Spasticity in adults: management using botulinum toxin

National guidelines

January 2009

Royal College of Physicians

Setting higher medical standards

BSRM

British Society of Rehabilitation Medicine

Spasticity in adults: management using botulinum toxin

National guidelines

January 2009

Royal College of Physicians

Setting higher medical standards

BSRM

British Society of Rehabilitation Medicine

Acknowledgements

This document has been produced with the assistance of an educational grant from Ipsen Ltd and coordinated by Louise Blakeborough, Chapter Five. Financial assistance for editing and preparation of the final manuscript was kindly provided by the Luff Foundation and the Dunhill Medical Trust.

The Royal College of Physicians

The Royal College of Physicians plays a leading role in the delivery of high-quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 20,000 Fellows and Members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

Citation for this document

Royal College of Physicians, British Society of Rehabilitation Medicine, Chartered Society of Physiotherapy, Association of Chartered Physiotherapists Interested in Neurology. *Spasticity in adults: management using botulinum toxin. National guidelines*. London: RCP, 2009.

ISBN 978-1-86016-350-0

ROYAL COLLEGE OF PHYSICIANS
11 St Andrews Place, London NW1 4LE
www.rcplondon.ac.uk

Registered charity No 293196

Review date: 2014

Typeset by Dan-Set Graphics, Telford, Shropshire

Printed in Great Britain by Cambrian Printers Ltd, Aberystwyth

Contents

Guidance Development Group

Professor Lynne Turner-Stokes (Chair and lead editor)
Consultant in Rehabilitation Medicine, Northwick Park Hospital, Harrow, Middlesex; Herbert Dunhill Chair of Rehabilitation, King's College London

Mr Stephen Ashford (Co-editor)
Clinical Specialist and Research Physiotherapist, Regional Rehabilitation Unit, Northwick Park Hospital, Harrow, Middlesex; Honorary Research Fellow, King's College London

Professor Bipin Bhakta
Charterhouse Professor of Rehabilitation Medicine, University of Leeds, Leeds

Dr Kate Heward
Senior Lecturer in Occupational Therapy, Sheffield Hallam University, Sheffield; Private Practitioner

Dr A Peter Moore
Consultant Neurologist and Honorary Senior Lecturer, The Walton Centre for Neurology and Neurosurgery, Liverpool

Mr Adrian Robertson
Clinical Specialist Physiotherapist, Mid-Yorkshire Hospitals NHS Trust

Professor Anthony Ward
Consultant in Rehabilitation Medicine, North Staffordshire Rehabilitation Centre, Stoke-on-Trent; Honorary Senior Lecturer, University of Keele

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.

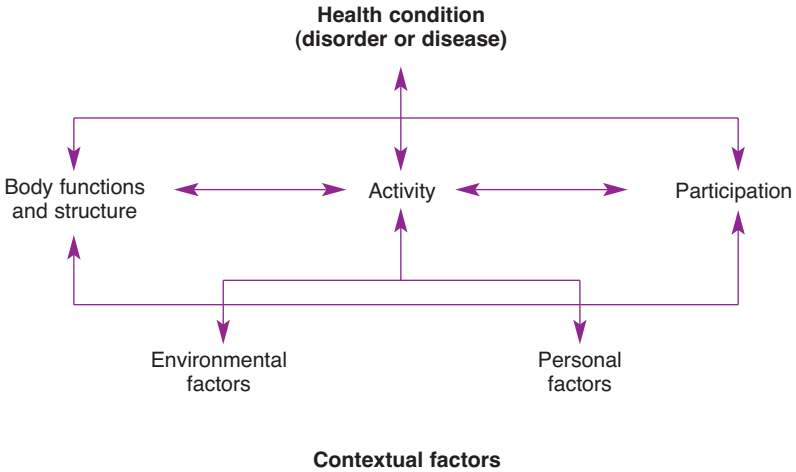


Fig 1 The International Classification of Functioning, Disability and Health

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.

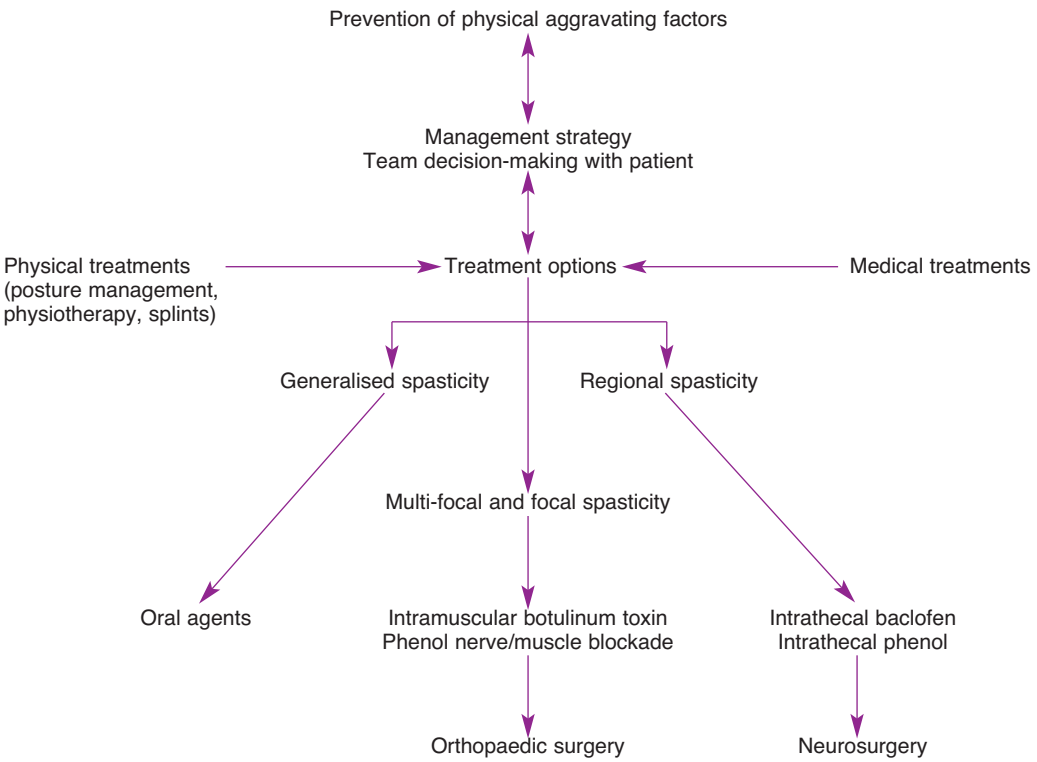


Fig 2 Management strategy for adults with spasticity. Note: It is not uncommon to have a mixed pattern of spasticity and interventions are almost always combined, eg physical management programmes and systemic medication.

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.

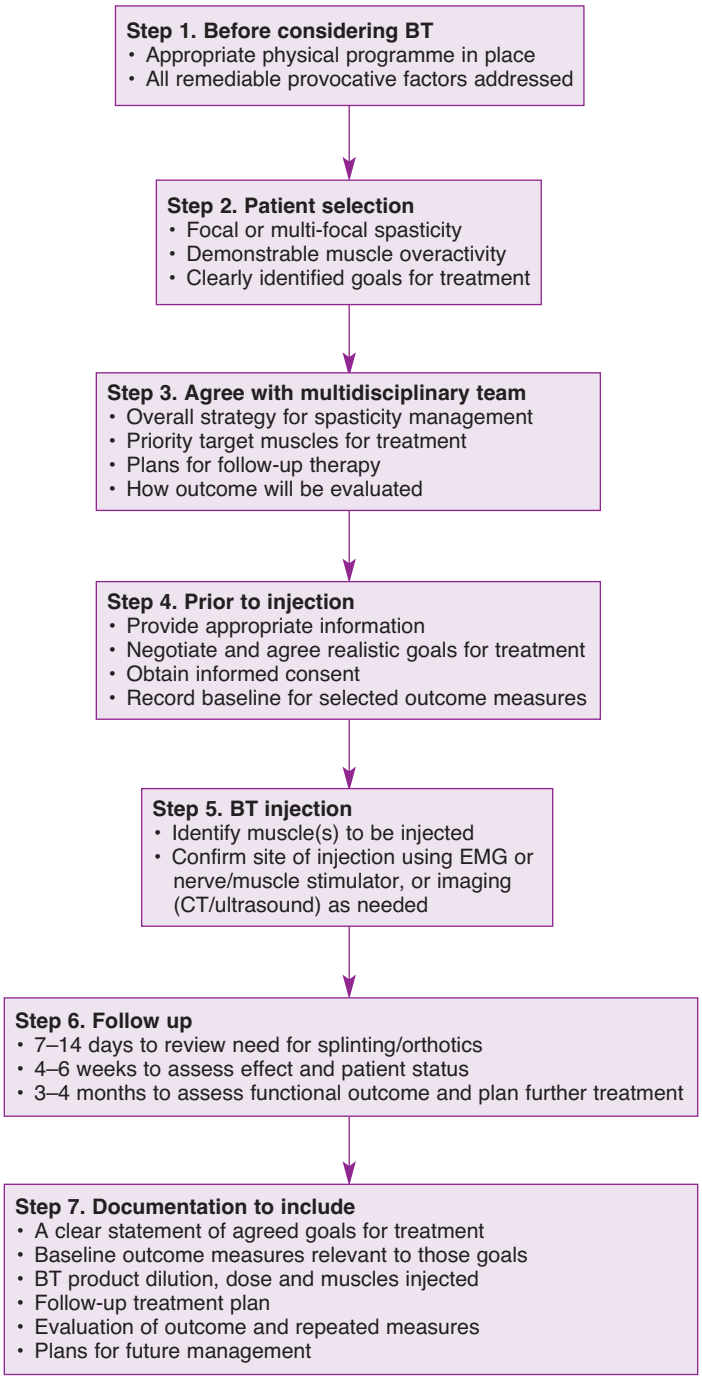


Fig 3 The key steps to treatment of spasticity with botulinum toxin (BT).

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

Appendix 1

Evidence for the effectiveness of botulinum toxin

The evaluation of literature to underpin this guidance was performed by members of the GDG, without the full machinery available to the major national guideline development bodies. Nevertheless, it included a systematic review of the randomised controlled trial (RCT) evidence for the effectiveness of BT in spasticity management, and also a review of the outcome measures that have been applied in those trials.

As with many guidelines, while trial-based evidence may be available to support the overall effectiveness of intervention, specific evidence to support the detailed steps of management is lacking. As a result the majority of recommendations are at level C, supported primarily by consensus of the GDG, underpinned by their respective experience and their knowledge of the published non-trial-based literature in this context.

Evidence

Details of the review methodology are published elsewhere (Ashford *et al* 2008b). Evidence tables A1.1–A1.2 summarise to date the main RCTs of BT in the treatment of spasticity in adults:

- Table A1.1 lists trials in upper limb spasticity
- Table A1.2 lists trials in lower limb spasticity.

The majority are fairly small, short-term studies.

The principal conclusions that may be drawn from these studies are that improvements at the level of impairment (ie reduction of tone and increased range of movement) are readily demonstrated, but it is harder to show that these are actually translated into changes at the level of activity or participation. Nevertheless, studies by Bhakta 2000 and Brashear *et al* 2002 showed improvements in function and carer burden.

A meta-analysis of pooled data from two trials of BT in upper limb spasticity (Francis *et al* 2004) targeted specifically the Barthel Index items that might reasonably be expected to change (dressing, grooming and feeding). This improved the sensitivity of functional assessment, so that it was then possible to demonstrate a clear relationship between reduction of spasticity and improved function. Moreover, the analysis demonstrates that maximal change in function was delayed until after the maximal change in spasticity for a significant number of patients. This could account for failure to demonstrate functional change in studies that used a single end-point for evaluation of outcome, and emphasises the need for continued follow-up with measurement of the relevant parameter at appropriate time points.

Dose-ranging studies for the upper (Bakheit *et al* 2000) and lower (Hyman *et al* 2000) limb suggest that a total of 1,000U of Dysport® is the optimum total dose for any one treatment cycle. Higher doses may produce a greater reduction of spasticity and a longer lasting effect, but carry a greater risk of unwanted side effects such as weakness in either local or distant muscles.

Adjunctive therapy

Most studies of BT in spasticity management have been undertaken in the context of a rehabilitation programme or have included follow-up therapy to a greater or lesser degree (not always specified). It is therefore appropriate to administer BT only in the context of a general spasticity management programme, and to follow up with appropriate physiotherapy intervention. A RCT by Giovannelli *et al* (2007) provides evidence for the added advantage of adjunctive physiotherapy over BT alone in the reduction of spasticity.

