Spasticity in adults: management using botulinum toxin

National guidelines

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Royal College of Physicians

Setting higher medical standards

BSRM

British Society of Rehabilitation Medicine

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Executive summary

This text provides an update to the original guide prepared in 2001[1] and peer reviewed for publication in 2002.[2]

- Spasticity is an involuntary muscle overactivity which commonly follows damage to the central nervous system (brain and spinal cord). It presents in a variety of ways depending on the size, location and age of the lesion, and may have several harmful effects such as pain, deformity and impaired function. Spasticity management is complex.
- Local intramuscular injection of botulinum toxin (BT) is an established, well-tolerated treatment in the pharmacological management of focal spasticity. There is a strong body of Level I evidence for its effectiveness in the management of upper and lower limb spasticity.
- The purpose of these guidelines is to provide clinicians with the knowledge and tools to use BT appropriately in this context. The keys to successful intervention are appropriate patient selection, establishment of clear goals for treatment and appropriate follow-up therapy.
- BT is licensed in the UK for treatment of focal spasticity in the upper limb. It has also become an accepted part of routine management in other muscle groups.
- BT should only be injected by clinicians experienced in the assessment and management of spasticity. The mainstay of spasticity management is stretching and correct positioning. BT should therefore not be used in isolation, but as part of a coordinated multidisciplinary approach involving physical handling and therapy, which may include splinting, to achieve the desired effect. In addition to medical staff, physiotherapists and nurses are now being trained to inject BT in the UK. The current arrangements for prescribing, supply and administration of BT by non-medical injectors is described in this document.
- The selection of appropriate patients and the definition of clear, achievable, realistic and measurable goals are crucial to the successful use of BT in spasticity management. Common goals for intervention include pain relief, improved range of limb movement, ease of care and, in some cases, active functional gain. These treatment goals should be documented in the patient records, and all BT injections should be accompanied by a formal assessment of outcome. Outcome measures should be relevant to the documented goals for treatment.
- If used according to the guidance, BT has the potential to reduce the overall costs of on-going care in people with severe spasticity through the prevention of contracture and deformity, and improved ease of care and handling.
- A substantial body of evidence now exists for the overall effectiveness of BT in the treatment of spasticity. Further research should focus on the gathering of 'practice-based evidence' through systematic data collection in the course of routine practice, to inform effective and cost-efficient practice in the application of BT for spasticity management and should include the evaluation of person-centred outcomes such as the attainment of individual goals.

[1]Ward AB, Turner-Stokes L. *The management of adults with spasticity using botulinum toxin: a guide to clinical practice.* London: Radius Healthcare, 2001.
[2]Turner-Stokes L, Ward AB. *Guidelines for the use of botulinum toxin (BTX) in the management of spasticity in adults.* Concise Guidance to Good Practice. London: Royal College of Physicians, 2002.

Recommendations

Summary of the guidelines

	Recommendation	Grade of evidence*
1 Principles of coordinated spasticity management		
1.1	The management of spasticity should be undertaken by a coordinated multidisciplinary team (MDT), rather than by clinicians working in isolation.	**C**
1.2	Before using botulinum toxin (BT), the team must ensure that: • an appropriate physical management programme is in place • all remediable aggravating factors have been addressed • a suitable programme of on-going coordinated management is planned.	**C**
1.3	BT must only be injected by clinicians who have: • appropriate understanding of functional anatomy • experience in the assessment and management of spasticity, and the use of BT in this context • knowledge of appropriate clinical dosing regimes and the ability to manage any potential complications.	**C**
1.4	BT injection must be part of a rehabilitation programme involving post-injection exercise, muscle stretch and/or splinting to achieve an optimal clinical effect.	**A**
2 Botulinum toxin injection		
2.1	Patients should be selected for BT on the basis of: • focal or multifocal problems due to spasticity • a dynamic spastic component as opposed to contracture • clearly identified goals for treatment and anticipated functional gains.	**C**
2.2	Patients and their families/carers should: • be given appropriate information • have an understanding of the realistic goals and expected treatment outcomes • agree treatment goals before BT is given.	**C**
2.3	Informed consent should be obtained from patients prior to injection. If the patient does not have the mental capacity to consent, current local (eg trust) policies for obtaining consent should be followed, with reference to the Mental Capacity Act 2005.	**C**
2.4	Clinicians must be aware that different BT products have different dosage schedules. The current recommended maximum doses used in a single treatment session are: • 1,000 units Dysport® or • 360 units Botox® Clinicians should refer to Appendix 2 for the recommended doses for individual muscles.	**A**
3 Prescribing, supply and administration of botulinum toxin by non-medical practitioners		
3.1	Processes for the administration and/or prescription of BT by non-medical practitioners (eg nurses, physiotherapists and other allied health professionals) are currently under exploration and development. • As for all spasticity interventions, the administration of BT by medical and non-medical practitioners should be in the context of a MDT decision. • Support and supervision should be available from a medical clinician who has the appropriate expertise and knowledge of BT injections, and will provide medical back-up in the event of any complications. • A formal system (such as a Patient Group Directions) should be produced to enable the administration of BT under sound clinical governance principles. • Careful attention should be given to the additional training needs of staff involved eg sterile intramuscular injection techniques, anatomical assessment etc.	**C**

continued

*See Chapter 1 for grading of recommendations.

Summary of the guidelines – *continued*

	Recommendation	Grade of evidence*
4 Follow up, documentation and outcome evaluation		
4.1	All injections should be followed by: • therapy review in 7–14 days for assessment and if necessary orthotics/splinting • MDT review at 4–6 weeks to assess effect and patient status • MDT review at 3–4 months to plan future management.	**C**
4.2	Injections should be followed by a formal assessment of outcome. Appropriate measures should be identified as part of the goal-setting process.	**C**
4.3	Formal evaluation of outcome should include: • achievement of intended goals for treatment • evaluation of gains at the levels of: – impairment eg clinical spasticity, range of movement etc – function ie whether 'active' eg motor use, or 'passive' eg ease of care • for details of tools to assess outcome see Appendix 3.	**B**
4.4	Documentation for all injections should include: • patient and carer expectations for outcome • a clear statement of agreed treatment goals • baseline outcome measures appropriate to those goals • BT product, dose, dilution and muscles injected • follow-up treatment plan • evaluation of outcome and repeat measures • plans for future management.	**C**
5 Services		
5.1	Services administering BT should have access to staff with the relevant expertise and facilities, including adequate space, therapies and equipment for orthotics/splinting.	**C**
5.2	Clinicians should have access to facilities to aid assessment, selection and treatment planning eg electromyography, nerve/muscle stimulation etc.	**C**
5.3	A clinical service should routinely use a single preparation to avoid confusion over dosage and to ensure knowledge of the product characteristics (see 'Summary of product characteristics' on www.emc.medicines.org.uk).	**C**
6 Training		
6.1	Clinicians undertaking BT injection should be able to demonstrate that they have the appropriate competency and training. Training should take the form of supervised clinical practice, supplemented as appropriate by formal accredited courses.	**C**
6.2	Training programmes should be in place to ensure that all relevant disciplines are trained and up to date.	**C**
6.3	Formal evaluation methods should be established to ensure that the necessary knowledge, experience and skills are acquired to perform the procedures and provide a service.	**C**

continued

*See Chapter 1 for grading of recommendations.

Summary of the guidelines – *continued*

	Recommendation	Grade of evidence*
7 Future research		
7.1	A substantial body of evidence now exists for the overall effectiveness of BT in the treatment of spasticity. Further research should focus on the gathering of 'practice-based evidence' to inform critical questions such as: • which patients are most likely to respond? • what are the optimum strategies for follow-up therapy in different situations? • what are the real-life benefits for patients, and to society in general?	**C**
7.2	Research should incorporate a range of research methodologies to inform effective and cost-efficient practice in the application of BT for spasticity management, and should include the evaluation of person-centred outcomes such as the attainment of individual goals.	**C**
7.3	Prospective data should be systematically gathered in the course of routine clinical practice to provide an accurate description of current interventions, together with outcome evaluation.	**C**
7.4	A national system for collection and collation of a minimum dataset based on the information listed in Recommendation 4.4 should be developed and implemented, for the purposes of quality benchmarking and for the assembly of practice-based evidence.	**C**

*See Chapter 1 for grading of recommendations.

