lumbosacral nerve roots. The upper half of the patient's body should never be placed at the level of, or below the horizontal during the administration of intrathecal phenol even for a few seconds. This is because approximately 30% of the injected phenol binds to the neural structures within seconds of coming into contact with them. Almost all of the remaining phenol binds to the nerve tissue during the following few minutes; by 15 minutes from the start of the phenol administration, only 0.1% of the administered dose remains in the CSF (Ichiyanagi *et al.*, 1975)

The magnitude of the clinical effect of the intrathecal block depends on the concentration of phenol and also on the volume of phenol that is injected into the subarachnoid space (Nathan *et al.*, 1965). The most frequently used concentration of phenol in glycerine is 5%. The average safe and effective dose of 5% phenol in glycerine used in intrathecal block for

the relief of muscle spasticity and intractable muscle pain and spasms in an adult patient has been reported as 0.6 to 1.2 ml (Berry & Olszewiski, 1962), 1.5 to 2.5 ml (Jarrett *et al.*, 2002) and 2 to 4 ml (Bhakta & Cozens, 1997). When 10% phenol in glycerine is used, 0.3 ml is usually sufficient (Iwatsubo *et al.*, 1994). In most patients the beneficial effect of intrathecal phenol block lasts more than a year (Iwatsubo *et al.*, 1994).

Alcohol is sometimes is used instead of oily phenol, as its effect is usually more permanent than that of phenol (Merritt, 1981). When alcohol is used, the foot of the bed should be raised 18 inches and should remain elevated for 24 hours to prevent diffusion of alcohol rostrally into the spinal cord and brainstem (alcohol is lighter than CSF). Absolute alcohol is injected at a rate of 1 ml per minute until the limb is completely flaccid. The total effective dose is usually 7 to 12 ml.

Complications of lumbar intrathecal block

Intrathecal block is usually painless because of the immediate anaesthetic effect of the neurolytic agents. Some patients experience headaches and vomiting, but these symptoms are usually self-limiting and often resolve in a few hours.

Intrathecal block is often complicated by loss of bladder and bowel control, and it is generally thought that this procedure should be considered only in patients with complete paraplegia and no prospects of functional recovery. However, in rare circumstances, intrathecal block may be appropriate for patients with incomplete paraplegia. The possibility of destruction of the nerve fibres to the bladder and rectal sphincters is particularly high in these patients with neurolysis of L5 and S1–S3 roots, which is necessary for the treatment of hamstring muscle spasticity. The risk is less when only the hip flexors and adductors (L1–L4 roots) are treated.

The loss of muscle tone in the lower limbs, which occurs following intrathecal blocks, predisposes to thrombosis of the leg and pelvic veins and increases the risk of pulmonary embolism. However, neither the incidence of deep vein thrombosis nor the frequency of pulmonary thrombo-embolism following intrathecal blocks is known.

Phenol partially diffuses into the bloodstream following peripheral nerve blocks (Nomoto *et al.*, 1987) and, in high concentration, it may lead to serious systemic adverse effects. Systemic phenol toxicity (except that due to hypersensitivity reactions) is dose dependent. The main signs of severe phenol toxicity are central nervous system depression, pulmonary oedema, respiratory failure and cardiovascular shock, often resulting in death.

Summary

1. Chemical neurolysis is only one method of treatment of muscle spasticity and the best clinical outcomes are achieved when it is utilized as part of the overall management strategy.
2. A clear functional goal must be identified before treatment is given.
3. Treatment is generally indicated for the relief of the distressing symptoms associated with spasticity and to improve motor function or to facilitate activities of daily living.
4. Accurate placement of the injection is essential for successful nerve blocks. The use of an electrical stimulator with a needle probe is advisable.
5. The optimal concentration of aqueous phenol and ethyl alcohol for peripheral nerve blocks appears to be 4.5% and 50%, respectively. Four to 5 ml of the solution may be necessary for a successful nerve block. The duration of effect is usually 3 to 4 months and the beneficial effects of treatment often diminish when the procedure is repeated more than two or three times.
6. Peripheral nerve blocks should be avoided in the upper limbs because they may cause loss of skin sensation and also because of the risk of vascular damage. Botulinum toxin is a useful alternative for the treatment of upper limb spasticity.
7. Lumbar intrathecal blocks with phenol in glycerine should be used as a last resort for the treatment

of severe intractable spasticity in patients with paraplegia or tetraplegia. The optimal dose of 5% phenol in glycerine is 2 to 4 ml.

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9

Spasticity and botulinum toxin

Michael P. Barnes and Elizabeth C. Davis

Introduction

Botulinum toxin (BoNT) is the most potent neurotoxin known, and its clinical effects have been recognized since the end of the nineteenth century. The toxin is produced by the gram-negative anaerobic bacterium *Clostridium botulinum* and ingestion can produce botulism, a rare and often fatal paralytic illness.

The paralytic effect of the toxin is due to blockade of neuromuscular transmission (Burgen *et al.*, 1949). Injection of BoNT into a muscle causes irreversible chemodenervation and local paralysis. It was this discovery that led to the development of the toxin as a therapeutic tool. It is now used clinically for a wide range of conditions (Jankovic, 1994).

There has been burgeoning interest in the medical use of BoNT, particularly since its efficacy and safety have been demonstrated. Its use in the management of spasticity is now well established. This chapter reviews its mode of action and current therapeutic use in spasticity.

Clinical pharmacology

There are seven immunologically distinct serotypes of botulinum toxin (labelled A to G); there are two types in routine clinical use – BoNT type A (BoNT-A) and BoNT type B (BoNT-B). Most of the studies with regard to botulinum and spasticity have been conducted using type A toxin, but type B toxin is in commercial use and is also used in the management of spasticity. There have been clinical trials of type C toxins (Eleopra *et al.*, 1997) and type F (Ludlow *et al.*, 1992; Greene & Fahn, 1993; Houser *et al.*, 1998) with positive clinical outcomes but with short-lasting effects. It is unlikely that the other toxins will achieve widespread clinical usage (Eleopra *et al.*, 2006); as far as the present authors are aware, there are no longer any ongoing clinical trials of these the other types of toxin.

Botulinum toxin acts selectively on peripheral cholinergic nerve endings to inhibit the release of acetylcholine. It also inhibits transmitter release from pre- and post-ganglionic nerve endings of the autonomic nervous system, but it does not affect the synthesis or storage of acetylcholine.

Following the binding, internalization and activation of the toxin in the presynaptic nerve terminals of the neuromuscular junction, there is chemical denervation. This process is temporary, because the muscle is progressively reinnervated by nerve sproutings.

The BoNT-A toxin is synthesized as a single polypeptide chain (molecular weight, 150 kDa). These molecules are relatively inactive until their structure is modified by cleavage into a light (50-kDa) and a heavy (100-kDa) chain, which are linked by a disulphide bond.

Selective, high-affinity binding of BoNT-A occurs at the presynaptic neurone of the neuromuscular junction. It is the C terminal of the heavy chain, which determines cholinergic specificity and is responsible for this binding. After internalization,

the disulphide bond is cleaved and the N terminal of the heavy chain, which promotes penetration and translocation of the light chain across the endosomal membrane into the cytosol.

Here it interacts with, and cleaves the fusion protein SNAP 25 (synaptosomal associated protein) and inhibits the calcium-mediated release of acetylcholine from the presynaptic nerve terminal, thereby weakening the muscle (Blasi *et al.*, 1993). Chemical denervation is induced in both the alpha motor innervated extrafusal fibres and the gamma motor innervated intrafusal muscle fibre endings (Rosales *et al.*, 1996).

Botulinum toxins type B and F act similarly but cleave the fusion protein VAMP (vesicular-associated membrane protein), and type C acts by cleaving syntaxin. This process is reversed within 2 to 4 months as a result of nerve sprouting and muscle reinnervation.

It is believed that the clinical effects of the toxin are due to the peripheral effects described above; however, retrograde axonal transport and intraspinal transfer of botulinum toxin have been shown in a mammalian model (Wiegand, 1976). This is one explanation that is used with regard to the effects of the toxin, which occur distant to the site of the injection.

There is usually a 2- to 4-day delay between the administration of the toxin and the onset of clinical effects. This delay may be due to the time required for the enzymatic disruption of the acetylcholine release process by the toxin. The clinical duration of response to BoNT-A is usually around 3 months but is to some extent dependent on the dosage used, the condition being treated and the size and activity of the muscle injected.

Adverse effects are primarily due to excessive weakening of the muscles being treated, although there are reports of self-limiting fatigue, nausea, headache and fever (Greene *et al.*, 1990). Unfortunately, immunoresistance to BoNT-A can also develop. The frequency of BoNT-A antibody formation varies from around 3% to 5% over time (Zuber *et al.*, 1993; Greene *et al.*, 1994). Differences in antibody detection rates may relate to the methods used for their detection; it has been suggested that the only reliable method of detecting circulating neutralizing antibodies is by the mouse bioassay (Hatheway *et al.*, 1994). It is not yet known in detail whether patients who develop secondary nonresponsiveness to type A due to antibody formation will respond clinically to the other BoNT types. However, a recent study by Barnes and colleagues (Barnes *et al.*, 2005) demonstrated a poor clinical response to BoNT-B in those who had become clinically nonresponsive to BoNT-A. Just 7 people out of 20 who had become type A resistant responded to the type B toxin, without unacceptable side effects. Similar results have been found in other studies (Dressler & Eleopra, 2006).

BoNT-A is commercially purified for clinical use and marketed as Dysport® (Ipsen) and BOTOX® (Allergan). Recently a new form of BoNT-A has been made available for commercial use. At the time of writing, it is commercially available only in Germany. This toxin has been produced free of complexing proteins and is marketed as Xeomin® (Merz). There is currently limited data from trials on Xeomin®, but initial studies, at least in the context of dystonia, have indicated a similar efficacy to the other type A toxins (Benecke *et al.*, 2005; Jost *et al.*, 2005).

A vial of Dysport® contains 500 units (1 unit = 0.025 ng) and a vial of BOTOX® and a vial of Xeomin® contain 100 units (1 unit = 0.4 ng). However, there are significant differences between the observed potencies of two of these distinct products in the clinical situation. Suggestions of an equivalency ratio of Dysport®/BOTOX® ranging from 3:1 to 4:1 at standard vial dilutions have been made (Brin & Blitzer, 1993; Odergren *et al.*, 1998; Sampaio *et al.*, 1997a). It is likely that a similar ratio will apply to Dysport®/Xeomin®.

Botulinum type B, Myobloc® (USA) or NeuroBloc® (Europe) (Solstice Neurosciences) is available in vials containing 2500, 5000 and 10 000 units. There is no clear, accepted conversion ratio between the type A and B toxins. It is recommended that a normal starting dose of Myobloc®/NeuroBloc® should be around 2500 to 5000 units for cervical dystonia (prescribing information from Solstice Neurosciences). In clinical practice, it is important to emphasize that the

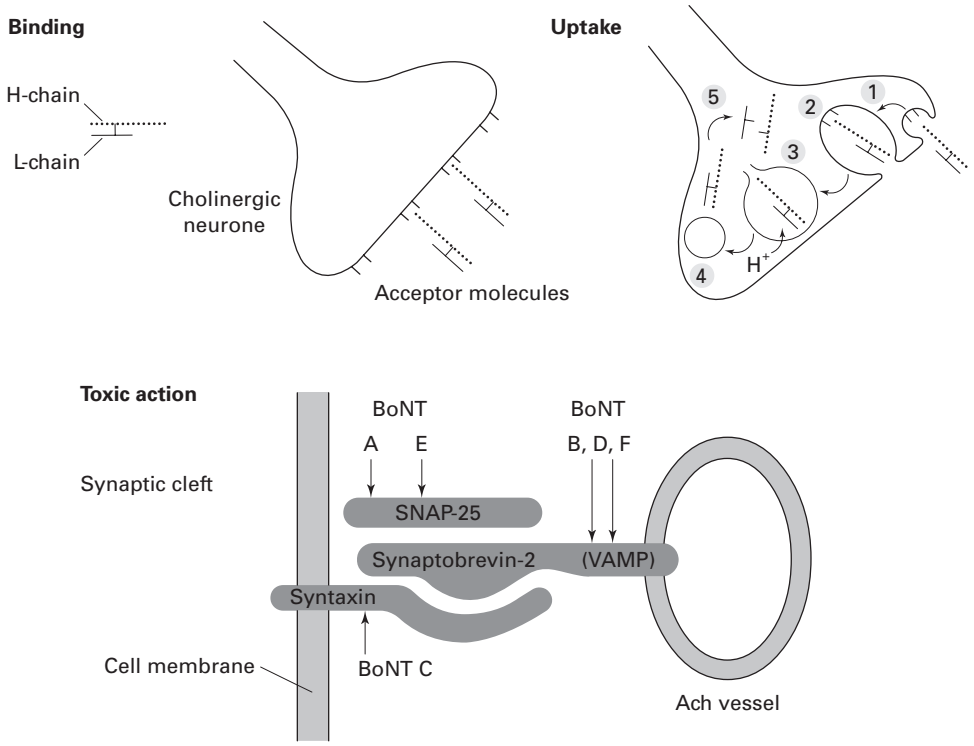

Figure 9.1. Diagram showing the mechanisms of binding and uptake and the toxic actions of the botulinum neurotoxins within the cholinergic nerve terminal. [Redrawn from Moore, P. (ed.). (1995). *Handbook of Botulinum Treatment*. Oxford: Blackwell, p. 21.]

different commercial products have different units and that there are no clear conversion ratios. It is important for the clinician to be aware of this point when prescribing any type of botulinum toxin.

Botulinum toxin as a therapy for spasticity

BoNT-A was first used therapeutically for strabismus (Scott, 1979). It is now considered the treatment of choice in a variety of focal dystonias including blepharospasm (Jankovic & Schwartz, 1993), oromandibular dystonia (Brin *et al.*, 1994), adductor spasmodic dysphonia (Truong *et al.*, 1991; Whurr *et al.*, 1993), cervical dystonia (Dauer *et al.*, 1998), task-specific dystonias (Tsui *et al.*, 1993) and hemifacial spasm (Jitpimolmard *et al.*, 1998).

In the last 10 years or so it has increasingly been recognized as an effective and useful tool for the treatment of spasticity.

Assessment

Prior to using botulinum toxin as a treatment for spasticity, a full clinical assessment is important. This is necessary to ensure that any deformity can be reduced to some extent by slow passive extension, because the toxin cannot free a joint that is fixed or stiff, nor in the main, is it believed that the toxin can lengthen muscles that are already shortened. It would therefore be inappropriate to use BoNT-A in such cases. In some centres a physiotherapist and a

medical doctor work together to carry out this assessment.

The Spasticity Study Group has produced an algorithm for the use of botulinum toxin in adult-onset spasticity (Brin, 1997). The Royal College of Physicians of London has also produced guidelines for the management of spasticity with botulinum toxin (Ward *et al.*, 2001). These are useful tools for any clinician intending to initiate the use of botulinum toxin as a therapy in the management of spasticity. It is also necessary to establish the objectives of treatment prior to implementation. Examples of treatment goals include the reduction of spasm frequency, the reduction of pain, to increase range of movement, to improve hygiene, to aid fitting of orthoses, to improve function, to delay or avoid surgery, to improve cosmesis and to ease the burden on carers. In clinical practice, a functional and practical treatment goal is probably more important than a simple measure of impairment. While, for example, improved range of motion across a joint is likely to have functional benefit, it is probably more relevant to measure actual functional improvement, such as timed walking, speed or functional hand tasks.

The injection technique

Botulinum toxin has to be injected into the involved muscle for the treatment of spasticity. The technique for injection is relatively simple. The toxin is reconstituted in normal saline and then injected intramuscularly into the affected area. However, there are some elements of controversy in the technique and often limited data that can act as a guide to best practice.

Dilution

Botulinum toxin type A requires reconstitution in normal saline. Botulinum toxin type B (NeuroBloc®/Myobloc®) does not need such reconstitution. A slight disadvantage for Dysport®/NeuroBloc®/BOTOX® is that the compounds have to be kept in a refrigerator/freezer. The new Merz compound (Xeomin®) can be kept at room temperature. The reconstituted volume for Dysport®/BOTOX®/Xeomin® has not been subjected to rigorous comparison of efficacy in different dilution volumes. The practice of the current authors is to reconstitute the toxins in 5 ml of normal saline, giving rise to 100 units of Dysport® per ml and 20 units of BOTOX® per ml. Some recent studies (in the context of cosmetic injections for wrinkle lines) have demonstrated a better spread of the toxin effect when BOTOX® was injected in a concentration of 20 units per ml as compared with a concentration of 100 units per ml (Hsu *et al.*, 2004). This finding was also confirmed in animal studies (Kim *et al.*, 2003). However, the situation is still not completely clear, as another single-blinded trial in the context of spasticity treatment in children with cerebral palsy indicated no differences between higher- and lower-volume injections (Lee *et al.*, 2004).

Dosage

Some publications have indicated dosage guidelines for the different muscles to be injected (Ward *et al.*, 2001). These guidelines are useful for the novice injector but, with such a wide variation of dosages, rigid adherence to dosage guidelines for a more experienced injector is not appropriate. The dosage will obviously vary according to muscle size. Larger muscles may need two, three or more injections for the muscle to be maximally relaxed. Smaller muscles may just require a single injection. The total dose will not only depend on muscle size but also on the clinical state of the patient. For example, individuals with no functional movement of the legs can be given larger doses than those who still require some strength in the muscles to remain ambulant. A few studies have compared dosages in different clinical circumstances. For example, a recent study by Pittock and colleagues (Pittock *et al.*, 2003) compared placebo or 500, 1000 and 1500 Dysport® units of botulinum toxin type A in 234 patients with stroke. Injections were given for calf muscle spasticity. All

Dysport® injections resulted in significant reductions of muscle tone, limb pain and dependence on walking aids. However, the greatest benefit was shown in patients receiving 1500 Dysport® units. A similar dose-dependent response, in terms of muscle tone reduction, was seen in another recent study by Childers and colleagues (Childers *et al.*, 2004). This study involved a comparison between placebo and 90, 180 or 360 units of BOTOX®. Muscle tone decreased in all the botulinum groups in all the muscles injected (upper limb muscles poststroke) and a dose-dependent response was seen with regard to tone reduction but not with regard to pain or other functional measures. However, the general message from published studies is that the dosage needs to be individualized to the specific goals in specific individuals (Slawek *et al.*, 2005).

Injection guidance

Some authorities would use electromyographic (EMG) guidance when injecting individual muscles. Other authorities feel that such EMG guidance is not required. It is generally accepted that the larger and easily identifiable and palpable muscles probably do not need EMG guidance, whereas for injections in the smaller muscles with less clear landmarks, EMG guidance can be useful. However, there are no clear studies indicating that EMG produces better efficacy than simple clinical palpation and injection. The current authors do not use EMG guidance for spasticity injections. The accuracy of non-EMG-guided injections has been questioned. One study by Chin and colleagues (Chin *et al.*, 2005) compared manual technique with electrophysiological guidance to aid needle placement. They found an "acceptable" accuracy for gastrocnemius/soleus injections (greater than 75%) and "less acceptable" accuracy for other muscles. For example, the accuracy of non-EMG–guided injections for tibialis posterior was only 11%; for the forearm and hand muscles, the figures ranged from 13% to 35%. These authors recommended electrical stimulation or other guidance techniques to aid accurate needle placement. However, as the toxin spreads a few centimetres from the injection site, precise needle placement may not actually be necessary to achieve a reasonable degree of muscle relaxation, particularly with higher dilution volumes. This matter is still open to debate.

Other guided injection techniques include ultrasound guidance, which is particularly useful for iliopsoas injections for hip flexor spasticity (Westhoff *et al.*, 2003). Some centres use general anaesthesia prior to injections, particularly in children. However, it is now generally accepted that general anaesthesia is not necessary and obviously will carry risks in its own right (Bakheit, 2003).

Long-term efficacy and safety

There are now many years of clinical experience with botulinum toxin in the management of spasticity. Some centres have been using botulinum on a regular basis, usually every 3 months, for over 10 years. There are no known long-term complications. As noted above, a small proportion of people (probably around 3%) develop neutralizing antibodies. In these people, from a clinical point of view, larger and larger doses will be required with less and less effect. Eventually the injection will stop working altogether. In theory, the higher doses required for spasticity management when compared to the lower doses needed for dystonia might lead to a higher risk of antibody formation in the longer term in the spasticity population. However, the experience at our own centre in Newcastle indicates that this is not the case. In our study there was a similar rate of antibody formation in individuals requiring lower doses for dystonia when compared to the higher doses needed for spasticity. However, it makes clinical sense to use the lowest efficacious dosage. The interval between injections might be important. Injections should probably not be repeated before the previous injection is beginning to wear off. This is normally at about a 3 months, although the efficacy duration can vary from patient to patient from 2 to 4 months. Antibody levels can be clini-

cally assayed but such techniques; but while valuable for research, they are probably not necessary in the clinical setting. If there was a decreasing clinical response at increasing dosage, then this is a reasonable and practical guide that suggests the formation of antibodies. If antibodies develop, an alternative toxin type can be tried (e.g. type B can be substituted for type A). However, despite initial indications, there does appear to be some cross-reactivity between type B and type A; thus, those with neutralizing antibodies to type A toxin may also have neutralizing antibodies to the type B toxin (Barnes *et al.*, 2005). Occasionally patients appear to respond to one manufacturer's version of the toxin and not another's, although the reasons for this are not clear. An alternative technique is simply to leave injections for a period of around 6 months and, in a small proportion of patients, when the injections are restarted, the efficacy appears to have returned. This is a poorly researched area and the mechanisms behind such responses are not clear. In theory, the recently developed Xeomin® toxin is free of complexing proteins and there should be less propensity to antibody formation with it. However, the compound has not been released into clinical practice long enough to determine whether this is the case.

Other than the risk of antibody formation, there do not appear to be any other long-term risks; indeed, a number of studies as well as clinical experience confirm long-term efficacy (Linder *et al.*, 2001; Bakheit *et al.*, 2004; Gordon *et al.*, 2004).

In the short term, the injections are remarkably safe and free of side effects. A small proportion of patients (around 1%) complain of flu-like symptoms for a few days and, occasionally (less than 1%), a localized rash appears around the injections site. A few authors also report nausea (around 2%). The botulinum B toxin produces some pain at the injection site, which is sometimes long lasting (Barnes *et al.*, 2005). Other complications have been very rare (Turkel *et al.*, 2006). The only other 'side effect' of note is excessive weakness. Obviously, muscle weakness is a desired effect of the injection, but in some instances the muscle weakness can have negative functional consequences. This is particularly the case in those who are ambulant. In such people a relatively minor level of increased weakness can impair ambulation. Some individuals need some residual muscle strength to aid transfers and such strength can be removed by excessive induced muscle weakness by the botulinum injection. Thus, caution is needed in those who are ambulant or require some muscle strength for transferring. Similar effects can be found in the arm when a weakened spastic limb can be transformed into a weaker limb with less spasticity but also with less functional abilities. This illustrates the importance of an individualized dosing regimen.

Economics

Botulinum toxin is expensive. The annual cost, while clearly depending on the total dosage used, can exceed £1000 per annum if the injections need to be repeated every 3 months. In many health economies this cost is prohibitive and precludes the widespread usage of botulinum toxin. However, whilst botulinum is superficially expensive, a full health economic appraisal may indicate savings in other areas. Oral medication, for example, can often be reduced or stopped altogether. If contractures can be prevented, for example, then this will save the cost of corrective surgery. Care costs for those with severe disabilities can also be reduced if contractures are prevented, as established contractures can often lead to the need for hoisting and, thus, the need for two carers. There have been a few studies of the health economic cost impact of botulinum toxin. A study in the UK (Ward *et al.*, 2005) demonstrated that botulinum toxin type A treatment was more cost effective than oral therapy, with a 'cost per successfully treated month' being £942 for the first-line botulinum toxin therapy compared to £1697 for oral therapy. Another study from Australia (Houltram *et al.*, 2001) compared the efficacy of botulinum toxin type A with serial casting in the management of equinus deformity in children with cerebral palsy. The study demonstrated equivalent efficacy between the two tech-

niques but found that the botulinum toxin effect lasted longer and was clearly the preferred treatment. For children with hemiplegia, the additional cost associated with botulinum was just $160 (Australian dollars) for each episode of treatment. This relatively modest increase led to acceptance by the Pharmaceutical Benefits Advisory Committee that BOTOX® should attract a full government subsidy in Australia. Finally, in the United States (Balkrishnan *et al.*, 2002), the costs of botulinum were compared in children with spastic cerebral palsy using a pair matching technique. The introduction of botulinum resulted in an increase of approximately $62 (US) per month in prescription costs, but these costs were offset by reductions in hospitalization. Overall, the Medicaid reimbursements of botulinum uses were not different from those of pair-matched nonbotulinum users.

Botulinum alone or in combination?