The use of specific adjunctive treatments, such as stimulation or splinting, often forms part of these general treatments, but has been formally evaluated in only a few studies:

- electrical stimulation: Hesse *et al* (1998) conducted a small randomised, placebo-controlled study to assess the use of BT with short-term electrical stimulation. Electrical stimulation (30 minutes three times a day for three days) was associated with some modest but statistically significant gains
- strapping/splitting: another small single blind RCT by Reiter *et al* (1998) showed that low dose BT (100U Botox®), followed by strapping of the ankle was as effective as standard dose (190–320U Botox®) without strapping in the management of spastic equinovarus.

Although it is generally accepted that BT needs to be given in combination with other ongoing spasticity management techniques, the optimal time to initiate treatment and the potential for combination treatments needs more research.

Evidence for cost-effectiveness

A secondary analysis of post-stroke patients compared the cost-effectiveness and outcomes of oral therapy versus BT type A treatment strategies in patients with flexed wrist/clenched fist spasticity. Treatment outcome and theoretical cost data based on resource use were collected from an expert panel experienced in the treatment of post-stroke spasticity. BT type A treatment was reported to be more cost-effective than oral therapy with the 'cost-per-successfully-treated month' being £942, £1,387 and £1,697 for BT type A first-line, BT type A second-line and oral therapy, respectively (Ward *et al* 2005).

The only other published study was another secondary analysis published as an abstract by Wallesch *et al* (1997) who looked at the effectiveness of BT injections in patients with spasticity following stroke. The authors estimated the cost-effectiveness of three treatment strategies for spasticity following a stroke: physiotherapy only, BT plus physiotherapy, and oral baclofen plus physiotherapy. The study suggests overall that the average extent of improvement in spasticity with BT plus physiotherapy, as measured by the Ashworth Scale, was three times greater than for baclofen plus physiotherapy and 10-fold greater than for physiotherapy alone.

Formal cost evaluation data have yet to be reported, but a multi-centre, multinational study is in progress and is expected to report in 2009/10.

Future research

While the body of existing research provides good evidence for the overall effectiveness of BT in relieving spasticity, critical questions remain to be answered including:

- 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?

These are questions that cannot necessarily be answered by RCTs or other experimental designs. Future research will need to incorporate a range of research methodologies (including quantitative and qualitative approaches) and should include the evaluation of the person's own perspective (including the achievement of personal goals), as well as informing effective and cost-efficient practice.

Elsewhere in the world, systematic data collection in the course of routine clinical practice is increasingly seen as an important contribution to establish 'practice-based evidence' for health interventions (Horn and Gassaway 2007). This is particularly relevant in situations where strength of evidence that already exist makes randomisation to 'no treatment' arms unethical, or where diversity of the intervention and/or patient group makes it impossible to account adequately for all the potential confounding factors.

Over the past decade, the gathering of large multi-centre datasets, such as the Post Stroke Rehabilitation Outcomes Project (DeJong *et al* 2005), has contributed to opening of the black box of rehabilitation. By providing detailed information on very large consecutive numbers of patients, all gathered in the course of real-life practice, this approach has started to address the types of questions raised above.

A pilot multi-national project is currently underway to develop a common minimum dataset for BT treatments in spasticity. The proforma in Appendix 5 is based on the currently proposed dataset, although it is anticipated that this will undergo further development and change before it reaches a stable state. As well as providing benchmarking for service quality, future roll-out of this project has the potential to provide systematic information on which to determine optimum treatment strategies in different clinical situations and thus guide individual treatments on a sound evidence base.

Table A1.1 Evidence table for the use of botulinum toxin (BT) in spasticity management: upper limb

Author year	Design/nos	Subjects	Agent	Outcomes	Findings
Simpson *et al* 1996	Multi-centre PC-RCT 3-month follow up	n=39 Mixed CNS disease	BT 75U,150U, 300U Elbow/wrist flexors	MAS	BT reduced tone safely
Yablon *et al* 1996	Open label study 2–4-week follow up	n=21 TBI	BT followed by physiotherapy Wrist/fingers	MAS ROM	BT improves tone and ROM safely
Bhakta *et al* 1996	Open label study	n=17 Stroke	Botox® or Dysport® Elbow/wrist	ROM Pain UL Function (hygiene, dressing, walking)	BT improves function safely
Hesse *et al* 1998	PC-RCT of BT plus FES	n=24 – four groups six in each Stroke	Dysport® 1,000U into 6 UL muscles	MAS, limb position Three functional tasks (palmar hygiene, cutting finger nails, and arm through sleeve)	Patients with BT and FES showed significantly greater reduction in difficulties with palm hygiene, with trend towards lower spasticity Small numbers though
Bakheit *et al* 2000	PC-RCT Dose-ranging study 4-month follow up	n=83 Stroke	Dysport® 500U, 1,000U or 1,500U Five muscles – fixed regimen	MAS ROM RMA (arm scale) Barthel Index Subjective evaluation of function: dressing, palmar hygiene, fingernails	Dysport® reduces tone Optimal dose 1,000U Safe No effect on RMA or Barthel Trend towards effect on subjective functional gain
Bhakta 2000	PC-RCT 3-month follow up	n=40 Stroke	Dysport® 1,000U Flexible regimen	Eight-item patient disability scale* Four-item carer burden scale* *Secondary measures: MAS, strength, ROM pain*	Significant improvement in patient disability at week 2–6, but wearing off at week 12 Improvement in carer burden maintained at 12 weeks
Richardson *et al* 2000	PC-RCT 3-month follow up	n=52 (27Rx/25pc) 16/16 upper limb 11/9 lower limb Mixed CNS disease	Botox® Flexible regimen	Problem severity and goal attainment MAS, ROM, nine-hole peg test, 10 m walk RMA (arm, trunk and leg scales)	Significantly better MAS, ROM, problem severity and RMA in Rx group Goal attainment achieved in both

continued

Table A1.1 Evidence table for the use of botulinum toxin (BT) in spasticity management: upper limb – *continued*

Author year	Design/nos	Subjects	Agent	Outcomes	Findings
Smith *et al* 2000	PC-RCT 3-month follow up	n=21 Stroke or TBI	Dysport® Flexible dose regimen Elbow/wrist/fingers	MAS, ROM, posture Disability – upper body dressing time, Frenchay arm test Patient reported global assessment scale	Reduction in tone and increased ROM in wrist and fingers at six weeks – lost by 12 weeks No change in disability, but improvement on pts global assessment
Bakheit *et al* 2001	PC-RCT 4-month follow up	n=59 Stroke	Dysport® 1,000U Flexible regimen	MAS, ROM, pain Barthel Index Subjective evaluation of function: dressing, palmar hygiene, fingernails GAS, global assessment of benefit	No significant difference in ROM, pain, GAS or BI at four weeks, but ROM at elbow better in BT group at 16 weeks and global assessments significantly better
Brashear *et al* 2002	Multi-centre PC-RCT 3-month follow up	n=126 Stroke	Botox® Flexible dose regimen Wrist/fingers	Disability assessment scale (hygiene, dressing limb position, pain) MAS Global assessment	Significant treatment effects on tone, functional ability and global assessment
Francis *et al* 2004	Secondary analysis	n=142	Pooled data from Bakheit *et al* 2000 and 2001	MAS Amalgamated functional scale	Clear relationship between changes in spasticity and arm function
Childers *et al* 2004	Multi-centre PC-RCT 6-month follow up	n=91	Botox® 90U, 180U, 360U or placebo Fixed regimen	MAS FIM Global assessment, SF-36	Dose dependent reduction in spasticity did not translate into improved function or quality of life
Bhakta *et al* 2008	PC-RCT 3-month follow up	n=40 Stroke	Dysport® 1,000U Flexible regimen	Biomechanical and EMG measure of upper limb associated reaction GAS using 10-point categorical scale	Significant improvement in biomechanical measure of associated reaction Significant reduction of the interference of associated reactions with daily activities (but small numbers)

Now known as the Leeds Arm Spasticity Impact Scale (LASIS) – see Appendix 3 for details. Bhakta *et al* (2008) involves patients recruited to Bhakta *et al* (2000).
BI = Barthel Index; CNS = central nervous system; EMG = electromyography; FES = functional electrical simulation; FIM = functional independence measure; GAS = Goal Attainment Score; MAS = Modified Ashworth Scale; MS = multiple sclerosis; PC-RCT = placebo controlled randomised clinical trial; RMA = Rivermead motor assessment; ROM = range of motion TBI = traumatic brain injury; UL = upper limb.

Table A1.2 Evidence table for the use of botulinum toxin (BT) in spasticity management: lower limb

Author year	Design/nos	Subjects	Agent	Outcomes	Findings
Snow *et al* 1990	Placebo controlled crossover study	n=9 MS patients	Botox® 400U Adductors	Composite score: spasms, pain, hygiene	First demonstration of effectiveness of BT in spasticity BT produced a significant reduction in spasticity and in nursing care. No adverse effects
Hesse *et al* 1994	Open label study 8-week follow up	n=12 Chronic hemiparetic patients	Botox® 400U to soleus, Tibialis posterior and gastrocnemius	MAS Gait analysis	Definite improvement in spasticity in 10 patients, two weeks after injection four patients able to achieve active dorsiflexion Demonstrated improvement in various aspects of gait, including velocity, stride length and stance symmetry Effects waned after eight weeks
Grazko *et al* 1995	Placebo controlled DB crossover study	n=12 MS patients Plus n=8 PD patients with rigidity	Botox® Adductors	Spasticity Function and nursing care	In spasticity group: improvement in tone, function and nursing care in 8/12 patients In rigidity group: tone improved in 7/8, function in 4/7 and pain in 4/5
Burbaud 1996	PC-RCT	n=23 Stroke patients (long-standing spasticity in some – up to 10 years)	Dysport® or placebo to gastrocnemius	MAS, Fugl–Meyer Video gait	Reduction in dependency on aids, but no change in gait velocity or Fugl–Meyer Longer-standing spasticity – poorer result BT effective, but better given earlier on
Kirazli 1998	Controlled trial BTX *v* phenol No placebo 12-week follow up	n=20	Botox® 400U or motor end-plate phenol	ROM, MAS, global assessment. Brace wear scale, ambulation	BT group showed better reduction in spasticity, increase in ROM and improvement in walking as compared with the phenol group. Both groups improved brace tolerance. Long-term benefits not explored

continued

Table A1.2 Evidence table for the use of botulinum toxin (BT) in spasticity management: lower limb – *continued*

Author year	Design/nos	Subjects	Agent	Outcomes	Findings
Reiter *et al* 1998	Single blind RCT 12-week follow up	n=18 Stroke	Botox® to Group A: Standard dose (90–320U) into several calf muscles Group B: low dose (100U) Tibialis posterior plus taping	ROM, MAS Step length and gait velocity	ROM improved better in group A, but gait velocity and step length improved equally Authors conclude that low-dose BT plus taping is as effective as higher does treatment, but this could just be type I error given small size of study
Hyman *et al* 2000	Multi-centre parallel group study 12-week follow up	n=74 MS patients	Dysport® dose-ranging study: 500, 1,000, 1,500U *v* placebo Hip adductors	MAS, ROM, spasm frequency	Significant dose-related reduction in spasticity with BT over placebo. 500U or 1,000U optimum dose – sometimes too weak with 1,500U although it gave better ROM and longer treatment effect Reduced need for re-treatment Trend towards improvement in hygiene and tone scores
Pittock *et al* 2003	Multi-centre PC-RCT 12-week follow up	n=234 Stroke patients	Dysport® dose-ranging study: 500, 1,000, 1,500U *v* placebo to gastrocnemius	2 min walking distance, stepping rate use of aids, pain, MAS	Small but significant improvements in calf spasticity, pain, and use of walking aids over placebo 68 patients reported 130 adverse events but no difference between groups. Serious events not related to treatment

DB = double blind; MAS = Modified Ashworth Scale; MS = multiple sclerosis; PC-RCT = placebo controlled randomised clinical trial; PD = Parkinson's disease; ROM = range of motion; UL = upper limb.

Appendix 2

Injection sites for botulinum toxin*

Adapted from Brin 1997; *Muscle & Nerve*, Vol 20, S6, 1994: S208–S220. Copyright John Wiley & Sons, Inc. 1994. Reprinted with permission of John Wiley & Sons, Inc.