Acronyms and abbreviations

ACPIN	Association of Chartered Physiotherapists Interested in Neurology
AGREE	Appraisal of Guidelines Research and Evaluation
ArMA	Arm Activity Measure
BI	Barthel Index
BT	Botulinum toxin
CMC	Carpometacarpal
CNS	Central nervous system
DB	Double blind
eMC	electronic Medicines Compendium
EMG	Electromyography
FCR	Flexor carpi radials
FES	Functional electrical stimulation
FIM	Functional Independence Measure
GAS	Goal Attainment Scaling
GDG	Guidance Development Group
ICF	International Classification of Functioning, Disability and Health
IP	Interphalangeal
LASIS	Leeds Arm Spasticity Impact Scale
MAS	Modified Ashworth Scale
MC	Metacarpal
MDT	Multidisciplinary team
MS	Multiple sclerosis
MT	Metatarsal
MTP	Metatarsophalangeal
NGRS	Numeric Graphic Rating Scale
NMI	Non-medical injector
NMJ	Neuromuscular junction
NMP	Non-medical prescriber
PC-RCT	Placebo controlled randomised clinical trial

PGD	Patient Group Directions
PIP	Proximal interphalangeal
PSD	Patient Specific Direction
RCP	Royal College of Physicians
RCT	Randomised controlled trial
RMA	Rivermead motor assessment
ROM	Range of motion
SMART	Specific, Measurable, Achievable, Realistic, Timed
SPC	Summary of product characteristics
SPIN	Scale of Pain Intensity
TBI	Traumatic brain injury
U	Units
UL	Upper limb
VAS	Visual Analogue Scale
VRS	Verbal Rating Scale
WHO	World Health Organization
WTE	Whole time equivalent

1 The guidance development process

Botulinum toxin (BT) has an established place in the pharmacological management of spasticity. There is now considerable experience of use, knowledge of its indications, effects and safety in clinical practice.

Guidance for the management of adults with spasticity was produced in 2001 (Ward and Turner-Stokes 2001) and was published as part of the Royal College of Physicians' Concise Guidance series in 2002 (Turner-Stokes and Ward 2002a,b). This latest text has been produced as an update to the original. Its purpose is to guide clinical practice in the treatment of adults with spasticity in the correct use of BT as part of an overall patient management programme; and to provide a background understanding of this complex field of intervention, as well as providing some practical tools for implementation.

This guidance has been developed in accordance with the principles laid down by the Appraisal of Guidelines Research and Evaluation (AGREE) collaboration (www.agreecollaboration.org).

The system for grading of evidence is outlined in Table 1. There is a substantial body of Level I evidence for the effectiveness of BT in reducing spasticity in the upper and lower limb, which is detailed further in Appendix 1. However, as is often the case, there is little direct trial-based evidence to inform the exact process and context of BT administration and the surrounding management of spasticity: this is the main focus of this guidance. Where research-based evidence is not available, guidance is based on the experience of the guidance development group (GDG).

Table 1 Levels of evidence

Level of evidence	Type of evidence	Grade of recommendation
Ia	Meta-analysis of randomised controlled trials (RCTs)	A
Ib	At least one RCT	A
IIa	At least one well-designed controlled study, but without randomisation	B
IIb	At least one well-designed quasi-experimental design	B
III	At least one non-experimental descriptive study (eg comparative, correlation or case study)	B
IV	Expert committee reports, opinions and/or experience of respected authorities	C

The guidance development process is summarised in Table 2.

Table 2 Summary of the guidance development process

Scope and purpose	
Overall objective of the guidance	To promote the appropriate use of botulinum toxin (BT) in the management of spasticity, give guidance on its administration and the wider principles of management. This guidance updates *The management of adults with spasticity using botulinum toxin: a guide to clinical practice* (Ward and Turner-Stokes 2001) which was peer reviewed for publication in 2002 (Turner-Stokes and Ward 2002a,b).
The patient group covered	Adults with spasticity due to neurological illness or injury.
Target audience	Doctors and health professionals involved in management of spasticity, providers and purchasers of rehabilitation services.
Clinical areas covered	• How should patients be selected for treatment with BT and how should it be administered? • What are the principal goals for treatment and how should outcomes be measured?
Stakeholder involvement	
The guidance development group (GDG)	The guidance was instigated by the British Society of Rehabilitation Medicine, in association with: • Royal College of Physicians (RCP) • The Association of British Neurologists • The Chartered Society of Physiotherapy • College of Occupational Therapists Specialist Section – Neurological Practice • Adult Physiotherapy Spasticity Forum • Association of Chartered Physiotherapists Interested in Neurology • Society for Research in Rehabilitation. In addition, the draft guidance was shared with the following user representative organisations during its development: • The Stroke Association • Headway • The Neurological Alliance • Multiple Sclerosis Society • Different Strokes • Scope • Spinal Injuries Association.
Funding	Costs of travel and accommodation for attending meetings, and for guidance production were met by an educational grant from Ipsen Ltd.
Conflicts of interest	All authors and group members have declared, and provided details of, any actual or potential conflicts of interest (see Appendix 9).
Rigour of development	
Evidence gathering	Evidence for this guidance was provided by a systematic review of the clinical trials for BT in spasticity. In addition, Cochrane Library and Medline searches were conducted by individual members of the group to address specific issues according to their area of expertise.
Review process	Identified studies were reviewed by at least two members of the GDG.
Links between evidence and recommendations	The system used to grade the evidence and guidance recommendations is that used by the RCP (see Table 1).
Piloting and peer review	The final draft was widely circulated to all relevant parties and their comments incorporated together with the results of pilot exercises on patient referral.
Implementation	
Tools for application	A documentation proforma is included along with some practical examples of outcome measures.
Plans for review	The guideline will be reviewed in five years (2014).

2 Spasticity – what is it and why does it matter?

2.1 Pathophysiology

The technical definition of spasticity is 'velocity-dependent increased resistance to passive limb movement in people with upper motor neurone syndrome' (Lance 1980). The pathophysiology is complex and readers are referred to detailed accounts by Brown (1994) and Sheean (2002).

At a clinical level, there are two main contributing factors to resistance to movement in the context of limb spasticity following damage to the brain or spinal cord:

- neurogenic component: overactive muscle contraction
- biomechanical component: stiffening and shortening of the muscle and other soft tissues.

If left untreated, a vicious cycle occurs in which unopposed contraction due to spastic dystonia in affected muscle groups leads to an abnormal limb posture, resulting in soft tissue shortening and further biomechanical changes in the contracted muscles. This in turn prevents muscle lengthening and perpetuates further tonicity.

The primary aim of the treatment of spastic muscles is to maintain length and allow normal positioning of the limbs to prevent secondary soft tissue shortening. The mainstay of treatment is muscle stretching, and splinting/orthotics provide a means to maintain prolonged stretching in between sessions of physiotherapy and manual handling (Verplancke *et al* 2005).

BT can facilitate this process by producing temporary weakness and relaxation of the targeted muscles, allowing them to be stretched more easily, thus reducing the neurogenic and biomechanical components of spasticity. However, it is important to remember that BT itself is only effective in reducing the neurogenic component of spasticity. Hence, there are two key prerequisites for the successful use of BT in management of spasticity:

- there must be a significant component of muscle overactivity
- injection must be followed by an appropriate programme of stretching and/or splinting to maximise the effects of muscle relaxation.

2.2 Epidemiology

There are no accurate figures currently available for the prevalence of spasticity. However, it is estimated that approximately one-third of stroke patients (van Kuijk *et al* 2007; Watkins *et al* 2002), 60% of patients with severe multiple sclerosis (MS) and 75% of patients with physical disability following severe traumatic brain injury will develop spasticity requiring specific treatment. Of these, approximately one-third may require treatment with BT (Verplancke *et al* 2005).

2.3 Why does treating spasticity matter?

Spasticity is not always harmful. Patients with a combination of muscle weakness and spasticity may rely on the increased tone to maintain their posture and aid standing or walking. There are

patients with spasticity who need little or no treatment. However, muscle tone may change over time and therefore requires repeated assessment and management.

For some patients spasticity can be painful, distressing, and a potentially costly cause of disability. Secondary complications arising from spasticity include impaired movement, hygiene, self-care, poor self-esteem, body image, pain and pressure ulcers (see Table 3). These may be distressing for the patient and difficult to manage for involved carers and health professionals. In some cases they may interfere with rehabilitation and can increase the cost of this and longer-term care over time. For example the direct cost of healing a pressure ulcer (Grade 4) has been estimated at £10,551 over the period of healing (Bennett *et al* 2004).

Successful treatment can improve physical functioning and can also prevent secondary complications (Boyd *et al* 2000).

2.4 Describing the effects of spasticity

The World Health Organization (WHO 2001) has developed an International Classification of Functioning, Disability and Health (ICF) as a model to describe the impacts of the health condition on (a) the body, (b) the ability to perform activity and (c) participation in society (see Fig 1).

- *Impairment* describes the effect on body structures and functions, eg paralysis, contracture or deformity
- *Activity* refers to the execution of a task, eg in activities of daily living
- *Participation* refers to the individual's ability to participate in society.