This book clearly demonstrates that the management of spasticity is multidisciplinary. A single treatment entity is unlikely to be sufficient for the overall management of the individual patient. Botulinum toxin can certainly reduce muscle tone, but it is likely that such treatment will need additional input from various physiotherapy techniques and perhaps other treatment modalities, such as orthoses and/or oral medication. Indeed, there is now emerging evidence that botulinum toxin is more efficacious when used in combination with other antispasticity measures rather than simply being used in isolation. Early studies involved the use of short-term electrical stimulation (Hesse *et al.*, 1998). Hesse and colleagues used four treatment groups in 24 people with stroke. They injected either placebo or toxin (1000 units of Dysport®) into six upper limb flexor muscles. The placebo or toxin was then combined with additional electrical stimulation given three times daily for $^1/_2$ hour over 3 days. Most improvement was seen in the combination group of botulinum toxin plus electrical stimulation, with a statistically significant improvement in palm cleaning as well as significant differences in tone and the ability to place the arm through a sleeve. Other studies have shown the efficacy of botulinum combined with taping (Carda & Molteni, 2005). The authors injected botulinum toxin in 65 adult subjects affected by spasticity of the wrist and finger flexors. After injection, one group was treated with adhesive taping for 6 days and the other with electrical stimulation and splinting for 6 days. There were statistically better improvements (as measured by the modified Ashworth scale) in the taping group. A more direct comparison was performed by Ackman and colleagues in Chicago (Ackman *et al.*, 2005). This study compared botulinum toxin alone, casting alone or a combination of the two techniques for the management of dynamic equinus in ambulatory children with spastic cerebral palsy. Thirty-nine children were enrolled in the study. This study actually showed that botulinum alone provided no improvement in the parameters measured in the study (ankle kinematics, velocity and stride length were the primary outcome measures) but that casting alone and botulinum combined with casting were effective in both the short and long term. In a study from Italy (Bottos *et al.*, 2003) 10 children with spastic diplegia were divided into two groups – one using botulinum toxin and the other using botulinum toxin plus casting – for the management of dynamic equinus foot. The study showed that botulinum reduced spasticity and improved functional performance in both standing and walking, but there were better and longer-term improvements when the botulinum was associated with casting. In fairness, not all studies have shown this combination to be efficacious. One study demonstrated that casting alone was sufficient for the management of calf contracture after severe head injury, and there was little additional benefit with botulinum toxin (Verplancke *et al.*, 2005). Also, a recent Cochrane review did not find sufficient evidence to support or refute the use of intramuscular botulinum as an adjunct to managing the upper limb in children with spastic cerebral palsy. The authors only found two randomised controlled trials that met their strict inclusion criteria, and only one of these studies demonstrated an improvement after botulinum toxin. This paper illustrates the need

for larger sample sizes and more rigorous methodology, particularly in terms of measurement of upper limb function in future studies (Wasiak *et al.*, 2004). Other studies have confirmed the original work of Hesse with regard to the efficacy of electrical stimulation. A study from the UK (Johnson *et al.*, 2004) demonstrated that combined treatment (botulinum toxin plus functional electrical stimulation for spastic foot drop) improved walking and function in a nonblinded and randomized controlled trial. Only 21 adults were studied in this trial, and while the results demonstrated promising combined efficacy of these two treatment modalities, larger studies are required. This result was replicated in a similar study from Italy (Frasson *et al.*, 2005) that studied changes in the amplitude of the compound muscle action potential recorded from the extensor digitorum brevis muscle in response to perineal nerve stimulation at the ankle after injection of botulinum toxin type A alone or combined with short-term nerve stimulation. The amplitude of the compound muscle action potential was significantly greater in the group that combined botulinum with low-frequency (4 Hz) nerve stimulation. The authors suggested that short-term low-frequency nerve stimulation accelerated the effectiveness of the botulinum injections and might produce a more rapid and persistent improvement in spasticity. This work needs further confirmation. Other early work has indicated the usefulness of combining botulinum toxin with occupational therapy (Fehlings *et al.*, 2000) and with modified constraint-induced therapy (Page *et al.*, 2003).

While the evidence is still somewhat patchy, the authors do recommend the involvement of a physiotherapist in the botulinum clinic. We are loathe to inject botulinum alone without the involvement of the multidisciplinary team.

Clinical trials

In the first edition of this book this chapter discussed many of the early studies in the use of botulinum toxin for the management of spasticity. Most of these studies dated from the early 1990s. The original report was by Das and Park in 1989 (Das & Park, 1989a, 1989b). The initial findings were followed by several open-labelled studies that continued to define and refine the use of botulinum in spasticity management. As most of these studies were published in the mid-1990s there is a further 10 years experience in the field, and it is probably no longer necessary to fully review the early literature. Botulinum toxin now has a clearly established place in the management of spasticity, and many studies have confirmed both the efficacy and safety of this treatment. The early studies concentrated on changes in impairment as the primary outcome measure. Many of the early studies measured reduction in muscle tone using the Ashworth scale or similar scores. However, the more recent studies tend to concentrate on the functional improvements that can follow botulinum injections. Obviously, such functional change is the main aim of the treatment for the individual patient and studies looking at function (activity) and broader aspects of participation are to be encouraged. Also, the earlier studies tended to concentrate on specific diagnostic groups – such as stroke, traumatic brain injury or multiple sclerosis. While such studies of homogeneous populations are important in terms of pharmaceutical licensing, they are less relevant for the overall management of spasticity, which will tend to have the same clinical characteristics regardless of the underlying aetiology.

Thus, for the purposes of this updated chapter, we discuss some of the larger-scale and more recent studies that have looked at functional outcome. We also mention some of the smaller-scale studies that are beginning to explore other areas of potential clinical relevance, such as the use of botulinum for spastic clawed toes and for the reduction of troublesome associated reactions.

One of the earlier studies looking at functional outcomes was reported by Dunne in 1995 (Dunne *et al.*, 1995). This study, which looked at 40 patients with mixed diagnoses, indicated that 85% of subjects derived worthwhile benefit in terms of posture and range of movement as well as pain reduction and increased function. In the same year Grazko

and colleagues (Grazko *et al.*, 1995), in a placebo-controlled crossover study using botulinum type A in 12 patients, demonstrated significant reduction in tone as well as increase in function and ease of nursing care in 8 of the 12 individuals; 5 also benefited from alleviation of muscle spasm. Pierson and colleagues (Pierson *et al.*, 1996) recorded similar functional improvement in 39 cases of spasticity of mixed aetiology. This study reported not only improvements in impairment level, such as range of motion, but also more relevant outcomes, such as better brace tolerance, pain relief and subjective functional improvement. Bhakta and colleagues (Bhakta *et al.*, 1996) studied 17 patients with a non-functioning arm assessed at baseline and 2 weeks after botulinum treatment. The treatment consisted of a single course of injections into four upper limb muscle groups (biceps and hand and finger flexors). They found improvements on the standard impairment measures, such as the modified Ashworth scale and goniometry, but they also found improvements on a rating scale based on patient-defined goal assessment. A total of 14 out of the 17 patients reported some functional benefit, which occurred within 2 weeks and lasted, surprisingly, from between 1 to 11 months. Not all early studies demonstrated such functional benefit. Sampaio and colleagues (Sampaio *et al.*, 1997b) confirmed improvements in impairment measures in a study of 19 patients following botulinum injections into the hand and finger flexors but, disappointingly, the population rated their functional improvement as none or mild. However, the authors acknowledge that only hand and finger flexors were injected and further functional improvements may have been obtained if elbow flexors had also been injected. More recent studies have looked at the impact of injections on disability and carer burden. Bhakta and colleagues (Bhakta *et al.*, 2000) included 40 patients after stroke with spasticity and a functionally useless arm randomized to receive either botulinum type A (Dysport®) or placebo. A total dose of 1000 units was divided between elbow, wrist and finger flexors. This study, as well as using impairment measures such as the Ashworth scale and joint movement, looked at disability and carer burden, using an eight- and four-item scales, respectively. Disability improved compared to placebo at week 6 and had worn off by week 12. There was also a reduction in carer burden in week 6 and continuing for at least 12 weeks. Grip strength was reduced in this study, but there were no significant adverse effects. The investigators concluded that botulinum was useful for treating people after stroke with self-care difficulties due to arm spasticity. They also made the point that one goal of treatment can be relief of carer burden. The concept of using self-reported disability as the primary outcome measure was interestingly explored in a study by Brashear and colleagues (Brashear *et al.*, 2002). The authors performed a randomized double-blind placebo-controlled multicentre trial to assess the efficacy and safety of a single injection of botulinum toxin (BOTOX®) in a dosage of 240 units in 126 subjects with increased flexor tone in the wrist and fingers after stroke. The primary outcome measure was self-reported disability in four areas: personal hygiene, dressing, pain and limb position at 6 weeks. Those subjects that received botulinum toxin had a greater improvement in tone in the wrist and fingers as well as greater improvement in the principal target of treatment at weeks 4, 6, 8 and 12. At week 6, for example, 62% of the botulinum group had improved on their target disability measure, compared to just 27% of the placebo group. There were no major adverse events.

Similar functional improvements have been confirmed in the lower limb. There have been few studies of traumatic brain injury, but one by Fock and colleagues (Fock *et al.*, 2004) confirmed improvements in gait velocity, cadence and stride length after a single treatment session of botulinum toxin to the spastic calf muscles. Three months after the injection all participants (however, there were only seven subjects) had a significant improvement in their walking parameters. Many studies in the lower limb have concentrated on amelioration of spasticity in children with cerebral palsy. A recent study from Germany (Mall *et al.*, 2006) enrolled 61 children at a mean age of just over 6 years with leg-dominant cerebral palsy. The authors treated

the children for adductor spasticity and found significant improvements in impairment measures (knee-knee distance) and Ashworth scale but also significant improvements in the Goal-Attainment Scale in the botulinum group compared to the placebo group. The troublesome problem of spastic equinus foot has been extensively studied in the literature. One recent example was the published work from Cardoso and colleagues in Brazil (Cardoso *et al.*, 2006). This was a meta-analysis of the published double-blind randomized clinical trials. This analysis revealed a statistical superiority of botulinum toxin over placebo on gait improvement tested using a Physician Rating Scale and Video Gait Analysis in those with spastic equinus foot. The botulinum group also showed better results in subjective assessments than the placebo group. Adverse events were mild and self-limited in all the studies.

There are similar good-quality studies of the efficacy of botulinum toxin in upper limb spasticity in children with cerebral palsy. Yang and colleagues (Yang *et al.*, 2003) studied 15 children with spastic cerebral palsy who were undergoing regular physical and occupational therapy. Botulinum toxin was injected for arm spasticity and, as usual, the spasticity was reduced in the treated muscle groups significantly between the control period (preinjection) and the study period. Physicians Rating Scales also improved and fine motor skills improved as measured by the Bruininks-Oseretsky Test of Motor Proficiency. Self-care capability also improved after the botulinum injection, and it was also noted that there was a reduction of caregivers' burden and improvement in quality of life throughout the study period. Reeuwijk and colleagues (Reeuwijk *et al.*, 2006) recently produced a systematic review of the effect of botulinum toxin type A on upper limb function in children with cerebral palsy. The authors carried out an extensive search in the literature for controlled and uncontrolled studies. They found a total of 645 identified studies, but only 12 were randomized controlled trials (RCTs) of sufficiently high methodological quality. In one of the three controlled trials a short-term significant decrease in spasticity was found in favour of botulinum toxin, and this was supported by 5 of the 7 uncontrolled studies. In another RCT, significant changes in the range of motion were reported for wrist and thumb extension and this was supported by two out of seven uncontrolled studies. In another uncontrolled trial, significant improvements in activities of living were found after 1 month which was supported in 5 out of 9 uncontrolled studies, which reported an improvement in functional activity. Overall, the authors felt there was currently insufficient evidence to conclude that botulinum type A could reduce spasticity and improve range of movement in the upper limb in children with cerebral palsy. However, they found that the lack of evidence was mainly due to use of invalid assessment instruments and insufficient statistical power in the studies to demonstrate treatment effects. This illustrates the point that small-scale uncontrolled studies are no longer appropriate in this arena. There is still a need for large-scale and probably multicentre randomized studies that particularly look at functional capabilities after botulinum injections.

In summary, there is now a considerable literature on the efficacy of botulinum toxin for the management of spasticity. The above study identified a total of 645 published trials, both controlled and uncontrolled. While one has to accept that many of these studies are inadequate in terms of methodology, it is clear that the overwhelming weight of evidence confirms the efficacy of botulinum as part of an overall management plan for spasticity in both adults and children. The literature is also clear that botulinum has an excellent safety record. The risk–benefit analysis is clearly in favour of the continued use of botulinum toxin, but there is room for further studies to refine the indications and to confirm the efficacy of various injection techniques.

Other spasticity indications

Most of the large-scale studies on botulinum toxin have been related to upper and lower limb spasticity. The former studies have largely concentrated on

elbow flexor spasticity as well as wrist and finger spasticity. The lower limb studies have largely concentrated on adductor spasticity, hamstring spasticity leading to knee flexion and calf spasticity leading to equinus and equinovarus spastic deformities. However, botulinum is finding a place in the management of less common but equally troublesome spastic conditions in both adults and children. There is very limited literature on these less usual indications, but the literature available and increasing clinical experience indicate that botulinum toxin does have a role to play in the management of other spastic conditions.

Toe clawing

Spastic toe clawing usually involves extension of the metatarsophalangeal joints of the foot, with flexion of the proximal and distal interphalangeal joints. Toe clawing can be a nuisance in terms of adequate fitting of footwear or orthotic appliances, and it can also be painful. A few studies have demonstrated the efficacy of injections of botulinum toxin into the long and short flexors of the toes to relieve this condition. Lim and colleagues (Lim *et al.*, 2006) included seven patients in a study and injected botulinum type A (40 to 90 units of BOTOX®) into the long and the short flexors of the feet and observed improvement in all outcome measures (except timed walking). The authors used electrical motor point stimulation under EMG guidance. Similar benefits were noted in an earlier study by Suputtitada (2002).

Spastic shoulder

A typical hemiplegic arm is adducted and internally rotated at the shoulder as well as being flexed at the elbow, pronated at the forearm and flexed at the wrist and hand. Shoulder spasticity can be painful and give rise to significant functional disability. Injection around the shoulder is often indicated in the subscapularis as well as the pectoralis group and, to a lesser extent, the lattissimus dorsi. One of the first published studies was by Yelnik and colleagues (2003). These authors studied just three post-stroke hemiplegic patients and injected botulinum type A into the subscapularis muscles with a total of 250 units of Dysport® toxin under electrostimulation guidance. In all cases the injections reduced pain and improved range of movement, particularly abduction and external rotation of the hemiplegic shoulder. Painful shoulder, particularly after stroke, is such a common and disabling problem that any alleviation achieved by botulinum toxin is likely to be useful.

Clawed hand

A common problem, particularly after stroke, is secondary to flexion of the wrist and fingers. Quite often the disability associated with flexed fingers and wrist is compounded by a thumb-in-palm deformity which consists of an adducted, flexed thumb secondary to overactivity of opponens pollicis and often combined with thumb flexion due to overactivity of flexor pollicis longus and flexor pollicis brevis. Injection into opponens pollicis as well as the small and long flexors can often help this problem. However, the authors are aware of only a single study confirming the efficacy of this treatment (Wall *et al.*, 1993). Probably the use of botulinum toxin is preferable to surgical alternatives (Smeulders *et al.*, 2005).

Hip flexion spasticity

Hip flexion spasticity can cause significant disability, pain and difficulties in seating in a wide variety of conditions, particularly after traumatic brain injury, stroke and in multiple sclerosis. There have been a few papers describing ultrasound-guided injection techniques into the iliopsoas muscle (e.g. Westhoff *et al.*, 2003). The technique is reasonably straightforward but, nevertheless, is not widely practised. Further studies are to be encouraged.

Associated reactions

Involuntary movements of a paretic arm during ambulation or other motor activities are known as associated reactions. These occur in around 80%

of people after stroke with a spastic hemiparesis. The movement can often interfere with balance and makes walking difficult. In a single study by Bakheit and Sawyer (2002), eight patients received a single injection of 500 Dysport® units of botulinum toxin into the biceps brachii of the paretic arm. The patients' balance and mobility were assessed before and up to 6 weeks after treatment using observational gait analysis and subjective assessment measures. The investigators found a significant reduction in the associated reactions after treatment, while 7 of the 8 patients reported improvement in their own walking abilities, although their balance and mobility was not significantly improved as assessed by the clinicians. However, this was an interesting pilot study, which may indicate a use in this troublesome and common complication.

Conclusions

The usefulness of botulinum toxin in the management of spasticity secondary to a variety of clinical conditions is increasing. It is now well accepted for the management of movement disorders, particularly dystonia. There is an increasing evidence base for the use as a management tool in spasticity. The products now have a licence for use in focal spasticity. Dysport® is indicated for focal spasticity specifically including arm symptoms associated with focal spasticity in conjunction with physiotherapy. It is also licensed for dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients. BOTOX® is similarly licensed for equinus foot deformity in paediatric cerebral palsy as well as for wrist and hand disability due to upper limb spasticity after stroke in adults. Neurobloc (Myobloc®) is not currently licensed for spasticity usage, and neither is Xeomin®.

Botulinum toxin has a number of advantages over other forms of local treatment:

- Simplicity of injection technique
- Lack of requirement for precise localization of motor endpoints
- Absence of a sensory disturbance
- Ease of dose adjustment according to previous response
- Reversibility of overall effect after 2 to 3 months of treatment
- Paucity of systemic side effects

However, there are a number of disadvantages, including the cost, the need for repeat injections and, in the longer term, the potential, albeit small, for the development of antibodies.

The main logistic problem is with regard to the increasing awareness of botulinum toxin and thus increasing referrals to the relatively few botulinum clinics. Our botulinum clinic in Newcastle upon Tyne, for example, started as a monthly clinic run by a single consultant in 1992 but has now grown to a clinic that is run four and, sometimes, five times a week with the involvement of at least three to four injecting staff. This clinic has developed the use of the trained nurse practitioner and the physiotherapist to undertake injections. A study based in Newcastle (Whitaker *et al.*, 2001) demonstrated that the trained nurse practitioner was as efficacious and as safe as the medical practitioners in the clinic and that the nurse was able to provide a service that was more appreciated by the patients, given the increased time for consultation and increased flexibility of a home visiting programme. This nurse injecting service has now been extended to involve a trained physiotherapist.

There is still much to be learnt about the efficacy of botulinum toxin in the management of spasticity. There are relatively few studies that have assessed the effect of different dilutions and different injection techniques, such as the need, or otherwise, to use EMG guidance. There are few studies in some of the less common indications, such as the use of botulinum toxin in spastic shoulders and toes. In the more common indications, there are many controlled and uncontrolled studies. However, a number of meta-analyses and systematic reviews have indicated the poor quality of many of these studies, with poor methodologies and small patient numbers. Thus, there is no room for complacency, and further more rigorous and detailed studies are still required to determine more precisely the place of

botulinum toxin in the management of spasticity. However, there is no doubt that the treatment is both efficacious and safe and has an increasingly important part to play in the overall multidisciplinary management of spasticity in both adults and children.

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10

Intrathecal baclofen for the control of spinal and supraspinal spasticity

David N. Rushton

Introduction

Intrathecal baclofen (ITB)

Penn and Kroin (1985) first described the benefits that could be obtained by long-term infusion of baclofen into the spinal subarachnoid space, reporting the treatment of six patients with severe continuing spasticity and spasms resulting from spinal injury or multiple sclerosis. They found a dramatic dose-related benefit which was highly valued by patients. Patients reported functional improvements in their activities of daily living (ADLs), reduced discomfort, improvement in sleep patterns, continence and nocturia. Voluntary power did not necessarily improve, but one patient in the initial series was enabled to walk provided that the dose was carefully titrated. Control of her spasticity and spasms was needed, but some lower limb tone had to be retained.

Penn and Kroin found that the optimum dose varied widely and that the effects were strongly dose-related. There was some evidence of drug tolerance: during the first few months, the average daily dose rose from 100 to 150 μg to something approaching 500 μg. Because they were so much improved, patients were unwilling to take part in controlled trials involving placebo infusions.

All of the significant findings put forward in this initial report have been amply confirmed during the following years, in subsequent larger and longer trials undertaken by the same authors and in many other centres. The initial and many subsequent trials were open; but double-blind, randomized, placebo-controlled trials of ITB have more recently been conducted in spinal spasticity and have reported a similar magnitude of benefit (Ordia *et al.*, 1996).

Pharmacology of baclofen

Baclofen and γ-amino butyric acid (GABA)

Baclofen is agonist to the bicuculline-insensitive variety of GABA receptor known as GABA-B. There is a high density of GABA-B receptors in the dorsal horn, particularly in laminae II (substantia gelatinosa) and III. Unlike the GABA-A receptor, GABA-B is not a complete ionic channel but is coupled indirectly to calcium (Ca^{2+}) channels. Activation of presynaptic GABA-B receptors therefore causes an inhibition of calcium-mediated inward current, thus inhibiting the release of excitatory neurotransmitters such as aspartate and glutamate in the polysynaptic pathways of the dorsal horn. This alters and reduces the excitability of monosynaptic and polysynaptic reflexes. Baclofen is thought also to exert a postsynaptic action, which also acts to reduce reflex excitability (Azouvy *et al.*, 1993). This may be the basis of its action in reducing H-reflex amplitude in patients with spinal lesions.

Baclofen and pain

Perhaps not surprisingly, given its site of action in the dorsal horn, there is also pharmacological evidence that baclofen exerts antinociceptive effects.

These are not mediated by opiate receptors and are not antagonized by naloxone. There is evidence of a carbamazepine-like suppression of excitatory neurotransmission in the cat trigeminal nucleus, and baclofen has been used successfully in the clinical treatment of trigeminal neuralgia (Fromm *et al.*, 1992).

Pharmacokinetics of intrathecal baclofen

Baclofen in cerebrospinal fluid (CSF)

Baclofen is hydrophilic and crosses the blood–brain barrier poorly. Spinal intrathecal administration bypasses the blood–brain barrier, allowing effective treatment of spasticity with a dose range that is 100 to 1000 times smaller than that required for oral treatment. It also allows a higher baclofen concentration to be achieved in the spinal cord than in the brain because of the characteristics of the circulation of the CSF from the ventricles to the spinal subarachnoid space. The effective distribution volume of intrathecally administered baclofen approximates to the volume of spinal CSF (about 75 ml) rather than total CSF volume. This is one reason why more effective treatment of spasticity of limbs and trunk is possible through this delivery route, with fewer side effects resulting from central actions of baclofen on the brain.

Localization of ITB

When the delivery catheter tip is placed at upper lumbar level, the concentration of baclofen in the lumbar CSF is several times higher than at the cervical level (Kroin & Penn, 1992), so it is possible preferentially to address spasticity focal in the lower limbs. Nevertheless, there is some mixing of spinal CSF, particularly with activity, while baclofen, being hydrophilic, penetrates spinal cord tissue slowly. The response therefore always extends much more widely than the level of the catheter tip. The clinical response to a bolus infusion or injection of baclofen suggests that the drug takes about 1 to 2 hours to diffuse to the relevant layers in the dorsal horn of the cord.

Excretion of ITB

The plasma levels of baclofen in patients undergoing intrathecal infusion have been found to be vanishingly low (Muller *et al.*, 1988). This is simply because the quantity used is so small; intrathecal baclofen, like orally administered baclofen, is not metabolized but is mainly excreted unchanged in the urine.

Neurophysiological effects of ITB

Spasticity score

ITB reduces spasticity, as clinically assessed using the Ashworth scale (Bohannon & Smith, 1987). ITB has been found to result in a diminution of 2 points or more in Ashworth scores in spasticity of both spinal and supraspinal origin (discussed below).

Spasm score

Flexion or extension spasms, more common in the lower limbs, may occur spontaneously or in response to cutaneous stimuli in association with spasticity. They may be painful and are likely to be aggravated by any local source of discomfort. The clinical spasm frequency score is a 5-point scale of self-reported spasm frequency. It has been shown to respond in a dose-related and predictable way to ITB (Penn *et al.*, 1989).

Flexion reflex excitability

The threshold of the electrically induced flexion reflex in the lower limb (stimulate sural nerve, record from *biceps femoris* using electromyography) has been found to be reduced in spinal spasticity and the response amplitude to be increased. The response was normalized in some cases with ITB, a change that did not necessarily correlate with changes in Ashworth or spasm frequency scores (Parise *et al.*, 1997).

Anterior Horn Cell Excitability

The effect of ITB on anterior horn cell excitability in spasticity has been assessed using F-wave amplitude as an index. The F-wave is usually of low threshold, increased amplitude and increased duration in spasticity. Latency is not significantly abnormal. The abnormality of F-wave amplitude and duration was found to be reduced by 40% to 80% following ITB, either as a bolus or as a continued infusion (Dressandt *et al.*, 1995).

Effects of ITB on function and quality of life

Functional independence measure (FIM)

In one study (Albright *et al.*, 1995), average FIM scores rose during the postimplantation follow-up period by 18 points. In those with good upper limb function, the rise was larger (25 points) and covered most of the items apart from 'eating' and 'stairs'. In those with poor upper limb function, the rise was less (4.8 points) and mainly focused on 'eating' and 'wheelchair function'. However, comfort was also improved, nursing made easier and care burden reduced.

Quality of Life (QoL)

Patients who previously had become institutionalized on account of unmanageable spasticity may be enabled to return to live in the community following the start of ITB. Admissions with acute medical problems may be greatly reduced. In one study (Becker *et al.*, 1995), a group of patients who between them had spent 755 days in acute care hospital during the year before implantation, spent between them only 259 days in hospital during the year after surgery. A larger randomized placebo-controlled multicentre trial of 22 patients (Middel *et al.*, 1997) examined the response on the sickness impact profile (SIP) and the Hopkins symptom checklist. After 3 months of randomized placebo-controlled study, all patients were switched to ITB. After 1 year, there were modest but significant benefits of ITB on some dimensions of the SIP ('mobility', 'body care and movement'), and in health behaviour ('sleep and rest', 'recreation and pastimes'), but not in psychosocial behavior in comparison with the preoperative condition. In progressive diseases such as multiple sclerosis, it may be particularly hard to demonstrate a sustained benefit to quality of life, despite a sustained benefit to measures of impairment, such as spasticity or spasms (Zahavi *et al.*, 2004).

Cost-benefit analysis

There are still relatively few studies of the cost–benefit impact of ITB. One retrospective review of 17 published studies, including a total of 324 patients (Sampson *et al.*, 2002) calculated the change in quality of life and estimated the costs in UK terms from data given. Depending on the severity of disability the cost/QALY for ITB ranged between £6900 and £12 800, thought to be good value in carefully selected patients. No comparison was made with alternative methods of spasticity management. Nance *et al.* (1995), in a small prospective study, found a net cost saving of over $150 000 in 2 years following implantation, attributable mainly to reduced hospitalizations. On the other hand, Albright *et al.* (1995) made a comparison of ITB and selective functional posterior rhizotomy over 1 year in 19 children with cerebral palsy. They showed that the cost of ITB was nearly four times higher but made no attempt to compare the efficacy of the two treatment methods.

Indications and patient screening tests for ITB

General considerations

ITB may benefit function, comfort or carer burden; it may help more than one of these, and occasionally it may benefit all three. However, it is an elaborate, invasive and expensive form of treatment. It calls for regular follow-up for pump refills, which typically have to be done several times a year. The pump itself, if it is battery powered and not rechargeable,

has to be replaced every 5 to 6 years. It is therefore fortunate that only a minority of patients with spasticity require ITB. Which ones are they?