Table A2.1 Injection sites for botulinum toxin

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Trunk muscles						
Psoas major	Transverse processes and vertebral bodies of T12–L5	Lesser femoral trochanter	Flexes hip	150–200	400–600	Approach posteriorly advancing spinal needle between transverse processes at L2, L3 and L4. 50–60 mU at each site
Iliacus	Floor of iliac fossa	Joins psoas tendon to form iliopsoas tendon to insert into lesser trochanter	Flexes hip	75–150	200–400	Anterior approach under lateral third of inguinal ligament – lateral to femoral nerve and avoiding lateral cutaneous nerve of thigh
Quadratus lumborum	Iliolumbar ligament and iliac crest	12th rib and L1–5 transverse processes	Flexes vertebral column laterally	100	300	Posterior approach lateral to vertebral column
Hip extensors and abductors						
Gluteus maximus	Posterior aspect ilium, sacrum, coccyx and sacrotuberous ligament	Greater trochanter	Extends thigh Laterally rotates hip	Rarely injected		
Gluteus medius	Large area of sacrum below iliac crest	Postero-superior angle of greater trochanter	Internally rotates leg	100	300	
Gluteus minimus	Broad area of ilium between anterior and inferior gluteal lines	Lower lateral part of greater trochanter	Abducts leg	Rarely injected		

continued

* It should be noted that the injection sites and doses other than in the upper limb are not yet approved by the UK licensing authority (Medicines and Healthcare products Regulatory Agency). In the absence of definitive research the guide doses are based on clinical experience and knowledge within the GDG. They are given as a guide only and should be adjusted according to individual clinical circumstances.

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Thigh – knee extensors						
Rectus femoris	Anterior inferior iliac spine (straight head) and ilium (reflected head)	Tibial tubercle via quadriceps and patellar tendons	Hip flexion and knee extension	100–150	300–500	Four points along the middle of quadriceps muscle mass
Vastus lateralis, intermedius and medialis	Anterior aspect of femur	Tibial tubercle via quadriceps and patellar tendons	Knee extension	100–150	350–500	Two points in lateral aspect of thigh; one deep centrally in lower half of thigh and one–two medially
Thigh adductors and knee flexors						
Pectineus	Superior pubic ramus	Posterior aspect of femur below less trochanter	Adducts thigh and assists hip flexion	50–100	150–400	Difficult to inject because of overlying neurovascular bundle below inguinal ligament medial to femoral vein
Adductor magnus	Ischial tuberosity	Posterior two thirds of femur down to adductor tubercle on medial femoral condyle	Adducts and extends thigh. Main action while sitting	100–200	300–600	Large muscle in upper medial thigh. Inject into upper third of thigh
Adductor longus	Body of pubis below pubic crest and symphysis	Post aspect of middle of femur into linea aspect	Adducts thigh. Main action on standing	50–100	100–300	Antero medial aspect of thigh one hand's breadth below inguinal ligament medial to femoral vein
Adductor brevis	Below pubic crest in superior pubic ramus	Upper femur posteriorly between lesser trochanter and linea aspera	Adducts and laterally rotates thigh	50–100	100–200	Behind adductor longus and pectineus and in front of adductor magnus
Gracilis	Inferior pubic ramus	Pes anserinus on posterior aspect of medial tibial condyle	Adducts thigh and flexes knee. Medially rotates flexed leg	80–120	100–300	Postero medial edge of thigh several points of injection down medial thigh

continued

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Thigh adductors and knee flexors – *continued*						
Semi membranosus	Ischial tuberosity	Pes anserinus on posterior aspect of medial tibial condyle	Flexes knee. Medially rotates flexed leg and extends hip	100–150	200–400	Medial muscles in posterior thigh – multiple injection sites
Semi tendinosus	Common origin with long head of biceps femoris	Pes anserinus on posterior aspect of medial tibial condyle	Same as semi membranosus	100–150	200–400	Medial muscles in posterior thigh – multiple injection sites
Biceps femoris	Long head: ischial tuberosity short head: linea aspera on back of femur	Head of fibula	Flexes knee, rotates leg externally and extends hip	100–150	200–400	Lateral muscle in posterior thigh – multiple injection sites
Popliteus	Popliteal groove on lateral epicondyle anteriorly	Pierces joint capsule to post. Aspect of upper medial tibia	Flexes knee and internally rotates lower leg at beginning of flexion	30	100	Deep over back of medial tibial condyle. Down to bone medial aspect of popliteal fossa and then withdraw
Lower leg – antero lateral compartment						
Tibialis anterior	Upper half of lateral surface of tibia and interosseous membrane	Medial cuneiform bone	Dorsi flexes and inverts foot	75–120	200–400	Front of shin, lateral to tibia
Extensor digitorum longus	Upper three fourths of anterior surface of fibula	Bases on 2nd and 5th middle and terminal phalanges	Dorsi-flexes foot and foot	50–80	150–250	Lateral to tibialis anterior in front of and border of fibula
Extensor hallucis longus	Anterior surface of middle two thirds of fibula and interosseous membrane	Base of distal phalanx of great toe	Extends great toe	50–60	100–150	Between tibialis anteror and extensor digitorum longus in middle of shin
Peroneus tertius (not always present)	Distal fourth of anterior surface of fibula	Dorsal surface of 5th MT base	Dorsi flexes and events foot	30–40	80–120	Attached to ext digitorum longus lateral surface

continued

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Lower leg – antero lateral compartment – *continued*						
Peroneus longus	Upper two thirds lateral surface of fibula	Under base of 5th MT and groove in cuboid to medical cuneiform and base of 1st MT	Everts and plantar flexes foot	50–80	100–250	Lateral aspect of shin anterior to fibula
Peroneus brevis	Lower two thirds of fibula shaft	Base of 5th MT	Everts foot	30–40	80–120	Lower half of lateral shin anterior to peroneus longus
Lower leg – posterior compartment						
Gastrocnemius – medial head	Back of medial femoral condyle	Via AT to calcaneum	Plantar flexes foot and flexes knee	100	150–400	Superficial muscle of medial aspect of calf
Gastrocnemius – lateral head	Back of lateral femoral condyle	Via AT to calcaneum	Plantar flexes foot and flexes knee	100	150–400	Superficial muscle of lateral aspect of calf
Soleus	Posterior surface of shaft of fibula and medial border of tibia	Via AT to calcaneum	Plantar flexes foot	100	200–400	Back of calf, midway down between muscle bellies of gastrocnemius
Flexor hallucis longus	Posterior surface of fibula below soleus	Through groove in posterior talus to terminal phalanx great toe	Flexes great toe (IP and MTP joints) maintains longitudinal arch	50	100–200	Under soleus mid calf immediately posterior to peroneus longus and fibula
Flexor digitorum longus	Posterior surface of tibia	Terminal phalanges of 2nd and 5th toes	Flexes toes 2–5 (IP and MTP joints) and maintains longitudinal arch	50	100–200	Behind medial border of tibia in its upper mid area. Inject near origin just behind tibia
Tibialis posterior	Interosseous membrane and adjoining posterior surfaces of tibia and fibula	Tuberosity of navicular bone and medial cuneiform bone	Plantar flexes and inverts foot	50–80	100–300	Mid calf, deep behind tibia and in depression between tibia and fibula

continued

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Lower leg – posterior compartment – *continued*						
Abductor hallucis	Medial aspect calcaneum and flexor retinaculum	Medial aspect base of great toe proximal phalanx	Abducts and plantar flexes great toe	10–20	30–80	Medial aspect 1st metatarsal
Flexor hallucis brevis	Cuboid bone and tibialis tendon	Two bellies inserted into each side of the base of the 1st proximal phalanx	Flexes 1st MTP joint	10–20	30–80	Plantar aspect of foot under 1st metatarsal
Flexor digitorum brevis	Medial aspect calcaneum and septal fascia	Middle phalanges of toes 2–5	Flexes 1st IP joint and lateral four MTP joints	10–20	30–80	Plantar aspect of foot at base of metatarsals
Pectoral girdle						
Trapezius	Occiput down median line to last thoracic vertebra	Lateral third of clavicle, acromion and scapular spine	Scapular elevation and rotation	50–75	150–250	Large muscle between neck and shoulder
Rhomboid	Spinous processes C7–T5	Medial border scapula	Extension of scapulae	50–60	150	Superficial, between scapula and spine
Supraspinatus	Supraspinatus fossa scapula	Greater tubercle of humerus	Abduction of arm from 0–15° above 90°	40	100–150	Supraspinous fossa on scapula
Infraspinatus	Post aspect scapula below spine	Greater tubercle of humerus	External rotation of arm	50	100–150	Infraspinous surface of scapula (caution: plays an important role in glenohumeral stability)
Subscapularis	Anterior aspect of scapula	Lesser tubercle of humerus	Internal rotation of arm	50	100–150	Inject under lateral border of scapula (usually requires imaging for accurate placement)
Deltoid	Scapular spine, acromion and clavicle	Deltoid tuberosity of humerus	Arm adduct from 15–90°	50–75	100–200	Inject anterior, middle and posterior fibres

continued

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Pectoral girdle – *continued*						
Teres major	Dorsum of scapula at inferior angle	Crest of lesser tubercle of humerus	Adducts, medially rotates and extends arm	30	100	Lateral aspect lower scapula (accurate injection very important – if too far cranio-laterally, may inject Teres minor (external rotator)
Teres minor	Lateral aspect of scapula	Back of greater tubercle of humerus	Adducts and laterally rotates	30	100	Lateral aspect scapula above
Latissimus dorsi	Tips of lower six thoracic spines, thoracolumbar fascia and iliac crest	Floor of intertubercular groove of humerus	Adducts, retracts and medially rotates upper limb	80	150–300	Find in posterior fold of axilla while asking patient to pull down elevated arm (caution: only inject in the presence of sufficient trunk stability)
Serratus anterior	Upper eight ribs in three parts	Medial border of scapula	Protracts upper limb	60–70	150–300	Lateral aspect of upper eight ribs
Pectoralis major	Clavicle and 3rd–8th anterior ribs	Greater tubercle of humerus	Adducts and medially rotates	75	200–300	Anterior axillary fold
Pectoralis minor	3rd, 4th and 5th ribs at costo-chondral cartlidges	Coracoid process	Draw scapula down and forwards, depresses shoulder	40	150	Deep to upper part of pectoralis major
Arm						
Biceps brachii	Short: coracoid process Long: supra glenoid tubercle scapula	Bicipital aponeurosis	Supination and elbow flexion	75–100	200–300	Anterior aspect of upper arm. Inject both heads
Triceps brachii	Scapula and humerus	Olecranon	Elbow extension	75–100	200–300	Three heads on post aspect of arm
Coracobrachialis	Coracoid process	Middle medial border humerus	Flexes and adducts upper arm	40	120	Medial to upper humerus between it and neurovasc bundle
Brachialis	Front of distal half humerus	Coronoid procress of ulna	Flexes elbow	50	150–200	Lower anterior humerus medial and lateral of biceps tendon

continued

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Extensor aspect forearm						
Brachioradialis	Left supracondylar ridge of humerus	Lateral surface distal radius	Elbow flexion	50	150–200	Radial side upper forearm
Supinator	Radial notch of ulna	Shaft of proximal radius	Supinates forearm	30–40	100–200	Extensor aspect of arm below radial neck – deep
Extensor carpi radialis longus	Distal third of lateral supracondylar ridge of humerus	Base of 2nd MC	Extends and adducts hand at wrist	30–40	100–200	Posterior to brachioradialis on back of forearm
Extensor carpi radialis brevis	Common extensor origin (lateral humeral epicondyle)	Base of 3rd MC	Extends and adducts hand at wrist	20–30	60–100	Posterior and medial to ECR longus
Extensor carpi ulnaris	Common extensor origin	Base of 5th MC	Extends wrist and elbow and adducts hand	30–40	100–150	Most medially placed extensor muscle. Halfway down ulna shaft
Extensor digitorum communis	Common extensor origin	Bases of middle and distal phalanges	Extends wrist and fingers	30–40	100–150	Middle of back of forearm distal to radial tuberosity
Extensor digiti minimi	Common extensor origin	Bases of middle and distal 5th phalanges	Extends 5th finger	30–40	50–100	Medial to ext digitorum
Extensor pollicis longus	Posterior surface middle third ulna	Base of distal phalanx thumb	Extends all joints of thumb	20–30	50–100	Midway down back of forearm
Extensor pollicis brevis	Posterior surface of radius and interosseous membrane	Base of proximal phalanx of thumb	Extends CMC and MCP joints of thumb	20–25	50–75	Distal third of forearm. Palpate by moving CMC and MCP joints
Adductor pollicis longus	Back of interosseous membrane and both radius and ulna	Base of 1st MC	Adducts thumb and hand	20–40	50–100	Proximal to ext pollicis brevis on back of forearm. Palpate action
Extensor indicis	Back of distal ulna and interosseous membrane	Extensor expansion of dorsum of 1st phalanx	Extends forefinger	20–30	50–100	Found medial of most lateral tendon of ext digit communis

continued

Table A2.1 Injection sites for botulinum toxin – *continued*

Muscle	Origin	Insertion	Action	Dose (U)		Injection point
				Botox®	Dysport®	
Flexor aspect of forearm						
Superficial flexor muscles Pronator teres	Humeral head medial humeral epicondyle. Ulna head from medial border of ulna coronoid process	Middle of lateral surface of radius	Pronates forearm and flexes elbow	30–40	100–200	Medial border of anterior cubital fossa – medial to brachial artery
Flexor carpi radialis	Medial humeral epicondyle	Base of 2nd MC	Flexes wrist and elbow	30–40	100–200	Upper forearm just below bicipital aponeurosis and medial to pronator teres
Flexor carpi ulnaris	Humeral head from medial humeral epicondyle. Ulna head from olecranon and upper two-thirds of its posterior border	Pisiform bone in wrist	Flexes and adducts hand at wrist	30–40	100–150	Upper forearm medial aspect of flexor surface below bicipital aponeurosis. Medial to FCR. Observe action of wrist flexion
Flexor digitorum superficialis	Humero-ulnar head from medial epicondyle and coronoid process. Radial head from upper half of anterior border of radius	Middle phalanges of medial four digits	PIP joint flexor and MCP joint flexor	25–30	100–200	Middle of forearm halfway down to either side of palmaris tendon
Flexor digitorum profundus	Proximal two-thirds of ulna	Terminal phalanges of fingers	Flexes all finger joints	30–40	100–200	Upper third of forearm. Deep muscle above lateral border of ulna
Flexor pollicis longus	Upper two-thirds of front of radius	Terminal phalanx of thumb	Flexes all joints of thumb	20–30	100–150	Mid forearm over anterior aspect of radius
Pronator quadratus	Front of ulna (distal)	Front of distal radius	Pronates forearm	20–30	100–150	Approach muscle from extensor aspect of forearm just proximal to wrist and advance through interosseous membrane