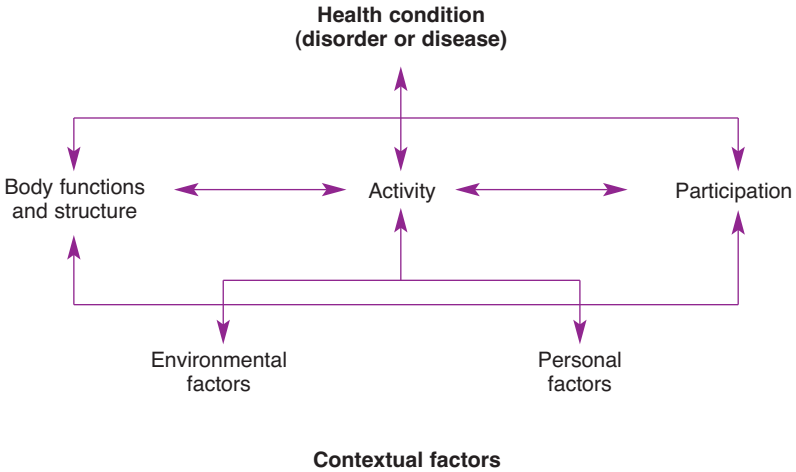

Fig 1 The International Classification of Functioning, Disability and Health

The ICF is a useful framework for describing the impact of disease and the benefits of effective treatment. In the context of spasticity management, it is important to demonstrate change not only at the level of impairment, but also at a functional level. Two categories of function have been described (Sheean 2001; Ashford and Turner-Stokes 2006):

- *active function* refers to the execution of a functional task by the individual themselves
- *passive function* refers to a task (such as a care activity) which is performed by a carer for the individual, or to an affected limb by the patient using an unaffected limb.

In some instances the treatment of spasticity may unmask voluntary muscle movement allowing the individual to manage active functional tasks that they were previously unable to perform. More often, however, the underlying weakness of the limb precludes the return to active function. Nevertheless, relieving spasticity may still have important benefits in terms of passive function, making it easier to care for the affected limb. Table 3 describes the harmful effects of spasticity classified according to the ICF.

Table 3 Harmful effects of spasticity

ICF level	Problem	Effect
Impairment	Muscle spasms	Pain Difficulty with seating and posture Fatigue
	Abnormal trunk and limb posture	Contractures Pressure sores Deformity
	Pain	Distress and low mood Poor sleep patterns
Activity	Active function loss	Reduced mobility Inability to use limbs in function Difficulty with sexual intercourse
	Passive function loss	Difficulty with self-care and hygiene Increased carer burden
Participation	Impact of any/all of the above	Poor self-esteem/self-image Reduced social interaction Impact on family relationships

3 Botulinum toxin in clinical practice

3.1 What is it?

Botulinum toxin is produced by *Clostridium botulinum* and strains of the bacterium have been found to produce seven antigenically distinct protein neurotoxins labelled A–G (Hambleton and Moore 1995). BT type A is a powerful neurotoxin that has been developed into a therapeutic agent.

3.2 Licensed products

This guidance refers to the use of BT in general, but product-specific advice is given only in relation to those products currently licensed for spasticity management in the UK.

Dysport® and Botox® type A toxins are both licensed for the treatment of focal spasticity in the UK:

- Botox® is licensed for the treatment of wrist and hand disability due to upper limb spasticity associated with stroke in adults
- Dysport® is licensed for the treatment of arm symptoms associated with focal spasticity in conjunction with physiotherapy.

Although both products are licensed for the treatment of dynamic equinus foot deformity in children with cerebral palsy from two years old, neither product as yet has a UK licence for treatment of lower limb spasticity in adults.

3.2.1 Storage

Unopened vials of Botox® and Dysport® should be stored at temperatures between 2–8°C. Once reconstituted, Dysport® is stable for up to eight hours in a refrigerator at 2–8°C and Botox® may be stored in a refrigerator at 2–8°C for up to 24 hours. If used in the community, appropriate measures must be taken to keep these products cool.

3.3 How does botulinum toxin work?

Botulinum neurotoxins all exhibit similar pharmacological activity; they prevent the release of acetylcholine from the pre-synaptic nerve terminal, thus blocking peripheral cholinergic transmission at the neuromuscular junction (NMJ). This results in a reduction in muscle contraction and a dose-dependent reversible reduction in muscle power. Active NMJs take up BT more avidly than NMJs at rest.

The clinical effects are temporary. The toxin degrades and becomes inactive within the nerve terminal (Hambleton and Moore 1995; Hambleton *et al* 2007). The NMJ atrophies and then regenerates with re-sprouting. The muscle weakness resolves over three to four months.

3.4 Administration

BT is injected intramuscularly into specifically selected muscles. Although it can diffuse through muscle fascial barriers, its effect is concentrated in the injected muscles so that it is

possible to generate highly focal weakness (Aoki 1999). The injections do not have to be placed precisely in the motor end-plate as BT diffuses to some extent within the muscle (see Chapter 5 for further details on injection technique).

3.5 Dosage

BT doses are measured in units (U), based on a mouse LD50 test intended to standardise doses (Hatherway and Deng 1994). Nevertheless various commercially available BT preparations have different dose schedules. The doses are not interchangeable with each other (see 'Summary of Product Characteristics' (SPC) on www.emc.medicines.org.uk).

Botox® is currently available in vials of 50U and 100U and Dysport® in vials of 500U. **It is vital to select the correct dose schedule (see Appendix 2).**

Early reports of BT trials commonly did not specify the preparation used. One report used the term 'botox' as a generic word when in fact the study used Dysport® (Dengler *et al* 1992). Some studies have combined results from patients using different preparations. It is the responsibility of the clinician administering BT to ensure that the name of the BT preparation is correctly documented in the clinical notes.

The maximum recommended dose in limb spasticity is 1,000U Dysport® or 360U Botox® in a single adult injection session. Larger doses carry increasing risk of systemic adverse effects. There is one report of occasional patients developing systemic symptoms at moderate doses after many previous injections of similar doses (Bhatia *et al* 1999). This is, however, rare.

Experience has generated 'standard' doses which are well-tolerated, and which work for most patients. Generally large, hypertrophied or highly active muscles need larger doses, and smaller less active muscles or lightweight patients need smaller doses. The degree and to some extent duration of weakness are dose dependent.

The dose should also be reduced if the target muscles are already weak, or if there is an increased risk of side effects in an individual patient. Pre-existing local tissue disruption (recent trauma or infections) or conditions causing systemic weakness such as in myopathy, myasthenia gravis, motor neurone disease, or neuropathy should provoke extreme caution, but are not absolute contraindications (Moore and Naumann 2003).

3.6 Duration of effect

BT is taken up by the NMJ within 12 hours (Schiavo *et al* 1992) and its clinical effect occurs gradually over 4–7 days, occasionally longer. It interferes with neuromuscular synaptic transmission for about 12–16 weeks, and causes clinically detectable weakness for 3–4 months in most situations, sometimes rather longer (Aoki 1999). The weakened muscles recover their activity after cessation of the BT administration. This recovery can be an advantage when a BT injection gives an unexpectedly poor result, but has the disadvantage that the injection may need to be repeated for prolonged effect (Ward and Barnes 2007).

The clinical benefit can persist for many months (particularly when accompanied by an appropriate physical management regimen) but wears off gradually. Repeat injections generally follow a similar course. Experience in other neurological conditions has demonstrated that

patients may become biologically resistant to BT as a result of antibody formation, especially with frequent, large dose injections (Greene and Fahn 1992, 1993; Hambleton and Moore 1995). This has led to the general advice to avoid repeated injection at less than three month intervals. Although secondary non-response is theoretically an issue for the use of BT in spasticity, it is rarely reported in practice. This may be because spasticity is often self-limiting in the course of natural recovery, eg following stroke or brain injury, so that long-term repeated injections are required for only a minority of patients. Advice regarding repeat injections may therefore be different for the post-acute situation, as opposed to chronic spasticity management, and is further discussed in Chapter 5.

3.7 Adverse effects

Serious adverse events are rare, but mild and transient adverse effects may occur; for a full list clinicians should refer to the product SPC at www.emc.medicines.org.uk. However, adverse events may include:

- *local muscle weakness* from toxin spread to nearby muscles. This may cause temporary functional loss. Local muscle atrophy may occur. Rarely, more generalised muscle weakness may be seen, particularly if high doses are given in multiple muscles (Bakheit *et al* 1997)
- *dysphagia* occurs mainly when high doses are used around the neck or proximal upper limb. Nevertheless, it should be remembered that patients with brain injury or stroke may have impaired swallowing reflexes, so care should be taken when injecting larger doses of BT in patients with a history of dysphagia, especially if they do not have percutaneous endoscopic gastrostomy feeding tubes
- *respiratory failure* has not been reported in adults, although there have been isolated case reports in children with cerebral palsy. Nevertheless it remains a theoretical risk for higher dose treatments and should be considered when planning injections for patients with profound neuromuscular compromise
- *autonomic dysfunction*, if it occurs, is almost always sub-clinical. Once again, however, it is something to bear in mind in patients who may already have a degree of autonomic dysfunction, eg some patients with Parkinson's disease or diabetes
- *'flu-like' symptoms* for up to a week, at some point in the month after injection, but are transient and mild
- *rash*
- *brachial neuritis* (very rare) following local injections
- *altered taste.*

These adverse effects are self-limiting and do not appear to affect the activity of BT. The peak period for adverse effects is usually at 2–4 weeks post-injection. The same dose and pattern of injections can produce variable results, with adverse effects occurring even after several apparently identical and successful injections. Similarly, subsequent exposure to BT does not always reproduce side effects seen on earlier occasions, but it may be prudent to adjust the dose and pattern of injections.

