

Unique Therapeutic Qualities of Botulinum Toxin A
Products – A review of the 3 current toxins in Canada
and their similarities and differences



Nancy Simonot Disclosure

Honoraria	AbbVie, Roche, Allergan, Amgen
Investments	None
Advisory Boards	Amgen, AbbVie

Learning Objectives

- 1 Understand the differences in the manufacturing, formulation, and potency testing amongst Botulinum Toxin A products available in Canada**
- 2 Discuss the role of Botulinum Toxin A in post stroke spasticity**
- 3 Identify available spasticity screening tools**



Understanding the Characteristic Differences of Botulinum Toxin A Products

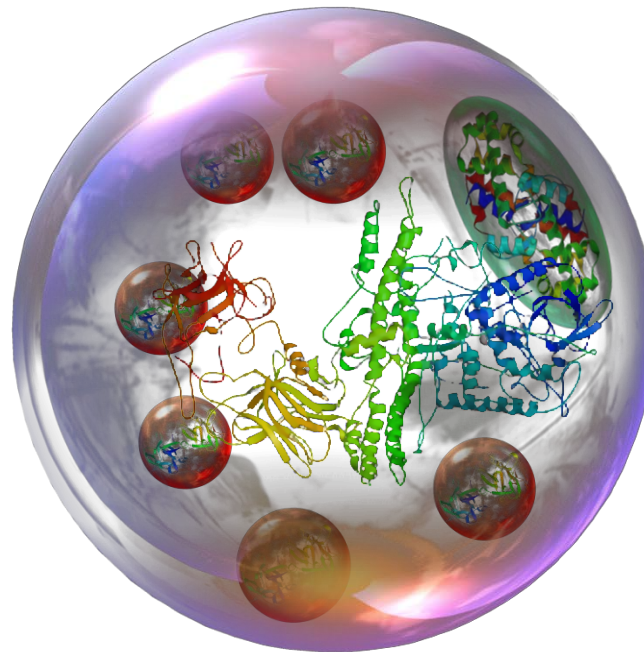
The Unique Molecular Structure of Botulinum Toxin A

Clostridium botulinum is a gram positive, anaerobic, rod-shaped bacterium that produces seven serologically distinct neurotoxins (A, B, C1, D, E, F, G).

Non-Toxic Accessory Proteins

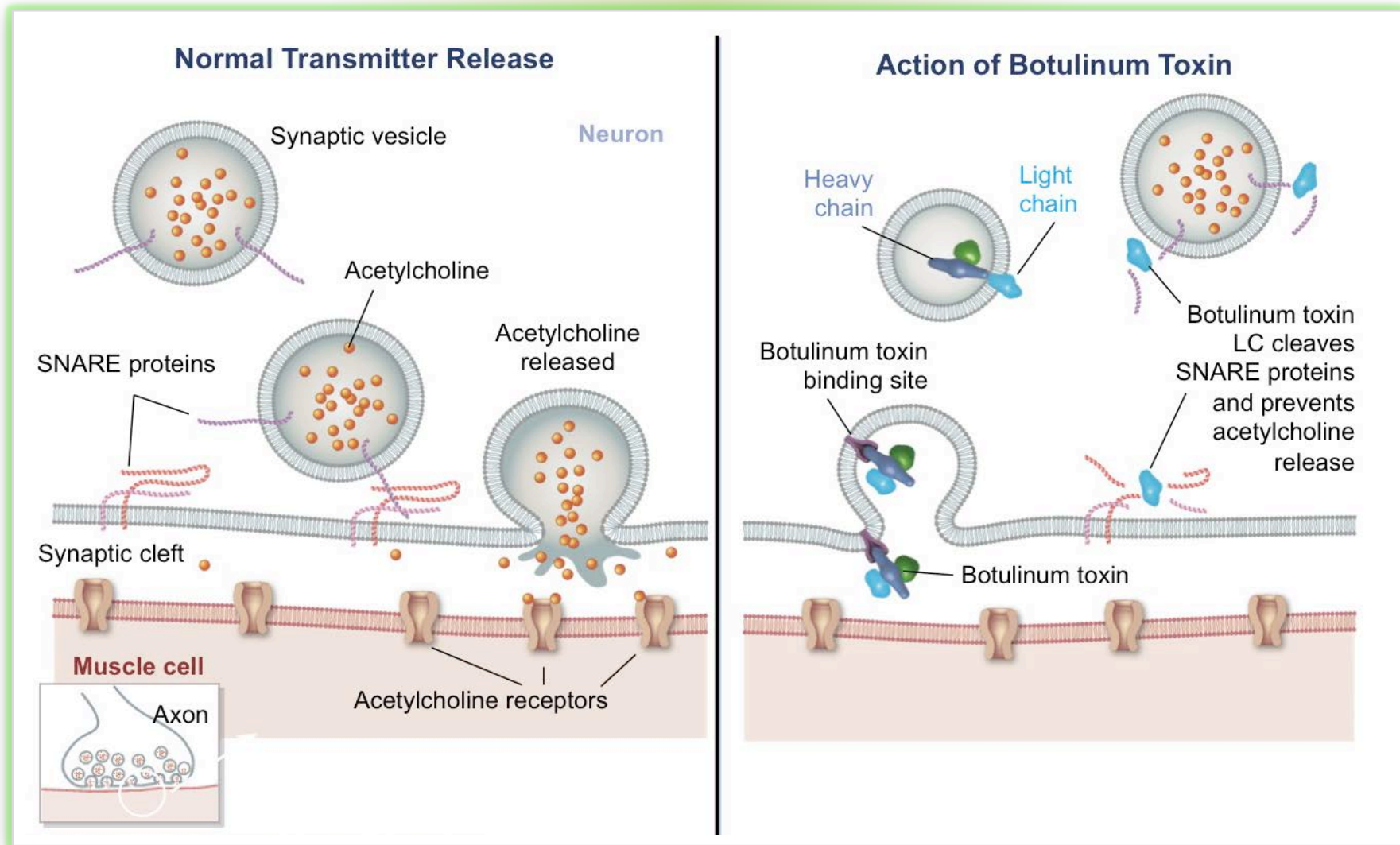
Non-toxic,
non-hemagglutinin
(NTNH)