Indications for ITB

ITB is used in patients with widespread spasticity in whom alternative methods of spasticity management are ineffective or inadequate or cause unacceptable side effects. In all patients with spasticity, remediable aggravating factors such as urinary retention or infection, skin infection or pressure sores, uncomfortable seating and poor posture will have been addressed in their own right. Passive muscle stretching, active physiotherapy, hydrotherapy and active exercise are all important aids to controlling and minimizing spasticity, particularly during the stage when spasticity is developing. Oral antispastic drugs such as baclofen, dantrolene, diazepam or tizanidine will have been introduced and titrated to find the optimum drug combination and dose range. This leads to a protocol wherein ITB is considered only in those patients in whom severe spasticity has developed in spite of preventive measures and who cannot be controlled in any less invasive way.

Alternatives to ITB in widespread spasticity

In many centres dealing with patients with severe spasticity, unselective dorsal rhizotomy and intrathecal phenol as treatments for spasticity have been largely supplanted by ITB. Unselective rhizotomy often results in significant loss of sensory function, and nonreflex stiffness and spasms may supervene. The effects of intrathecal phenol are found to be unpredictable in all but the most experienced hands, and it can be used only in patients who have already lost bladder and bowel control. Selective posterior rhizotomy has been used extensively in some centres for the treatment of spasticity, particularly in cerebral palsy. It has been compared with ITB in one centre and found to be about equally effective; relative indications for one or the other form of treatment have been described (Albright *et al.*, 1995). Epidural spinal stimulator implants have been used, often in patients who have pain as well as spasticity, although the efficacy has not been compared with ITB (Barolat *et al.*, 1995). Cerebellar stimulation is sometimes used in the control of spasticity and found to be effective, particularly in cerebral palsy, but again no comparison with ITB for efficacy has been made (Davis, 2000).

Indications for botulinum toxin

Patients whose spasticity is focal and involves accessible muscles will have been offered local treatments such as intramuscular botulinum toxin and are usually better managed in that way. Some patients with focal spasticity are managed with nerve blocks, but neurodestructive injections are much less used now that botulinum toxin is widely available.

Trial dose

A trial dose of intrathecal baclofen is done for two reasons. First, it is necessary to demonstrate that ITB will make a significant impact on the level of spasticity and spasms. Secondly, it is necessary to demonstrate that it will, as a result, significantly benefit function, comfort, posture, care or hygiene. In order to achieve these demonstrations, the patient must be taken through a functional assessment as well as bedside tests of tone and spasms. The patient must therefore be mobilized, into walking or wheelchair as appropriate, during the action of the single intrathecal dose, which typically lasts for several hours. The period of bed rest following the lumbar puncture must therefore be not more than an hour or so. It is therefore considered to be advantageous to use as fine a needle as possible, preferably of the noncutting fibre-splitting type, so as to minimize the risk of low-pressure headache.

An initial intrathecal trial dose of 25 or 50 μg of baclofen is used. The smaller initial trial dose should be used if the patient is not on oral baclofen, in case of sensitivity. If the response to the initial trial is

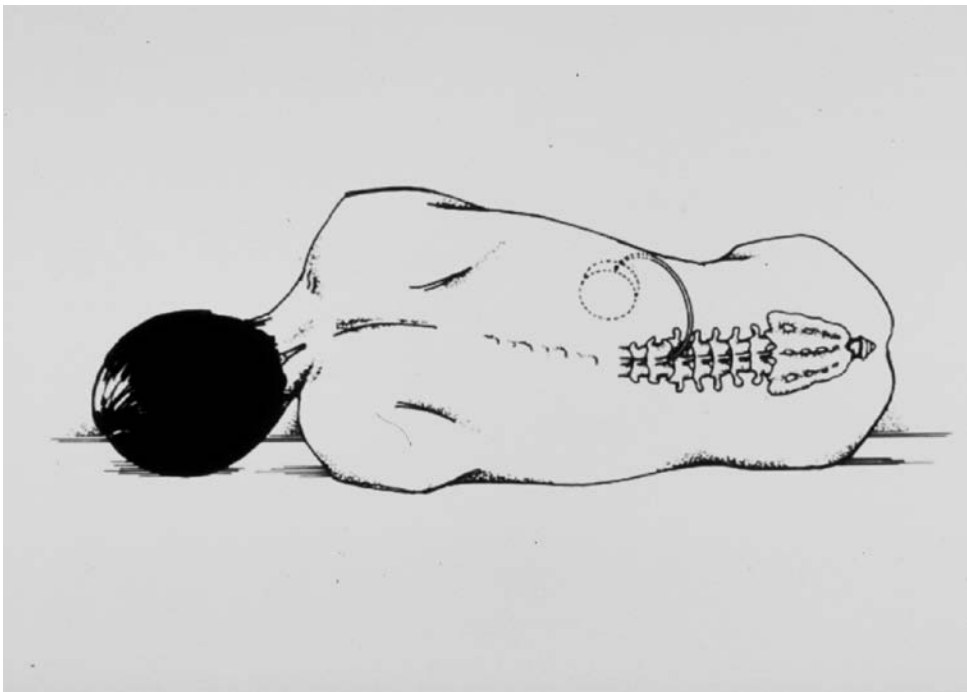

Figure 10.1. Pump pocket location is usually in the anterolateral abdominal wall. Catheter is tunnelled to the lumbar region and into the spinal canal at lumbar level, turning craniad and terminating at conus level. (From Medtronic Ltd., with permission.)

inadequate, a second trial dose of 75 or 100 μg can be given the next day. The maximum single bolus trial dose recommended is 100 μg. Opinions vary as to whether oral baclofen should be continued unchanged through the trial. It is probably better to do so, on the grounds that to alter it would complicate the assessment; the intrathecal bolus dose response is in any case a poor guide to titration of the likely daily infusion rate which will subsequently be needed.

ITB infusion is often found to improve bladder and sphincter function and has been found to improve urodynamic parameters such as bladder capacity, reflex detrusor contractions, bladder compliance and detrusor-sphincter dyssynergia. However, any bladder effects are often difficult to evaluate during the time available in the preimplantation trials. Sometimes it causes sphincteric weakness, resulting in stress incontinence (Bushman *et al.*, 1993). Varying effects on erectile and ejaculatory function have been recorded (Denys *et al.*, 1998).

Implant surgery

After exposing the laminae, the subarachnoid space is accessed at lumbar level using a Tuohy needle (Fig. 10.1). Paramedian location of the needle helps avoid catheter kinking later, as the spine moves. The catheter is passed up to about T10 vertebral level. It is screened to ensure that it is not kinked in location. It is tunnelled through paraspinal muscle, which is sutured around it to help avoid CSF leakage past the catheter. The catheter is anchored to prevent slippage and is tunnelled through to the selected pump-pocket location, usually in the right iliac fossa deep to the external oblique muscle. The guide wire is removed, and CSF should ooze from the catheter. The catheter is then trimmed to length (with sufficient

surplus to ensure that it will never be stretched) and is joined to the pump according to the manufacturer's instructions using the correct connector and strain-relief fairing. Programmable powered pumps are filled and started before implantation.

Postoperative procedure

The patient is managed in the recumbent position for the first 7 to 10 postoperative days. This is in order to discourage the development of CSF leakage alongside the catheter. Subsequently, the dosage rate is adjusted according to response to achieve the desired degree of spasticity reduction. The rate will need further adjustments as the patient mobilizes. The oral baclofen treatment, if given, will be tailed off over 2 to 3 weeks as part of the same process; it should not be stopped precipitately. Any other oral antispastic drugs will then also be considered for tailing off.

Follow-up organization and procedures

The follow-up of patients with implanted pumps should in the first instance preferably be managed at centres where a clinic can be set up for the purpose. This enables continuity of care, appointments for pump refills and dosage titration can be planned efficiently and medical and patient time is not wasted waiting in the ward or theatre. Our patients usually require refill about four times a year (range 2 to 10); once the dose is stabilized, they sometimes ask for more local refill arrangements. Often this cannot be implemented for lack of local skills and facilities.

Dosage adjustments

For the programmable pumps such as the Medtronic SynchroMed® (Fig. 10.2), the rate can be adjusted using the external programmer, which interrogates and reprogrammes the chip in the pump by telemetry via a radiofrequency link (Fig. 10.3). The pump can be set up to deliver a varying dosage rate. In theory, up to 10 different periods can be set up in the 24 hours, with a different pump rate in each. In practice, two rates are usually sufficient, one for day and one for night. When setting up the timing of rate changes, it should be borne in mind that the clinical effect lags by 1 to 4 hours.

Pump refills

The programmable pumps emit a low-reservoir alarm sound when a preset level (usually 2 ml of their 20- or 40-ml capacity) remains. When telemetered after filling, they give the date on which their alarm will sound, and this facilitates setting the next appointment. When working in the reserve 2-ml volume, the pump output may fall because it is working with a reduced filling pressure. This may result in a clinically noticeable reduction in efficacy when a refill is due.

Pumps are refilled percutaneously by injection through the filling port. Before filling, the reservoir must be drained by aspiration. Air must not be allowed into the empty reservoir, so an isolating tap is used when changing syringes. Strict precautions must be taken against introducing infection when the implant is refilled. Infection can be introduced either from the drug solution or atmospheric air, causing infection within the pump reservoir, or else from the needle, causing infection in the potential space around the pump. Both of these spaces are immunologically privileged, and infection in them is therefore to be rigorously avoided. Implantable pumps do incorporate bacterial filters, so that any infection within their reservoir cannot be spread via the pump and catheter to the subarachnoid space. Refill systems also incorporate a bacterial filter as an added precaution.

Results in clinical practice

Multiple sclerosis (MS)

In most series (Penn, 1992; Patterson *et al.*, 1994), MS patients have been implanted for the relief of severe lower limb spasticity and flexor spasms. The goals then are improved comfort and wheelchair posture,

Figure 10.2. A programmable pump, and spinal catheter with centimetre length markings. The refill port is at the centre of the pump body. The aspiration (test) port is in the delivery nacelle. (From Medtronic Ltd., with permission.)

improved transfers, and ease of personal hygiene. Most patients reported have been wheelchair-bound by the time they were implanted, and restoration of gait was not an issue. There are few reports of implantation in patients who are ambulant or near-ambulant with earlier disease; this may be because of a reluctance to perform elective implantation surgery in this group.

Spinal cord injury (SCI)

ITB is widely considered to be the treatment of choice for SCI patients who suffer from widespread spasticity if it is inadequately controlled using conventional antispastic medication. This may represent about 5% of the SCI population. Conventional spasticity management will be fully employed during their primary spinal rehabilitation, including passive stretching, active physiotherapy, control of nociceptive stimuli, effective bladder and bowel management and adequately titrated doses of oral antispastic drug treatment. The majority are successfully managed in these ways. Not surprisingly, the longest follow-ups of ITB treatment have been achieved in this stable, often youthful, group. Besides abolishing spasticity, ITB has been found to alleviate pain of musculoskeletal origin in SCI (i.e. pain resulting from spasticity), though not neurogenic pain (Loubser &

Figure 10.3. Hand-held programmer for use in pump adjustment and refill. (From Medtronic Ltd., with permission.)

Akmann, 1996). For SCI patients as for MS patients, FIM score is found to improve more in paraplegia than in tetraplegia (Azouvy *et al.*, 1996), but scores relating to the quality of life are improved in both groups (Albright *et al.*, 1995; Middel *et al.*, 1997).

Traumatic brain injury (TBI)

The effect of ITB on spasticity and spasm scores in patients with TBI has been found to be marked (Meythaler *et al.*, 1996). Function was gained with long-term infusion (Meythaler *et al.*, 1997), and there were no untoward side effects. Early consideration for implantation has been recommended for TBI patients with severe spasticity (Becker *et al.*, 1997). However, the dosage required for the treatment of supraspinal spasticity seems to be about twice that required for spinal spasticity (Saltuari *et al.*, 1992), and there have been occasional reports of seizures apparently precipitated by ITB in this group (Rifci *et al.*, 1994).

Cerebral palsy (CP)

ITB may be effective against spasticity in this group, but it does not significantly influence athetosis or dystonia (Muller, 1992). It should be considered as an alternative to tenotomy, muscle lengthening or posterior rhizotomy where appropriate. In those who are able to walk, the main goal is to improve gait quality. Some residual extensor spasticity may need to be retained if there is significant lower limb weakness. In those who are wheelchair bound, the main goals are to improve wheelchair posture and comfort without compromising trunk stability or head control. A small minority may achieve a functional gait with the assistance of ITB. Upper limb function and speech may be significantly improved in both walking and nonwalking groups (Albright *et al.*, 1993).

The average ITB dose rate required is lower for the walking group than for the nonwalking group. As for other patient groups, the dose rate often needs to be increased during the first year; it tends to remain unchanged thereafter.

ITB and the rehabilitation team

Physical and occupational therapists in neurological and spinal rehabilitation units and community-based teams need to be aware of the potential and limitations of ITB treatment. Often, therapists will be the first to become aware of functional limitations attributable to spasticity and may need to initiate the process of consideration for ITB. Patients may hear about ITB and discuss the question with their therapists rather than their doctors. The charting of range and function before and after a trial dose of ITB is usually done by a therapist. The charts concerned are not standardized; they often focus more on impairment-based variables such as passive range of motion and less on functional variables. There are reasons for this: the functional variables are more individual and more subjective. However, there is a need for a manageable, broadly based assessment protocol (Campbell *et al.*, 1995). After implantation, there may be complex functional changes requiring expert therapy advice. For example, if orthoses are discarded as a result of ITB, gait and movement re-education may be needed. An improved level of physical functional independence may call for additional aids or instruction in order to take safe advantage of the gain.

Complications of ITB

Catheter failure

Spinal catheters can become blocked, kinked, leaky, disconnected, dislodged, or their outlet encased in secondary dura. The likelihood of catheter failure is minimized by care in checking the course and location of the catheter at the time of operation. It should be arranged so that it will not be pinched or kinked by the full range of lumbar motion. The catheter should be firmly fixed to paraspinal muscles, using the fixing anchor devices provided, to prevent it from being dislodged. If symptom control is lost and catheter failure is suspected, then the problem should be investigated rather than dealing with it by turning up the pump rate. An increased pump rate followed by spontaneous unkinking of a kinked catheter may result in a drug overdosage. Catheter faults are particularly likely to occur in children (Albright, 1996; Armstrong *et al.*, 1997), probably because they are more active than adults and have less paraspinal muscle bulk.

If the catheter is blocked, kinked or disconnected, this will usually become apparent if an attempt is made to aspirate from the delivery port. If CSF is aspirated, this means that the catheter is patent and in continuity. However, there have been occasional reports of faults in which a microscopic crack in the catheter has led to drug loss by leakage without apparent loss of catheter patency (Bardutzsky *et al.*, 2003; Gaffen *et al.*, 2005).

Effects of pump or catheter failure

Catheter or pump failure leads to a sudden withdrawal of medication, which can occasionally cause a serious withdrawal syndrome of of tachycardia, labile blood pressure, impaired consciousness, spasticity, itching, paraesthesiae or priapism (Coffey *et al.*, 2002). There have been occasional case reports of hyperthermia, rhabdomyolysis and disseminated intravascular coagulation associated with sudden withdrawal of ITB due to catheter disconnection or programming error. The clinical condition improved only when the fault was corrected, and a causative relation was presumed (Reeves *et al.*, 1998; Mohammed & Hussain, 2004). In the vast majority of instances, sudden pump failure is followed only by a marked exacerbation of spasticity, and patients can be managed (temporarily and less effectively) with oral baclofen.

Baclofen overdosage

Minor degrees of ongoing overdosage are dealt with by adjusting the dose rate. Major bolus overdosage is usually caused by operator error, usually either inadvertently programming a bolus, attempting to fill the reservoir through the flushing port or wrong calculation of a bridging bolus. (A bridging bolus is a bolus dose designed to flush a delivery catheter filled with saline or CSF and fill it with drug solution.) The patient may become weak, hypopnoeic or apnoeic or unconscious following severe overdosage. The development of such symptoms require immediate transfer to an intensive therapy unit so that ventilatory support can be given if required. The pump should be stopped until the patient recovers. Supportive therapy is usually adequate; no specific antagonists to baclofen are clinically available, though mild respiratory depression may be reversed with physostigmine 1 to 2 mg IV (Muller-Schwefe & Penn, 1989; Saltuari *et al.*, 1990). Both baclofen bolus dosage (Kofler *et al.*, 1994) and sudden baclofen withdrawal (Rivas *et al.*, 1993) have occasionally been associated with seizures.

CSF leakage

The pressure of the lumbar CSF rises to 20 to 30 mm Hg in the upright position and is further raised on coughing or straining. In these circumstances CSF may find a way along the outside of the catheter and accumulate in the potential space around the pump, forming a palpable or visible fluid swelling. Rapid escape of CSF from the theca in this way can lead to low-pressure headache, which is therefore usually postural. If such a CSF leak occurs in the early postoperative period, it may often be cured by a period of recumbent nursing. If it persists, the fistula will have to be repaired. If a leak begins late, it is unlikely to resolve spontaneously. A CSF leak to the exterior (e.g. through the stitches closing the pump pocket) is dangerous and must be repaired immediately. It would be preferable for future designs of intrathecal catheter to incorporate a sealing system to prevent CSF from flowing along their outer surface.

This method has been used successfully in other lumbar intrathecal implant devices (Brindley *et al.*, 1986).

Implant infection

In skilled hands and where correct procedures are followed, implant infection is rare. When it occurs, the whole implant should be removed. Perioperative infection may not become evident for weeks or months, particularly if a low-grade skin commensal is involved. The risk of perioperative infection of neurological implants may be reduced by preoperative antibiotic coating of the implant (Rushton *et al.*, 1989). Haematogenous infection of an implant is excessively rare but is a theoretical risk, for example, in association with bacterial endocarditis.

Implant limitations

Different types of pump have different limitations, failure rates and failure modes (Gardner *et al.*, 1995; Teddy, 1997). The Medtronic SynchroMed© programmable pump, while expensive, has been found to be highly reliable within its lifetime; but its internal nonrechargeable battery fails predictably in 5 to 6 years, so that the pump then has to be replaced. The manually operated Cordis Secor is cheap but has been associated with a higher complication rate. Also, if implanted too deep, it is difficult to operate; if too shallow, it tends to erode through the skin. The fixed-rate, gas-liquid–powered pumps (Therex, Infusaid) are simple and reliable but offer no scope for adjusting the drug dosage rate other than by varying the concentration of the drug solution with which they are filled. Also, the flow rate varies with body temperature and atmospheric pressure.

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11

Surgical management of spasticity

Patrick Mertens and Marc Sindou

Introduction

Spasticity is one of the commonest sequelae of neurological diseases. In most patients spasticity is useful in compensating for lost motor strength. Nevertheless, in a significant number of patients it may become excessive and harmful, leading to further functional losses. When not controllable by physical therapy, medications and/or botulinum toxin injections, spasticity can benefit from neurostimulation, intrathecal pharmacotherapy or selective ablative procedures.

Neuro-stimulation procedures

Stimulation of the spinal cord was developed in the 1970s on the basis of the 'gate-control theory' of Melzach and Wall (1974) for the treatment of neurogenic pain. This method has been found to be partially effective in the treatment of spastic syndromes, such as those encountered in multiple sclerosis (Cook & Weinstein, 1973; Gybels & Van Roost, 1987) or spinal cord degenerative diseases, such as Strumpell–Lorrain syndrome. However, this method is generally most effective when spasticity is mild and the dorsal column has sufficient functional fibres, as assessed by somatosensory evoked potentials. Stimulation electrodes are implanted, either percutaneously through a Tuohy needle under X-ray fluoroscopy or surgically via an open interlaminar approach in the extradural space posteriorly to the dorsal column, at the level of the thoracolumbar spinal cord for spasticity in the lower limbs of paraparetic patients or at the level of the cervical spinal cord for spasticity in the upper and/or lower limbs of quadriparetic patients. The electrodes are connected by means of flexible electrical wires to a generator inserted in the subcutaneous tissue and located under the abdominal skin for electro-stimulation of the thoracolumbar spinal cord, or under the skin of the subclavicular region for cervical stimulation.

Cerebellar stimulation has been extensively and seriously tried for spasticity from cerebral palsy (Davis *et al.*, 1982). For most of the studies, cerebellar stimulation did not prove to be sufficiently effective for it to be widely adopted (Seigfried & Lazorthes, 1985).

Deep brain stimulation – which yields positive results in patients with tremor, dystonia, akinesia, dyskinesia and/or nonspastic hypertonia (i.e. rigidity), especially in patients with Parkinson's disease – is not effective for the treatment of spasticity.

We have recently found precentral cortical stimulation, which was indicated for poststroke pain in hemiplegic patients, to have some effect on spasticity in some patients (unpublished data).

Neuroablative procedures

When spasticity cannot be controlled by conservative methods or by botulinum toxin injections, ablative procedures must be considered. The surgery should be performed so that excessive hypertonia is reduced without suppression of useful muscular

tone or impairment of the residual motor and sensory functions. Therefore, neuroablative techniques must be as selective as possible. Such selective lesions can be performed at the level of peripheral nerves, spinal roots, spinal cord or the dorsal root entry zone.

Peripheral neurotomies (PNs)

Selective PNs were introduced first for the treatment of spastic deformities of the foot by Stoffel (1913). Later, Gros *et al.* (1977) and Sindou and Mertens (1988) advocated making neurotomies more selective by using microsurgical techniques and intraoperative electrical stimulation for better identification of the function of the fascicles constituting the nerve. Selectivity is required to suppress the excess of spasticity without producing excessive weakening of motor strength and severe amyotrophy. To achieve this goal, preserving at least one-fourth of the motor fibres is necessary.

Neurotomies are indicated when spasticity is localized to muscles or muscular groups supplied by a single or a few peripheral nerves that are easily accessible. To help the surgeon decide if neurotomy is appropriate, temporary local anaesthetic block of the nerve (with lidocaine or with long-lasting bupivacaine) can be useful. Such a test can determine if articular limitations result from spasticity or musculotendinous contractures and/or articular ankyloses (only spasticity is decreased by the test). In addition, these tests give the patient an idea of what to expect from the operation. Botulinum toxin injections may also act as a 'prolonged' test for several weeks or months.

Lower limbs

For spasticity in the lower limbs (Mertens & Sindou, 1991), neurotomies of the tibial nerve at the popliteal region (Fig. 11.1) and of the obturator nerve just below the subpubic canal (Fig. 11.2) are the most common for the so-called spastic foot and for spastic flexion-adduction deformity of the hip, respectively.

Tibial neurotomy is performed as follows. After exposure of the tibial nerve from the popliteal region down to the soleus muscular arcade under general anaesthesia not using curare, all the branches are individualized and identified one by one, using the operating microscope and bipolar stimulation. Each branch (or fascicle) considered as supporting harmful spasticity on the basis of stimulation is then partially resected over a 5-mm length to prevent regeneration. Conservation of one-third to one-fifth of the fibres of each branch is sufficient to avoid loss of motor function and amyotrophy. Comparing the results of stimulation of the distal and proximal parts of the resected fibres proved useful in controlling the effects of the operation on muscular contraction. The particular branches of the nerve to be operated on are determined preoperatively by analyzing all the components of the spastic disorder, according to the following schedule: (1) equinus and/or ankle clonus requires sectioning of the soleus nerve(s) and, if necessary, the two gastrocnemius branches; (2) varus necessitates interruption of the posterior tibial nerve; and (3) tonic flexion of the toes requires sectioning of the flexor fascicles situated inside the distal trunk of the tibial nerve. Their precise identification, avoiding sensory fascicles, is of paramount importance in avoiding hypoaesthesia and dysaesthetic disturbances as well as trophic lesions of the plantar skin.

In 180 patients, 82% of tibial PNs resulted in suppression of the disabling spasticity with improvement of the residual voluntary movements (P. Mertens & M. Sindou, unpublished data). We have recently published the results of a multicentre study of the long-term results of tibial neurotomy (Buffenoir *et al.*, 2004). This multicentre, prospective study was conducted between 1999 and 2003 and 55 patients with spastic equinus foot were treated in five neurosurgical centres. No postoperative complications were observed in this series. Gait analysis demonstrated a statistically significant increase in the speed of gait after the surgical treatment and improvements in the equinus score and foot appearance. Overall 92.7% of preoperative objectives had been achieved in the series, and there seemed to be

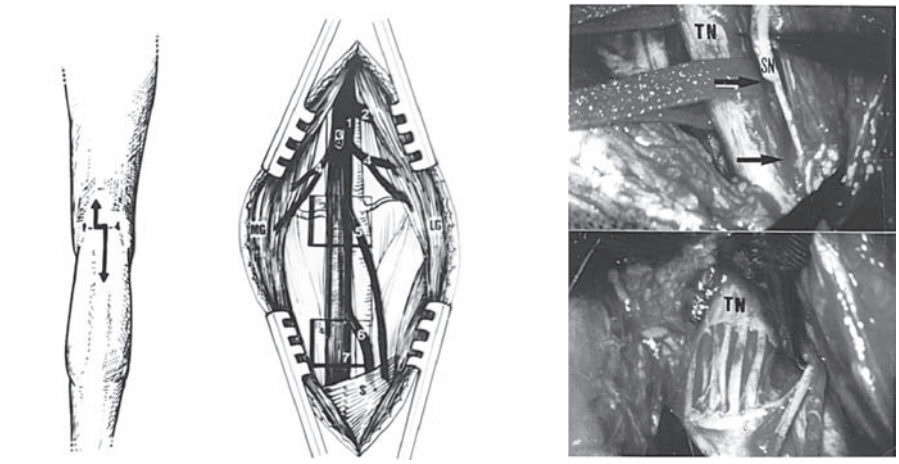


Figure 11.1. Selective tibial neurotomy. Left: Skin incision in the right popliteal fossa. Centre: Dorsal view showing tibial (1), and peroneal (2) nerves, sural (sensory) nerve (3), medial gastrocnemius and lateral gastrocnemius branches (4), soleus nerve (5), posterior tibialis nerve (6). The distal trunk of the tibial nerve, just above the soleus arch (S), contains 15 to 18 fascicles averaging 1 mm in diameter each; two thirds are sensory. Equinus and ankle clonus require section of the soleus nerve (5) and, if necessary, of the medial and lateral gastrocnemius nerve (4). Varus necessitates interruption of the posterior tibialis nerve (6). Tonic flexion of the toes requires section of the flexor fascicles situated inside the distal trunk of the tibial nerve (7); their precise identification apart from the sensory fascicles by electrical stimulation is of paramount importance to avoid hypoaesthetic and dysaesthetic disturbances, as well as trophic lesions of the plantar skin. Upper right: Operative view of the resection, over 7 mm in length (between the two arrows), of two-thirds of the soleus nerve (SN). Lower right: Operative view of five dissected fascicles inside the distal part of the tibial nerve (TN) at the level of the soleus arch, after the epineural envelope has been opened.