Clinicians should inform patients and family practitioners of the possible adverse effects and should take steps to minimise or avoid them by modifying the subsequent injections. Where BT is administered or prescribed by non-medical injectors (NMIs), specific arrangements must be in place for medical back-up in case a significant adverse event occurs, however unlikely this may be.

3.8 Contraindications

For a full list of contraindications and special warnings and precautions for the use of BT, clinicians should refer to the product SPC at www.emc.medicines.org.uk.

4 Management and treatment of spasticity

4.1 Principles

The management of spasticity is complex and requires a multidisciplinary team (MDT) working together with the patient and family/carers. The MDT may include:

- medical specialists eg rehabilitation medicine physician, neurologist, geriatrician
- nurse/professional care staff
- therapists eg physiotherapist, occupational therapist
- others eg rehabilitation engineer, orthotist.

The underlying principle is to treat spasticity when it is causing problems for the patient's functioning or care provision. The basis of management is physical and BT treatment is aimed at symptom relief, improving function and preventing deterioration. BT is an adjunct to meeting the wider rehabilitation aims of the patient, carer and treating team. It should be used in parallel with appropriate physical therapy and other anti-spastic strategies and, importantly, postural management programmes.

4.2 Physical treatment

4.2.1 Prevention of aggravating factors

Because spasticity results in part from the abnormal processing of sensory input, nociceptive stimuli, such as pain and discomfort, will exacerbate it and make it harder to treat. Initially therefore, the MDT should identify and eliminate any remedial factors, which may be aggravating spasticity. These include:

- pain or discomfort
- constipation
- infection (eg urinary or respiratory tract infection, pressure sores etc)
- tight clothing or catheter bags
- poor postural management.

4.2.2 24-hour postural management

High-quality nursing is vital for the effective management of spasticity. Nurses and carers play a key role in spasticity management as they are responsible for positioning and handling of the patient throughout the 24-hour period. Other members of the MDT also play an important role in advising on positioning and providing for example special seating and postural support systems. Education and advice are important for good physical management of spasticity; it takes considerable staff time, and all carers need to be involved.

When planning the postural management programme, it should be recognised that the body needs to change position. There is not just one correct position, but a range of different positions that may act to vary the stretch on different muscles and body parts throughout the day. Careful positioning in bed, supported sitting in the wheelchair, periods in a standing frame and splinting/orthotics all contribute to the maintenance of muscle length and control of spasticity. In addition, these measures reduce the risk of complications, such as pressure sores, which may result from abnormal pressure points and shearing forces.

4.2.3 Physical therapy

There should be a programme of stretching and physical therapy intervention (Giovanelli 2007). Further details of physical management are given in Pope (2007) and Edwards (1996).

The principal aims of physical therapy are to:

- maintain muscle and soft tissue length across joints
- facilitate care giving (passive functional improvements)
- facilitate active control of any residual movements to allow for active participation in tasks (active functional improvements).

The physical therapy programme should be directed by professionals experienced in the management of neurological disease.

4.3 Medical treatment

Physical treatment alone may be insufficient to overcome the effect of increased muscular tone or its mechanical consequences, particularly in moderate to severe spasticity. Medical treatment and other interventions should therefore be considered early in the management of the patient.

Firstly, the clinician should consider whether the spasticity is actually harmful and what impact treatment will have on the patient's functioning. Patients may rely on spasticity for standing and walking, and treatments may aggravate further disability.

Secondly, the pattern of spasticity is important and it may give rise to generalised, focal or multi-focal problems. Intramuscular BT injections or nerve blockade with phenol in aqueous solution are the pharmacological treatments of choice for focal spasticity. If spasticity causes multi-focal problems, BT will again be helpful. However, dose limitations may reduce its long-term effectiveness and additional strategies such as intrathecal baclofen, or a combination of BT and phenol would have to be considered. Oral anti-spasmodic agents may be considered for generalised spasticity but frequently carry the unwanted side effects of drowsiness and muscle weakness. Figure 2 summarises an overall management strategy.

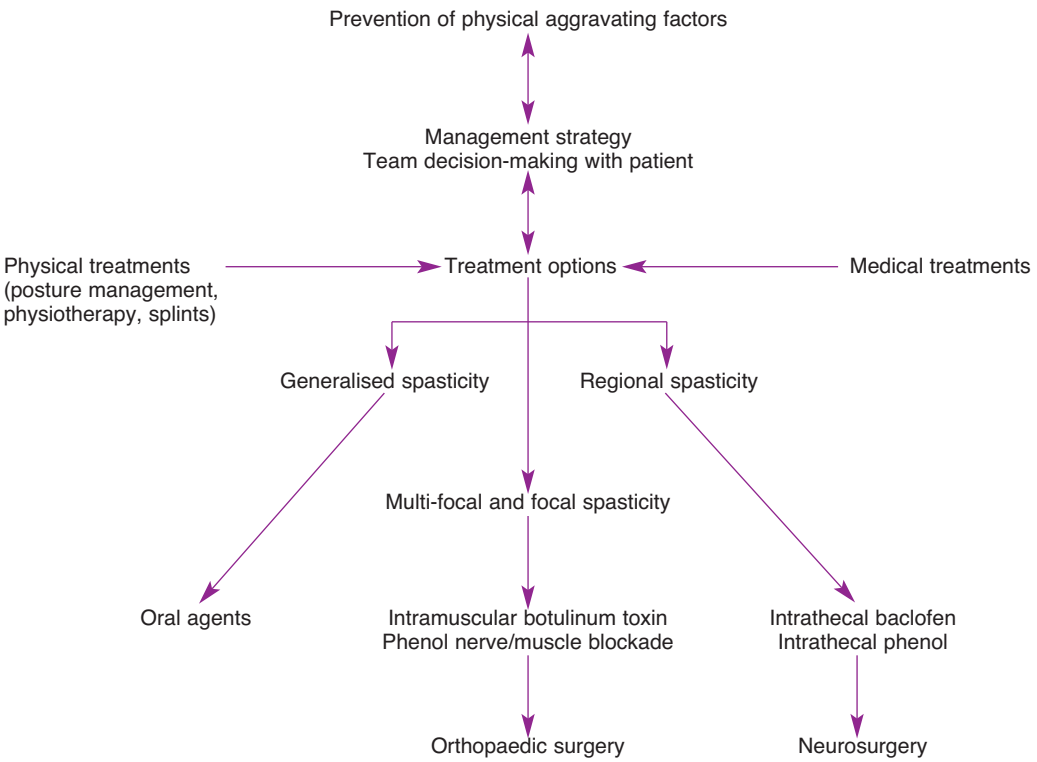

Fig 2 Management strategy for adults with spasticity. Note: It is not uncommon to have a mixed pattern of spasticity and interventions are almost always combined, eg physical management programmes and systemic medication.

5 Using botulinum toxin to treat spasticity

5.1 Summary of key principles for use of botulinum toxin

- BT is useful in the management of focal spasticity, whether of cerebral or spinal origin (Jankovic and Schwartz 1995), but it should be used as part of an integrated multidisciplinary approach and accompanied by a rehabilitation programme
- BT should be used to address specific functional limitations resulting from focal spasticity (ie muscle over-activity confined to one or a group of muscles that contribute to a specific functional problem)
- BT will not recover lost function, except where that function has been lost due to antagonist muscle over-activity.

5.1.1 Use in the post-acute setting

BT can result in long-term gains in people with sudden onset neurological conditions such as stroke. If used appropriately in the early phases of rehabilitation it may prevent soft tissue shortening arising from the combined effect of spasticity and limb immobility. This may potentially help to avoid learned disuse and facilitate neurological recovery. For example, in some patients with regional spasticity (eg a paretic upper limb), a serial approach with injections into several different muscle groups over a relative short timescale has been reported to be successful in curtailing upper limb spasticity, and has led to a good functional recovery (Turner-Stokes and Ashford 2007). In these circumstances, although the subsequent injections follow on soon after one another, the total number of treatments is limited to three or four. The potential benefits may outweigh the theoretical risk of antibody formation, which in any event has not been a problem in spasticity treatment to date.