AT = Achilles tendon; CMC = carpometacarpal; FCR = flexor carpi radials; IP = interphalangeal; MC = metacarpal; MT = metatarsal; MTP = metatarsophalangeal; PIP = proximal interphalangeal.

Appendix 3

Tools to assess outcome

Measurement of goal attainment

Table A3.1 shows some common goals for treatment and tools that might be applied to assess outcome.

Table A3.1 Common treatment goals and suggested outcome measures

Goal	Suggested outcome measure
Active function/mobility	
Improved gait pattern	• Timed walking tests • Gait analysis/video recording
Improved gait efficiency	• Physiological cost index
Passive function/care	
Ease of applying splint/orthosis	• Time taken to apply splint/number of helpers required • Carer rating of ease of application using NGRS or VRS • The amount of time for which the splint is worn
Ease of maintaining hygiene	• Time taken to wash/number of helpers required • Carer rating of ease of maintaining hygiene using NGRS or VRS
Ease of dressing	• Time taken to dress/number of helpers required • Carer rating of ease of dressing using NGRS or VRS
Improved seating position	• Time taken to position in chair/number of helpers required • Photographic record – assessed by independent assessor
Symptom relief	
Reduction of pain	• NGRS • VRS

NGRS = Numeric Graphic Rating Scale; VRS = Verbal Rating Scale.

Alternatively, goals for intervention may be set on a more descriptive level and their achievement or otherwise noted at the agreed outcome assessment point. The incorporation of set goals into formal measurement through the Goal Attainment Scaling (GAS) is further described in Appendix 4.

Visual Analogue Scale (VAS) and Numeric Graphic Rating Scale (NGRS)

Graphic rating scales may be useful for scoring a number of patient- or carer-rated items; for example pain, ease of undertaking care tasks etc. As noted in Chapter 6, the addition of numbers to a 10-cm scale may produce a more reliable score than a standard VAS. An example of a NGRS is given in Fig A3.1.

The Numeric Graphic Rating Scale (NGRS)

Say ***to the patient:***
- This is a scale to measure [symptom]
- 0 indicates 'none at all'
- The numbers on the scale indicate increasing levels of [symptom] up to 10 which is the most severe pain imaginable
- Which point on the scale shows how much [symptom] you have today?

To the administrator
In your opinion was the person able to understand this scale?

Yes No

Comment

Fig A3.1 A numeric graphic rating scale

Verbal scale

Some patients may find it easier to complete a verbal questionnaire. While this will offer fewer possibilities and is therefore less sensitive, it may be more reliable. Such scales may be administered before and after treatment, or applied retrospectively so that the individual provides an evaluation of change as illustrated below:

Example of a verbal rating scale for pain

Which of the following best describes the severity of your pain? (Circle one)

No pain Mild pain Moderate pain Severe pain

Example of a retrospective evaluation scale

How is your pain now, compared with your pain before treatment? (Circle one)

Much better A bit better The same A bit worse Much worse

Pictorial scales

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 (SPIN) (Fig A3.2).

The SPIN provides pictorial representation of pain at different sites, rated on a six-point graphic scale that includes increased proportions of red shading to indicate pain intensity. A series of pictures illustrates different scenarios. The scale itself may be used with either verbal or pictorial anchors.

The SPIN has been validated in patients with communication and cognitive difficulties and some patients are able to use this where they are unable to report their symptoms using standard rating scales (Jackson *et al* 2006).

A screening version of the SPIN is also available (Turner-Stokes *et al* 2008).

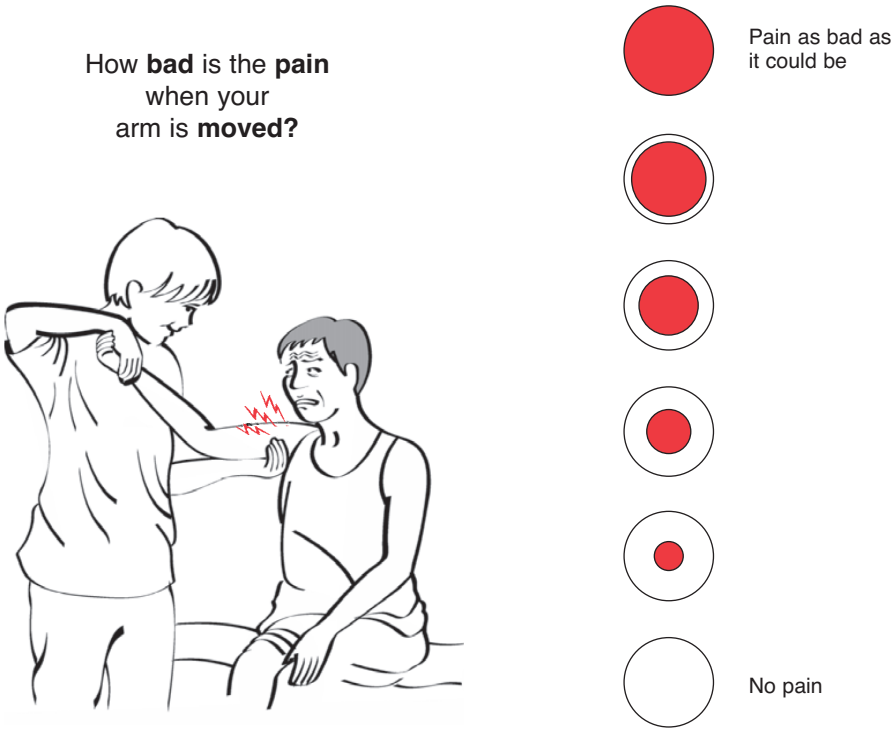


Fig A3.2 The Scale of Pain Intensity

Measurement of spasticity

The Ashworth Scale

The original Ashworth Scale was developed for MS patients, but with little attempt at validation. Bohannon and Smith (1987) modified it by adding the 1+ grade and demonstrated acceptable reliability for assessing spasticity of elbow flexors. The Modified Ashworth Scale (MAS) has been used on many of the studies on BT, where it is often shown to be sensitive (Table A3.2). However, its validity is questionable in joints other than the elbow.

Table A3.2 Modified Ashworth Scale

Grade	Description
0	No increase in tone
1	Slight increase in tone giving a 'catch and release', or minimal increase in resistance at end-range, when the limb is moved in flexion or extension
1+	Slight increase in tone giving a catch, followed by minimal resistance throughout the remainder of range of movement
2	More marked increase in tone through most of the range of movement, but affected parts easily moved
3	Considerable increase in tone – passive movement difficult and joint range of movement restricted
4	Affected parts rigid in flexion or extension

The Tardieu Scale

The Tardieu Scale was originally developed for children with cerebral palsy. More recently it has been evaluated in adults with post-stroke spasticity with Mehrholz *et al* (2005) finding some evidence that it was more reliable than the MAS. The key criticism of the Tardieu Scale, however, is that it is time-consuming and requires considerable skill to apply in clinical practice which affects its feasibility and may affect its reliability in standard clinical practice.

The Tardieu Scale is rated for each muscle group, and reaction to stretch is rated at a specified stretch velocity with two parameters:

- X: the quality of muscle reaction (see Table A3.3)
- Y: the angle at which muscle reaction occurs measured relative to the position of the minimal stretch of the muscle for all joints (except hip, where it is relative to the resting anatomical position).

Table A3.3 Quality of muscle reaction (X) in the Tardieu Scale

Grade	Description
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 a precise angle
2	Clear catch at a precise angle, interrupting the passive movement, followed by release
3	Fatigable clonus (in less than 10 seconds when maintaining pressure) occurring at a precise angle
4	Infatigable clonus (greater than 10 seconds when maintaining pressure) occurring at a precise angle

Technically the Tardieu Scale is rated at three speeds:

- V1: as slow as possible: ie this measures the passive range of movement
- V2: speed of the limb segment falling under gravity
- V3: as fast as possible.

In clinical practice, rating is often limited to V1 and V3 in the interests of time.

Measurement of function

Some functional activity measures are listed in Table A3.4.

Table A3.4 Focal measures of functional activity

Lower limb	Upper limb
10-m walking time*	Leeds Arm Spasticity Impact Scale
Six-minute walking distance*	Arm Activity Measure
Functional Ambulation Category*	Nine-hole peg test*
Paper walkway/gait analysis – to measure stride length, cadence and symmetry	Frenchay arm test*
	Action research arm test*

* Descriptions of these scales are given in Wade (1992).

The Leeds Arm Spasticity Impact Scale (LASIS) and the Arm Activity Measure (ArMA) are more recently developed scales specifically designed for use in this context. They are therefore described in detail below.

Leeds Arm Spasticity Impact Scale

This is a scale designed to measure the impact of spasticity on the functional use and care for the hemiparetic arm. It is administered by a clinician, but is based on the individual's normal activities in the preceding seven days.

In each case the respondent is asked if a task is possible for them to do or not, if the patient or carer does the task and to score the difficulty of doing the task between 0 and 4.

Instructions for LASIS

1 Investigator asks questions to the patient and carer; the responses are noted on a proforma. Each question should be qualified in terms of the usual level of difficulty when performing the task *over the preceding seven days*. The investigator may supplement the questions by demonstrating the action required for a particular activity.

2 If either the patient or carer reports difficulty then the answer to the first part of each question is yes.

3 The responses are chosen to the following the question 'How difficult is this activity?' by the patient or carer from the rating chart.

4 If patients or carers have not performed a particular activity within last seven days, then leave blank.

5 A summary score for patient disability is obtained by adding together all the patient scores and dividing this total by the number of questions on which responses were made. This results in a summary score between 0 (no disability) and 4 (maximum disability). A summary score for physical carer burden can be derived in a similar way.

6 Preliminary analysis of the psychometric properties has only been performed on the patient ratings thus far. This scale has not been published yet so any data obtained should be analysed with caution.