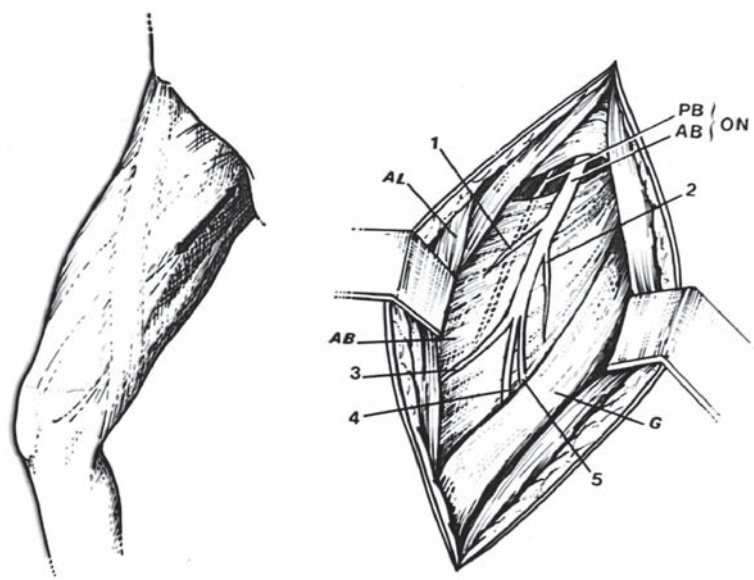


Figure 11.2. Obturator neurotomy. Skin incision on the relief of the adductor longus muscle. Dissection of the anterior branch (AB) of right obturator nerve (ON). The adductor longus muscle (AL) is retracted laterally and gracilis muscle (G) medially. The nerve is anterior to the adductor brevis muscle (AB). The adductor brevis nerve (1 and 2), adductor longus nerve (3) and gracilis nerve (4 and 5) are shown. The posterior branch (PB) of the obturator nerve lies under the adductor brevis muscle (AB).

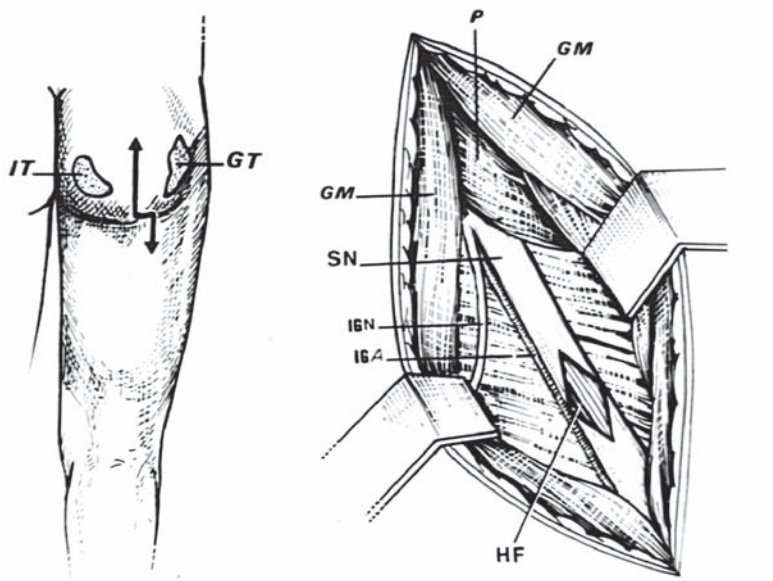


Figure 11.3. Hamstring neurotomy. Skin incision between the ischial tuberosity (IT) and the greater trochanter (GT). Dissection of the right sciatic nerve (SN), under the piriformis muscle (P), after passing through the fibres of the gluteus maximus muscle (GM). The epineurium of the nerve is opened and fascicles for hamstring muscles (HF) are located in the medial part of the nerve. IGN: inferior gluteal nerve; IGA: inferior gluteal nerve artery.

a lasting response at least over the mean follow-up period of 10 months.

In contrast to the adult, in the spastic hemiplegic child the effects of tibial PN may be only transient. In our series of 13 paediatric cases, 8 cases had a recurrence (Berard *et al.*, 1998).

Selective neurotomy of the branches to the knee flexors (hamstrings) can also be performed at the level of the sciatic trunk through a short skin incision in the buttock (Fig. 11.3). For spastic hyperextension of the first toe (so-called permanent Babinski sign), a selective neurotomy of the branch(es) of the deep fibular nerve to the hallux extensor can be useful.

Upper limbs

Neurotomies are also indicated for spasticity in the upper limbs (Mertens & Sindou, 1991). Selective fascicular neurotomies can be performed in the musculocutaneous nerve for spastic elbow flexion (Fig. 11.4), and in the median (and ulnar) nerve for spastic hyperflexion of the wrist and fingers (Fig. 11.5).

The last procedure, which consists of sectioning the branches to the forearm pronators, wrist flexors and extrinsic finger flexors, is indicated for spasticity in the wrist and the hand – the aim being to open the hand and improve prehension. As the fascicular organization of the median and ulnar nerves does not allow for differentiation of motor from sensory fascicles at the level of their trunks, it is necessary to dissect the motor branches after they have left the nerve trunk in the forearm. Special care must be taken with the sensory fascicles to avoid painful manifestations.

Neurotomies of brachial plexus branches have now been developed for treating the spastic shoulder (Decq *et al.*, 1997). The pectoralis major muscle and teres major muscle are the main muscles implicated in this condition. This excess of spasticity restrains the active (and passive) abduction

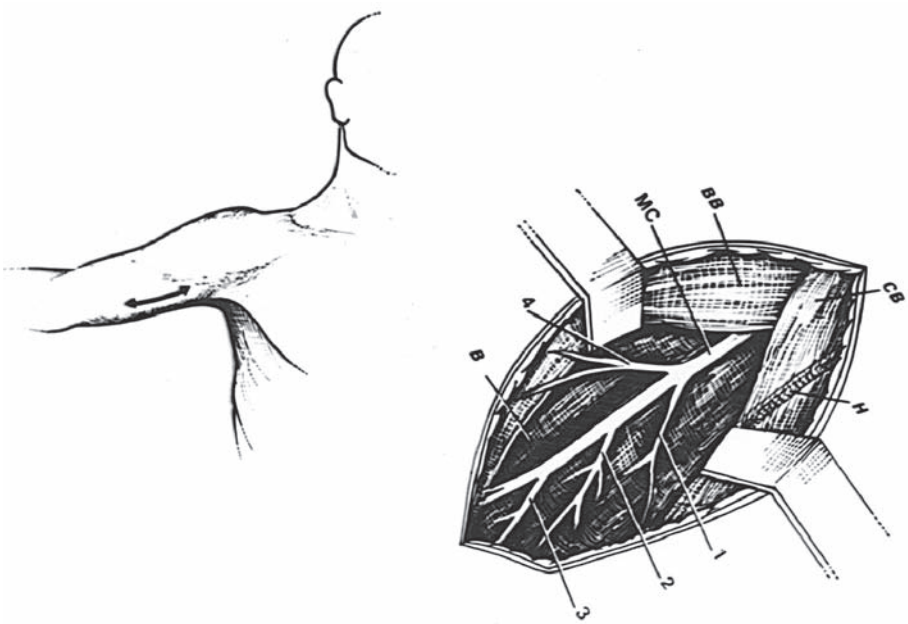


Figure 11.4. Musculocutaneous neurotomy brachialis. Skin incision along the medial aspect of the biceps brachii. Dissection of the right musculocutaneous nerve (MC) in the space between the biceps brachii (BB) laterally, the coracobrachialis (CB) medially, and the brachialis (B) posteriorly. Branches to brachialis (1 and 2) and to biceps brachii (3 and 4). The humeral artery (H) and the median nerve are situated medially (they are not dissected).

and external rotation of the shoulder. The pectoralis major nerve can be easily reached via an anterior approach of the shoulder. With the patient supine and the upper limb lying alongside the body, an incision is made at the innermost part of the deltopectoral sulcus and curves along the clavicular axis. The teres major nerve can be approached posteriorly to the shoulder. With the patient in procubitus position and the upper limb lying alongside the body, a vertical incision is made along the inner border of the teres major. Decq *et al.* (1997) found a significant increase in amplitude and speed in the active mobilization of the spastic shoulder, leading to better functional use in five patients after surgery. Selective peripheral neurotomy for the treatment of spastic upper limb does seem to lead to long-term satisfactory improvement in functional and/or comfort with a low morbidity rate in appropriately selected patients, as recently confirmed in a prospective study in 31 patients published by Maarrawi and colleagues (Maarrawi *et al.*, 2006).

Improvement of motor function

Basically, selective neurotomies are able not only to reduce excess of spasticity and deformity but also to improve motor function by re-equilibrating the tonic balance between agonist and antagonist muscles (Fig. 11.6). This was certainly true for 82% of 180 adult patients operated on for spastic foot using tibial PN. In our experience – since 1980 and more than 300 operations – tibial neurotomy has been the most frequently used PN (Mertens & Sindou, unpublished data).

With regard to the spastic hand, which is a very difficult problem to deal with, a functional benefit in prehension can only be achieved if patients retain a residual motor function in the extensor and

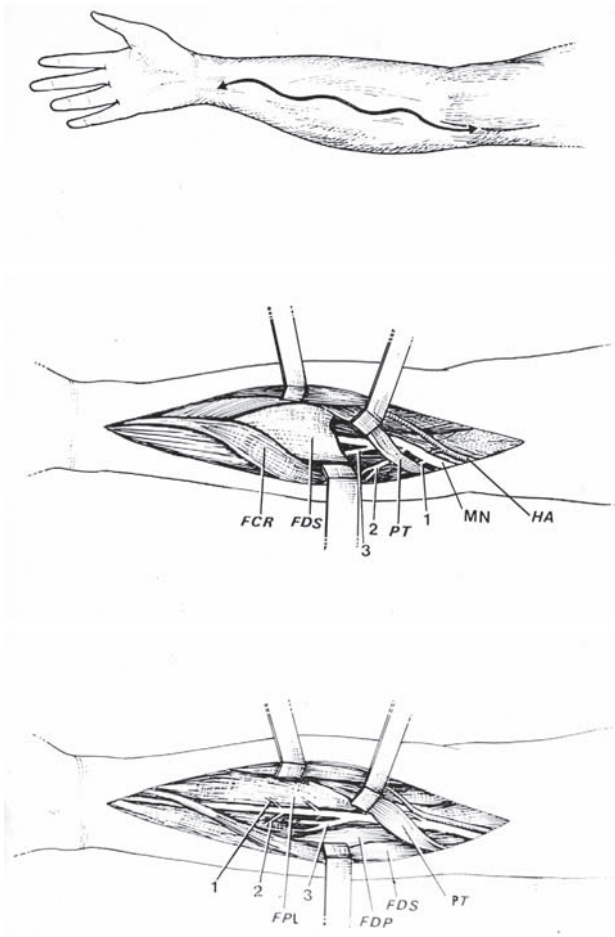


Figure 11.5. Median neurotomy (slightly modified from Brunelli's technique). Top: Skin incision on the right forearm from the medial aspect of the biceps brachii at the level of the elbow to the midline above the wrist. Centre: First stage of the dissection; the pronator teres (PT) is retracted upward and laterally, and the flexor carpi radialis (FCR) is retracted medially. Branches from the median nerve (MN), before it passes under the fibrous arch of the flexor digitorum superficialis (FDS), are dissected. These branches are (1) to the pronotor teres and (2,3) two nerve trunks to the flexor carpi radialis, palmaris longus and flexor digitorum superficialis. Bottom: Second stage of the dissection; the fibrous arch of the FDS is sectioned to allow more distal dissection of the median nerve. The FDS is retracted medially, and branches from the median nerve are identified to the (1) flexor pollicis longus (FPL), (2) flexor digitorum profundus (FDP) and (3) the interosseous nerve and its proper branches to these muscles.

supinator muscles together with a sufficient residual sensory function. If these conditions are not present, only better comfort and better cosmetic aspect can be achieved.

We recently performed 25 median (and ulnar) neurotomies combined with tenotomies (predominantly of the epicondyle muscles) in the forearm (namely a Page–Scaglietti operation) (Brunelli & Brunelli, 1983) to treat spastic flexion of the wrist and fingers with tendinous contractures. All patients in this special group – who did not have any voluntary effective motor function preoperatively – had a better comfort and good cosmetic effect, but without any significant functional benefit.

Posterior rhizotomies

Posterior rhizotomy was performed by Foerster for the first time in 1908 to modify spasticity (Foerster, 1913), after Sherrington had demonstrated in 1898 using an animal model that decerebrate rigidity could be abolished by sectioning the dorsal roots, that is, by interruption of the afferent input to the monosynaptic stretch and polysynaptic withdrawal reflexes. Its undesired effects on sensory and sphincter functions limited its application in the past. To diminish these disadvantages, several surgeons in the 1960s and 1970s attempted to develop more selective operations, especially for the treatment of children with cerebral palsy.

Posterior selective rhizotomy

To reduce the sensory side effects of the original Foerster method, Gros *et al.* (1967) introduced a technical modification that consisted of sparing one rootlet in five of each root, from L1 to S1. Using similar principles, Ouaknine (1980), a pupil of Gros, developed a microsurgical technique that

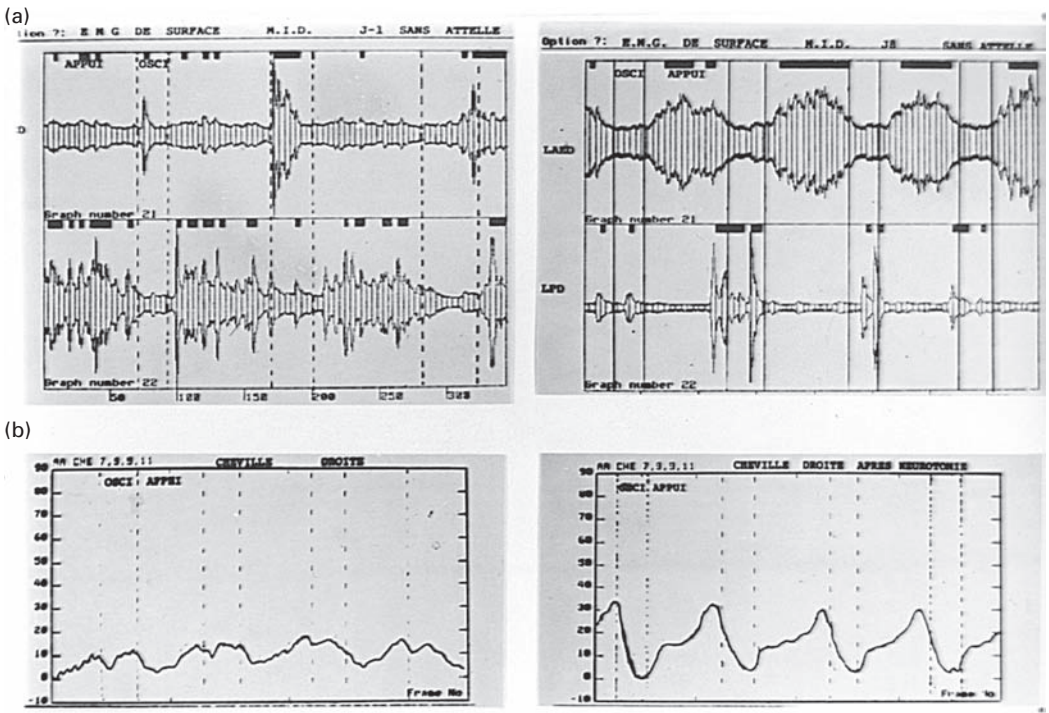


Figure 11.6 Movement analysis in a hemiplegic patient with a spastic foot (equinovarus) before and after selective tibial neurotomy. (a) Surface polyelectromyography of the tibialis anterior (LAED) and the triceps surae (LPD) muscles on the spastic leg during walking. Left: Preoperative recordings showing desynchronized activities of the triceps surae, with abnormal co-contractions of antagonist muscles – triceps surae and tibialis anterior. Right: After selective tibial neurotomy there is a reappearance of muscular activities in the tibialis anterior muscle, a clear decrease in triceps surae activities and normal alternance of contractions of these muscles (i.e. triceps surae at the end of the stance phase and tibialis anterior during the swing phase). (b) Tridimensional movement analysis of the ankle flexion-extension amplitude during the gait with VICON system. Left: Preoperatively, the amplitude of the spastic ankle is limited to 18 degrees of dorsal flexion. Right: After selective tibial neurotomy, the dorsal flexion increased to 32 degrees. Thus, the tonic balance of the ankle has been re-equilibrated by the selective tibial neurotomy; consequently, motor function and gait have been improved.

consisted of resectioning one third to two thirds of each group of rootlets of all the posterior roots from L1 to S1.

Sectorial posterior rhizotomy

In an attempt to reduce the side effects of rhizotomy on postural tone in ambulatory patients, Gros (1979) and his pupils Privat *et al.* (1976) and Frerebeau (1991) proposed a topographic selection of the rootlets to be sectioned. Firstly, a preoperative assessment is done to differentiate the 'useful spasticity' (i.e. the one sustaining postural tone – abdominal muscles, quadriceps, gluteus medius) from the 'harmful spasticity' (i.e. the one responsible for vicious posture – hip flexors, adductors, hamstrings, triceps surae). This is followed by mapping the evoked motor activity of the exposed rootlets, from L1 to S2, by direct electrostimulation of each posterior group of rootlets. Finally, the rootlets to be sectioned are determined according to this preoperative programme.

Partial posterior rhizotomy

Fraioli and Guidetti (1977) reported on a procedure for dividing the dorsal half of each rootlet of the selected posterior roots a few millimetres before its entrance into the posterolateral sulcus. Good results were obtained, without significant sensory deficit. This can be explained by the fact that partial sectioning leaves intact a large number of fibres of all types.

Functional posterior rhizotomy

The neurological search for specially organized circuits responsible for spasticity led Fasano *et al.* (1976) to propose the so-called functional posterior rhizotomy. This method is based on bipolar intraoperative stimulation of the posterior rootlets and analysis of the types of muscle responses by electromyography (EMG). Responses characterized by a permanent tonic contraction, an after-discharge pattern or a large spatial diffusion to distant muscle groups were considered to belong to disinhibited spinal circuits responsible for spasticity. This procedure, which was especially conceived for use with children with cerebral palsy, has been also used by other outstanding surgical teams, each one having brought its own technical modifications to the method (Peacock & Arens, 1982; Cahan *et al.*, 1987; Storrs, 1987; Abbott *et al.*, 1989).

Personal technique

Our personal adaptations of these methods are summarized below. Selection of candidates for surgery was done in a multidisciplinary way, with the rehabilitation team, the physiotherapist, the orthopaedic surgeon and the neurosurgeon being present, as well as of course the patient's family. Candidates were retained only if spasticity was responsible for a halt in motor skill acquisitions and/or evolutive orthopaedic deformities in spite of intensive physiotherapy. The main goals of the surgery were clearly defined for every patient: improvement in comfort; decrease in orthopaedic risks; improvement for sitting, standing and/or walking; and improvement in urinary function. The muscles in which there was a harmful excess of tone and their – anatomically – corresponding lumbosacral roots (i.e. those to be resected, as well as the degree of their resectioning according to amount of spasticity to be reduced) were determined by the multidisciplinary team. The surgical procedure used is detailed in Figure 11.7. Until recently, we have operated only on very severely affected children – quadriplegic and not able to locomote on their own. The results are reported in Hodgkinson *et al.* (1996) and summarized in Table 11.1. Since 1995 we have extended the indications to diplegic children able to walk; the effects are good, but follow-up in this group is not yet sufficient to report on the results in detail.

The results of posterior rhizotomies

The results obtained in children with cerebral palsy, whatever the technical modality of surgery may be, have been extensively reported in the literature. A number of publications have confirmed the efficacy of the various dorsal rhizotomy techniques. In 2002, for example, McLaughlin *et al.* conducted a

Table 11.1. Results according to whether or not principal goal is reached

Principal goal	Number of cases	Goal reached	Goal not reached
Improvement in comfort	2	1	1
Orthopaedic risks	6	2	4
Improvement of sitting position	1	1	–
Improvement of standing and walking	8	6	2
Improvement of vesical function	1	0	1
Total	18	10	8

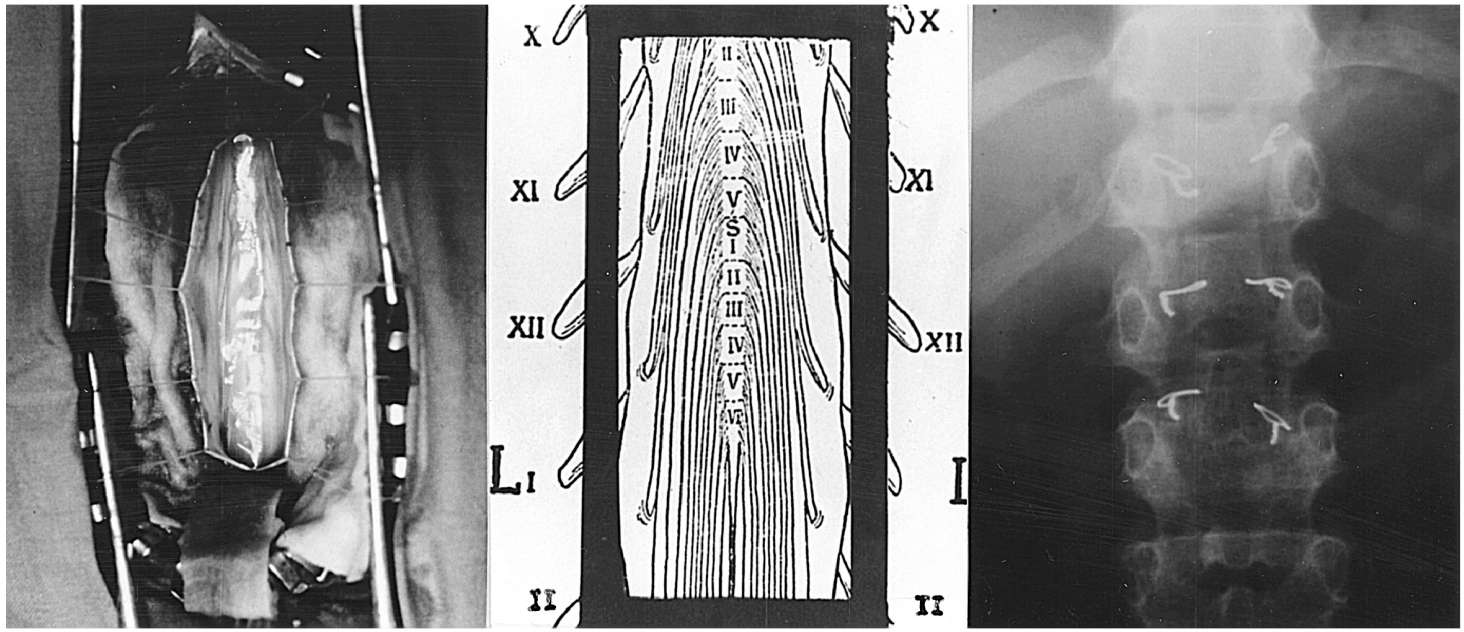


Figure 11.7. Lumbosacral posterior rhizotomy for cerebral palsy children. Our personal technique consists of performing a limited osteoplastic laminotomy using a power saw, in one single piece, from T11 to L1 (left). The laminae will be replaced at the end of the procedure and fixed with wires (right). The dorsal (and ventral) L1, L2 and L3 roots are identified by means of the muscular responses evoked by electrical stimulation performed intradurally just before entry into their dural sheaths. The dorsal sacral rootlets can be seen at the entrance into the dorsolateral sulcus of the conus medullaris. The landmark between S1 and S2 medullary segments is located 30 mm approximately from the exit of the tiny coccygeal root from the conus. The dorsal rootlets of S1, L5 and L4 are identified by their evoked motor responses. The sensory roots for bladder (S2–S3) can be identified by monitoring vesical pressure, and those for the anal sphincter (S3–S4) can be identified by rectomanometry (or simply using a finger introduced into the patient's rectum) or electromyography recordings. Surface spinal cord SEP recordings from tibial nerve (L5–S1) and pudendal nerve (S1–S3) stimulation may also be helpful.

For the surgery to be effective a total amount of 60% of dorsal rootlets must be cut, of course with a different quantity cut according to the level and function of the roots involved. Also, of course, the correspondence of the roots with the muscles having harmful spasticity or useful postural tone must be considered in determining the amount of rootlets to be cut; in most cases L4 (which predominantly gives innervation to the quadriceps femoris) has to be preserved.

meta-analysis of three randomized controlled trials and confirmed a significant reduction in spasticity using both the Ashworth score and the Gross Motor Function Measure. They showed a direct relationship between percentage of dorsal route tissue transected and functional improvement. There was better improvement when selective dorsal rhizotomy was combined with physiotherapy, at least in the context of children with spastic diplegia. Salame and colleagues (Salame *et al.*, 2003) have also recently reported on a retrospective series of 154 patients who underwent selective posterior rhizotomy over a 30-year period. They showed a reduction of spasticity in the lower limbs in every case, with improvements in movement in 86% of cases. They also showed alleviation of painful spasms in 80% of cases and amelioration of neurogenic bladder in 42%. They found no significant perioperative mortality or major complications. In a slightly different context, Bertelli and colleagues (Bertelli *et al.*, 2003) have also shown the efficacy of brachial plexus dorsal rhizotomy for hemiplegic cerebral palsy and demonstrated that grasp and pinch strength were improved together with movement, speed and dexterity. In their experience, procedures are mainly carried out in children 5 to 6 years of age with cerebral palsy. Briefly, these publications show that about 75% of the patients at 1 year or more after surgery had nearly normal muscle tone that no longer limited the residual voluntary movements of limbs. After a serious and persisting physical therapy and rehabilitation programme, most children demonstrated improved stability in sitting and/or increased efficiency in walking. In most cases with installed contractures, deformities were not retrocessive, so that complementary orthopaedic surgery was justified.