5.1.2 Longer-term treatment

In people with severe and longstanding spasticity, the focus will be more on symptom control or passive function outcomes (eg pain relief, wearing of splints) (Ashford and Turner-Stokes 2006). For example, severe flexion deformity of the fingers as a result of spasticity may cause pain, affect hand hygiene and cause skin breakdown. In these people, repeated BT treatments may be required over several years. Careful attention to physical management in between injections can help to reduce the frequency of BT treatments, and reduce the likelihood of secondary non-response. Here the general advice of avoiding repeat injections within three months should be adhered to.

5.1.3 Distinction of spasticity from contractures

Severe spasticity is often difficult to differentiate from contracture. Electromyography (EMG) may be useful to identify the presence of unwanted muscle activity during passive and active movement as well as during effortful activity to identify associated reactions. Examination under anaesthesia or sedation may be useful to assess the presence of contracture for which other interventions may be more appropriate.

5.2 Key steps to treatment of spasticity with botulinum toxin

Figure 3 summarises the key steps to treatment of spasticity with BT.

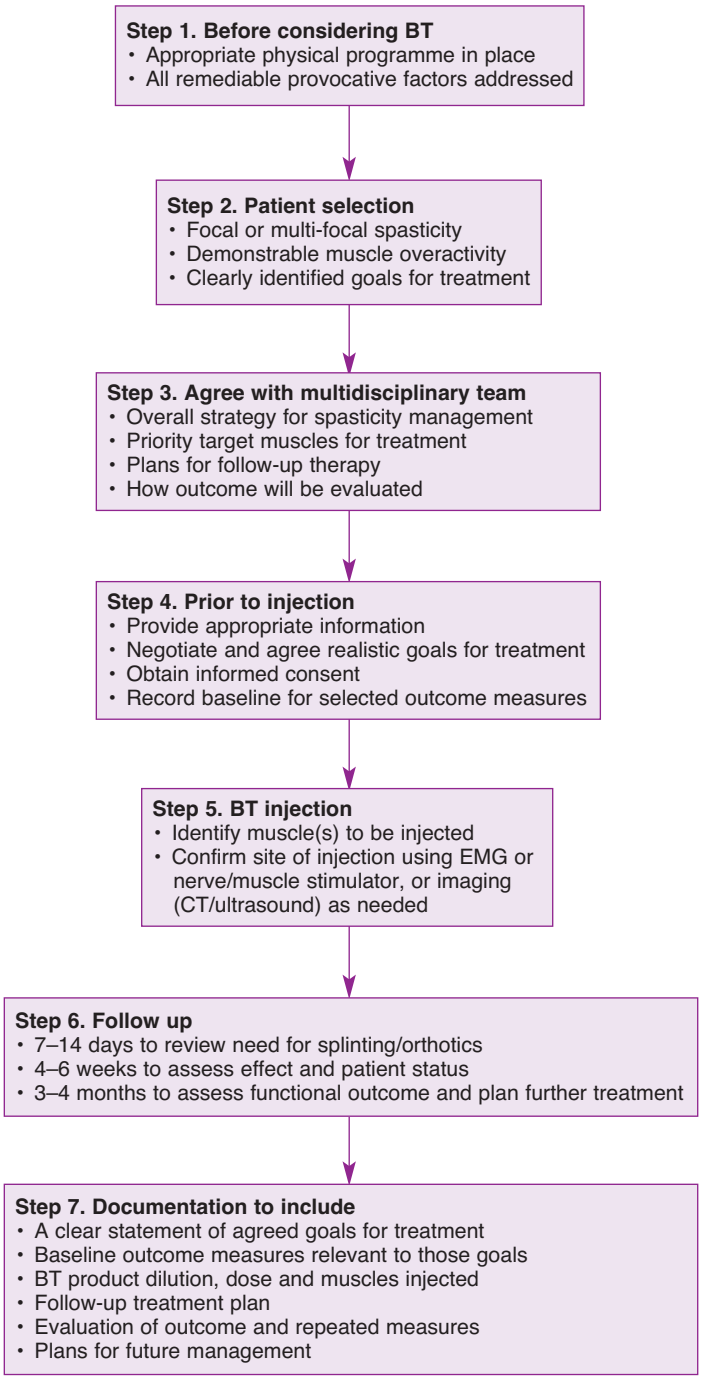

Fig 3 The key steps to treatment of spasticity with botulinum toxin (BT).

5.3 Patient selection

Appropriate patient selection is crucial to the successful treatment of spasticity. Patients must have focal or multi-focal spasticity with demonstrable evidence of muscle overactivity and there must be clearly agreed goals for treatment. The selection checklist shown in Table 4 may be helpful.

Table 4 Patient selection checklist

What is the problem and is it amenable to treatment with BT?
Is the problem a result of focal spasticity; if so, which muscles are involved?
Is BT the most appropriate treatment?
Are there any contraindications to BT injection?
Have treatment goals been identified and agreed with the patient and treating MDT?
Who will provide the on-going physical treatment and monitoring?
How will treatment outcomes be evaluated and will the measures used be appropriate?
Has the patient consented to treatment, or does the family assent on their behalf?

5.4 Treatment goals

The first step is to consider the likely outcomes from treatment. In some cases, active functional goals may be appropriate, but there may also be important gains to be made in terms of passive function or avoiding progression of impairment. Some common treatment goals are shown in Table 5.

Table 5 Treatment goals

Symptom management and impairment	
Relief of symptoms	Pain relief Muscle spasm frequency Involuntary movements eg associated reactions
Active function	
Functional improvement	Improved ability in the following tasks: • mobility eg speed, balance, quality or gait pattern or endurance of walking or wheelchair propulsion • transfers eg getting from chair to bed and back • dexterity and reaching • self-care eg washing, dressing • eating/drinking • sexual activity
Passive function	
Decrease carer burden	Ease of moving, handling and positioning Routine day-to-day care (eg perineal hygiene, dressing)

continued

Table 5 Treatment goals – *continued*	
Avoiding progression of impairment	
	Prevention of contractures and deformity – ease of splint application and prolonged use Optimising posture and seating to improve tissue viability
Aesthetic and postural appearance	
	Improve body image Improve fit of clothes
Enhance impact of conventional rehabilitation intervention	
	Optimise effectiveness of therapies Reduce use of systemic medication to treat spasticity Inform potential surgical treatment

5.5 Muscle selection

Identifying the cause of the problem is fundamental to planning treatment. It is important to distinguish between spasticity and weakness because both cause limb deformity but their treatment differs considerably (Richardson *et al* 2000). Spasticity usually involves several muscles and may occur in common postural patterns. The MDT will need to consider the predominant active muscles in relation to the intended goals for treatment (see Table 6).

Knowledge of functional anatomy and the action of muscles is essential. Muscle selection and the order/priority of treatment should be agreed between the treating clinician and the MDT.

Table 6 Common patterns of spasticity and treatment benefits

Pattern	Muscle involved	Benefits
Upper limb		
Shoulder adduction, internal rotation and retraction (Turner-Stokes 2007)	Pectoralis major Latissimus dorsi Teres muscle group Subscapularis Rhomboids and interscapular muscles	Sitting posture Ease of dressing Axillary hygiene Improve balance and symmetry of gait and can sometimes help to reduce unwanted spasticity in the elbow and hand
Elbow flexion	Biceps brachii Brachialis Brachioradialis	Improve flexion deformity Improve reach/retrieve
Pronation of the forearm	Pronator teres Pronator quadratus	Hand function
Flexed wrist and clenched hand	Flexor carpi ulnaris and radialis Flexor digitorum superficialis and profundus Flexor pollicis longus	Maintain palmar skin hygiene Improve grasp release

continued

Table 6 Common patterns of spasticity and treatment benefits – *continued*

Pattern	Muscle involved	Benefits
Upper limb – *continued*		
Thumb in palm, intrinsic muscle stiffness	Opponens pollicis Adductor pollicis Flexor pollicis brevis Lumbricals Interossei	Improve grasp
Lower limb		
Hip adductor spasticity and spasms (Hyman *et al* 2000; Snow *et al* 1990)	Adductor magnus, longus and brevis	Improve 'scissor gait' Ease of perineal hygiene and urinary catheterisation Easier sexual intercourse
Hip and knee flexion deformity/spasm (Ward 2002)	Psoas major Iliacus Medial hamstring group (gracilis, semi-tendinosus, semi-membranosus) Biceps femoris	Improve weight bearing Improve gait pattern and seating posture
Knee extension spasm	Quadriceps group	Seating posture (note potential to worsen sit to stand and standing)
Plantar flexed and inverted foot (Das *et al* 1989; Burbaud *et al* 1996)	Gastrocnemius, soleus and posterior tibialis	Correct equinus deformity, and foot inversion to allow heel strike
Toe clawing	Flexor hallucis longus, flexor digitorum longus	Ease of donning foot wear and comfort
Hyperextension of great toe	Flexor hallucis longus Extensor hallucis longus	Ease of donning foot wear and comfort

5.6 Pre-injection patient consultation

5.6.1 Agreed goals for treatment

Patients often have high expectations of functional gain. Before treating with BT, the treatment goals and expected outcomes should be negotiated and agreed with the patient and their family to ensure that the expected outcome is realistic and worthwhile. All parties should be clear about what is involved, and the need for compliance and commitment to the subsequent therapy. The procedure for Goal Attainment Scaling (GAS) described in Appendix 4 can be a helpful step in the negotiation of realistic goals.