How difficult is this activity?	
0	I have **no** difficulty
1	I have **a little** difficulty
2	I have **moderate** difficulty
3	I have **a great deal** of difficulty
4	I **cannot do** this activity

Leeds Arm Spasticity Impact Scale

1	**Cleaning the palm of the hand**				
	Do you or your carer have difficulty cleaning the palm of your affected hand?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
2	**Cutting fingernails**				
	Do you or your carer have difficulty cutting the fingernails of your affected hand?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*

continued

Leeds Arm Spasticity Impact Scale – *continued*

3	**Cleaning around the elbow**				
	Do you or your carer have difficulty cleaning around the elbow of your affected arm?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
4	**Cleaning the armpit – affected arm**				
	Do you or your carer have difficulty cleaning the armpit of your affected arm?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
5	**Cleaning the armpit – unaffected arm**				
	Do you or your carer have difficulty cleaning the armpit of your affected arm?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
6	**Putting arm through sleeve**				
	Do you or your carer have difficulty putting your affected arm through the sleeve of your coat?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
7	**Putting on a glove**				
	Do you have difficulty putting a glove on your affected hand?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
8	**Rolling over in bed**				
	Do you have difficulty rolling over in bed because of tightness in your arm?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
9	**Doing physiotherapy exercises**				
	Do you have difficulty doing physiotherapy exercises to your affected arm?	*Yes/No or Not attempted*	Who does this activity most of the time? Degree of difficulty experienced by patient Degree of difficulty experienced by carer	*Patient* *0 1 2 3 4* *0 1 2 3 4*	*Carer*
10	**Balance when standing alone**				
	Does the position of your affected arm cause difficulty in balancing when you are standing by yourself?	*Yes/No or Cannot stand*	Degree of difficulty experienced by patient	*0 1 2 3 4*	

continued

Leeds Arm Spasticity Impact Scale – *continued*

11 **Balance when walking**			
Does the position of your affected arm cause difficulty in balancing when you are walking by yourself (including use of walking aid)?	*Yes/No or Cannot walk*	Degree of difficulty experienced by patient	*0 1 2 3 4*
12 **Stabilising objects – with affected arm**			
Do you have difficulty using your affected arm to hold objects steady while you use your unaffected arm?	*Yes/No or Cannot use affected arm*	Degree of difficulty experienced by patient	*0 1 2 3 4*

Arm Activity Measure

This measure is designed to assess the functional use or impact on care for the hemiparetic arm, of interventions used in the rehabilitation of the arm. It is constructed along similar lines to the LASIS, but the primary differences are:

1 It is designed for completion by self-report, so that it can be sent to patients/their carers to respond from a distance

2 It includes active as well as passive function items.

The ArMA

Date and time of completion:.....

Patient name:.....

Instructions for completion:

If the patient is unable to complete the questionnaire independently they may:

- receive assistance from a carer or professional to either act as scribe
- or facilitate understanding and completion question by question.

Who has completed this questionnaire?

☐ Patient alone

☐ Carer alone

☐ Patient/carer in combination

Guidance for completion:

For each of the activities listed, please indicate:

1 If the task is possible for you or your carer.

2 The amount of *difficulty* that you or your carer experience in doing the activity.

3 **Please answer every question based on your activity over the *last 7 days*.**

If you are able to do the task but have not done so in the last 7 days please estimate the amount of difficulty you would have had with each task. Indicate if the score is an **estimate or actual** in every case.

ArMA – Section A (caring for the affected arm)

In *each column*, please *CIRCLE* as appropriate

Care activities (affected arm)	Possible to do task or not?	Difficulty 0 = no difficulty 1 = mild 2 = moderate 3 = severe difficulty 4 = unable to do activity	Estimate/Actual (If the task was not actually done in the last 7 days, circle 'estimate')
1 Cleaning palm	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
2 Cutting finger nails	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
3 Putting on a glove	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
4 Cleaning armpit	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
5 Putting arm through a sleeve	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
6 Put on a splint (if required)	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
7 Positioning arm on a cushion or support in sitting	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**

ArMA – Section B (using the affected arm)

In *each column*, please *CIRCLE* as appropriate

Activities using affected arm	Possible to do task or not?	Difficulty 0 = no difficulty 1 = mild 2 = moderate 3 = severe difficulty 4 = unable to do activity	Estimate/Actual (If the task was not actually done in the last 7 days, circle 'estimate')
1 Do up buttons on clothing	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
2 Pick up a glass, bottle, or can	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
3 Use a key to unlock the door	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
4 Write on paper	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
5 Open a previously opened jar	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
6 Eat with a knife and fork	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
7 Hold an object still while using unaffected hand	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
8 Effect of affected arm on balancing when walking	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
9 Dial a number on home phone	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
10 Tuck in your shirt	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
11 Comb or brush your hair	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
12 Brush your teeth	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**
13 Drink from a cup or mug	**Yes/In part/No**	**0 1 2 3 4**	**Estimate/Actual**

Appendix 4

Goal Attainment Scaling – how to do it

What is Goal Attainment Scaling and why use it?

Measurement with the Goal Attainment Scale (GAS) was first introduced by Kiresuk and Sherman (1968) for assessing outcomes for complex intervention in mental health settings. Since then GAS has been applied in many other areas of rehabilitation (Williams and Steig 1987; Rockwood *et al* 1997; Stolee *et al* 1992, 1999; Rushton and Miller 2002).

GAS is a method of scoring the extent to which patient's individual goals are achieved in the course of intervention. In effect, each patient has their own outcome measure but this is scored in a standardised way to allow statistical analysis. While traditional standardised measures include a standard set of tasks (items) each rated on standard levels, in GAS tasks are individually identified to suit the patient, and the levels are individually set around their current and expected levels of performance.

GAS is conceptually different from standardised measures, in that it can incorporate different goals on different timescales. However, many clinicians reared on the highly structured platform of standardised measurement at fixed time points find GAS hard to accept on first encounter.

The potential advantages of GAS are that it focuses specifically on the outcomes that are important to the patient and relevant to the treatment. The patient is actively involved in determining the goals and evaluating their achievement. A further advantage is that it may be used to bring together a range of different outcomes into one overall score.

GAS has been criticised on the basis that it is dependent not only on the response to treatment, but the therapists' ability to predict outcome accurately. For this reason it cannot be used in isolation from standardised outcome measures. However, it may also be argued that it is appropriate to test the clinicians' skill in predicting outcome as this is essential to the selection process for BT.

How is Goal Attainment Scaling rated?

An important feature of GAS is the *a priori* establishment of criteria for a 'successful' outcome in that individual, which is agreed with the patient and family before intervention starts so that everyone has a realistic expectation of what is likely to be achieved, and agrees that this would be worth striving for.

Each goal is rated on a five-point scale, with the degree of attainment captured for each goal area:

If the patient achieves the expected level, this is scored at 0.

If they achieve a *better* than expected outcome this is scored at:

+1 (somewhat better)

+2 (much better)

If they achieve a *worse* than expected outcome this is scored at:

–1 (somewhat worse)

–2 (much worse)

Goals may be weighted to take account of the relative importance of the goal to the individual, and/or the anticipated difficulty of achieving it (Rushton and Miller 2002). Normally three to four goals are identified, which are incorporated into the single GAS score.

Overall Goal Attainment Scores are then calculated by applying a formula:

$$\text{Overall GAS} = 50 + \frac{10\,\Sigma(w_i\,x_i)}{[(1-\rho)\,\Sigma w_i^2 + \rho(\Sigma(w_i)^2]^{1/2}}$$

Where:

w_i = the weight assigned to the *i*th goal (if equal weights, $w_i = 1$)

x_i = the numerical value achieved (between –2 and + 2)

Σ = the expected correlation of the goal scales

In effect, therefore the composite GAS (the sum of the attainment levels x the relative weights for each goal) is transformed into a standardised measure with a mean of 50 and standard deviation of 10.

Given that the results should exceed and fall short of expectations in roughly equal proportions, over a sufficiently large number of patients, one would expect a normal distribution of scores and the GAS thus performs at interval level. Demonstrating that the mean GAS for the study population is around 50 is a useful quality check of GAS scoring. If a team attempts to inflate their results by scoring over-cautiously, the mean score will be >50. Similarly, if they are consistently over ambitious it will be <50.

The procedure for Goal Attainment Scaling is summarised in Fig A4.1.

Application of GAS specifically in relation to BT injection for spasticity has been described by Ashford and Turner-Stokes (2006) and Turner-Stokes and Ashford (2007).

Proforma for recording Goal Attainment Scaling

Patient ID:

Start date:…… Outcome date:……..

Goal	Goal stated by patient	SMART goal	Imp (0–3)	Diff (0–3)	Baseline score	Outcome score	Reason for variance
1	I want the injection to relieve my pain	To achieve a reduction in pain score from 7/10 to 3/10	3	3	–1	+1	Achieved better than expected pain relief to score 1–2/10
2	I want to be able to dress more easily	To get left arm through sleeve of jacket without help by <date>	2	3	–1	–1	Donning jacket easier, but still requires some assistance
3	I want to be able to open my hand so that my fingernails stop digging into my palm	To open the hand sufficiently to clean the palm and to accommodate a 2 cm diameter palm guard	3	2	–2	0	

Baseline composite score	Attained composite score	Change
32.5	51.9	19.4

continued

1 Identify the goals

- Interview the patient to identify the main problem areas
- Establish an agreed set of priority goal areas (with the help of the team) for achievement by an agreed date (usually discharge or the end of the programme)

2 Weight the goals (optional)

- Assign a weight to each goal if required: **weight = importance × difficulty**

Importance and difficulty may each be rated on a four-point scale.

Importance	Difficulty
0 = not at all (important)	0 = not at all (difficult)
1 = a little (important)	1 = a little (difficult)
2 = moderately (important)	2 = moderately (difficult)
3 = very (important)	3 = very (difficult)

If a weighting system is not used, a value of '1' is simply applied to weight in the formula.

3 Define expected outcome

The 'expected outcome' is the most probable result if the patient receives the expected treatment. Ideally, levels should also be pre-defined for:

- 'somewhat less' and 'much more'
- 'somewhat more' and 'much more'.

These are defined by the team or investigator. They should be *as objective and observable as possible.*

The process provides an opportunity to negotiate with the patient if they have unrealistic expectations. For example if the patient wants active hand function, but realistically the expected outcome is to be able to use the affected hand as a prop, then the active function task can be set at level 2, and use as a prop at level 0. This way, the patient's aims are not dismissed, but are clearly defined as beyond the level of expectation.

4 Score baseline

This is usually rated –1, unless the patient is as bad as they could be in that particular goal area, in which case the baseline rate is –2.

5 Goal attainment scoring

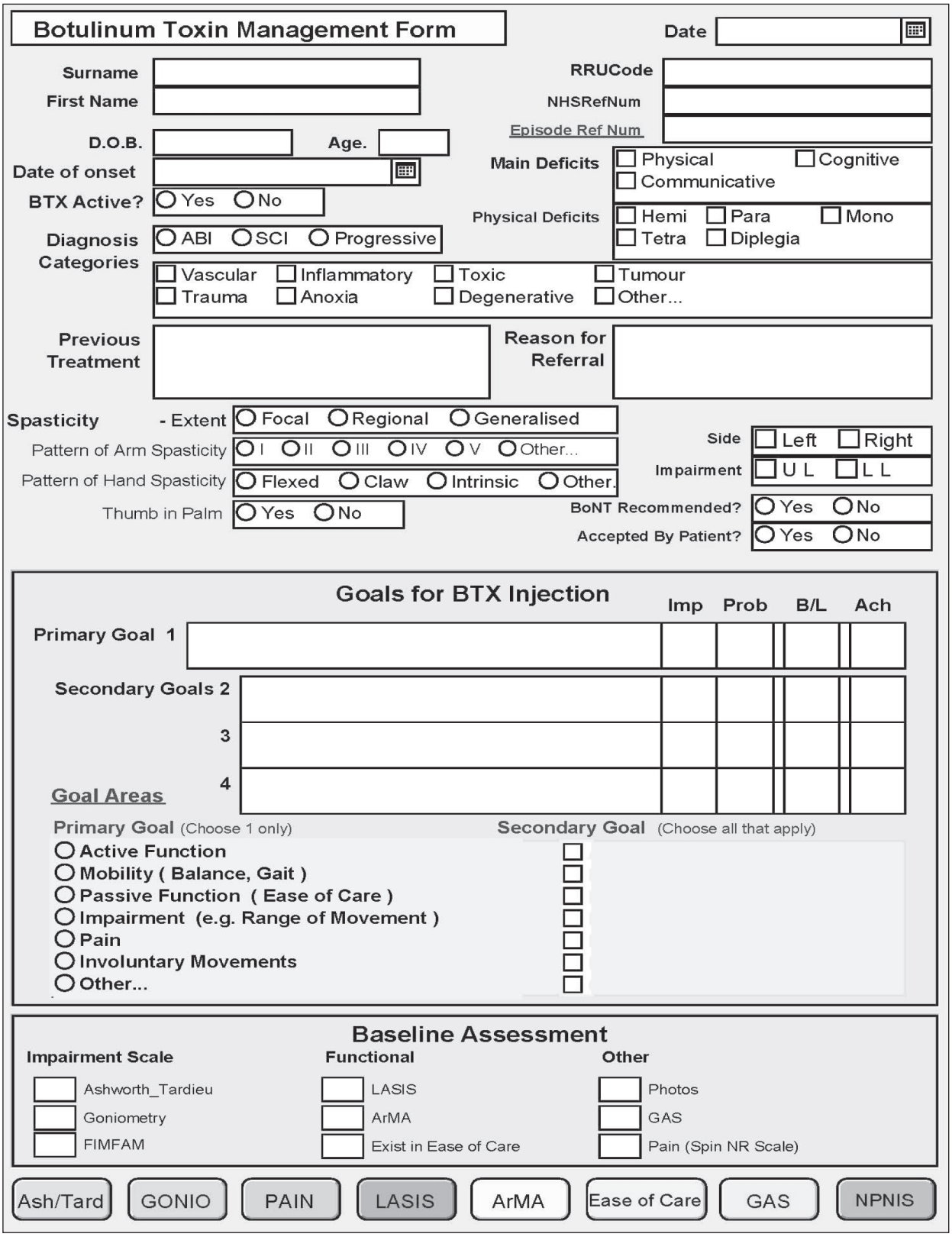
Rate the outcome scores at the appointed review date. Calculate the GAS by applying the formula or looking the summated scores up in the published tables (Kirusek *et al* 1994). The change in GAS score may be determined by subtracting the baseline from the outcome GAS rating.