Percutaneous thermorhizotomies and intrathecal chemical rhizotomies

Percutaneous radiofrequency rhizotomy, initially performed for the treatment of pain (Uematsu *et al.*, 1974), was later applied to the treatment of neurogenic detrusor hyperreflexia (Young & Mulcachy, 1980) and of spasticity in the limbs (Herz *et al.*, 1983; Kenmore, 1983; Kasdon & Lathi, 1984). The procedure in the lumbar spine is generally performed in the lateral recumbent position, the affected side uppermost, because the prone position would be very uncomfortable, with fixed tendons and joint resulting in abnormal postures. The entry point is about 7 cm from the midline just below the level of the intervertebral space. The needle is pushed obliquely upwards to the corresponding foramen under fluoroscopy so as to reach the target root tangentially. The radiofrequency (RF) probe is placed through the stylet and a stimulation current is applied with an increasing voltage until a motor response is obtained in the appropriate muscular group. The probe must be readjusted if a good motor response is not obtained with a threshold of less than 0.5 volts. The RF lesion is made at 90°C for 2 minutes. A stimulation test is then applied; an increase in threshold of at least 0.2 volts is desired to be certain of a significant relief of spasticity. Otherwise, the procedure must be repeated. For the placement of the electrode at S1, the needle is inserted in the midline between the spinous processes of L5 and S1 and pushed laterally towards the elbow of the S1 nerve root (without penetration of the dura). RF–sacral rhizotomies can be performed at the foramen of S1 to S4 with cystometric monitoring for neurogenic bladder with detrusor hyperactivity. RF–thermorhizotomy can be also performed in the cervical spine. The patient is in the supine position. The tip of the needle is placed in the posterior compartment of the vertebral foramen to avoid damage to the vertebral artery. Percutaneous rhizotomies have the advantage of being less aggressive than the open procedures in very debilitated patients. The procedure seems more appropriate for spastic disturbances limited to a few muscular groups that correspond to a small number of spinal roots (as occurs in spastic hip, which can be treated by thermorhizotomy of L2–L3). The effects are most often temporary. In long-term follow-up, a high rate of recurrent spasticity is observed (5 to 9 months on average),

but the preoperative level of spasticity is most often not totally reached and the procedure can be repeated.

Intrathecal injection of alcohol was first introduced for cancer pain (Dogliotti, 1931); only later was it used for hypertonia in patients with severe spastic paraplegia (Guttman, 1953). Alcohol was then replaced by phenol (a hyperbaric solution), which is easier to control (Maher, 1955; Kelly & Gauthier-Smith, 1959; Nathan, 1959). The best candidates for phenol intrathecal injections are paraplegic patients suffering from severe spasms who do not have useful residual motor, sensory or sphincter function below the level of the lesion (see Chapters 8 and 10).

Longitudinal myelotomy

Longitudinal myelotomy was introduced by Bischof (1951); it was made more selective by Pourpre (1960) and later by Laitinen and Singounas (1971). The method consists of a frontal separation between the posterior and anterior horns of the lumbosacral enlargement from T11 to S2 performed from inside the spinal cord after a posterior commisural incision that reaches the ependymal canal. Laitinen and Singounas (1971) found that of 25 patients, 60% had complete relief of spasticity while 36% showed some residual spasticity in one or both legs. Within 1 year, some muscular tone returned in most patients, but it seldom produced troublesome spasticity. However, a harmful effect on bladder function was present in 27% of the patients. Longitudinal myelotomy is indicated only for spastic paraplegias with flexion spasms, when the patient has no residual useful motor control and no bladder or sexual function.

Surgery in the dorsal root entry zone

Surgery in the dorsal root entry zone was introduced in 1972 (Sindou, 1972) to treat intractable pain. Because of its inhibitory effects on muscular tone, it has been applied to patients with focalized hyperspasticity (Sindou *et al.*, 1974, 1982, 1985a,b). This method – named microDREZotomy (MDT) – attempts to selectively interrupt the small nociceptive and the large myotatic fibres (situated laterally and centrally, respectively), while sparing the large lemniscal fibres which are regrouped medially. It also enhances the inhibitory mechanisms of Lissauer's tract and dorsal horn (Eccles *et al.*, 1961) (Fig. 11.8).

MDT (Sindou *et al.*, 1986, 1991a; Sindou & Jeanmonod, 1989) consists of microsurgical incisions that are 2 to 3 mm deep and at a 35-degree angle at the cervical level and at a 45-degree angle at the lumbosacral level followed by bipolar coagulations performed ventrolaterally at the entrance of the rootlets into the dorsolateral sulcus, along all the cord segments selected for operation (Fig. 11.8, right). For patients with paraplegia (Sindou & Jeanmonod, 1989), the L2–S5 segments are approached through a T11–L2 laminectomy (Fig. 11.9), whereas for the hemiplegic upper limb (Sindou *et al.*, 1986), a C4–C7 hemilaminectomy with conservation of the spinous processes is sufficient to reach the C5-T1 segments (Fig. 11.8). Identification of the cord levels related to the undesirable spastic mechanisms is achieved by studying the muscle responses to bipolar electrical stimulation of the anterior and/or posterior roots. The motor threshold for stimulation of anterior roots is one third that of the threshold for posterior roots. The lateral aspect of the DREZ is now exposed, so that the microsurgical lesions can be performed, 2 to 3 mm in depth and at 35- to 45-degree angles in the ventrolateral aspect of the sulcus all along the selected segments of the spinal cord. Intraoperative neurophysiological monitoring may be of some help to identify cord levels, quantify the extent of MDT and avoid impairing long fibre tracts.

MDT is indicated in paraplegic patients, especially when they are bedridden as a result of disabling flexion spasms, and in hemiplegic patients with irreducible and/or painful hyperspasticity in the upper limb (Sindou *et al.*, 1986, 1991a; Sindou & Jeanmonod, 1989; Beneton *et al.*, 1991; Sindou, 1997). MDT also can be used to treat neurogenic bladder

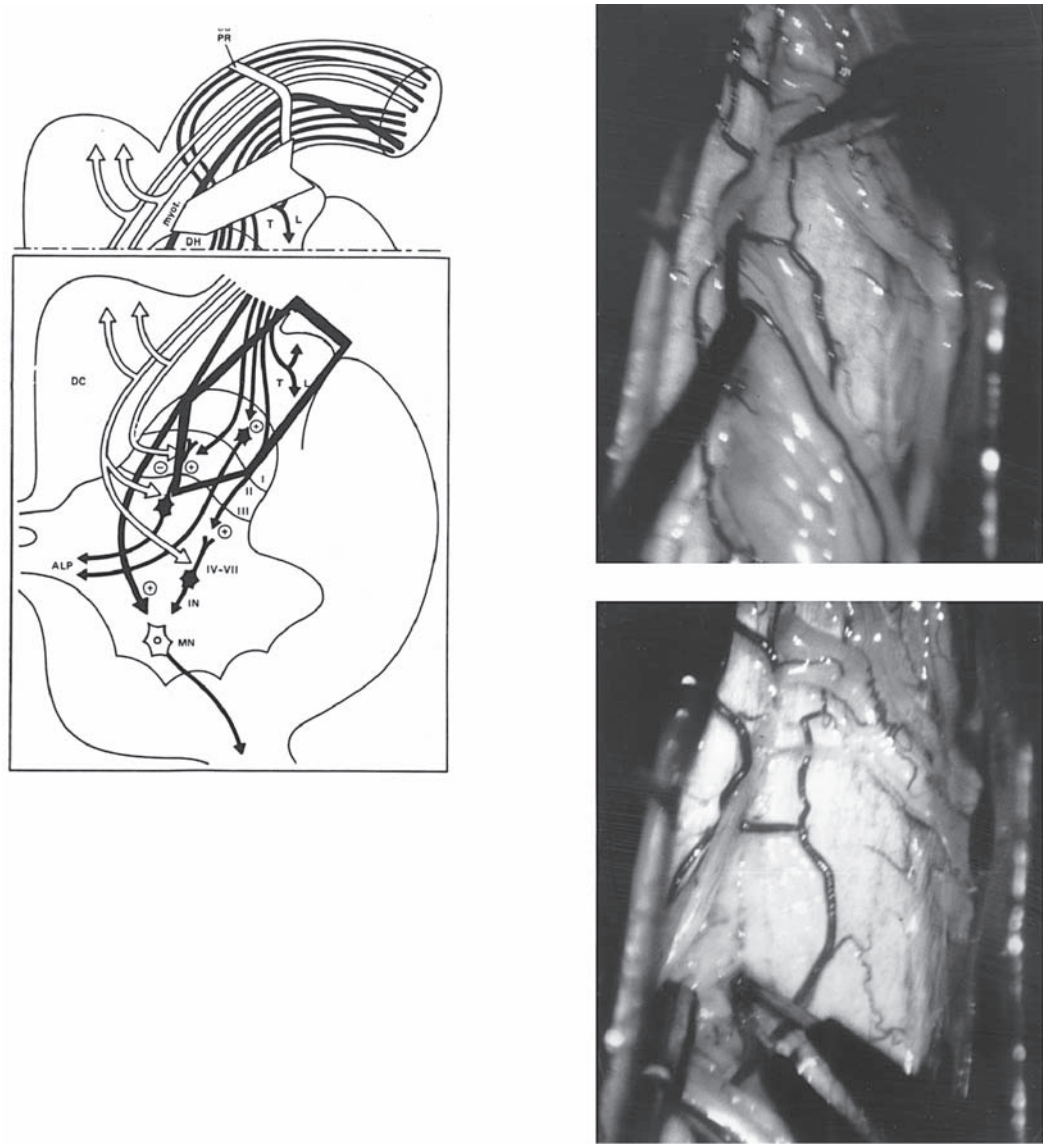


Figure 11.8. MicroDREZotomy (MDT). Left: Organization of fibres at the dorsal root entry zone (DREZ) in humans. The large arrow shows the proposed extent of the MDT, that is, the lateral and central bundles formed by the nociceptive and myotatic fibres, as well as the excitatory medial part or the TL and the upper layers of the dorsal horn. Right: Principles of the technique of the MDT. Example at the cervical level through a right cervical hemilaminectomy (the procedure for the lumbosacral roots is the same). The right C6 posterior root has been retracted toward the inside to make the ventrolateral region of the DREZ accessible. The incision is performed into the dorsolateral sulcus using a small piece of razor blade (upper photograph). The incision is 2 to 3 mm deep and is made at 35-degree angle (at 45-degree angle for the lumbosacral level). Then microcoagulations are created with a very sharp and graduated bipolar microforceps down to the apex of the dorsal horn (lower photograph).

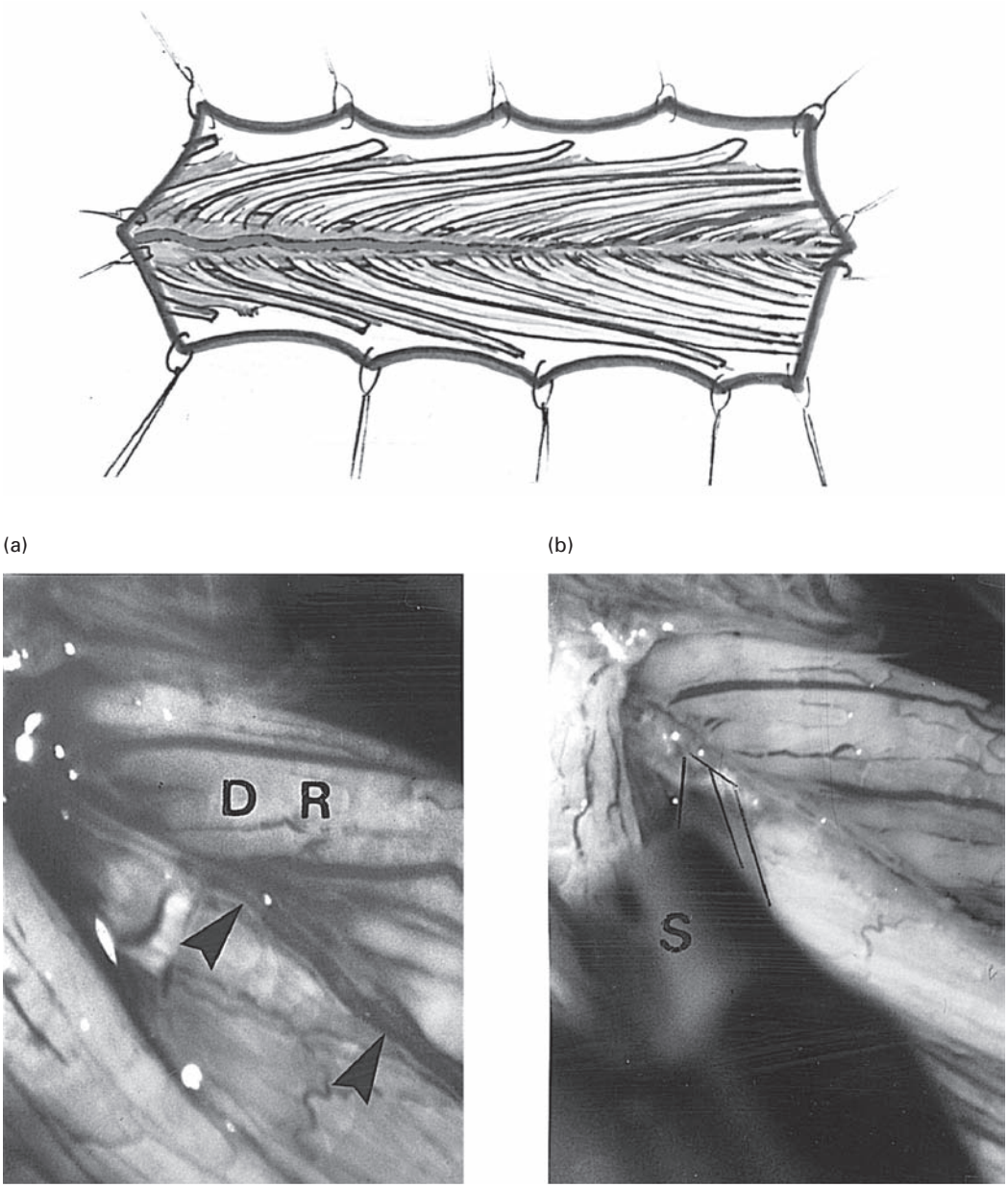
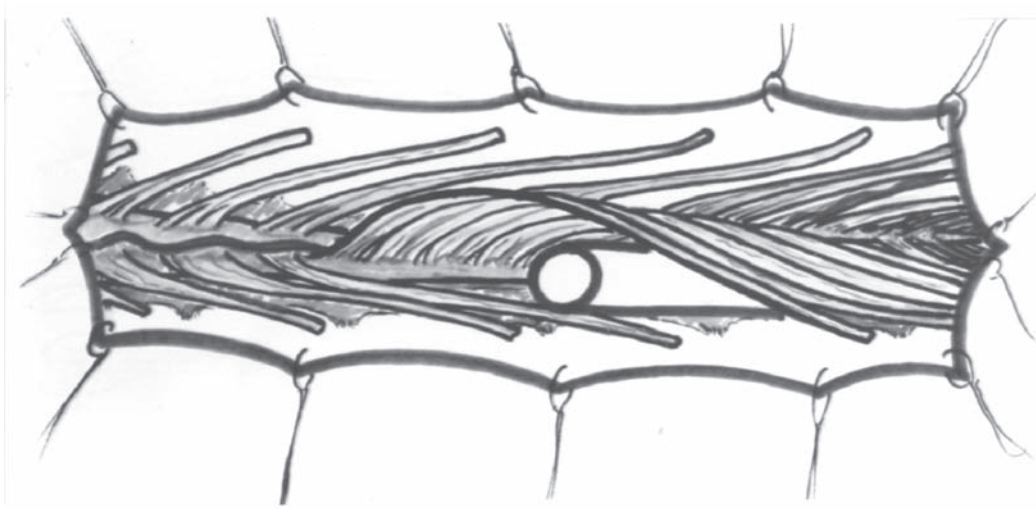


Figure 11.9. MDT technique at the lumbosacral level. Top: For paraplegia, the conus medullaris is approached through a (T10) T11–L2 laminectomy. Exposure of the left dorsolateral aspect of the conus medullaris on the left side. Bottom: Exposure of the left posterolateral aspect of the conus medullaris. (a) The rootlets of the selected lumbosacral dorsal roots (D) are displaced dorsally and medially to obtain proper access to the ventrolateral aspects of the dorsal root entry zone in the posterolateral sulcus. Only the tiny pial vessels (arrows) will be coagulated with a thin, pointed, graduated bipolar microforceps. (b) Microscalpel (S) made from a small, elongated fragment of a razor blade mounted on a holder is ready to start the incision, which will be at an angle of 45 degrees ventromedially and 2 to 3 mm deep (arrows, posterolateral sulcus).

(*cont.*)



(c) (d)

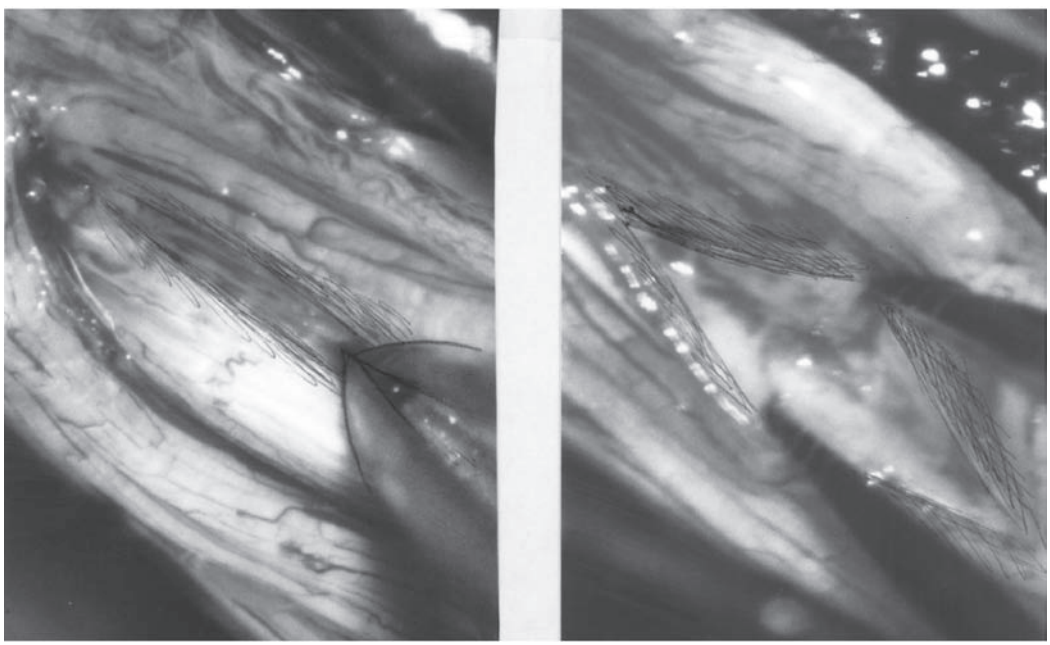


Figure 11.9 (*cont.*)**.** (c) Microcoagulations are performed inside the incision, 2 to 3 mm in depth, down the upper layers of the dorsal horn. (d) The line of incision is opened (between the two tips of the bipolar forceps) and reveals its depth and the apex of the dorsal horn.

with uninhibited detrusor contractions resulting in voiding around a catheter (Beneton *et al.*, 1991).

Our studies to date consist of 45 cases of unilateral cervical (C5-T1) MDT for harmful spasticity in the upper limb, 121 cases of bilateral lumbosacral MDT (L2 to S1 or S5) for disabling spasticity in the lower limbs and 12 cases of bilateral sacral S2–S3 (S4) MDT for hyperactive neurogenic bladder only. Effects on muscular tone can be judged only after a 3-month follow-up. A 'useful' result on spasticity allowing withdrawal of antispastic medications, was obtained in 78% of patients with a spastic upper limb. A similarly useful effect was obtained in 75% of patients with spasticity in the lower limbs.

When spasms were present in paraplegic patients, they were suppressed or markedly decreased in 88% of cases. The results were better in spasticity (and spasms) caused by pure spinal cord lesions (in the order of 80% useful effects), followed by multiple sclerosis (75%). The least improvement was observed in patients with spasticity resulting from cerebral lesions (60%). Reduction in spasticity usually leads to a significant improvement of abnormal postures and articular limitations. This was achieved in about 90% of our patients. For the hemiplegic upper limb, the increase in articular amplitude was most remarkable for the elbow and shoulder (when not 'frozen') but was much more limited for the wrist and fingers, especially if there was retraction of the flexor muscles and no residual voluntary motor activity in the extensors. For the lower limb(s) with abnormal postures in flexion, the increase in articular amplitude was dependent on the degree of the preoperative retractions. When the post-MDT gains were deemed insufficient because of persistent joint limitations, complementary orthopaedic surgery was indicated. With regard to the five patients who had paraplegia with irreducible hyperextension, all were completely relieved.

In the patients with some voluntary movements hidden behind spasticity, reduction in the hypertonia results in an improvement in voluntary motor activity. Of the patients operated on for spasticity in the upper limb, 50% had better motor activity of the shoulder and arm, but only half of those with some preoperative distal motor function obtained additional hand prehension. Only 10% of the patients with spasticity in the lower limb(s) had significant motor improvement after surgery, because most patients in this group had no functional preoperative motor function. In these very severely affected patients the main benefit was better comfort, less pain, ability to resume physical therapy and less dependence in their daily lives (Fig. 11.10). See Sindou (1997) for pre- and postoperative assessment of patients (with details on the functional scores used) (Tables 11.2 and 11.3).

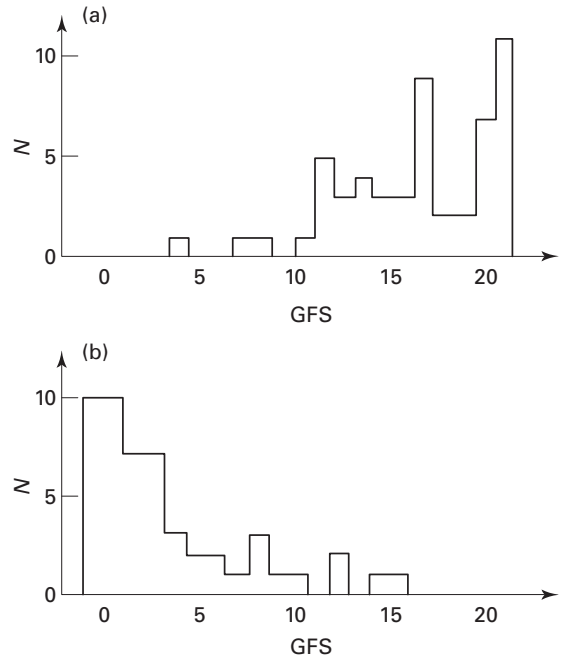


Figure 11.10. Distribution of pre- (a) and postoperative (b) global functional scores (GFS) in patients with spasticity in the lower limbs. N: number of patients. (See Table 11.3 for explanation of the scoring system.)

Bladder capacity was significantly improved in 85% of the 38 patients who had hyperative neurogenic bladder with urine leakage around the catheter. These 32 improved patients were those in whom the detrusor was not irreversibly fibrotic. Pain, when

Table 11.2. Functional score for hemiplegic patients with spasticity in the upper limb

Grade	Description
I	Absence of useful active mobility and uneasy and painful passive mobilization, making it difficult to dress and wash
II	Easy passive mobilization but without any useful voluntary movements
III	Slight but useful voluntary motor function
IV	Good active mobility with the possibility of prehension in the hand and fingers

present, was in general favourably influenced. MDT constantly produced a marked decrease in sensation.

Because most patients were in a precarious general and neurological state, death occurred in 5 (4%) patients, resulting from respiratory problems in 4 and bed sores in 1. Two multiple sclerosis patients presented with an acute but transient increase in their pre-existing neurological symptoms during the postoperative period, whereas two others had a new postoperative clinical manifestation of the disease.

Finally, mention should be made of one patient who had been operated on at the cervical level and who continued to have a persistent motor deficit in the ipsilateral leg after surgery.

With rigorous selection of patients, MDT can be very effective in relieving pain and suppressing excess spasticity. Good long-lasting relief of excess spasticity had been achieved in 80% of our patients. As a result, MDT, sometimes combined with complementary orthopaedic surgery, resulted in significant improvement in patient comfort and articular deformities and even enhancement of residual voluntary motility hidden preoperatively behind hypertonicity.

Orthopaedic surgery

Orthopaedic procedures can reduce spasticity by means of muscle relaxation that results from tendon lengthening and may help in restoring articular function when deformities have become irreducible.

Table 11.3. Global functional score for paraplegic patients with spasticity in the lower limb(s)

Pain
0 absent
1 rare and mild
2 frequent: minimal disability
3 marked and frequent: marked disability
4 permanent and severe

Spasms
0 absent
1 rare and mild spasms only during mobilizations: no disability
2 frequent, spontaneous but moderate spasms: moderate disability
3 frequent
4 almost constant and severe spasms: severe disability, major problems for sitting or lying

Sitting position
0 normal
1 mild difficulty
2 moderate to marked difficulty, causing reduction of sitting periods
3 severe difficulty: patient has to be tied down in position
4 impossible

Body transfers
0 normal
1 mild difficulty
2 moderate difficulty
3 marked difficulty, need for a person helping
4 severe difficulty, need for two persons helping

Washing and dressing
0 normal
1 mild difficulty
2 moderate difficulty
3 marked difficulty, need for a person helping
4 severe difficulty, need for two persons helping

Note:
This score developed by Millet *et al.* (1981) cited in Sindou *et al.* (1991b) quantifies five components that are directly influenced by spasticity, abnormal postures and articular limitations and are parts of the patient's everyday life. The score goes from 0 to 4 for each component, with a total of 20/20 denoting a bedridden and totally dependent patient. A score of 10/20 was seen to correspond to the threshold between a decent condition and an unacceptable condition.

Current techniques for correcting excessive shortness of the muscle tendon assembly are muscular desinsertion, myotomy, tenotomy and lengthening tenotomy. The lengthening operations most often used are (1) the muscular desinsertion of the epicondylian muscles for flexed wrist and fingers (Scaglietti's procedure); (2) the flexor digitorum lengthening for the hemiplegic hand; (3) the tendon lengthening of the heel cord for foot equinism; and (4) the hamstring-tendon lengthening associated with patellar-tendon shortening. Such techniques aim to obtain a more functional position for the limb or limbs involved. Excessive lengthening can lead to a decrease in muscular strength.