5.6.2 Information about the treatment

The clinician should explain to the patient, their family or carers what the treatment will entail; which muscles will be involved, the number of injections, the potential benefits and adverse effects, and the importance of the advice from the MDT. Liaison is required with the local team if the patient is being treated in the community.

5.6.3 Consent

The treating clinician must obtain informed consent from the patient prior to the injection and take account of appropriate ethical issues including those relating to the Mental Capacity Act 2005.

5.7 Injection technique

The BT injection must be prepared according to the manufacturers instructions and the appropriate disposal facilities should be available for unused BT.

5.7.1 Planning and siting of injections

The planning and siting of the injections should be undertaken by the clinician in consultation with the MDT. Larger superficial muscles may be identified with knowledge of surface anatomy. Smaller, less accessible muscles may require additional techniques to ensure correct placement of the injection, especially in the presence of adipose tissue, or where normal anatomy is contorted by deformity:

- EMG can be useful to confirm placement within the muscle and to confirm the presence of muscle activity (Keenan *et al* 1990)
- nerve or muscle stimulation may be useful to confirm placement by producing a 'twitch' in the target muscle
- imaging, such as ultrasound (or occasionally computed tomography/magnetic resonance imaging scanning) may also be used.

The best sites for injection are theoretically the nerve end-plate zones deep in the muscle bulk. The patterns of end-plate zones are not yet clearly mapped, but it is not necessary to make multiple passes using needle EMG looking for their subtle, characteristic electrical signature. BT diffuses sufficiently from the site of injection to make this unnecessary.

Small and moderate-sized muscles will usually respond to BT injected simply into the belly of the muscle. Injection location is often not critical perhaps because BT tends to 'seek out' the active NMJ. Although there is some diffusion through muscle fascia (Shaari *et al* 1991, 1993), muscles with well-delineated separate components, such as quadriceps, need separate injections for each major section. Conversely unwanted muscle weakness can occur in adjacent muscles because of this diffusion. This needs to be explained to the patient. Muscles with fibres arrayed in parallel may be more effectively weakened by multiple injections transversely across the muscle belly, while muscles with fibres arranged longitudinally may require a spread of injections along their length (Moore and Naumann 2003).

Some authorities recommend multiple scattered smaller injections to spread the toxin even in medium-sized muscles. The justification for multiple injections within a single muscle partly depends on the theoretical concept of BT saturation of a volume of muscle (50U Botox® or 200U Dysport® has been suggested as a maximum dose per site). However, multiple injections may be uncomfortable for some patients and may lead to temporary pain-induced increase in muscle tone.

It is important to document the dose and dilution, the type, and the location of BT, and the number of injection sites per muscle. A sample proforma is given in Appendix 5.

5.8 Post-injection management

The effect of BT and the duration vary between individuals. The effects of BT should be monitored over time, and standardised assessment and evaluation should be performed at realistic intervals.

5.8.1 Physical management

The team members involved in pre-injection assessment should be included in the post-injection treatment, measurement of outcome, re-assessment and review of goal achievement. It is important to:

- assess the need for orthotics/splinting or review existing orthoses as appropriate once the clinical effect of muscle weakening is observed (usually 7–14 days post-injection) and ensure there is a system to review the orthotics/splinting provision, provide new orthoses as required and assess patient compliance
- provide patient education on stretching regimes and guidance on participating in activities
- take care over stretching weakened muscles. The intensity of the stretches should be graded over time to prevent intramuscular haematomas due to tearing of stiffened muscle fibres
- provide therapy to increase muscle strength of the opposing muscle groups, when indicated
- facilitate activity in opposing muscle groups
- consider other treatments that may enhance the effects of BT such as constraint therapy or electrical stimulation as appropriate
- active NMJs take up BT more avidly than NMJs at rest, and there is some evidence that electrical stimulation of the *injected muscle* may enhance the anti-spastic effects of BT (Hesse *et al* 1998). However, it is necessary to stimulate the motor point or the nerve to the muscle, in order to activate the NMJs to achieve this effect
- functional electrical stimulation of the *antagonist muscle* may help to build up muscle strength and so enhance functional benefits (Hesse *et al* 1998).

5.8.2 Orthotics/splinting provision

Orthotics/splinting provision covers a range of devices which include thermoplastic splints, casts, Lycra® garments, neoprene, inflatable splints, dynamic splints.

Splinting provides a prolonged stretch to a muscle and, when used together with BT, aims to improve muscle length, correct and prevent contractures and maximise function. 'Off-the-shelf' orthoses can sometimes be useful if carefully applied and adapted for the individual. However, the presence of deformity often requires bespoke solutions.

The use of orthotics/splinting is an adjunct to other therapies. The assessment and provision of orthoses must only be carried out by trained staff with the knowledge of how to position and align a limb, an understanding of muscle tone, and the skills to fabricate the appropriate device (ACPIN 1998). The patient and/or carer must be educated regarding donning and doffing the splint.

Pre-existing splints/orthotics should be reviewed, or new ones applied approximately 7–14 days post-injection, which is when the effect of BT usually starts to become clinically apparent. The

optimal duration of splinting is unclear. There is some evidence that splints should be worn for at least six hours and tolerance often needs to be built up slowly. The splints should be reviewed and revised regularly (Tardieu *et al* 1988). However, the duration and frequency of orthotic use will depend on the individual patient characteristics. Advice should be sought from the treating therapist.

Frequent inspection should be undertaken as a precaution to prevent pressure injury in the following circumstances:

- skin fragility
- allergy to splint materials
- pressure areas and oedema
- other limb pathologies (eg rheumatoid arthritis)
- vascular disorders
- cognitive and communicative deficits
- sensory and perceptual deficits
- limb being used for vital sign assessment or drug administration.

5.9 Clinical review

5.9.1 7–14-day review

This review is normally undertaken by the therapy team to assess the need for splinting/orthotics and other therapy interventions.

5.9.2 4–6-week review

A formal follow-up assessment is required at four to six weeks to determine whether or not the treatment goals have been achieved and to identify any adverse effects and patient compliance with post-injection regime (if serial injection is planned, the need for injection of further muscles may be considered at this point).

5.9.3 3–4-month review

The treating clinician must review at three to four months post-injection, when the effect of the toxin is likely to have worn off and to determine the need for further BT treatment.

5.10 Documentation

Documentation for all injections should include:

- a clear statement of treatment aims
- baseline outcome measures appropriate to those aims
- BT brand, dose, dilution and muscles injected
- follow-up treatment plan
- evaluation of outcome, including goal attainment and repeat measures
- plans for future management
- adverse effects
- user satisfaction questionnaire.

(A sample proforma is given in Appendix 5.)

6 Formal evaluation of effectiveness

All interventional procedures should have a formal assessment of outcome. Outcome should be evaluated at least three levels:

- Goal attainment: have the intended goals for treatment been achieved?
- Impairment: has BT intervention produced a reduction in spasticity?
- Function: if so, has this had any impact on function, either in terms of 'passive' (ease of care) or 'active' functional activity?

In some cases it will also be appropriate to consider whether this has produced an improvement at the level of participation, such as well-being or quality of life for patients and their carers; and also to consider evidence of cost-effectiveness.

Because individual goals for treatment vary widely, there is no single outcome measure that will capture the benefits of treatment in all cases. Instead, a range of measures will be required. While agreeing the goals for treatment with the patient and their family, the treating team should consider which measures will be appropriate to assess outcome, and ensure that these are measured and recorded at baseline.

The purpose of this section is to describe the principles of outcome measurement. Further details and practical tools to assist with outcome evaluation are given in Appendices 3 and 4.

6.1 Measurement methods

Some key measurement methods are summarised in Table 7.

Table 7 Key measurement methods

Method	Examples
Physical measurements (generally at the level of impairment)	Range of movement, eg goniometry Anatomical distance, eg inter-knee distance Spasm frequency
Rating scales (for symptoms or tasks)	Graphic rating scales, eg numeric or visual analogue scales for pain Verbal rating scales, eg Likert scale
Goal attainment	Simple recording of treatment goals achieved Goal Attainment Scaling
Formal standardised scales	Impairment scales, eg Ashworth, Tardieu Passive function, eg carer burden scales Active function, eg motor function tests

6.2 Have the treatment goals been achieved?

As discussed above, clear goals for treatment should always be documented in the medical records. Even if they record nothing else, the clinicians should note whether these have been achieved or not.