A simple GAS calculation programme written in Excel is available on request from Professor Lynne Turner-Stokes at the Regional Rehabilitation Unit at Northwick Park Hospital: lynne.turner-stokes@dial.pipex.com

Fig A4.1 Procedure for Goal Attainment Scaling

Appendix 5

Dataset and proforma (example)



Botulinum Toxin Management Form

Date

Surname
First Name
D.O.B. Age.
Date of onset
BTX Active? ○ Yes ○ No
Diagnosis Categories ○ ABI ○ SCI ○ Progressive

RRUCode
NHSRefNum
Episode Ref Num

Main Deficits ☐ Physical ☐ Cognitive ☐ Communicative

Physical Deficits ☐ Hemi ☐ Para ☐ Mono ☐ Tetra ☐ Diplegia

☐ Vascular ☐ Inflammatory ☐ Toxic ☐ Tumour
☐ Trauma ☐ Anoxia ☐ Degenerative ☐ Other...

Previous Treatment

Reason for Referral

Spasticity - Extent ○ Focal ○ Regional ○ Generalised
Pattern of Arm Spasticity ○ I ○ II ○ III ○ IV ○ V ○ Other...
Pattern of Hand Spasticity ○ Flexed ○ Claw ○ Intrinsic ○ Other.
Thumb in Palm ○ Yes ○ No

Side ☐ Left ☐ Right
Impairment ☐ U L ☐ L L
BoNT Recommended? ○ Yes ○ No
Accepted By Patient? ○ Yes ○ No

Goals for BTX Injection

		Imp	Prob	B/L	Ach
Primary Goal 1					
Secondary Goals 2					
3					
4					

Goal Areas

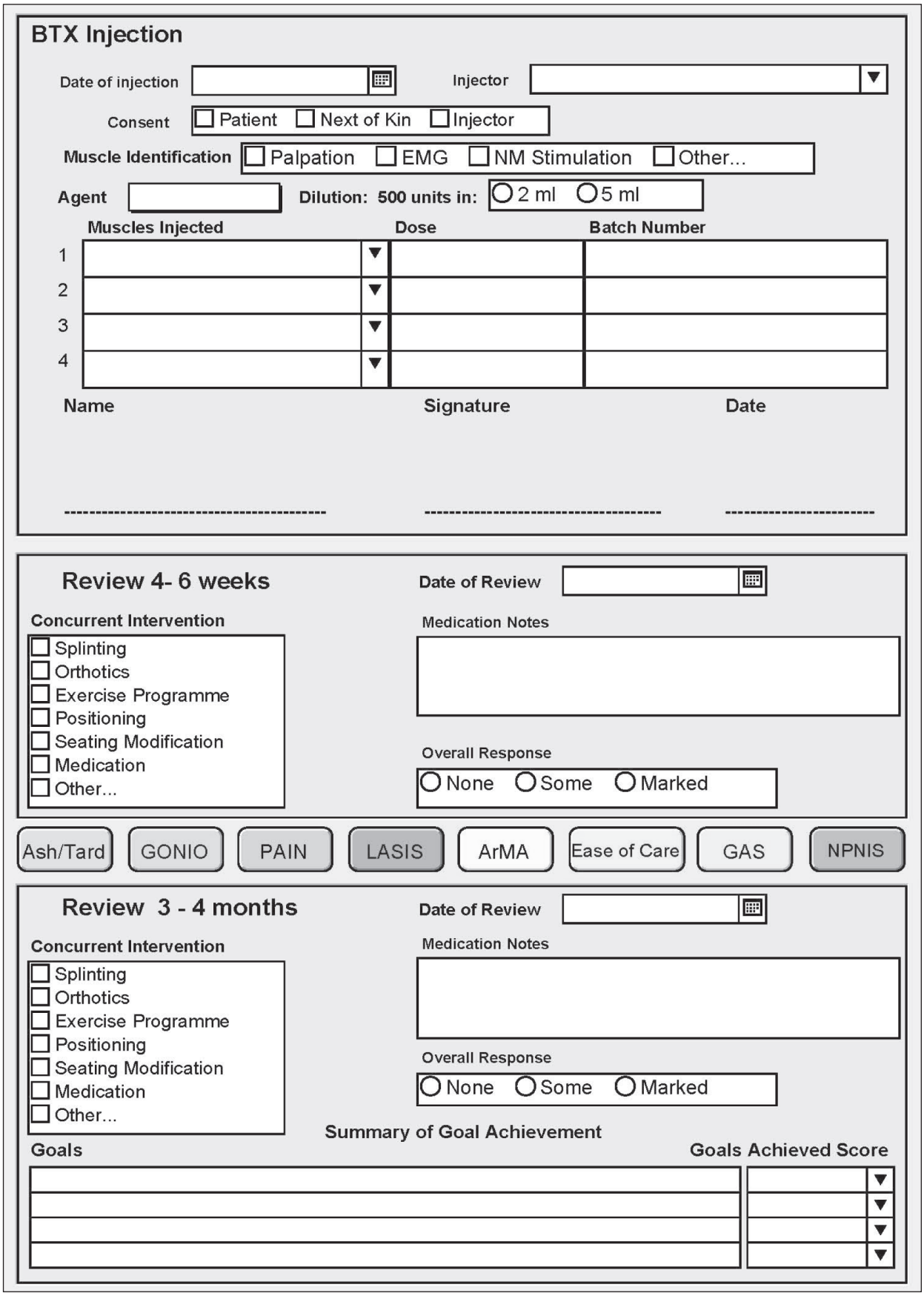
Primary Goal (Choose 1 only)
○ Active Function
○ Mobility (Balance, Gait)
○ Passive Function (Ease of Care)
○ Impairment (e.g. Range of Movement)
○ Pain
○ Involuntary Movements
○ Other...

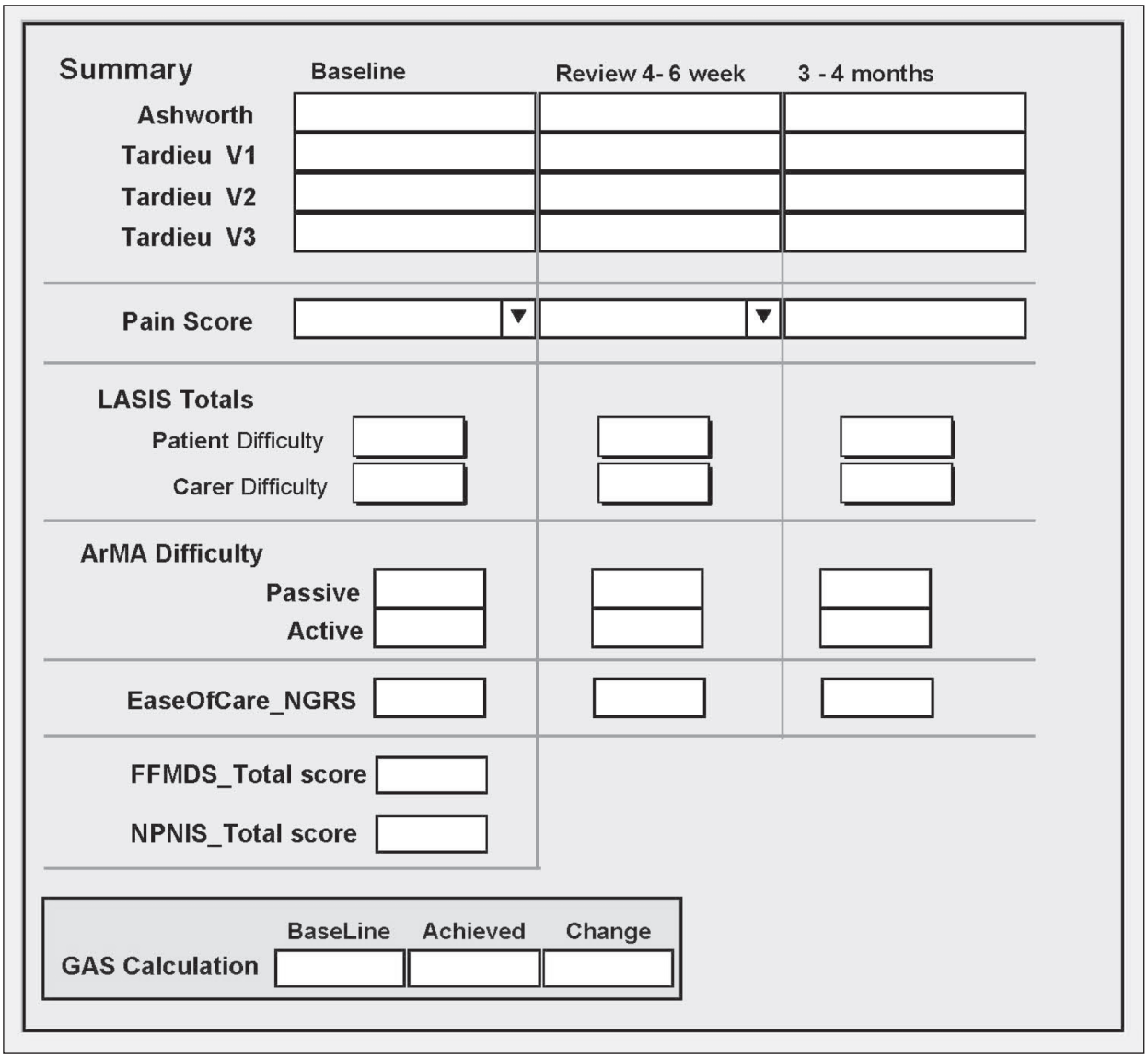
Secondary Goal (Choose all that apply)
☐
☐
☐
☐
☐
☐
☐

Baseline Assessment

Impairment Scale	Functional	Other
☐ Ashworth_Tardieu	☐ LASIS	☐ Photos
☐ Goniometry	☐ ArMA	☐ GAS
☐ FIMFAM	☐ Exist in Ease of Care	☐ Pain (Spin NR Scale)

Ash/Tard | GONIO | PAIN | LASIS | ArMA | Ease of Care | GAS | NPNIS





ABI = acquired brain injury; Ach = achieved; ARMA = Arm Activity Measure; ASH/Tard = Ashworth/Tardieu; B/L = baseline; BoNT = botulinum toxin; BT = botulinum toxin; BTX = botulinum toxin; EMG = electromyography; FFMDS = FIM + FAM Minimum Dataset; GAS = Goal Attainment Scaling; GONIO = goniometry; Imp = importance; LASIS = Leeds Arm Spasticity Impact Scale; LL = lower limb; NGRS = Numeric Graphic Rating Scale; NM = neuromuscular; NPNIS = Northwick Park Neurological Impairment Scale; NR = numbered rating; SCI = spinal cord injury; UL = upper limb.

Appendix 6

Botulinum toxin advice sheet

Botulinum toxin (BT) has been shown to be a well-tolerated and effective treatment for individuals with local spasticity in a localised group of muscles. Spasticity is an abnormal increase in the tone of your muscles and is common following injury to the brain.

BT is used as a support to physiotherapy or occupational therapy treatment. The specific goal for treatment is dependent on the individual, in some cases this will be removal of spasticity or sometimes it will just be a reduction in its presentation.

BT is administered using a simple local injection into the muscle. This produces temporary weakness and relaxation of the muscle. This effect is produced by the BT blocking communication between the muscle and its connecting nerve. The effects of BT are temporary and will last approximately three to four months after which it gradually wears off.

Side effects from BT injection are usually mild and transient. However, the following have been known to occur:

1 Pain at the injection site
2 'Flu-like' symptoms
3 Excessive muscle weakness and temporary swallowing problems
4 Potential for anaphylaxis, which is an immune reaction to the medication and requires urgent medical attention.

Further information is available on the internet at the electronic medicine compendium site: www.emc.medicines.org.uk

SEEK ADVICE FROM YOUR DOCTOR OR PHYSIOTHERAPIST IF YOU HAVE ANY CONCERNS ABOUT THE INJECTION OR INTERVENTIONS ASSOCIATED WITH IT, SUCH AS SPLINTING.