Tendon transfer has a different goal – to normalize articular orientation when it has been distorted by muscular imbalance. Transfer of spastic muscles must be avoided. If necessary, suppression of spasticity must be achieved by neurosurgical procedure before tendon transfer. A frequently indicated tendon transfer is the fixation of the distal tendon of the peroneus brevis onto the tibialis anterior for equinovarus foot (i.e. Bardot's procedure).

Osteotomies aim to correct bone deformity resulting from growth distorsion in a child (e.g. femoral derotation osteotomy to correct excessive anteversion in patients with cerebral palsy) or to treat stiffened joints (e.g. supracondylar femoral osteotomy for irreducible flexed knee). Articular surgery is indicated only when osteoarticular deformity cannot be corrected by osteotomy or tendon surgery alone. When a foot varus deformity is very severe and fixed, one can have recourse to a triple hind-foot arthrodesis – subtalar and midtarsal; with this technique the ankle remains free. Arthrodesis must not be performed in children until they have stopped growing.

Orthopaedic surgery can be undertaken to correct or even prevent irreducible deformities, to increase comfort in the more severely affected patients or to improve function in those who have recovered a sufficient level of voluntary motor function, but only after spasticity has been reduced.

Some useful recent references of the orthopaedic management of problems secondary to spasticity have recently been published by Landi *et al.* (2003), Presedo *et al.* (2005) and Hogan *et al.* (2006).

Indications for surgery

In adults

ITB administration is indicated for para- or tetraplegic patients with severe and diffuse spasticity especially when from spinal origin. Because of its reversibility, this method has to be considered before considering an ablative procedure. However, the range is very narrow between excess of hypotonia with loss of strength and an insufficient effect. An intrathecal test through a temporary access port can be useful before indicating permanent implantation.

Neuroablative techniques are indicated for severe focalized spasticity in the limbs of paraplegic, tetraplegic or hemiplegic patients.

Neurotomies are preferred when spasticity is localized to muscle groups innervated by a small number of nerves, or a single, peripheral nerve. When spasticity affects an entire limb, MDT is preferred. Several types of neuroablative procedures can be combined in the treatment of one patient, when needed.

Whatever the situation and the aetiology may be, orthopaedic surgery must be considered only after spasticity has been reduced by physical and pharmacological treatments and, when necessary, by neurosurgical procedures.

Guidelines for surgical indications have been detailed elsewhere (Sindou & Mertens, 1991; Sindou *et al.*, 1991b) and are summarized in Figure 11.11. The general rule is to tailor individual treatments as much as possible to the particular problems of the patient.

In children with cerebral palsy

In children, surgical indications depend on preoperative abilities and disabilities and the eventual functional goals. As guidelines, we have adopted

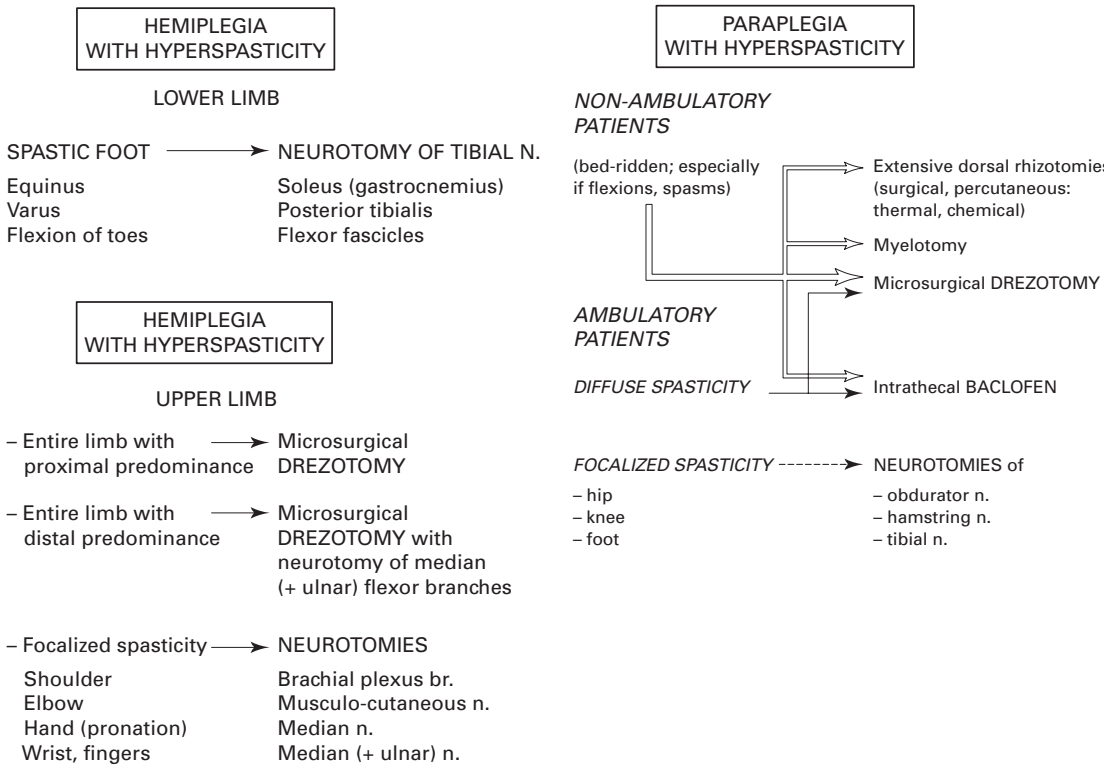


Figure 11.11. A summary of the guidelines for surgical indications.

the classification of six groups as defined by Abbott (1991):

1. In independent ambulatory patients, the goal is to improve efficiency and cosmesis in walking by eliminating as many abnormally responsive neural circuits as can be identified through functional posterior rhizotomy. Surgery is best performed as soon as possible after the child has demonstrated the ability to work with a therapist, usually between ages 3 and 7 years, and frequently must be done in conjunction with operations on tendons because of concomitant shortened muscles.
2. For ambulatory patients dependent on assistance devices (i.e. canes, crutches, rollators, walkers), the goal is to lessen that dependence. A child with poor trunk control or lack of protective reaction but with good underlying strength in the antigravity muscles can safely undergo a functional posterior rhizotomy. In children dependent on hypertonicity in the quadriceps to bear weight, a limited sectorial rhizotomy is preferable. For children who are in the process of developing ambulatory skills and need an assistance device only temporarily, it is important to delay surgery until they have perfected these skills.
3. For quadriped crawlers (or bunny hoppers) the goal is to achieve assisted ambulation during mid-childhood to early adolescence. A functional posterior rhizotomy will decrease hypertonicity in the leg musculature and allow better limb alignment in the standing position for a child with adequate muscular strength. However, a child who exhibits quadriceps weakness can be considered for a sectorial posterior rhizotomy. Children in this group can present at a young age with progressive hip

dislocation. The goal is to stop the progressive orthopaedic deformity by using obturator neurotomy with adductor tenotomies or functional posterior rhizotomy.
4. For commando (or belly) crawlers disabled by severe deficiencies in postural control, the goal of posterior rhizotomy is only to improve functioning in the sitting position by increasing stability.
5. In totally dependent children with no locomotive abilities, the goals are simply to improve comfort and facilitate care. As with group 4, the preferred treatment is posterior rhizotomy, but there is also a need for exploring the efficacy of ITB.
6. For asymmetrical spasticity, selective peripheral neurotomies must be considered, especially obturator and tibial for the spastic hip and foot, respectively. For upper limb spasticity, the MDT procedure and/or selective neurotomies of the flexor muscles of wrist and fingers can be considered.

In summary, for children, the main goal is to stop and prevent progressive and irreversible orthopaedic deformities. Lumbosacral posterior rhizotomies can be indicated for reducing the excessive general level of spasticity in diplegic (and even quadriplegic, thanks to distant effects in upper limbs) patients. ITB is an alternative, but the range between an insufficient effect and an excessive effect responsible for a global decrease in tone impairing gait and reducing muscular strength, is often very narrow. In cases with localized hyperspasticity threatening a joint, peripheral neurotomy(ies) can be the solution, as for instance obturator neurotomy for hip spasticity. Frequently orthopaedic surgery can be usefully performed in conjunction with neurological surgery to lengthen tendons.

Conclusion

Spasticity is often a useful substitute for deficiency of motor strength, and therefore to that extent must be preserved. However, not infrequently, it may become harmful, leading to an aggravation of motor disability. When excessive spasticity is not sufficiently controlled by physical therapy and pharmacological means, patients can have recourse to surgery, especially neurosurgical procedures. By suppressing excessive spasticity, correcting abnormal postures and relieving the frequently associated pain, surgery for spasticity allows physiotherapy to be resumed and it sometimes results in the reappearance of, or improvement in, useful voluntary motility. When dealing with these patients, the surgeon must know the risks of the available treatments. To minimize those risks, the surgeon needs a strong anatomic, physiological and chemical background; rigorous methods to assess and quantify the disorders and the ability to work in a multidisciplinary team (Sindou *et al.*, 1991b).

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12

Management of spasticity in children

Rachael Hutchinson and H. Kerr Graham

Introduction

Spasticity can be defined as a velocity-dependent resistance to passive movement of a joint and its associated musculature (Lance, 1980; Rymer & Powers, 1989; Massagli, 1991). Although spasticity is usually present before contracture in children with cerebral palsy, true muscle shortening or contracture also appears at an early stage. The majority of children will have a mixture of spasticity and contracture. Distinguishing spasticity from contracture is important from a management point of view.

1. 'Dynamic' shortening is most commonly caused by spasticity but may also be associated with dystonia and mixed movement disorders. Typically, 'dynamic' contracture is recognized in younger children with cerebral palsy or spasticity of recent onset. Such children are likely to exhibit hyperreflexia, clonus, co-contraction and a velocity-dependent resistance to passive joint motion. Children who exhibit 'dynamic' calf shortening may walk on their toes with an equinus gait, but on the examination couch the range of passive ankle dorsiflexion may be full or almost full.
2. 'Fixed' shortening or 'myostatic' contracture describes the typical stiffness found in muscles of older children with cerebral palsy or spasticity of longer duration. The stiffness is much less velocity dependent and is still present during couch examination and under anaesthesia.

Causes of spasticity in children

With the eradication of poliomyelitis and the dramatic fall in the prevalence of spina bifida, the most common motor disorder in children in developed countries is cerebral palsy. The incidence of cerebral palsy in developed countries is static or even rising. The reductions in the prevalence of kernicterus due to neonatal jaundice has been overshadowed by improved survival of very low birth weight and premature infants, many of whom suffer from spastic diplegia and quadriplegia (Stanley & Alberman, 1984; Petterson *et al.*, 1993a,b; Pellegrino & Dormans, 1998; Marlow *et al.*, 2005). Other common causes of spasticity in children are acquired brain injury and spinal cord injury. Table 12.1 shows the cause of spasticity in a consecutive sample of 341 children seen in a variety of clinics at the Royal Children's Hospital in Melbourne in 1998.

Spasticity in children will continue to be a common and challenging problem for the foreseeable future. While reduction in the incidence of cerebral palsy would have the most impact in reducing the overall incidence of spasticity in children, prevention of traumatic brain injury and spinal cord injury is probably more realistic (Glasgow & Graham, 1997).

The pathology of spasticity

Given that the most common cause of spasticity in our clinics is cerebral palsy, subsequent discussion

Table 12.1. Aetiology of spasticity in 341 children (cerebral palsy, orthopaedic and spasticity clinics)

Cerebral palsy	79%
Acquired brain injury	6%
Spina bifida	5%
Spinal cord injury	2%
Miscellaneous	8%

on pathology and management focuses mainly but not exclusively on spasticity in the context of juvenile cerebral palsy. The effects of spasticity cannot be separated from the overall effects of the upper motor neurone (UMN) syndrome (Fig. 12.1). The child with diplegia who walks on his toes because of calf spasticity may also be unable to voluntarily control the dorsiflexors of the ankle during gait. No matter how effective management of the calf spasticity is, gait may remain impaired because toe clearance cannot be achieved during the swing phase of gait (Perry, 1985, 1992). Indeed there is virtually always an effective solution to calf spasticity/stiffness/shortening, but inability to control the ankle dorsiflexors during swing phase may mean life-long dependence on an orthosis. Weakness and impaired selective motor control have a much greater impact on gait and function than spasticity. They are also more difficult to manage.

Fixed musculoskeletal pathology in cerebral palsy is acquired during childhood. Children with cerebral palsy do not have contractures, dislocated hips or scoliosis at birth. These common deformities are acquired during childhood. Muscle growth in children is a race between the pacemakers (i.e. the physes of the long bones) and the muscle tendon units, in which the muscles are doomed to second place (Graham & Selber, 2003). The prerequisites for normal muscle growth is frequent stretching of relaxed muscle. In children with cerebral palsy, the muscles do not readily relax because of spasticity, and they are infrequently stretched because of reduced activity. Spasticity plus reduced activity leads to failure of longitudinal muscle growth, contractures and fixed deformities (Ziv *et al.*, 1984; Cosgrove & Graham, 1994). The limb pathology can be considered in three stages (Fig. 12.2):

In **stage 1**, typically the younger child with cerebral palsy, the deformities are all dynamic or reversible. This is the phase when spasticity management, gait training and the use of orthoses may be most useful. Orthopedic surgery is not indicated.

In **stage 2**, there are fixed contractures, which may require surgical lengthening of muscles or tendons.

In **stage 3**, there are changes in bones and joints, including torsion of the long bones and joint instability. The most common torsional problems are medial femoral torsion and lateral tibial torsion. Joint instability problems include hip subluxation and subtalar collapse in the hindfoot (Graham & Selber, 2003).

Spasticity, dynamic and fixed contractures coexist in varying proportions in most children. The transition from dynamic to fixed contracture occurs at different rates in different topographical types of cerebral palsy and at different rates in different limb segments and even in different muscle groups in the same limb segment. There appears to be a 'biological clock' running at different speeds for different muscles in children with cerebral palsy, governing the timing of the transition from dynamic to fixed contracture (Eames *et al.*, 1999; Preiss *et al.*, 2003).

In hemiplegia, there is an earlier transition from dynamic to fixed contracture than in diplegia. The dynamic component can be exploited by spasticity management (Eames *et al.*, 1999). In spastic hemiplegia, fixed contracture usually develops in the lower limb earlier than in the upper limb. Spasticity management may be appropriate in the upper limb at an age when surgery is required for a fixed equinus deformity. In the hemiplegic upper limb, the first muscle to develop a fixed contracture is almost invariably the pronator teres (Preiss *et al.*, 2003). This may result more from the absence of active supination than increased spasticity in the pronator teres. A useful strategy may be to combine a lengthening or rerouting of the pronator teres, with spasticity management of the wrist and finger flexors using botulinum toxin A (BoNT-A). Recognition of these types of patterns may greatly improve the outcome of both spasticity and contracture management and

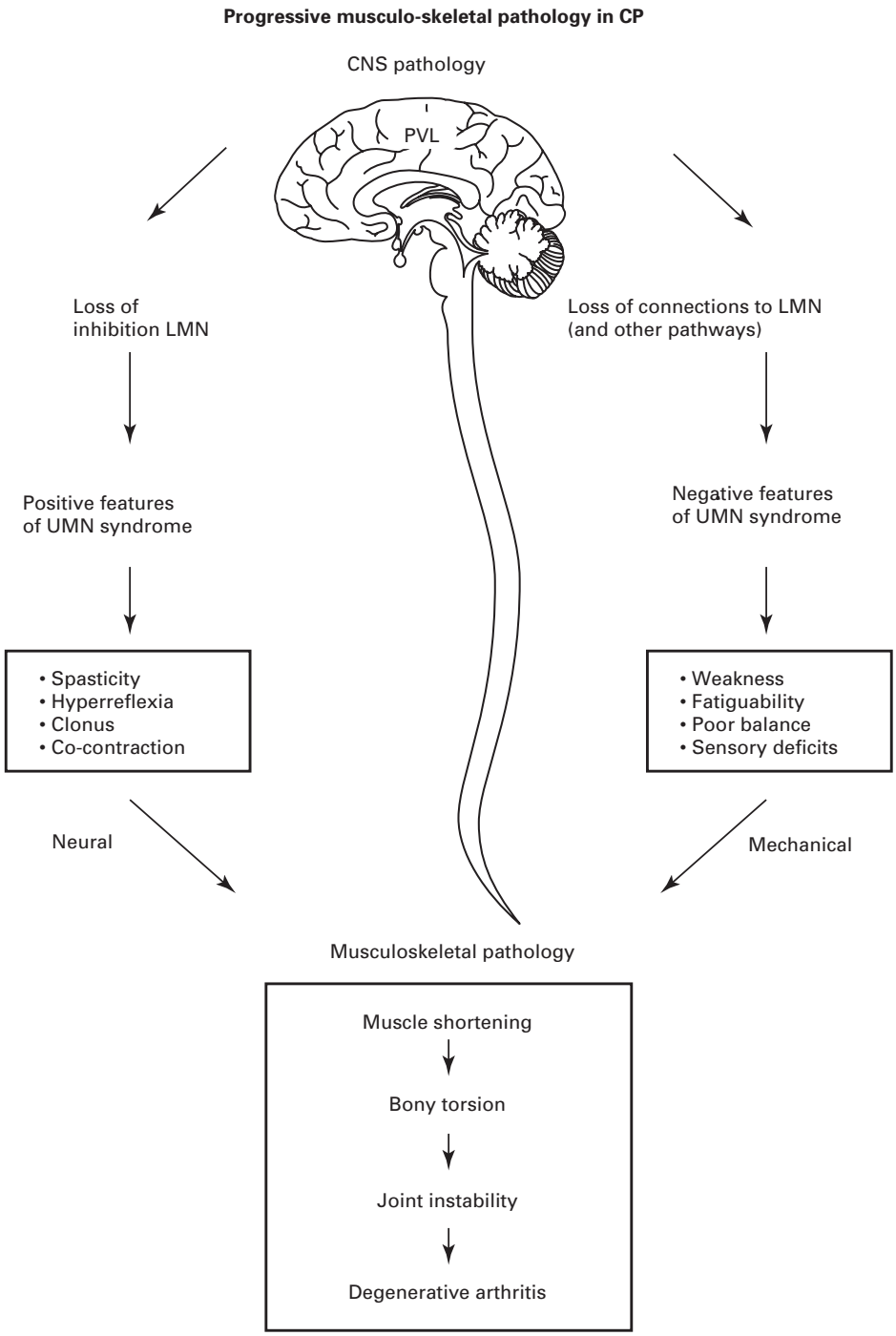

Figure 12.1. Progressive musculoskeletal pathology in cerebral palsy. (From Graham & Selber, 2003. Reproduced with permission. Copyright © British Editorial Society of Bone and Joint Surgery.)

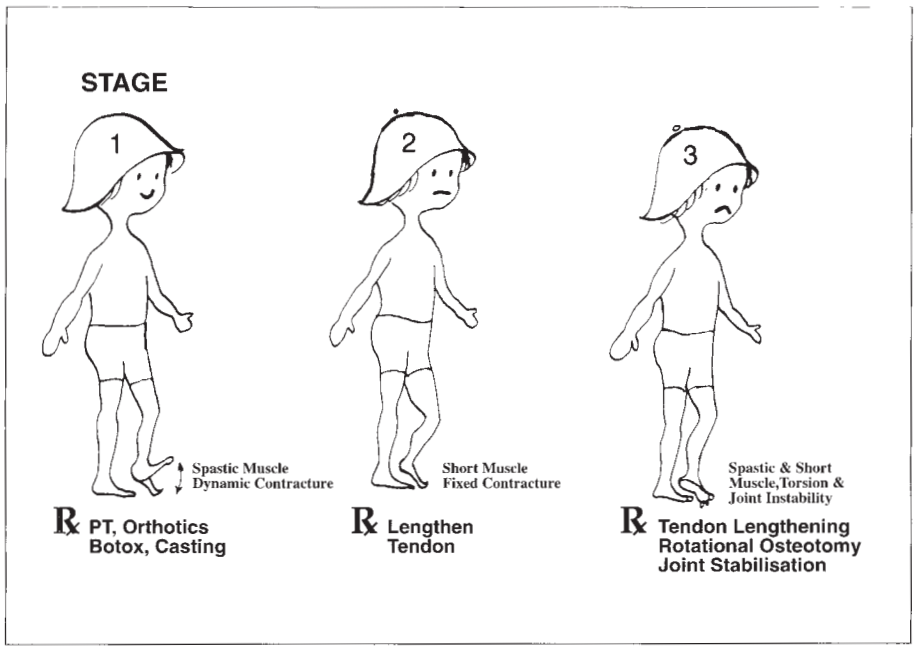

Figure 12.2. The stages of lower limb pathology in the child with cerebral palsy. (Modified after Rang, 1990.)

lead to the development of creative strategies to deal with common clinical presentations (Preiss *et al.*, 2003)(Fig. 12.3).

Measuring spasticity in children: clinical

The Ashworth scale

There are few useful clinical measures of spasticity and none validated for use in children. The Ashworth and modified Ashworth scales are blunt and unresponsive tools in the assessment of the child with cerebral palsy (Ashworth, 1964; Bohannon & Smith, 1987). Their evaluations are subjective and reliability between investigators may be a problem. Most muscles in most children are grade 1+ to grade 3. Most useful clinical responses to spasticity management are within and not across a single Ashworth grade. Of much greater utility is the measurement of dynamic joint range, which can be used across most major joints as a quantitative measure of spasticity (Tardieu *et al.*, 1954; Fosang *et al.*, 2003).

The dynamic and static joint range of motion

The range of motion of joints in both the upper and lower limbs is classically used as a proxy measure of the length of muscles crossing that joint. In the upper limb, the range of elbow extension is taken to be a measure of the length of the elbow flexors, the biceps and brachialis. Loss of elbow extension (fixed flexion deformity) is taken to mean shortening of the elbow flexors, although it should be noted that other factors such as intrinsic joint contractures must be excluded. In the lower limb, the range of dorsiflexion at the ankle is considered to be a measure of the calf muscle length. A further refinement is that the range of ankle dorsiflexion with the knee flexed is a measure of soleus length, and the range of ankle dorsiflexion with the knee extended is a measure of gastrocnemius length (Silfverskiold, 1924). This is

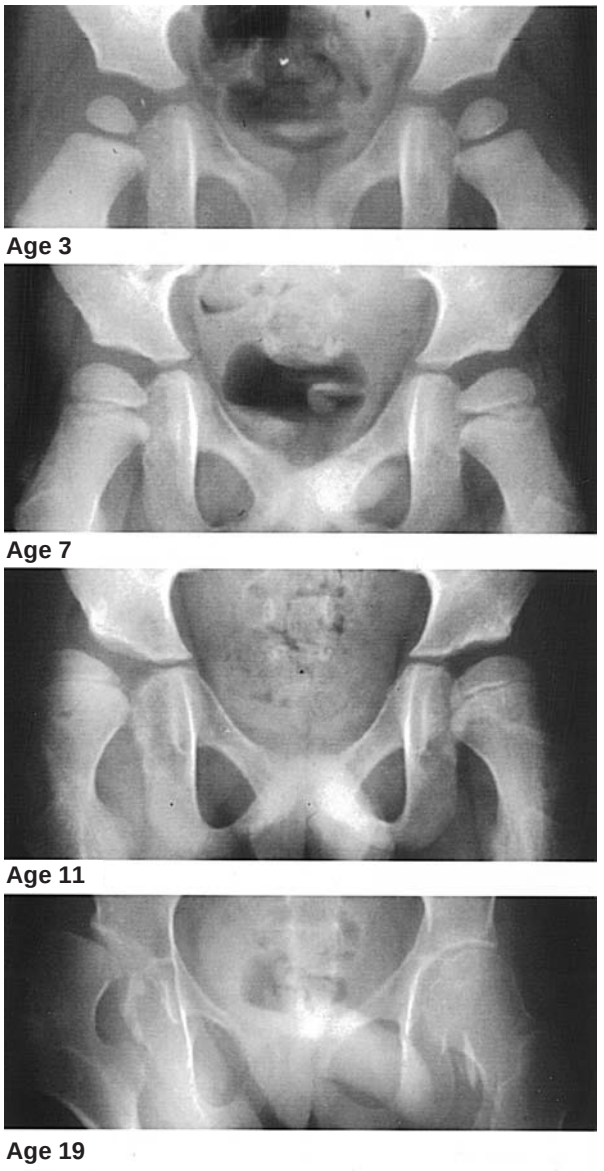

Figure 12.3. The pathology in the lower limbs in children with cerebral palsy is progressive as this sequence of hip X-rays shows. At the age of 3 the hip X-ray is normal; at age 7 there is a very mild uncovering of the right hip. At age 11 the hip is subluxed and more than 50% is outside the acetabulum. At age 19 there is painful degenerative arthritis with few management options remaining.

the basis for the Silfverskiold test, and although it may be only completely reliable under anaesthesia, it is of great value as a simple test to differentiate between gastrocnemius versus gastrocnemius and soleus contracture. Typically, in hemiplegia there is usually shortening of both the gastrocnemius and soleus but in diplegia, isolated gastrocnemius shortening is common. The criticism of the Silfverskiold test (Silfverskiold, 1924) by Perry has in our view led to an unwarranted devaluation of this most useful clinical test (Perry *et al.*, 1974, 1976, 1978).

Dynamic joint range of motion is measured by provoking a stretch reflex if it is present. Typically this first catch, or R1, comes in at a repeatable joint angular position. This is usually 20 to 50 degrees prior to R2, the static muscle length (Tardieu *et al.*, 1954). The variation is due to the proportion of the deformity, which is dynamic, and not fixed. R2 approximates to the degree of 'myostatic contracture' or fixed shortening, which may require tendon

Example 1

A 3-year-old child with spastic diplegia has an equinus gait affecting both lower limbs equally.

R1: −35 degrees (35 degrees of equinus)
R2: +5 degrees (5 degrees of dorsiflexion)
R2 − R1 = 40 degrees

Spasticity management is likely to be beneficial because there are 40 degrees of dynamic shortening to be exploited by spasticity management. Surgical lengthening of the heel cord is contraindicated because the degree of fixed contracture is so small.

Example 2

A 10-year-old boy with hemiplegia walks with an equinus gait on the affected side.

R1: − 30 degrees (30 degrees of equinus)
R2: −20 degrees (20 degrees of equinus)
R2 − R1: 10 degrees

Surgical lengthening of the Achilles tendon is indicated because R2 minus R1 = 10 degrees. This is not enough dynamic shortening for spasticity management and there would be too much residual contracture.

lengthening and R1 the degree of spasticity or dynamic shortening, which may respond to spasticity management. These simple clinical tests of R1 and R2, static and dynamic muscle length can be performed to assess the length of the adductors of the hip, the hamstrings, quadriceps and the calf muscles, some of the most important lower limb muscle groups to be affected by spasticity.