Goals for intervention vary from patient to patient and a single outcome measure cannot capture all domains.

Goal Attainment Scaling can overcome this variation to record the successful attainment of several goals that are important to the individual. First introduced in the 1960s by Kiresuk and Sherman (1968), this technique is found to be suitable for health problems which warrant a multidimensional and individualised approach to treatment planning and outcome measurement. It has been successfully used to demonstrate clinically important change in the context of spasticity management (Ashford and Turner-Stokes 2006). Goal attainment is rated on a five-point scale and combined into a single score through the application of a standard formula. Appendix 4 provides a brief overview and practical guide to GAS.

6.3 Impairment – has botulinum toxin intervention produced a reduction in spasticity?

Spasticity is hard to measure directly in routine clinical settings. However, it is important to assess the change in muscle tone if possible, because if BT has not been effective in reducing unwanted muscle overactivity, it is unlikely that any functional gains may be attributed to BT itself.

Two clinical scales have been devised to provide a clinical assessment of spasticity, based on clinical evaluation of involuntary muscle contraction in response to movement:

- the Ashworth Scale is widely used although validity, reliability and sensitivity are acknowledged to have limitations (Mehrholz *et al* 2005). However, it forms a useful baseline indicator of severity and may provide some indication of change
- the Tardieu Scale is reported to have slightly better reliability than the Ashworth Scale (Mehrholz *et al* 2005). However it is more time consuming to complete and the full scale is rarely recorded (see Appendix 3).

These scales are commonly used although their validity has never been demonstrated as their reliability is variable.

6.3.1 Physical effects of spasticity

In addition to muscle overactivity, the physical effects of spasticity (eg limited range of movement) are often recorded through:

- goniometry to measure the range of movement across a joint, or
- anatomical distances such as inter-knee distance following injection of hip adductors, or finger–palm distance in the case of treatment for a clenched hand.

6.4 Evaluation of symptoms

Symptoms such as pain or perceived muscle stiffness are often the features of spasticity that bother patients the most:

- a VAS or other graphic rating scale, recorded before and after treatment, may help to provide an objective assessment of change. The patient marks along a 10 cm line how severe their target symptom is
- verbal rating scale: some patients may find it easier to report on a simple verbal rating scale – for example ‘none – mild – moderate – severe’, or to say whether their pain is ‘the same, better or worse’.

6.4.1 Evaluation symptoms in people with cognitive and communication problems

It should be remembered that patients with brain injuries may have visuospatial problems, making the VAS less reliable. The following may help in this situation:

- vertical, as opposed to the horizontal, orientation of the scale can help to avoid distortion due to unilateral neglect
- some patients prefer to report symptoms based on a numerical score of 0–10
- the Numeric Graphic Rating Scale may provide the best of both through a combination of the visual scale and numbers.

People with severe cognitive and communication problems may require particular support for symptom reporting:

- rating scales should be presented in a format that is accessible for the individual. Tools such as the AbilityQ have been designed to test the persons ability to use different types of scale, and thus present questions in a form to suit their strengths (Turner-Stokes and Rusconi 2002)
- people who lack verbal and numerical skills may be able to respond to a suitably adapted pictorial rating scale (such as the Scale of Pain Intensity: see Appendix 3).
- assistance from a speech and language therapist or psychologist may help to facilitate self-report in the presence of more severe impairment.

6.5 Impact on function

Standardised scales allow comparison between individuals and groups, although many of the recognised measures have limited applicability in this area. The choice of scale will depend on the goals for treatment.

6.5.1 Active function

Global measures, such as the Barthel Index or the Functional Independence Measure (FIM), are rarely sensitive to change arising from focal intervention. Where patients have underlying selective voluntary movement in the limb, but increased tone limits 'active' function, eg by affecting the quality or speed of movement, it is usually necessary to use a focal motor function test to detect functional gains. Some useful focal measures include:

Upper limb:

- Frenchay arm test
- Action research arm test
- Nine-hole peg test.

Lower limb:

- functional ambulation category
- 10 m walking time, or six minute walking distance (to capture fatigue)
- gait analysis, or paper walkway if this is not available.

Even if formal motor function tests are not used, simple video recordings of the patient undertaking the same activity before and after treatment can provide objective evaluation of functional change.

6.5.2 Passive function

Rather more commonly, there may be little opportunity to restore active function, but improving the ease of caring for the affected limb, eg in washing and dressing, can nevertheless make significant impact on carer burden, and can potentially have significant cost benefits in reducing the time taken, or the number of people required, to perform care tasks.

Techniques for assessing passive function include:

- verbal or visual analogue ratings of 'ease of care'
- timed care tasks eg time taken for dressing/washing
- formal scales that measure dependency or carer burden.

A number of scales in particular have been developed specifically for assessment of outcome from spasticity management (see Appendix 3 for details):

- the Leeds Arm Spasticity Impact Scale (LASIS) (Bhakta *et al* 1996) (originally published as the Patient Disability and Carer Burden Scales (Bhakta *et al* 1996)) is a measure of passive function
- the Arm Activity Measure (ArMA) is a self-report scale which includes active and passive function subscales (Ashford *et al* 2008a)
- Snow *et al* (1990) used a standardised measure of focal tone, spasm frequency and ease of hygiene for evaluating outcome from BT injection for hip adductors.

To date, there is some limited evidence for the validity and reliability of these tools but further work is required to fully understand their psychometric properties and utility in the course of routine practice.

In severe contractures, maintaining hygiene in skin crease areas, eg in the palm, axilla or at the elbow can be difficult. Digital photography before and after treatment can provide a useful record of skin maceration for comparison.

6.6 Participation and quality of patient experience

Because of the wide range of different goals and outcomes for BT injection and the focal nature of the intervention, scales which provide a global assessment of well-being or quality of life tend to be poor indicators of the success of treatment. Nevertheless it is important to capture patient experience. Possible outcome measures at this level include:

- global assessment of benefit using a verbal or visual analogue rating scale
- patient and carer satisfaction questionnaires
- goal attainment rating especially where goals are weighted for importance to the patient and reflect goals at the level of participation.

7 Prescribing, supply and administration by non-medical injectors

Therapists and nurses play a critical role in all aspects of spasticity management using BT from patient selection, through treatment planning and goal setting to follow-up and outcome evaluation. A logical extension to this role is the prescribing, supply and administration of the BT itself:

- prescription of medicines in the UK is controlled by the Medicines Act 1968
- in the Medicine Act 1968, supply and administration of medicines is considered a separate issue to prescribing.

Particular challenges in BT prescribing, supply and administration lie in the potentially toxic nature of the drug, which mean that administration by NMIs must be very carefully managed and monitored, in order to safeguard not only the patient but also the professional. While side effects are very rare, they could (at least in theory) be life threatening, so that adequate arrangements for emergency medical back-up and support must always be in place.

At the time of producing this document, spasticity management services already routinely involve therapists in clinical decision making and follow-up management of patients. In a number of services, therapists and nurses have now become involved in the administration of BT and this is likely to develop further in the future. The level of involvement will vary and develop depending on the individual clinicians' experience, legal rights held, knowledge and the service need.

There are four methods whereby NMIs may be involved in BT supply and administration in the UK. Two of these involve supply and administration but not prescribing, under either a Patient Specific or a Patient Group Direction (PSD/PGD). The other two involve prescribing, as well as supply and administration – either as a supplementary or an independent prescriber (see Appendix 7 for further details).

At the current time in the UK:

- nurses may prescribe using either independent or supplementary prescribing rights, providing they have the required training and certification
- allied health professionals do not yet have independent prescribing rights. They can only undertake supplementary prescribing, again with the required training
- both groups may use PSDs or PGDs for supply and administration.

PSDs, PGDs and supplementary prescribing can all include uses of licensed medicines outside their SPC (so called 'off-label' uses). Independent non-medical prescribers (NMPs) may theoretically prescribe medications for off-label use, but they must accept professional, clinical and legal responsibility for that prescribing, and should only prescribe 'off-label' where it is accepted clinical practice. It should be noted than many of the uses of BT described in these guidelines are currently off-label and, given the potentially toxic nature of the product, we strongly recommend at the current time that independent NMPs restrict their prescription of BT to its licensed uses, and that any off-label injections are prescribed by a registered medical practitioner.

This area of practice and legislation is changing quite rapidly. At the time of publication, however, the majority of therapists or nurses undertaking supply and administration of BT are

doing so under a PGD, but a small minority are supplying, administering and prescribing under supplementary prescribing rights. Both medical and NMIs require additional training, which may vary dependent of experience (see Section 8.4 for the training requirements).

The scope of each method is detailed in Appendix 7, and the role of the NMI is summarised in Table 8.