Appendix 7

Methods for prescribing, supply and administration of botulinum toxin by non-medical injectors

Patient Specific Directions (PSD)

A PSD is a written instruction from a doctor, dentist or other independent prescriber for a medicine to be supplied or administered to a *named patient* by another health professional.

- The patient must be individually identified on the PSD.
- The written instruction must be signed and dated by the doctor/dentist or other independent prescriber.
- Provisions in medicines legislation allow for the supply and/or administration of an unlicensed product under a PSD provided it has originated from a doctor or dentist.
- For a PSD to be valid, the named patient must also have been seen by the doctor/dentist or other independent prescriber (Department of Health 2006).

Examples of a written instruction include:

- the traditional prescription
- an instruction written in the patient's medical records
- an instruction written on a hospital drug chart or
- an instruction given in a letter written from a doctor to a physiotherapist.

The administration of medicines prescribed using a PSD may be delegated to other appropriately qualified health professionals. Medical prescribers may delegate the administration of licensed and off-label medicines. While non-medical (independent) prescribers (NMPs) may technically delegate the administration of off-label medicines, in view of the potentially toxic nature of BT, we strongly recommend the restriction of non-medical prescribing to licensed users only in this context.

Patient Group Directions (PGD)

A PGD is a written instruction for the supply or administration of a named medicine in a defined clinical situation to *groups of patients* who may not have been identified before presenting for treatment.

- PGDs are formal documents written by individual health provider organisations (eg NHS trusts) for supply and administration.
- The formulation of the document should include the signed agreement of an NHS trust's medicines management committee and/or medical directors is required.
- Variation to the specific site of injection can be undertaken, but must be identified in the PGD, and relate to the initial presentation of spasticity.
- PGDs should also allow for variation to the dose of BT based on sound clinical judgement and in accordance with factors such as the weight of the patient, amount of spasticity present and the reduction in spasticity required to address the clinically identified goal.
- In order to be valid, a PGD must meet specific legal criteria. This includes the requirements that the therapist/nurse is registered with the Health Professions Council

(HPC)/Nursing and Midwifery Council, and that the supply and administration of the drugs listed in the PGD is not delegated to anyone else (Prescription Only Medicines (Human Use) Amendment Order 2000 SI 2000/1917).

- PGDs tend to be used in hospital and primary care settings but are also valid in other non-NHS clinical settings.

PGDs can include medicines for use outside the terms of their 'Summary of product characteristics' (SPC) (so called 'off-label' use), provided such use is supported by best clinical practice. The PGD should state when the product is being used outside the terms of the SPC and why this is necessary. However, clinicians should be aware that, if information given in a product's SPC states that a certain technique/action is not advised, then members should consider an alternative approach in the first instance unless 'off-label' use really is justified.

Supplementary prescribing

Supplementary prescribing is a voluntary prescribing partnership between the independent prescriber (doctor or dentist) and supplementary prescriber, to implement an agreed patient-specific clinical management plan (CMP), with the patient's agreement.

- Following agreement of the CMP, the supplementary prescriber may prescribe any medicine for the patient that is referred to in the plan, until the next review by the independent prescriber.
- There is no formulary for supplementary prescribing, and no restrictions on the medical conditions that can be managed under these arrangements.
- To undertake supplementary prescribing, practitioners must have completed a HPC-approved course and have their record annotated on the HPC register.

Supplementary prescribers can prescribe *controlled drugs* and *off-label medicines* in partnership with a doctor, where the doctor agrees within a patient's CMP (Department of Health 2006). This enables the supplementary prescriber to manage a range of medications including BT, and allow for administration in collaboration with the MDT.

Independent prescribing

Independent prescribing entails the clinician taking on full responsibility for prescription as well as administration and monitoring of BT intervention. Practitioners must again have obtained a specific qualification to become an independent prescriber and have their professional registration amended accordingly.

Therapists do not have independent prescribing rights at the current time as opposed to nurses who do have, but still have restrictions on those rights. Nurses who are suitably qualified are termed NMPs. They can prescribe any licensed medicine (ie products with a valid marketing authorisation in the UK) for any medical condition, with the exception of all controlled drugs. They are restricted by the British National Formulary, local formularies and local/national guidelines eg National Institute for Health and Clinical Excellence. A nurse who is a NMP cannot prescribe unlicensed medicines. They may instruct another professional to administer licensed medicines to a patient under the terms of a PSD, but not unlicensed medicines.

Training

Medical and non-medical injectors require additional training, which may vary dependent of experience (see Section 8.4 for the training requirements).

Further information

For further information on PGDs and supplementary prescribing please see the following references:

- Department of Health. *Medicines matters: a guide for the prescribing, supply and administration of medicines*. London: DH, 2006. www.dh.gov.uk
- National Prescribing Centre. *Patient Group Directions: a practical guide and framework of competencies for all professionals using patient group directions Incorporating an overview of existing mechanisms for the supply and prescribing of medicines*. London: NPC, 2004. www.npc.co.uk/publications/pgd/pgd.pdf
- Royal Pharmaceutical Society of Great Britain. *Patient group directions: a resource pack for pharmacists*. London: Royal Pharmaceutical Society of Great Britain, 2004. www.rpsgb.org
- The Department of Health website on supplementary prescribing. www.dh.gov.uk/en/Policyandguidance/Medicinespharmacyandindustry/Prescriptions/TheNon-medicalPrescribingProgramme/Supplementaryprescribing/index.htm

Appendix 8

Patient organisations

The Stroke Association
Stroke House
240 City Road, London EC1V 2PR
T: 020 7566 0300
www.stroke.org.uk

Headway
7 King Edward Court
King Edward Street, Nottingham NG1 1EW
T: 0115 924 0800
www.headway.org.uk

The Neurological Alliance
Stroke House
240 City Road, London EC1V 2PR
T: 020 7566 1540
www.neural.org.uk

The Multiple Sclerosis Society
MS National Centre
372 Edgware Road, London NW2 6ND
T: 020 8438 0700
www.mssociety.org.uk

Different Strokes
9 Canon Harnett Court
Wolverton Mill, Milton Keynes MK12 5NF
T: 0845 130 7172
www.differentstrokes.co.uk

Scope
6 Market Road
London N7 9PW
T: 020 7619 7100
www.scope.org.uk

Spinal Injuries Association
SIA House
2 Trueman Place
Oldbrook, Milton Keynes MK6 2HH
T: 0845 678 6633
www.spinal.co.uk

Appendix 9

Conflicts of interest

The following conflicts of interest were declared by members of the GDG.

Professor Lynne Turner-Stokes (Chair and lead editor)	• I practise in clinical rehabilitation and use BT regularly in the management of spasticity for my patients • I have a specific interest in outcome measurement for rehabilitation and have been responsible for the development of some of the measures included in these guidelines • I have undertaken research sponsored by investigator-led grants from Ipsen Ltd • I have undertaken consultancy work for Ipsen and Allergan and have received sponsorship from both companies at various times to attend conferences and meetings in the UK and overseas • I have no personal financial interest in BT or any related product
Mr Stephen Ashford (Co-editor)	• I practise in clinical rehabilitation and use BT regularly in the management of spasticity • I have a specific interest in outcome measurement for rehabilitation and have been responsible for the development of one of the measures included in these guidelines • I have undertaken research sponsored by investigator-led grants from Ipsen Ltd • I have received sponsorship from Ipsen and Allergan to attend conferences and meetings in the UK and overseas • I have no personal financial interest in BT or any related product
Professor Bipin Bhakta	• I practise in clinical rehabilitation and use BT regularly in the management of spasticity for my patients • I have undertaken research sponsored by investigator-led grants from Ipsen ltd • I have received sponsorship from Ipsen and Allergan at various times to attend conferences and meetings in the UK and overseas • I have no personal financial interest in BT or any related product
Dr Kate Heward	• I practise in neurological rehabilitation carrying out splinting and spasticity management post-BT injections • I have received reimbursement from Ipsen Ltd for attending meetings in the UK • I have no personal financial interest in BT or any related project
Dr A Peter Moore	• I practise in clinical neurology and use BT regularly in the management of spasticity for my patients • I have undertaken research sponsored by grants from Ipsen Ltd, Allergan and Merz • I have undertaken consultancy work for Ipsen, Allergan and Merz and have received sponsorship from these companies at various times to teach at and attend conferences and meetings in the UK and overseas • I have no personal financial interest in BT or any related product

continued

Mr Adrian Robertson	• I practise in clinical rehabilitation and use BT regularly in the management of spasticity for my patients • I have undertaken research sponsored by investigator-led grants from Ipsen Ltd • I have received sponsorship from Ipsen and Allergan at various times to attend conferences and meetings in the UK and overseas • I have no personal financial interest in BT or any related product
Professor Anthony Ward	• I practise in rehabilitation medicine and use BT regularly in the management of spasticity for my patients • I have undertaken research sponsored by investigator-led grants from Allergan • I have undertaken consultancy work over several years for Allergan, Ipsen and Merz and have received sponsorship from these companies at various times to teach at and attend conferences and meetings in the UK and overseas and have received sponsorship from Allergan at various times to attend conferences and meetings in the UK and overseas • I have no personal financial interest in BT or any related product

References

Aoki KR (1999) Pre-clinical update on BOTOX® (BT-A) purified neurotoxin complex relative to other botulinum neurotoxin preparations. *European Journal of Neurology* 6(4):53–510.

Ashford S, Turner-Stokes L (2006) Goal attainment for spasticity management using botulinum toxin. *Physiotherapy Research International* 11(1):24–34.

Ashford S, Turner-Stokes L, Slade M (2008a) Preliminary evaluation of reliability and internal consistency for Arm Activity Measure (ArMA). Abstract submitted for the Society of Research in Rehabilitation. *Clinical Rehabilitation* 22(9):856–63.

Ashford S, Slade M, Turner-Stokes L (2008b) Evaluation of functional outcome measures for the hemiparetic upper limb – A systematic review. *Journal of Rehabilitation Medicine* 40(10).

Association of Chartered Physiotherapists Interested in Neurology (ACPIN) (1998) *Clinical practice guidelines on splinting*. London: ACPIN.

Bakheit AMO, Ward CD, McLellan DL (1997) Generalised botulinum-like syndrome after intramuscular injections of botulinum toxin Type A: a report of two cases. *Journal of Neurology, Neurosurgery and Psychiatry* 62:198.

Bakheit AMO, Thilmann AF, Ward AB *et al* (2000) A randomized, double-blind, placebo-controlled, dose-ranging study to compare the efficacy and safety of three doses of botulinum toxin type A (Dysport) with placebo in upper limb spasticity after stroke. *Stroke* 31(10):2402–6.

Bakheit AMO, Pittock S, Moore AP *et al* (2001) A randomized, double-blind, placebo-controlled study of the efficacy and safety of botulinum toxin type A in upper limb spasticity in patients with stroke. *European Journal of Neurology* 8(6):559–65.

Bennett G, Dealey C, Posnett J (2004) The cost of pressure ulcers in the UK. *Age and Aging* 33(3):230–5.

Bhakta BB, Cozens JA, Bamford JM *et al* (1996) Use of botulinum toxin in stroke patients with severe upper limb spasticity. *Journal of Neurology, Neurosurgery and Psychiatry* 61:30–5.

Bhakta BB (2000) Management of spasticity in stroke. *British Medical Bulletin* 56(2):476–85.

Bhakta BB, Cozens JA, Chamberlain MA *et al* (2000) Impact of botulinum toxin type A on disability and carer burden due to arm spasticity after stroke: a randomised double blind placebo controlled trial. *Journal of Neurology, Neurosurgery and Psychiatry* 69(2):217–21.

Bhakta BB, Cozens JA, Bamford JM, Chamberlain MA (2001) Measuring associated reactions in the paretic arm in stroke and their relationship to spasticity. *Clinical Rehabilitation* 15:195–206.

Bhakta BB, O'Connor RJ, Cozens JA (2008) Associated reactions after stroke: a randomized controlled trial of the effect of botulinum toxin type A. *Journal of Rehabilitation Medicine* 40:36–41.

Bhatia K, Münchau A, Thompson P *et al* (1999) Generalised muscular weakness after botulinum toxin injections for dystonia: a report of three cases. *Journal of Neurology, Neurosurgery and Psychiatry* 67:90–3.

Bohannon RW, Smith MB (1987) Inter-rater reliability of a modified Ashworth Scale of muscle spasticity. *Physical Therapy* 67:206–7.

Boyd RN, Pliatsios V, Stan R *et al* (2000) Biomechanical transformation of the gastrosoleus muscle with botulinum toxin A in children with cerebral palsy. *Developmental Medicine and Child Neurology* 42:1–10.

Brashear A, Gordon MF, Elovic E *et al* (2002) Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke.[comment]. *New England Journal of Medicine* 347(6):395–400.