The measurement of R2 and R1 are of great practical relevance in the management of spasticity because they help to:

- Differentiate between spasticity and contracture
- Quantify the degree of spasticity present
- Select which muscles might respond to spasticity management
- Serve to monitor the response to spasticity management

Measuring spasticity in children: instrumented

Although we believe that dynamic joint range of motion is a useful clinical tool in the measurement of spasticity in children, there is a clear need for objective measurements with a greater degree of validity and repeatability. A number of techniques have been described, and although most are useful within research settings, none have become popular in clinical practice.

Measurements of muscle stiffness address the biomechanical rather than the neurophysiological components of spasticity. These measurements may also be obtained on the examination couch or during walking. Static measurements include measurements of muscle torque and resonant frequency (Walsh, 1988; Corry *et al.*, 1998; McLaughlin *et al.*, 1998). In a placebo-controlled clinical trial, resonant frequency was found to be an objective means to quantify muscle stiffness in the hemiplegic upper limb. Reductions in resonant frequency were recorded after injecting the forearm muscles with BoNT-A (Corry *et al.*, 1997).

Video recording of gait and aspects of the static couch examination are very useful in clinical practice. Utility is further enhanced by split-screen, two-dimensional recording with freeze-frame facilities (Keenan *et al.*, 2004). Careful editing and archiving of patient records is also important.

Various scoring systems or 'physician rating scales' have been devised to increase the sensitivity and objectivity of information gained from video recordings of children's gait (Koman *et al.*, 1993, 1994; Corry, 1994). Although some have been tested for repeatability, few have been tested for validity (Corry, 1994). Instrumented gait analysis, including kinematics and kinetics, provide the clinician with valuable information regarding the effects of spasticity, contractures and other manifestations of the UMN syndrome on gait (Gage *et al.*, 1995). Typical kinematic and kinetic patterns can be recognized and interpreted in the light of the patient's history and clinical examination. Instrumented gait analysis is considered by many clinicians to be essential to plan such interventions as multilevel injections of BoNT-A and selective dorsal rhizotomy. The dilemma is that only instrumented gait analysis gives valid, repeatable and accurate measures of the effects of spasticity and associated limb pathology on gait. Instrumented gait analysis is limited in clinical utility because of cost and availability. Furthermore, many of the children who may need and benefit most from spasticity management are too small and lacking in co-operation for instrumented gait analysis using current techniques.

Managing spasticity in children

In our preliminary open label study into the use of BoNT-A in the lower limbs of children with cerebral palsy, the indications were summarized as 'children with dynamic deformities which were interfering with function, in the absence of fixed, myostatic deformities' (Cosgrove *et al.*, 1994).

Although we believe that this statement remains valid, we increasingly recognize the twin difficulties in differentiating between dynamic and fixed deformities and in measuring functional outcomes in motor disabled children. Spasticity should not be treated just because it is present. The natural

history of spasticity in children is not sufficiently well known nor are our present methods of management sufficiently safe and effective to warrant such an approach. Children with severe, 'whole body' involvement frequently use spasticity in functional activities. A total extensor pattern may aid standing transfers. In this scenario, 'successful' spasticity management, if measured by reduction in tone and improved range of motion, might reduce rather than enhance function. Hence the prime goal of spasticity management must be improved function.

Understanding of motor development and methods of assessing function in children is also crucial. A major characteristic of children who have cerebral palsy is the delayed acquisition of motor skills (Rosenbaum *et al.*, 2002). Given that spasticity management must often be undertaken against a background of growth and motor development, it is clear that only controlled clinical trials can reliably separate the effects of spasticity management on function from gains made as part of normal motor development. It is relatively straightforward to demonstrate reduction in tone, improved joint range of motion and improved muscle length after spasticity management, but evidence of functional gains is much more demanding.

The Gross Motor Function Classification System (GMFCS) is the most useful tool to stratify children with cerebral palsy into five major groups (Palisano *et al.*, 1997). The Functional Mobility Scale is a useful measure of functional mobility and is sensitive to change after major interventions (Graham *et al.*, 2004). The Gross Motor Function Measure (GMFM) is the most useful validated tool to measure functional outcomes in children with cerebral palsy (Russell *et al.*, 1989; Ketalaar *et al.*, 1998; Wei *et al.*, 2006).

The best candidates for spasticity management are children who share the following features:

- Mild to moderate spasticity
- Good cognitive ability
- No fixed contractures or deformities
- Good selective motor control
- Good general health
- Stable supportive home environment
- Access to appropriate physiotherapy

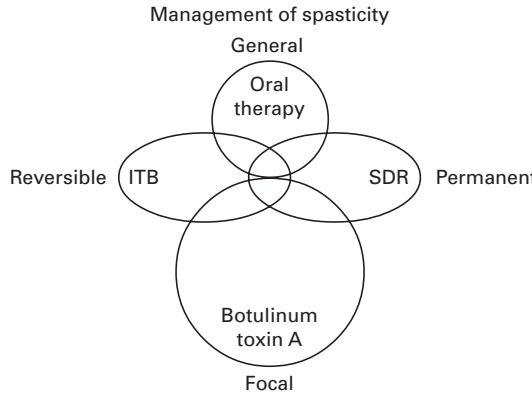

Figure 12.4. The four-way compass of spasticity management with general versus focal (north and south) and reversible versus permanent (west versus east).

- Access to appropriate orthotics

Spasticity management may fail for a variety of reasons including:

- Spasticity, too severe and generalized
- Poor cognitive ability
- Fixed deformity
- Poor selective motor control
- Associated medical disease
- Inadequate home support
- No access to appropriate physiotherapy or orthotics

Methods of spasticity management can be classified on a four-way compass (Fig. 12.4) according to whether they are focal or general in effect and as to whether the effects are permanent or temporary. Within this four-way matrix (permanent-temporary, focal-general) practical clinical guidelines may be derived. The child with acquired spasticity secondary to acquired brain injury may have a relatively short period of severe spasticity in a hemiplegic distribution. This could be managed by a program, which may include intramuscular BoNT-A to large muscle groups on the affected side including the elbow flexors, the forearm muscles and the gastrosoleus. In this scenario the focal and temporary nature of BoNT-A may be advantageous. Selective dorsal rhizotomy (SDR) would be contraindicated because it is permanent and bilateral.

A child with spastic diplegia who demonstrates lower limb spasticity may respond favorably to SDR; the permanence and generalized effects on the lower limbs may be advantageous. Multiple, repeated injections of BoNT-A would be less effective and risk systemic side effects.

The spasticity team and the spasticity clinic

Successful spasticity management in children depends as much on teamwork as it does on techniques and technology. Given that options in spasticity management in children include administration of drugs by oral and intrathecal routes, neurosurgical procedures and orthopaedic surgery, it should be self-evident that spasticity management is a multidisciplinary exercise. In many centres, the concept of a spasticity team and a spasticity clinic are well developed. At the Royal Children's Hospital in Melbourne, the members of the team are drawn from the following backgrounds:

- Physical Medicine and Rehabilitation
- Child Development and Rehabilitation
- Physiotherapy
- Occupational Therapy
- Clinical Nurse Coordinators
- Orthotics
- Neurosurgery
- Orthopaedic Surgery
- Motion Analysis Laboratory

Many children are managed successfully by individual clinicians. However, there are a sufficient number of very difficult management problems to justify a monthly spasticity clinic where the management of a small number of problem children is discussed in detail. Often investigations such as gait analysis or examination under anaesthesia are requested to aid decision making. We find the multidisciplinary discussions stimulating and the communication between specialties invaluable and management is frequently altered with benefit to our patients. The most frequent management issue is the interplay between spasticity management and orthopaedic surgery for deformity correction. Are the deformities dynamic or fixed? To resolve this common dilemma, an examination under the full relaxation of a general anaesthetic may be invaluable.

Oral medications: generalized temporary

Oral medications for the management of spasticity in children are in the temporary/generalized category of the treatment compass. The agents most frequently used are diazepam (Valium), baclofen (Lioresal) and dantrolene sodium (Dantrium). In general oral medications have a rather narrow therapeutic window between efficacy and side effects. Individual responses vary greatly, and a careful clinical trial is necessary for many children to determine the individual response/side-effect profile. The advantages and disadvantages of oral agents have recently been discussed (Ried *et al.*, 1998); see also Chapter 7).

Diazepam

Most clinicians are familiar with the role of diazepam as an anxiolytic agent. However evidence from animal work suggests that it possesses both muscle relaxant and spinal reflex blocking properties. The spinal actions of diazepam are the result of potentiation of the presynaptic inhibitory effects of GABA at $GABA_A$ receptors on spinal afferent presynaptic terminals. Central effects in the brainstem reticular formation result in sedation (Costa & Guidoffi, 1979; Young & Delwaide, 1981a; Davidoff, 1989; Blackman *et al.*, 1992). Diazepam is rapidly and almost completely absorbed following oral or rectal administration. Intravenous administration is occasionally used to gain rapid control of muscle spasms in a child who is excessively anxious and in pain after orthopaedic procedures, but there is a risk of respiratory depression, and this route is not recommended for routine use. Intramuscular injections are painful, rarely required and erratic in their absorption profile. Rectal administration is ideal when children are fasting, nauseated or unable to take medication orally. The half-life in children is shorter than in adults but still long at 18 hours. There tends to be a cumulative effect of diazepam and it may take

some time to reach the appropriate levels in body tissues and optimal clinical effect. The drug's volume of distribution is large, reflecting its extensive tissue penetration within the body. It is metabolized by the liver to pharmacologically active metabolites, including nordiazepam and oxazepam (Greenblatt *et al.*, 1980). The most common side effects are excessive sedation, respiratory depression, fatigue and ataxia. Paradoxical effects may occur, including hallucinations and increased spasticity. These must be recognized and not managed by increasing the dose.

Many children with cerebral palsy and other forms of spasticity demonstrate increased spasticity when they are anxious and especially when they are in pain. Anxiety and pain seem to interact in a vicious cycle to increase muscle tone after painful interventions such as orthopaedic surgery (Baillieu *et al.*, 1997). The central tranquilizing effects and peripheral tone-reducing effects of diazepam are extremely useful in this situation. However, this means equally that there is a very small threshold between effective reduction in spasticity and sedation, invalidating diazepam for chronic spasticity management in the vast majority of children. We use diazepam almost routinely in children with cerebral palsy who are facing painful invasive procedures, including orthopedic surgery, SDR, etc. Addiction and withdrawal symptoms are reported in patients who use diazepam in the long term (Young & Delwaide, 1981b). We have noted a 'rebound' phenomenon in children who have high doses of diazepam postoperatively if it is stopped suddenly. We routinely recommend that children be 'weaned' slowly from diazepam use after short-term/high-dose use.

Dantrolene

Dantrolene is valuable in the treatment and prevention of malignant hyperthermia (Arens & McKinnon, 1971; Waterman *et al.*, 1980). The main effect on skeletal muscle appears to be direct muscle relaxation rather than a central or a spinal level of action. Dantrolene inhibits the release of calcium from the sarcoplasmic reticulum of muscle cells (VanWinkle, 1976; Desmedt & Hainaut, 1979; Molnar & Kathirithamby, 1979). All muscles, both spastic and normal, tend to be affected, ranging from relaxation through to weakness. Dantrolene is rapidly and extensively absorbed, but there is a lack of pharmacokinetic data in children and especially in children who have spasticity (Lietman *et al.*, 1974; Young & Delwaide, 1981a; Lerman *et al.*, 1989). The utility of dantrolene has been limited by the potential for hepatotoxicity (Utili *et al.*, 1977; Wilkinson *et al.*, 1979; Chan, 1990). Fatal dantrolene-induced hepatitis has been reported in adults but not in children. In children, transaminase levels may rise, leading to a withdrawal of therapy. Liver function should be assessed prior to starting dantrolene therapy and at frequent intervals thereafter (Ried *et al.*, 1998).

A number of studies have been reviewed by Blackman and colleagues, who note that the numbers of patients within the published files are small and the outcome measures not particularly objective (Blackman *et al.*, 1992). However, most studies do report that in comparison with placebo, dantrolene has a positive effect in reducing muscle tone but not necessarily in improving function.

Tizanidine

Tizanidine is a benzothiodozol derivative of clonidine and acts centrally as an alpha-2-adrenergic agent. It may reduce spasticity by decreasing the release of excitatory neurotransmitters from afferent terminals and interneurones (Albright & Neville, 2000). Experience in children is limited and use is limited by sedation.

Baclofen

Baclofen was introduced in the mid-1970s and appears to act as a GABA agonist on the $GABA_B$ receptors (Rice, 1987). Baclofen inhibits transmitter release by competitive inhibition of excitatory neurotransmitters at the spinal level. There may be actions in the spinal cord or more centrally which are not yet fully described or understood (Pedersen *et al.*, 1974; Calta & Santomauro, 1976; Milla & Jackson, 1977; McKinlay *et al.*, 1980; Young & Delwaide, 1981a; Dolphin & Scott, 1986; Fromm & Terrence,

1987). Pharmacokinetic data in respect of baclofen children are lacking. Although baclofen is rapidly absorbed after oral administration, levels in the cerebrospinal fluid (CSF) are low because of its low lipid solubility and 30% binding to plasma proteins. This limits its transport across the blood–brain barrier (Knutson *et al.*, 1974; Gilman *et al.*, 1990). It can be administered orally or intrathecally but not parenterally. The response to baclofen in children varies widely (Milla & Jackson, 1977). In general the threshold between effective reduction in spasticity or muscle tone and side effects such as dizziness, weakness and fatigue is rather small. However, individual children can respond well, and a careful trial of various dose levels is worthwhile, although the majority will have their medication discontinued because of side effects. Hallucinations and seizures may occur with abrupt withdrawal of baclofen; therefore, as with diazepam, children who have become habituated to larger doses should be weaned off the drug slowly. A double-blind crossover trial of oral baclofen administration in children documented a decrease in spasticity with little change in functional abilities, such as ambulation and the performance of activities of daily living (ADLs)(Milla & Jackson, 1977; Molnar & Kathirithamby, 1979).

Much interest has been raised by the intrathecal administration of baclofen (Knutson *et al.*, 1974; Penn & Kroin, 1985). Using this technique, the low lipid solubility and binding to plasma proteins is avoided by administration of the drug directly to the target tissues. As will be seen in a later section, this introduces a new 'risk–benefit' profile with specific advantages and disadvantages.

Casting and orthoses: temporary/focal

The use of casting and orthoses can be classified as focal/temporary. Casting, orthoses, neurolytic injections and physiotherapy are often used in various combinations to manage spasticity in younger children with cerebral palsy (see also Chapter 6). The efficacy and duration of casting are related to the proportions of dynamic and fixed contracture before treatment and the responsiveness to the connective tissue to stretching forces. Many clinicians combine casting with intramuscular injections of botulinum toxin. It is still unclear as to whether the combined effect of injection and casting may be better than either intervention on its own (Boyd & Graham, 1997; Corry *et al.*, 1997; Booth *et al.*, 2004; Kay *et al.*, 2004); however, the evidence remains anecdotal.

Spasticity of the gastrosoleus, resulting in dynamic equinus, is usually treated by serial below-knee casting for periods of 1 to 4 weeks. Given the very widespread utilization of the technique by physiotherapists, there have been few outcome studies (Corry *et al.*, 1998; Brouwer *et al.*, 2000). In a randomized clinical trial, Corry and colleagues compared serial casting with injection of botulinum toxin in the management of dynamic equinus in children with cerebral palsy. They concluded that both interventions were effective but that the effects of botulinum toxin lasted longer (Corry *et al.*, 1998). Flett *et al.* (1999) reported the inconvenience of casting and child and family preference for botulinum toxin over serial casting.

Orthoses such as the ankle-foot orthosis (AFO) are widely used in the management of younger children who have calf spasticity. The effects of AFOs are difficult to study in younger children, but there are definite biomechanical benefits, confirmed by motion analysis (Rose *et al.*, 1991; Ounpuu *et al.*, 1993).

Intramuscular injections: chemoneurolysis: temporary/focal

Intramuscular injections are focal in nature. The duration depends on the agent, the concentration used and the site of injection. 'Chemoneurolysis' refers to a nerve block resulting in impaired neuromuscular conduction by the destruction of neural tissue, either temporarily or permanently (see Chapter 8). Injection can be performed at many levels in the peripheral nervous system from nerve root to motor end plate (Glenn, 1990). The more proximal the injection site, the more general and prolonged the effect. Sciatic nerve block results in a variable degree of weakness of all of the muscles supplied by the sciatic nerve in the distal thigh and leg. Injection of the gastrocnemius muscle affects small local

motor nerves and for this reason is classified as a motor point block (Bakheit *et al.*, 1996).

Local anesthetic blocks are used for a short-term effect, usually as a diagnostic test rather than for therapeutic effects. The duration can be varied according to the agent used (e.g. lignocaine, bupivicaine).

Alcohol and phenol have been used for many years and are both cheap and easily available. Phenol denatures proteins in the myelin sheath and is capable of destroying axons of all sizes (Fischer *et al.*, 1970; Felsenthal, 1974; Beckerman, *et al.*, 1996). Application is either direct to the nerve at the time of surgery or by electrical stimulation to localize the optimum injection site. This can be at the level of the peripheral nerve (Khalili & Benton, 1966; Spira, 1971; Petrillo *et al.*, 1980), the large motor branch (Easton *et al.*, 1979; Carpenter, 1983) or the end plate (DeLateur, 1972). The younger child tolerates this localization technique poorly and an anaesthetic is often required (Griffiths & Melampy, 1977). High concentrations of both agents may cause severe pain at the site of injection, dysaesthesia and tissue necrosis (Easton *et al.*, 1979; Petrillo *et al.*, 1980). For this reason, pure motor nerves are better targets for these agents than mixed motor and sensory nerves. We use phenol injections for the management of adductor spasticity by injecting the obturator nerve. In the hemiplegic upper limb, injection of the musculocutaneous nerve can be useful in the management of elbow flexor spasticity. Although both the obturator and musculocutaneous nerves have a small sensory component, dysaesthesias are rarely a problem.

These type of blocks produce muscular relaxation in the target area, providing a 'window of opportunity' for a focused programme of splinting, casting, gait training and strengthening of antagonist muscles. Children with mild spasticity do better than those with more severe spasticity.

With the introduction of BoNT-A, injections of phenol and alcohol have largely been superseded, especially when injection of a mixed sensory and motor nerve would pose a risk of painful dysaesthesias (e.g. sciatic nerve, posterior tibial nerve and median nerve). They can, however, be used in conjunction with BoNT-A allowing a larger number of neuromuscular units to be treated once the maximum dosage of BoNT-A is met.

Peripheral neurectomy: permanent/focal

Peripheral nerve surgery has a limited role in spasticity management. It can be classified as permanent/focal therapy. It is most widely used in the management of adductor spasticity and hip subluxation by neurectomy of the anterior branch of the obturator nerve, usually in conjunction with open adductor release. Children who exhibit spastic cerebral palsy in a quadriplegic or 'whole-body' pattern of involvement have a very high incidence of adductor spasticity and hip migration (Soo *et al.*, 2006)

Careful assessment of these children is necessary to determine the contribution of contractures of the adductor muscles as opposed to spasticity of these muscles. This assessment requires serial radiological examinations of the hips, to determine 'at risk' signs, as well as clinical examination, both in the clinic and under the relaxation afforded by a general anesthetic (Scrutton & Baird, 1997). The most appropriate management can then be selected. This includes various focal spasticity treatments and abduction bracing in early cases and surgery for more advanced cases when they manifest hip subluxation. The benefits of lengthening of the contracted adductor muscles can be enhanced by selective use of phenolisation of the obturator nerve. The role of obturator neurectomy is controversial. Its indiscriminate use can undoubtedly lead to poor outcomes, including the reverse deformity (abduction contracture), windswept hips and excessive weakening. It should not be employed in the ambulant child. When there is uncertainty regarding the indication for obturator neurectomy, a reasonable simulation can be achieved by the injection of BoNT-A or phenol neurolysis.

Selective dorsal rhizotomy: permanent/generalized

Selective dorsal rhizotomy (SDR) (see Chapter 11) is a neurosurgical procedure in which a percentage of the dorsal rootlets, which make up the roots of the lumbosacral plexus, are divided to reduce spasticity

in the lower limbs. SDR interrupts the reflex arc by selective ablation of sensory nerves that return the reflex arc to the spinal cord. This is a permanent procedure with selectivity for the lower limbs (Peacock & Arens, 1982). Some reduction in spasticity and occasionally improved function has been reported in the upper limbs after SDR by a mechanism, which has neither been fully investigated nor satisfactorily explained (Oppenheim *et al.*, 1992).

SDR has a long and interesting history but can be considered to have been refined and introduced as a reliable procedure in present spasticity management by the South African group, especially Warwick Peacock, the neurosurgeon responsible for refining the procedure (Peacock & Arens, 1982; Peacock *et al.*, 1987; Peacock & Standt, 1990).

The ideal candidate for SDR is a child with moderately severe spastic diplegia, good cognitive abilities, no fixed contractures, good underlying muscle strength and good voluntary muscle control. Contraindications include dystonia, weakness and previous muscle-tendon lengthening surgery. The optimum age is between 4 and 8 years (i.e. old enough to participate in a rigorous rehabilitation program and young enough not to have fixed deformities).

The key features of a successful SDR program would appear to include the following:

1. Multidisciplinary approach to patient selection
2. Availability of motion analysis for selection and monitoring outcome
3. Precise surgical program and intraoperative monitoring
4. Rehabilitation program

Expected outcomes include permanently reduced muscle tone, reduced co-contraction, improved joint range of motion and reduction of dynamic deformities. There is convincing evidence for improvements in gait using kinematics, electromyography and energy studies. Three randomized clinical trials of SDR compared to physiotherapy have been published, with variable outcomes (Steinbok *et al.*, 1997; McLaughlin *et al.*, 1998; Wright *et al.*, 1998). A meta-analysis of the three trials confirmed a marked reduction in spasticity and a small but significant gain in physical function according to the GMFM (McLaughlin *et al.*, 2002).

The relationship between SDR and deformities is of great significance (Oppenheim, 1990). Fixed contractures and bony torsional problems are unaffected by SDR and require corrective orthopedic surgery. Intuitively, SDR should be performed before the development of contractures and bony torsion for two reasons. First, children with mainly dynamic deformities may benefit most and SDR may prevent the progression of deformity, although no study has confirmed this (Vaughan *et al.*, 1988, 1991; Arens *et al.*, 1989). Unfortunately, some deformities may be caused or may progress more rapidly after SDR, including spinal deformity (lumbar lordosis, scoliosis), hip subluxation and foot deformities (Johnson *et al.*, 2004, Spiegel *et al.*, 2004; Lundkvist *et al.*, 2006).

The longer-term effects of SDR are not clearly known. Although there are several good short- to medium-term outcome studies with objective measures, too few children have been followed through the adolescent growth spurt to skeletal maturity (Cahan *et al.*, 1989; Perry *et al.*, 1989; Peacock & Standt, 1991; Vaughan *et al.*, 1991). In children with cerebral palsy, the adolescent growth spurt may pose a great challenge. Deformities may increase and become more fixed, function may deteriorate and borderline ambulators may opt for wheelchair mobility. Residual weakness of large antigravity muscles and sensory impairment post rhizotomy may add to this already challenging natural history.

Intrathecal baclofen (ITB): semipermanent/generalized

There has been a substantial experience with the use of baclofen as an oral medication in spasticity management, but the narrow therapeutic window between efficacy and side effects has limited its clinical utility. Delivering baclofen to the target tissue directly avoids this conflict (Penn & Kroin, 1985; Coffey *et al.*, 1993). Using a programmable implanted pump, baclofen can be delivered intrathecally (see Chapter 10). The delivery of a relatively high concentration of the drug to the lower motor neurons can be achieved, avoiding systemic side effects (Knutson *et al.*, 1974; Dralle *et al.*, 1985; Muller, 1992;

Kroin *et al.*, 1993). The requirement of a delivery system places ITB therapy in the semipermanent category. The pump has to be refilled every 2 to 3 months and replaced when the battery runs out, after 4 to 6 years. The programmable pump offering considerable flexibility in dose control and the ability to modulate the clinical effects (Albright, 1996). The drug acts mainly on the lower limbs, but there is some spread within the intrathecal space and there can be beneficial effects on the upper limbs (Zieglgansberer *et al.*, 1988; Muller, 1992; Albright *et al.*, 1993). As the pumps become smaller and more reliable, younger children can be offered this spasticity management option, although the costs of ITB are a major disadvantage and are limiting clinical trials and patient access (Albright, 1996).

There is very good evidence for efficacy in terms of short-term measures such as tone reduction and improved joint range of motion (Penn, 1992; Albright *et al.*, 1993). Functional improvements can be achieved, particularly in those patients with a large element of dystonia (Albright *et al.*, 2001; Van Schaeybroeck *et al.*, 2000; Lazorthes, 2006). Murphy *et al.* reported a consecutive case series of 25 ITB pumps with effective spasticity reduction and a high incidence of wound complications, leading to pump removal. Albright *et al.* reported a large prospective multicentre study of 68 patients with ITB pumps. The majority were under 18 years of age and had spasticity of cerebral origin. They reported effective long-term reduction in spasticity, with an acceptable incidence of adverse events and complications. Long-term studies comparing SDR to ITB and combined spasticity-orthopaedic procedures would be valuable but difficult to conduct (Flett & Graham, 2006).

Botulinum toxin A (BoNT-A): focal/temporary

BoNT-A is a reversible, focal agent which has been under evaluation since the early 1990s in the management of spasticity in children (Cosgrove *et al.*, 1994; Koman *et al.*, 1994, 1996; Corry *et al.*, 1995, 1998). The toxin was first identified as the causative factor in some forms of food poisoning and then investigated as a potential biological weapon. The first therapeutic applications were in the management of strabismus and focal dystonias, including blepharospasm, spasmodic torticollis and hemifacial spasm (Scott, 1980; Scott *et al.*, 1990; Jankovic & Brin, 1991). In these early indications the target muscles were small skeletal muscles and both the clinical and economic profile of BoNT-A is more suited to these applications than to the management of spasticity in large skeletal muscles (see Chapter 9 for further discussion).