Table 8 Summary of the role of the non-medical injector (NMI) under the various current methods to support prescribing, supply and administration of botulinum toxin

Method	Role of the NMI
Administration, but not prescription	
Patient Specific Direction (PSD) (A written instruction from an independent prescriber* for a medicine to be supplied/ administered to a named patient by an appropriately qualified health professional)	The NMI may administer the medication *to a specific patient* under instructions from an independent prescriber* PSDs do not allow for any clinical decision making at the point of administration, eg variation of dose or site, and may not meet the needs of the individual if dose variation is clinically indicated
Patient Group Directions (PGD) (A formal document drawn up by an NHS trust or other healthcare provider, providing written instruction for the supply and/or administration of • a named medicine • by a named registered health professional • in a defined clinical situation • to groups of patients who may not have been identified before presenting for treatment)	The NMI may administer medication for certain *patient groups* under circumstances specified in the PGD, thus avoiding the need for a specific PSD for each patient Clinical decision making (eg variation to dose and site) is allowed, providing it is acknowledged in the PGD, and is managed according to clear criteria or parameters
Prescription as well as administration – requires specific qualification	
Supplementary prescribing (A voluntary prescribing partnership between the independent* and supplementary prescriber, to implement an agreed patient-specific clinical management plan, with the patient's agreement)	In addition to administration, the NMI has a limited role in the prescription of medicines through the use of a patient-specific 'clinical management plan' – usually devised with a medical colleague The supplementary prescriber may prescribe any medicine that is referred to in the plan until the next review by the independent prescriber*
Independent prescribing (Full responsibility for the prescription, supply and administration of licensed medicines)	The non-medical prescriber (NMP) takes on full responsibility for the prescription, administration and monitoring of the treatment We strongly recommend that independent prescribing is applied to licensed uses of BT only At the current time in the UK, nurses can become NMPs, but not allied health professionals

*For all off-label or unlicensed uses of BT, the independent prescriber named in a PSD, PGD or supplementary prescribing arrangement must be a registered medical practitioner.

8 Organisation of services

8.1 Requirements

It is important for the MDT to have the necessary competencies to set up services to manage spasticity; this applies irrespective of the scope of the service. The optimal service configurations will vary according to staff skills, facilities, patient population, etc. A service will usually revolve around specialist rehabilitation units, neurology or stroke services or within departments of medicine for the elderly, but should be supported by a business case for all aspects of spasticity management.

The requirements include:

- clinician(s) trained in neurological rehabilitation and spasticity management in general, with specific additional training in BT treatment
- an integrated physiotherapy, rehabilitation nursing and occupational therapy service, with a role in:
  - selecting appropriate patients for treatment
  - arranging or delivering targeted physiotherapy after injection
  - ensuring appropriate provision of splinting and orthoses. There should be good links with physical therapy departments in referring units elsewhere.
- appropriate surgical advice should be available (eg orthopaedic, neurosurgical, plastics).

Many injections can be performed in dedicated outpatient clinics. This allows:

- more convenient, cost-effective assessment
- MDT follow up
- minimal wastage of BT
- easier access to equipment eg EMG to help with injections
- availability of nursing staff trained to assist in the care of patients.

Where possible, services should avoid the use of more than one of the available BT preparations in order to prevent confusion over doses.

All services should have:

- clear, concise documentation (see Appendix 5)
- a system for obtaining informed consent
- standardised evaluation and assessment, including outcome measurement
- provision of appropriate patient and carer information leaflets
- appropriate arrangements for follow up
- a clearly defined mechanism for paying for the spasticity management service. Ad hoc arrangements can be financially risky for host institutions.

Without these service elements, successful patient management will be limited.

8.2 Estimated treatment costs and potential cost savings

Although there is a cost to setting up the service, there is also potential to make significant savings through the use of BT. Box 1 shows the estimated annual cost implications of a service providing approximately 100 treatments per year.

Box 1 The estimated annual cost implications of a service providing approximately 100 treatments per year

The estimated annual total cost of a service providing approximately 100 treatment per year will include:

- BT and other medication costs approximately = £30,000
- Disposable EMG needles, syringes and other items = £800
- Splinting materials (estimated at three splints per treatment) = £7,500
- Imaging (required relatively infrequently (estimated at five patients per year)) = £1,500

Plus staff salaries for:

- 0.2 WTE medical consultant
- 0.5 WTE senior physiotherapist (Band 7–8)
- 0.5 WTE senior occupational therapist (Band 7–8)
- 1 WTE therapy assistant(s) (Band 3)
- 1 session (programme activity) for a treating physician
- Nursing, clinic and secretarial time

Capital costs:

A portable EMG machine or nerve/muscle stimulator = approximately £1,500

EMG = electromyography; WTE = whole time equivalent.

While this may at first sight seem expensive, at a total of approximately £950–1,000 per treatment, the cost of BT is relatively modest compared with the other interventions. Moreover, if cases are appropriately selected, it has the potential to reduce the costs of on-going care including:

- staff time/length of stay in prolonged therapy
- avoiding unnecessary surgical procedures and/or complications, such as pressure sores.

Even for severely dependent patients, the cost of care can be substantially reduced if BT injections produce critical changes in the number of carers or time taken for care tasks. This is illustrated by a brief case history described in Box 2.

8.3 Service evaluation

Regular audit of the use of BT should include the following, and documentation and follow up should be arranged to facilitate this.

Audit assessments include:

- quality of documentation and recording
- compliance with guidance including:
  - evidence of consent obtained in all cases
  - therapy intervention and follow up
- outcomes from treatment, in particular achievement of treatment goals
- adverse events.

A standardised international database is currently in development to facilitate consistent recording of treatment and outcomes (see Appendix 5).

Box 2 Example of a highly cost-effective (but as yet off-label) application of BT

A 33-year-old lady with MS had spasticity in her left hamstring muscles, resulting in knee flexion and inability to put her left foot to the floor. Because she was also mildly ataxic, she required two carers for all transfers and therefore a care package requiring two live-in carers.

Goals for BT treatment were to allow straightening of the left leg so that she could weight-bear on both feet. This would increase her stability during transfers, so that these could be managed with just one person and allow her care package to be reduced.

The anticipated weekly saving in care costs was estimated (based on current care costs at the time) using the Northwick Park Dependency and Care Needs Assessments (Turner-Stokes *et al* 1998, 1999).

Treatment included injection of Dysport® 500U into the hamstrings, followed by stretching serial casting (three splint applications) and institution of a standing regimen using an Oswestry® standing frame. The total cost of treatment (including the frame) was £1,250.

After treatment the patient was able to get her left foot to the floor, to weight-bear equally on both feet and to transfer safely and easily with just one person to assist her. Her care package reduced from two live-in carers (at a weekly cost of £1,232) to one live-in carer (with four hours cover for rest periods) (weekly cost £856), saving £376 per week.

The cost of her treatment was thus offset within just three to four weeks by savings in her ongoing care.

At her annual review five years later, the team recorded that she was still using her standing frame on a daily basis, and has required no further BT treatment. She is still transferring with the help of one person and requiring the same care package.

Allowing for inflation-related care costs, the mean annual saving in cost of care over this five-year period is £25,000, which means that this one treatment has now led to a total saving of over £125,000 – or 100 times the initial cost of treatment.

8.4 Training

BT should only be injected by clinicians with the appropriate skills and training. Ideally, the qualifications include in-depth knowledge, skills and practical experience of neurological rehabilitation.

All clinicians involved in spasticity management should be trained in the assessment and management of spasticity in general, together with specific treatment techniques and splinting related specifically to BT. Training may be delivered through a range of formats including:

- approved short courses with lectures and practical demonstrations
- MSc modules in spasticity management
- attachments to centres delivering BT treatments or working under the supervision of practitioners expert in spasticity management and the use of BT.

Key knowledge and skills should cover the areas shown in Box 3.

8.4.1 Minimum training requirements

- Attendance on BT training course (to include a formal certificate) approved by the relevant college.
- Observation of the assessment of and injection technique in at least five patients with arm and five patients with leg spasticity related problems.
- Ability to use the relevant equipment eg EMG, nerve stimulation or ultrasound.

Box 3 Key competencies for botulinum toxin (BT) injectors

Knowledge required

- What is BT?
- What is spasticity?
- What is the impact of spasticity on patients, carers and the rehabilitation process?
- The range of spasticity treatments and the role of BT
- Adverse effects
- Evidence base for the use of BT
- Relevant functional anatomy
- How to distinguish spasticity from contracture or soft-tissue shortening
- Service organisation:
  - role of physiotherapy, orthotics/splinting, information provision
  - development of a business case to obtain funding
- How to set up a BT service

Skills required

- Patient selection
- How to assess the patient
- Communication and negotiation skills
- Identifying target muscles
- Injection technique with or without electromyography guidance
- Post-injection follow up
- Use and interpretation of outcome measures, including goal attainment scaling