Brin MF, Spasticity Study Group (1997) Dosing administration and a treatment algorithm for use of botulinum toxin A for adult-onset spasticity. *Muscle and Nerve* 20(S6):S208–20.

Brown P (1994) Pathophysiology of spasticity. *Journal of Neurology, Neurosurgery and Psychiatry* 57:773–7.

Burbaud P, Wiart L, Dubos JL *et al* (1996) A randomised, double blind, placebo controlled trial of botulinum toxin in the treatment of spastic foot in hemiparetic patients. *Journal of Neurology, Neurosurgery and Psychiatry* 61:265–9.

Childers MK, Brashear A, Jozefczyk P *et al* (2004) Dose-dependent response to intra-muscular botulinum toxin type A for upper limb spasticity after a stroke. *Archives of Physical Medicine and Rehabilitation* 85:1063–9.

Das TK, Park DM (1989) Effect of treatment with botulinum toxin on spasticity. *Postgraduate Medical Journal* 65(762):208–10.

Dengler R, Neyer U, Wohlfarth K *et al* (1992) Local botulinum toxin in the treatment of spastic drop foot. *Journal of Neurology* 239(7):375–8.

DeJong G, Horn SD, Conroy B *et al* (2005) Opening the black box of post-stroke rehabilitation: stroke rehabilitation patients, processes, and outcomes. *Archives of Physical Medicine & Rehabilitation* 86(12 Suppl 2):S1–S7.

Department of Health (2006) *Medicines matters: a guide for the prescribing, supply and administration of medicines*. London: DH.

Edwards S (ed) (1996) *Neurological physiotherapy: a problem solving approach*. London: Churchill Livingstone.

Francis HP, Wade DT, Turner-Stokes L *et al* (2004) Does reducing spasticity translate into functional benefit? An exploratory meta-analysis. *Journal of Neurology, Neurosurgery and Psychiatry* 75:1547–51.

Giovannelli M, Borriello G, Castri P *et al* (2007) Early physiotherapy after injection of botulinum toxin increases the beneficial effects on spasticity in patients with multiple sclerosis. *Clinical Rehabilitation* 21(4):331–7.

Grazko MA, Polo KB, Jabbari B (1995) Botulinum toxin for spasticity, muscle spasms and rigidity. *Neurology* 45:712–7.

Greene P, Fahn S (1992) Development of antibodies to botulinum toxin type A in torticollis patients treated with botulinum toxin injections. *Movement Disorders* 7:134.

Greene P, Fahn S (1993) Development of antibodies to botulinum toxin type A in patients with torticollis treated with injection of botulinum toxin type A. In: DasGupta BR (ed), *Botulinum toxin and tetamine neurotoxins: neurotransmission and biomedical aspect*. New York: Plenum Press.

Hambleton P, Moore AP (1995) Botulinum neurotoxins: origin, structure, molecular actions and antibodies. In: Moore AP (ed), *Handbook of botulinum toxin treatment*. Oxford: Blackwell Science.

Hambleton P, Pickett AM, Shone CC (2007) Botulinum toxin: from menace to medicine. In: Ward AB, Barnes MP (eds), *Clinical uses of botulinum toxins*. Cambridge: Cambridge University Press.

Hatherway CG, Deng C (1994) Immunogenicity of the neurotoxins of Clostridium botulinum. In: Jankovic J, Hallett M (eds), *Therapy with botulinum toxin*. New York: Marcel Dekken.

Hesse S, Lucke D, Malezic M *et al* (1994) Botulinum toxin treatment for lower limb extensor spasticity in chronic hemiparetic patients. *Journal of Neurology, Neurosurgery and Psychiatry* 57:1321–4.

Hesse S, Reiter F, Konrad M *et al* (1998) Botulinum toxin type A and short term electrical stimulation in the treatment of upper limb flexor spasticity after stroke: a randomised, double-blind, placebo-controlled trial. *Clinical Rehabilitation* 12:381–8.

Horn SD, Gassaway J (2007) Practice-based evidence study design for comparative effectiveness research. *Medical Care* 45(10 Supl 2):S50–7.

Hyman N, Barnes M, Bhakta B *et al* (2000) Botulinum toxin (Dysport) treatment of hip adductor spasticity in multiple sclerosis: a prospective, randomised, double-blind, placebo-controlled, dose ranging study. *Journal Neurology, Neurosurgery and Psychiatry* 68:707–12.

Jackson D, Horn S, Kersten P, Turner-Stokes L (2006) A pictorial scale of pain intensity (SPIN) for patients with communication impairments. *International Journal of Therapy and Rehabilitation* 13(10):457–63.

Jankovic J, Schwartz K (1995) Response and immunoresistance to botulinum toxin injections. *Neurology* 45:1743–6.

Keenan MA, Haider TT, Stone LR (1990) Dynamic electromyography to assess elbow spasticity. *Journal of Hand Surgery (Am)* 15:607–14.

Kirazli Y, On AY, Kismali B, Aksit R (1998) Comparison of phenol block and botulinus toxin type A in the treatment of spastic foot after stroke: a randomized, double-blind trial. *American Journal of Physical Medicine & Rehabilitation* 77(6):510–5.

Kiresuk T, Sherman R (1968) Goal attainment scaling: a general method of evaluating comprehensive mental health programmes. *Community Mental Health Journal* 4:443–53.

Kiresuk T, Smith A, Cardillo J (1994) *Goal attainment scaling: application, theory and measurement*. New York: Lawrence Erlbaum Associates.

Lance JW (1980) Symposium synopsis. In: Feldman RG, Young RR, Koella WP (eds), *Spasticity: disordered motor control*. Chicago: Year Book Medical Publishers.

Mehrholz J, Wagner K, Meissner D *et al* (2005) Reliability of the modified Tardieu scale and the modified Ashworth scale in adult patients with severe brain injury: a comparison study. *Clinical Rehabilitation* 19:751–9.

Moore A, Naumann M (2003) General and clinical aspects of treatment with botulinum toxin. In: Moore A, Naumann N, *Handbook of botulinum toxin treatment*, 2nd edn. Oxford: Blackwell Science.

Pittock SJ, Moore AP, Hardiman O *et al* (2003) A double-blind randomised placebo-controlled evaluation of three doses of botulinum toxin type A (Dysport) in the treatment of spastic equinovarus deformity after stroke. *Cerebrovascular Diseases* 15(4):289–300.

Pope P (2007) *Severe and complex neurological disability – management of the physical condition.* Oxford: Butterworth-Heinemann Elsevier.

Reiter F, Danni M, Lagalla G *et al* (1998) Low dose botulinum toxin with ankle taping for the treatment of spastic equinovarus foot after stroke. *Archives of Physical Medicine and Rehabilitation* 79(5):532–55.

Richardson D, Greenwood R, Sheean G *et al* (2000) Treatment of focal spasticity with botulinum toxin: effect on the 'positive support reaction'. *Physiotherapy Research International* 5(1):62–70.

Rockwood K, Joyce B, Stolee P (1997) Use of goal attainment scaling in measuring clinically important change in cognitive rehabilitation patients. *Journal of Clinical Epidemiology* 50(5):581–8.

Rushton PW, Miller WC (2002) Goal attainment scaling in the rehabilitation of patients with lower-extremity amputations: a pilot study. *Archives of Physical Medicine & Rehabilitation* 83(6):771–5.

Schiavo G, Benfenati F, Poulain B *et al* (1992) Tetanus and botulinum toxin B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin. *Nature* 359:832–5.

Shaari CM, George E, Wu BL *et al* (1991) Quantifying the spread of botulinum toxin through muscle fascia. *Laryngoscope* 101(9):960–4.

Shaari CM, Sanders I (1993) Quantifying how location and dose of botulinum toxin injections affect muscle paralysis. *Muscle and Nerve* 16(9):964–9.

Sheean G (2001) Botulinum treatment of spasticity: Why is it difficult to show a functional benefit? *Current Opinion in Neurology* 14(6):771–6.

Sheean G (2002) The pathophysiology of spasticity. *European Journal of Neurology* 9(S1):3–9.

Simpson DM, Alexander DN, O'Brien CF *et al* (1996) Botulinum toxin type A in the treatment of upper extremity spasticity: a randomised, double-blind, placebo-controlled trial. *Neurology* 46(5):1306–10.

Smith SJ, Ellis E, White S *et al* (2000) A double-blind placebo-controlled study of botulinum toxin in upper limb spasticity after stroke or head injury. *Clinical Rehabilitation* 14(1):5–13.

Snow BJ, Tsui JKC, Bhatt MH *et al* (1990) Treatment of spasticity with botulinum toxin: A double blind study. *Annals of Neurology* 28(4):512–5.

Stolee P, Rockwood K, Fox RA *et al* (1992) The use of goal attainment scaling in a geriatric care setting. *Journal of the American Geriatrics Society* 40(6):574–8.

Stolee P, Zaza C, Pedlar A *et al* (1999) Clinical experience with goal attainment scaling in geriatric care. *Journal of Aging & Health* 11(1):96–124.

Tardieu C, Lespargot A, Tabary C *et al* (1988) For how long must the soleus muscle be stretched each day to prevent contracture? *Developmental Medicine and Child Neurology* 30:3–10.

Turner-Stokes L, Nyein K, Halliwell D (1999) The Northwick Park care needs assessment (NPCNA) – a directly costable outcome measure in rehabilitation. *Clinical Rehabilitation* 13:253–68.

Turner-Stokes L, Tonge P, Nyein K *et al* (1998) The Northwick Park Dependency Scale – a measure of nursing dependency which translates into care needs in the community. *Clinical Rehabilitation* 12:304–18.

Turner-Stokes L, Ward AB (2002a) Botulinum toxin in the management of spasticity in adults. *Clinical Medicine* 2(2):128–30.

Turner-Stokes L, Ward AB (2002b) *Guidelines for the use of botulinum toxin in the management of spasticity in adults.* Concise Guidance to Good Practice. London: RCP.

Turner-Stokes L, Rusconi S (2002) The AbilityQ and the ShoulderQ: A system to assess shoulder pain in stroke patients. *Clinical Rehabilitation* 17(2);150–7.

Turner-Stokes L, Ashford S (2007) Serial injection of botulinum toxin (BTX) for muscle imbalance due to regional spasticity in the upper limb. *Disability and Rehabilitation* 29(23):1806–12.

Turner-Stokes L, Disler R, Shaw A, Williams H (2008) Screening for pain in patients with cognitive and communication difficulties: Evaluation of the SPIN-Screen. *Clinical Medicine* 8(4):393–8.

van Kuijk AA, Hendricks HT, Pasman JW *et al* (2007) Are clinical characteristics associated with upper-extremity hypertonia in severe ischaemic supra-tentorial stroke? *Journal of Rehabilitation Medicine* 39(1):33–7.

Verplancke D, Snape S, Salisbury CF *et al* (2005) A randomised controlled trial of botulinum toxin on lower limb spasticity following acute acquired severe brain injury. *Clinical Rehabilitation* 19(2):117–25.

Wade DT (1992) *Measurement in neurological rehabilitation*. Oxford: Oxford University Press.

Wallesch C-W, Meas E, Lecomte P *et al* (1997) Cost-effectiveness of botulinum toxin type A injection in patients with spasticity following stroke: a German perspective. *European Journal of Neurology* 4(2):S53–S57.

Ward AB, Turner-Stokes L (2001) *The management of adults with spasticity using botulinum toxin: a guide to clinical practice*. London: Radius Healthcare.

Ward AB (2002) A summary of spasticity management – a treatment algorithm. *European Journal of Neurology* 9(S1):48–52.

Ward AB, Roberts G, Warner J, Gillard S (2005) Cost-effectiveness of botulinum toxin type A in the treatment of post-stroke spasticity. *Journal of Rehabilitation Medicine* 37(4):252–7.

Ward AB, Barnes MA (2007) *Clinical uses of botulinum toxin*. Cambridge: Cambridge University Press.

Watkins CL, Leathley MJ, Gregson JM *et al* (2002) Prevalence of spasticity post-stroke. *Clinical Rehabilitation* 16(5):515–22.

Williams RC, Steig RL (1987) Validity and therapeutic efficiency of individual goal attainment procedures in a chronic pain treatment centre. *Clinical Journal of Pain* 2:219–28.

World Health Organization (2001) *International classification of functioning, disability and health*. Geneva: WHO.

Yablon SA, Agana BT, Ivanhoe CB *et al* (1996) Botulinum toxin in severe upper extremity spasticity among patients with traumatic brain injury: an open labelled trial. *Neurology* 47:939–44.

ISBN 978-1-86016-350-0

Royal College of Physicians of London
11 St Andrews Place, London NW1 4LE

www.rcplondon.ac.uk