However, the focal and temporary nature of BoNT-A permit exploitation in spasticity management in a manner for which no other agent is available (Graham, 1995; O'Brien, 1995). In children with cerebral palsy there is a need for a minimally invasive method of spasticity management that can be targeted to specific muscles and the effects varied by dose levels. BoNT-A meets a least some of these requirements (American Academy of Neurology, 1990; NIH Consensus Development Conference, 1990; O'Brien, 1995).

The pharmacology and pharmacokinetics of BoNT-A is covered in Chapter 9. There is no important pharmacological difference in the effects of BoNT-A in different muscles or in different conditions but there can be very different clinical effects and priorities.

Children with cerebral palsy rarely have deformities at birth; most are acquired during growth, especially during periods of rapid growth (Rang, 1990). Although orthopaedic surgery is the mainstay of deformity correction in older children, corrective surgery in the younger child is unpredictable and should be avoided whenever possible. The obvious exception to this principle is surgery to prevent spastic hip dislocation.

Since 1992 we have investigated a possible role for the use of BoNT-A in children with cerebral palsy (Fig. 12.5). Our first study was a randomized controlled trial (RCT) in an animal model, the hereditary spastic mouse (Cosgrove & Graham, 1994). This strain of mice has a neurotransmitter deficiency, which is inherited in an autosomal recessive fashion and has a number of features that mimic cerebral

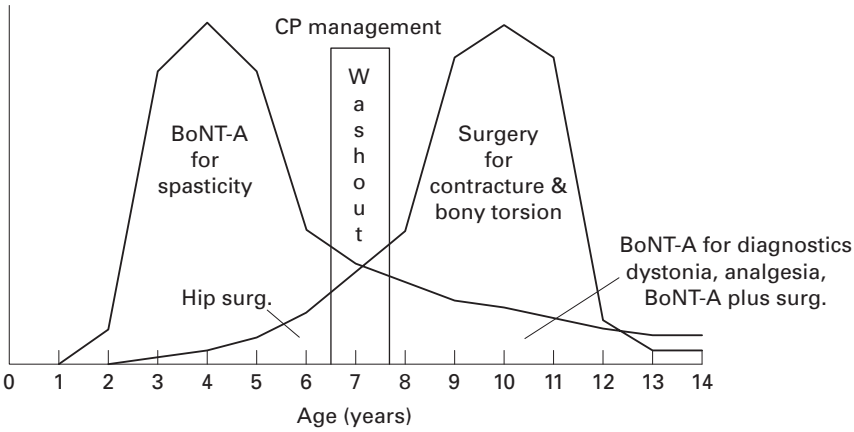

Figure 12.5. The approximate time line for the use of BoNT-A as an agent for spasticity management in the lower limb, in children with cerebral palsy. Surgery is reserved for older children. On the horizontal axis is the age in years. Note that the only early surgery is hip surgery to prevent dislocation when there are clinical and X-ray signs of the hips being 'at risk'. We reserve the use of botulinum toxin for younger children peaking at age 4. Surgery for fixed contractures and bony torsional problems is used in the age 8 to 12 years with a decreasing use in this age group of botulinum toxin for diagnostic purposes, postoperative analgesia and in the management of dystonia.

palsy. This model had been previously studied by Ziv and Rang, who described the failure of longitudinal muscle growth in affected mice leading to musculotendinous contractures (Ziv *et al.*, 1984).

We investigated muscle and tendon growth in a RCT in which the calf muscle was injected on day 6 of life with BoNT-A or normal saline. In summary, spastic mice injected with saline developed contractures in comparison with their normal littermates, but those injected with BoNT-A did not. This seemed to confirm the Ziv and Rang hypothesis of muscle growth inhibition by spasticity and suggested a preventative role from BoNT-A.

Our first clinical trial was of necessity an 'open label' uncontrolled study (Cosgrove & Graham, 1994). No information was available at that time regarding dose, method of administration, frequency of injection, outcomes or side effects. In effect, each injection was approached as an individual clinical trial. In order to reduce the risk to individual children and to gain the maximum information, we admitted each child to hospital for 3 to 5 days, during which objective measurements including gait analysis were performed. We quickly learned to titrate the dose to achieve our desired effect and developed practical injection techniques for the principal target muscles in both the upper and lower limbs (Couper-Brash, 1955; Corry *et al.*, 1997; Cosgrove *et al.*, 1994). We used simple tests to confirm needle placement in target muscles, including manual palpation, freehand needle placement and confirmation by moving the distal joint through a range of motion prior to connecting the syringe containing the toxin. We used a short general anesthetic (GA) in this first study and continue to use GA much more than other groups. Using GA has a number of important advantages, which may go some way to explain differences in the outcomes we have achieved and reported in comparison with other groups. Firstly, GA provides the definitive method of distinguishing dynamic from fixed contractures. Sometimes we remain in doubt until the child is fully relaxed under GA and we are prepared to cancel the injection, advise supplementary casting or proceed to surgery according to the clinical findings under GA (Graham, 1995; Boyd & Graham, 1997). It is pointless to proceed with injecting a contracted muscle. Secondly, the control afforded by GA permits us to inject target muscles

in an accurate relaxed manner using multiple injection sites. Multiple injection sites are probably safer and possibly more effective than fewer sites. Typically we inject four sites in the calf and two sites in the adductors and hamstrings. Although it is reasonable easy to target the calf under sedation/LA, the same cannot be said for the adductors and hamstrings. In the diplegic child who is receiving multiple injections in multiple muscles, we believe that GA is mandatory. We now use muscle stimulation for all target muscles except the gastrosoleus. We made this change to our practice following a trial in which we demonstrated alarming degrees of inaccurate needle placement using palpation and distal joint movement (Chin *et al.*, 2005).

The conclusions from our first clinical trial were that large doses of BoNT-A in children were safe and that reduction in tone was reasonably predictable but short lived. Some improvements in the kinematics of gait were noted and, in some children, these improvements persisted after the pharmacological effects of toxin would have been expected to wear off. Function was assessed crudely by the Hoffer classification of ambulatory status (Hoffer *et al.*, 1973) and was noted to improve in some children. No matter which outcome parameter we studied, there was an exponential decrease in benefit with age (i.e. older children responded less well than did younger children). This observation confirmed our clinical impression that the primary cause of clinical unresponsiveness was fixed contracture, which becomes increasingly prevalent as the children become older. This study raised more questions than it answered but provided a reasonable basis for our second phase of investigation, three controlled clinical trials.

RCT 1: hemiplegic upper limb

We felt very strongly that BoNT-A should be investigated in a placebo-controlled trial, and we selected the hemiplegic upper limb. Many of the parents of children who had received lower limb spasticity management asked for upper limb treatment in addition. These were mostly older children with spastic hemiplegia who could cooperate with injection under local anesthesia or sedation. This was at a time when most of our multiple lower limb injections were performed under general anesthesia, precluding randomization to receive placebo. The aims of the study were to determine if the effects of BoNT-A were consistent in an RCT/placebo-controlled environment by both subjective and objective means (Corry *et al.*, 1997). The subjective assessment was obtained by canvassing the opinion of the parents and therapist as to whether the child's condition after injection was improved/unchanged/worse after injection compared to pre-injection status. The results were very positive; the effects of BoNT-A in producing relaxation of spastic upper limb were easily and consistently recognized.

We also introduced an objective means of measuring muscle stiffness by using resonant frequency by a modification of the method and techniques described by Walsh (1988). The resonant frequency of the forearm muscle in the hemiplegic upper limb was significantly greater than that in the normal limb. This increased resonant frequency, reflecting increased stiffness, was significantly decreased by injection of BoNT-A.

Functional outcomes were equivocal. Improvements in range of motion were sometimes offset by decreased grip strength. As with other interventions in the upper limb, the improvements in cosmesis, related to decreased hemiplegic posturing, were more appreciated by our patients than the functional gains achieved. Two high-quality upper limb RCTs have been published since then, confirming significant functional improvements using validated measures of upper limb function (Fehlings *et al.*, 2000; Lowe *et al.*, 2006).

There is much more work to be done in the upper limb, including combining BoNT-A injection with surgery and exploiting the muscular relaxation achieved by BoNT-A with targeted splinting and therapy programs. Not all muscles make the transition from dynamic to fixed contacture at the same speed. In the hemiplegic upper limb, the pronator teres is almost always the first muscle to develop a contracture, and this can be a principal cause of failure after BoNT-A injection. In the younger child, we combine

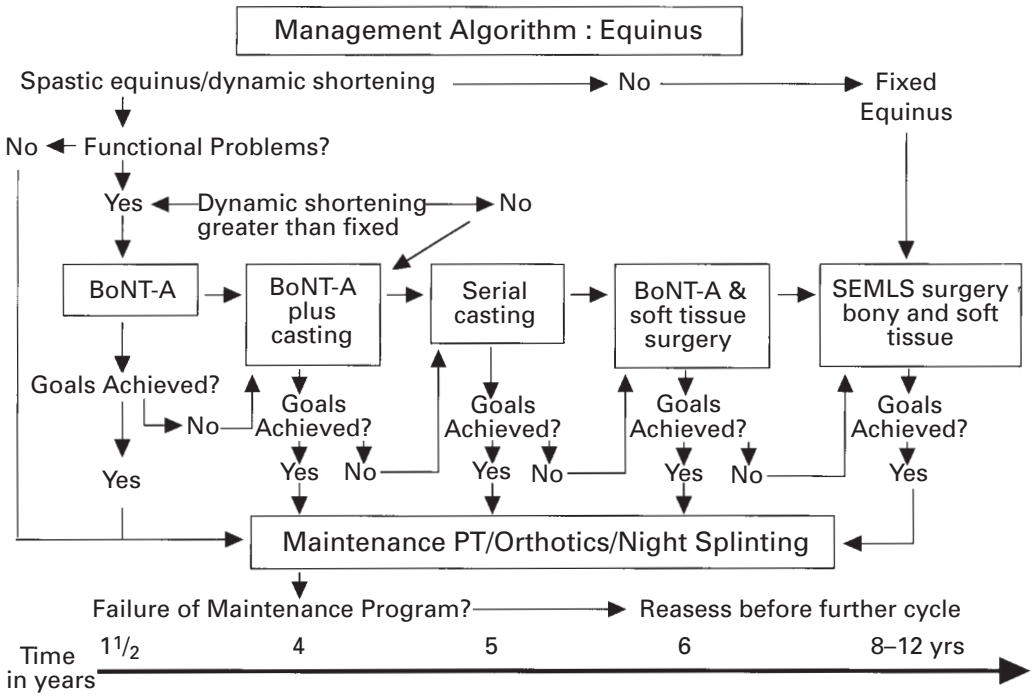

Figure 12.6. A 'stepped' approach to the management of equinus in the child with cerebral palsy commencing with botulinum toxin injections to the gastrosoleus for the younger child with a purely dynamic problem. It progresses through botulinum toxin plus casting, serial casting or toxin plus limited surgery. Finally there is multilevel surgery for those children who require it before the age of 8 and 12 years. (© R. N. Boyd, H. K. Graham.)

release or rerouting of pronator teres with BoNT-A injections to the wrist and finger flexors. Other uses of BoNT-A in the hemiplegic upper limb include pain relief and protection of upper limb tendon transfers from post-operative spasm.

RCT 2: BoNT-A vs casting for dynamic equinus

In this study we compared the effects of BoNT-A and casting in the management of dynamic equinus (Fig. 12.6) in a group of younger children with cerebral palsy (Corry *et al.*, 1998). Casting is a popular management option for the younger child who exhibits dynamic equinus, but despite its popularity and widespread utilization, there are few studies with objective outcome measures, and there were no clinical trials that have demonstrated efficacy. The entry criterion for our study was 'the intention to treat dynamic equinus'. Children were then randomized to receive serial casting or BoNT-A. Outcome measures included clinical measures and gait analysis. Younger, less cooperative children had a two-dimensional video recording of gait, and from this the Physician Rating Scale was applied by experienced observers blinded to the form of treatment. Older, more cooperative children had instrumented gait analysis, concentrating on sagittal plane kinematics.

Both interventions were equally effective in terms of correcting equinus gait, but the effects of BoNT-A were more prolonged. Given that both interventions were comparable in terms of cost, BoNT-A was at least as cost effective as casting and was preferred by the majority of parents. A longer-term study is

required to address cost–benefit issues more rigorously.

Similar results have been obtained recently by Flett and colleagues. They performed a prospective, randomized, single-blind controlled study comparing BoNT-A injections with fixed plaster cast stretching in the management of dynamic calf tightness. They concluded that BoNT-A injections were of similar efficacy to serial fixed plaster casting in improving calf tightness in ambulant or partially ambulant children with cerebral palsy. It was also noted that parents consistently favoured BoNT-A, highlighting the inconvenience of serial casting (Flett *et al.*, 1999). Houltram *et al.* (2001) analyzed the cost–benefit of BoNT-A compared to serial casting in the Corry and Flett trials and concluded that BoNT-A was associated with only a modest increase in costs and was the preferred treatment by the majority of families.

RCT 3: hamstring injection

In this trial children with flexed knee gait were managed by injections of BoNT-A to the hamstrings (Cosgrove *et al.*, 1994; Corry *et al.*, 1999). Children were randomly assigned to immediate injection or injection after a period of observation. The main outcome measures were kinematics and energy studies. The results were inconclusive. Popliteal angle measurements showed significant reductions, but only some of the patients had improvements in their gait. Some of the patients who had a good correction of crouch gait also had reduced energy expenditure. Our conclusions were that individual improvements were worthwhile for some children, but selection needed to be more rigorous and injections of other levels needed to be considered.

BoNT-A doses in children

In large skeletal muscles (calf, hamstrings, adductors) predictable responses occur at about 4 Botox units/kg, especially if the dose is spread over multiple sites. Some responses are seen at 2 Botox units/kg, but these are neither so predictable nor long lasting. It is rarely beneficial to exceed 6 Botox units/kg. A muscle that does not respond at a dose of 6 Botox units/kg will usually have a fixed contracture.

We previously used a standard dilution of 100 units of the Allergan preparation 'Botox' in 1 ml of normal saline. However, we now prefer a greater dilution, 100 Botox units in 4 ml of normal saline for all large muscle groups. This has been associated with increased efficacy and no appreciable increase in adverse events. We use the 100 Botox units in 1 ml dilution in the hemiplegic upper limb, where target muscles are long and thin and in close proximity to one another.

Allergan is the manufacturer of the U.S. product Botox®. The British product, Dysport®, and Botox®, are not of equivalent dosage. Care must be taken in following the dosage guidelines of clinical papers.

We follow empirical guidelines established by trial and error in toxin administration including the following:

Maximum dose at one site, 50 Botox units
Maximum dose per muscle, 6 Botox units/kg
Maximum dose per child, 12 Botox units/kg or 300 Botox units, whichever is lower (Graham *et al.*, 2000)

A muscle will respond to BoNT-A at a dose of 4 Botox units/kg if there is more than a 30-degree difference between R2 and R1 (i.e. more spasticity than contracture). This does not mean, however, that the child will automatically benefit in terms of achieving the desired functional goal.

Management of equinus can be simple or remarkably difficult. In younger children with hemiplegia, assessment of equinus is straightforward and management planning similarly simple. Dynamic equinus deformity will usually respond well to BoNT-A. If the response is incomplete, a short period of casting will usually help achieve the required correction, which can then be sustained by the use of an AFO and physiotherapy (Rodda & Graham, 2001).

In diplegia the situation is often much more complicated. The easiest scenario is a bilateral, symmetrical equinus gait with little proximal involvement. This can be managed in a similar manner to hemiplegia.

However, when there is proximal spasticity and hip and knee flexion as well as equinus, good judgement and a sound appreciation of biomechanics is required to plan logical and effective management. We find that many clinicians treat all equinus by calf injection, forgetting that 'apparent equinus' secondary to hamstring and/or psoas spasticity is very common in diplegia (Rodda *et al.*, 2004). If the equinus is secondary to hamstring spasticity, calf injection may achieve 'foot flat' and apparent correction, but at the high cost of increased 'crouch' gait. A better strategy may be to inject the psoas and hamstrings and use AFOs. The Leuven group have pioneered multilevel injections of BoNT-A in spastic diplegia and have achieved quite remarkable results (Molenaers *et al.*, 2001). They emphasize instrumented gait analysis to identify gait deviations and selection of target muscles. In addition, they employ a rigorous casting, orthotic and physiotherapy-rehabilitation approach to maximize the benefit (Molenaers *et al.*, 2006).

We do not advocate or practice long-term spasticity management with BoNT-A in children with cerebral palsy. Neither safety nor efficacy has been established. Given that the principal deficit in cerebral palsy is weakness, legitimate concerns have recently been raised about the use of an agent that further weakens muscle (Gough *et al.*, 2005).

We use BoNT-A for the younger child as part of a management plan that includes physiotherapy and the use of orthotics with a view to definitive surgical correction at the age of 6 to 12 years (Rodda & Graham, 2006). The use of BoNT-A in the younger child appears to have the following advantages:

- Improved motor function
- Reduced dynamic deformity
- Delayed progress to fixed deformity
- Later age at first surgery
- Less repeat surgery
- Simplified surgery

The use of BoNT-A in other forms of childhood spasticity is less well defined than in cerebral palsy. There do not appear to be any intrinsic differences between the responses of large skeletal muscles to BoNT-A in relation to the underlying cause of the spasticity, but the natural history of the spasticity is of great importance. BoNT-A has been of great value in the management of spasticity secondary to acquired brain injury, cerebrovascular accident and following surgery for arteriovenous malformation or tumour. BoNT-A is more applicable to short- or medium-term spasticity management in a restricted number of target muscles. Severe, generalized, long-term spasticity should be managed by other means.

Finally, an emerging application for the use of BoNT-A is in the management of pain associated with muscle spasm (Fig. 12.7). Soft tissue injury and surgery in children who have spastic cerebral palsy can be associated with disproportionately severe and prolonged pain. Relatively minor orthopaedic procedures such as adductor release surgery can be overshadowed by inadequate pain control. Musculoskeletal pain in spastic cerebral palsy responds poorly to standard analgesic regimens. Narcotic analgesics even in large doses seem to leave painful spasms untouched but are associated with side effects including nausea, vomiting and constipation.

We observed that when injections of BoNT-A were combined with orthopaedic surgery, children appeared to have a significant reduction in their pain, spasms and analgesic requirements (Baillieu *et al.*, 1997). We decided to investigate this further in a double-blind, randomized, placebo-controlled trial. We chose to investigate pain and analgesic requirements after adductor releases in children with cerebral palsy who had both clinical and radiological evidence of hip subluxation. When the decision to perform adductor surgery had been reached, the children were randomly allocated to have an injection of BoNT-A at a dose of 4 Botox units/kg to each adductor muscle group, or normal saline of an equal volume. Injections were performed in the outpatient department between 5 and 10 days before the scheduled date of surgery. All aspects of the perioperative care were standardized. Postoperative pain and analgesic consumption was carefully monitored. When the code was broken, it became evident that children who had received botulinum toxin chemodenervation prior to surgery had lower pain scores, reduced

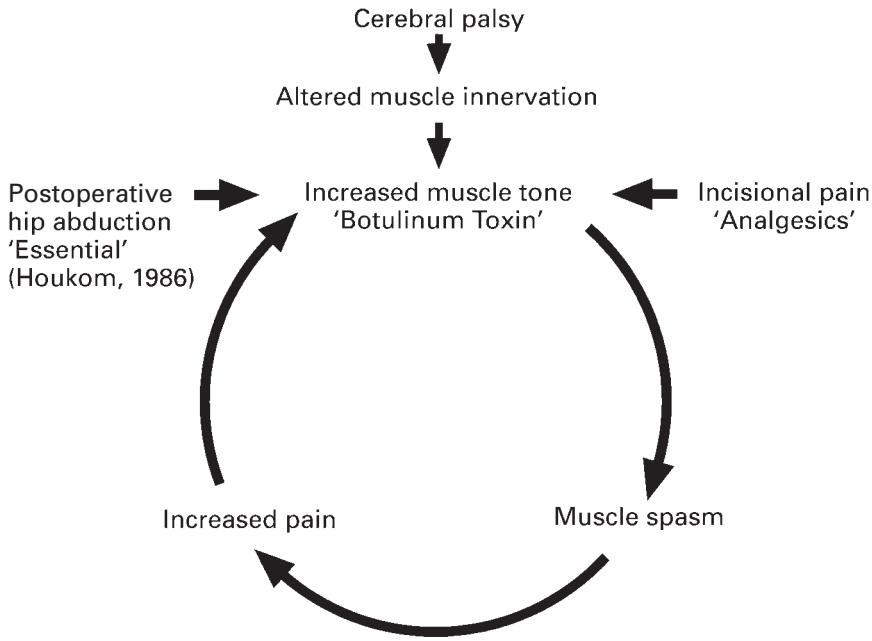

Figure 12.7. The pain/spasm vicious circle in the child with cerebral palsy after hip-release surgery. Muscle tone increases postoperatively because of the combination of incisional pain and postoperative hip abduction in plasters or splints. The incisional pain is managed by a various combination of analgesics and the hip abduction is considered to be essential. The cycle of spasm increasing pain which produces further spasms can be broken by preoperative chemodenervation by intramuscular adductor injection of BoNT-A.

analgesic consumption and earlier discharge from hospital than those in the placebo group. We feel that these findings confirmed our hypothesis that BoNT-A would break the postoperative cycle of pain and spasm. There are potentially many other applications for the use of BoNT-A in the perioperative period, including tendon transfers in the upper limb and tendon lengthenings and transfers in the lower limb.

Orthopaedic surgery

Orthopaedic surgery for children with spasticity due to cerebral palsy can be conveniently classified as soft tissue surgery or bony surgery. This is a form of focal and permanent treatment. Soft tissue operations include surgery on muscles and tendons. Tendons can be released, lengthened or transferred and muscle bellies can be recessed or detached from underlying fascia or their tendons (Dormans & Copley, 1998; Bache *et al.*, 2003).

Tenotomy, or complete division of tendon, is reserved for the management of contractures and spasticity in muscle units whose effect is considered to be harmful. When a tendon is completely severed, it probably reattaches to its original insertion point with scar tissue. This occurs over a period of time. Subsequently, it may begin to function with a possible reduction in its strength (Moseley, 1992).

Controlled lengthening of muscle bellies and tendons to correct the deformities often seen in children with cerebral palsy is the preferred option. This includes lengthening of the hip flexors, the knee flexors and the ankle plantar flexors. Complete loss of muscle function could be very harmful, as muscles are the important 'motors' working on

the skeletal levers to produce movement. The controlled lengthening usually required to retain useful function of individual muscle tendon units on bony levers translates into an improved gait pattern. Such surgery is best performed following a careful analysis of walking patterns with three-dimensional gait analysis (Bache *et al.*, 2003).

Lengthening of muscles and tendons has a profound effect on the physiology and biomechanics of muscle (Miller *et al.*, 1995). It is widely accepted that lengthening muscles produces a weakening effect (Moseley, 1992). However, careful restoration of muscle–tendon unit relationship, which allows the joint to work in its most functional position, may actually increase power generation as measured by a force plate.

Lengthening muscles has significant effects on the underlying component of spasticity. In the initial postoperative period, when children have pain and anxiety, muscle tone remote from the site of surgery is frequently increased. If this perioperative increase in spasticity is not managed appropriately, undesirable posture may result with resultant progression of deformities at other sites.

In the muscle tendon units that have been lengthened, clonus is frequently abolished and the deep tendon reflexes are reduced for a variable period of time. This may be the result of both biological and biomechanical effects of lengthening, including changes in the proprioceptive and muscle spindle inputs to the reflex arc. Part of the explanation may also lie in the servomechanism theory proposed by Moseley, in which the brain is described as part of the servomechanism whose activities are dependent on the perceived results of any of the activities in the feedback loop (Moseley, 1992). There has been little investigation of the magnitude of the reduction in spasticity by soft tissue surgery, its duration and its benefits.

A second important component of orthopaedic surgery for deformity correction is osteotomy and joint stabilization. Osteotomies in the management of children with cerebral palsy are usually rotational in nature. Typically medial femoral torsion is corrected by an external rotation osteotomy of the femur (Brunner & Baumann, 1997; Bache *et al.*, 2003; Pirpiris *et al.*, 2003). Lateral tibial torsion (Staheli *et al.*, 1968; Nicol & Menelaus, 1983; King & Staheli, 1984) is corrected by an internal rotation osteotomy of the tibia (Dodgin *et al.*, 1998; Stefko *et al.*, 1998, Selber *et al.*, 2004). Rotational osteotomies can be helpful in the management of gait disturbance, but the effects on muscle can also be very significant. An osteotomy of the femur in the intertrochanteric region will change the effective line of pull of muscle whose origins and insertion points cross the line of the osteotomy. These include the iliopsoas, hip adductors and hamstrings. Computer modeling indicates that some of these muscles may be relaxed by the rotational osteotomy, but others may have their tension increased. As described above, spasticity may increase in the postoperative period in children with cerebral palsy because of pain and anxiety. In addition, we must now add the potential for increased muscle tension due to the rotational osteotomy. Such increased muscle tone and spasticity should be anticipated and managed appropriately by acute spasticity management and, when necessary, associated prophylactic lengthening of musculotendinous units. As outlined above, the use of diazepam can be very effective in the perioperative period.

The main role of orthopedic surgery for children with cerebral palsy and other forms of spasticity is the management of fixed deformities. However, the correction of these deformities by both soft tissue and bony surgical procedures may have a very significant acute effect in the postoperative period and a more gradual, longer-term effect on the associated spasticity. These effects must be anticipated and included in an overall management plan. Much basic research remains to be done on these effects in both animal models and children with spasticity.

Conclusion

The management of spasticity in children is best achieved by a multidisciplinary team approach. Spasticity, muscle imbalance and restricted weight

bearing may initiate a chain of events that lead to progressive fixed contractures, torsional deformities in long bones and eventually joint instability and even frank degenerative arthritis. Because spasticity seems to play a key role in the development of deformity, spasticity management is very important in the growing child. There is now a range of options from which the clinician can choose in order to manage spasticity as safely and as effectively as possible. By considering whether the intervention is focal or general in its effects and whether it is permanent or temporary, appropriate choices can be made. By utilizing a range of clinical and objective measures, the clinician has an ability to measure spasticity and monitor the effects of intervention. Outcome studies, with objective measures including gait analysis and appropriate measures of functional activity, should be the focus of our efforts in spasticity management research in children.

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