Hemagglutinin (HA)



150 kDa neurotoxin
protein

Mechanism of Action: Botulinum Toxin A (BoNT)



There Are Significant Differences Between Toxin Manufacturing Processes, Which Leads to Distinctly Different End Products:

“The Product Is the Process”¹

Fermentation and isolation



C. botulinum



C. botulinum



C. botulinum

Purification

Ethanol precipitation and crystallization²

Ion exchange and pH change⁴

Ion exchange³



Formulation

Finishing

- Albumin
- NaCl

Botox

onabotulinumtoxin A

- Albumin
- Sucrose

Xeomin

incobotulinumtoxin A

- Albumin
- Lactose

Dysport

abobotulinumtoxin A

1. Schellekens H. *Nephrol Dial Transplant* 2005;20[Suppl 4]: iv31–iv36. 2. Schantz and Johnson. *Microbiol Rev.* 1992;56(1): 80-99; 3. Hambleton. *J Neurol.* 1992;239:16-20; 4. Canadian Intellectual Property Office patent #CA 2376193; Botox (onabotulinumtoxinA), Xeomin (incobotulinumtoxinA), Dysport (abobotulinumtoxinA); *Web FDA Dysport chemistry review. Exact weights and composition have not been reported by the manufacturer

Product Ingredients



BOTOX

OnabotulinumtoxinA

HSA: 500 µg (100U)
NaCl: 0.9 mg



Xeomin

IncobotulinumtoxinA

HSA: 1000 µg (100 U)
Sucrose: 4.7 mg



Dysport

AbobotulinumtoxinA

HSA: 125 µg (300 U)
Lactose: 2.5 mg

Botox® Product Monograph, Allergan, Inc., Markham, ON 2014, Xeomin® Product Monograph. Merz Pharma Canada Ltd. Burlington, ON 2015 Dysport® Product Monograph, Ipsen Biopharm Limited. Mississauga ON. June 2016 *Exact quantities of excipients described in Dysport® American PI (July 2015 US Prescribing Information) HSA: Human Serum Albumin; Botox (onabotulinumtoxinA), Xeomin (incobotulinumtoxinA), Dysport (abobotulinumtoxinA)

How Do the Botulinum Toxin A Products Differ?

	BOTOX® ¹	XEOMIN® ²	DYSPORT™ ³
Non-Proprietary Name	onabotulinumtoxinA	incobotulinumtoxinA	abobotulinumtoxinA

Health Canada and other regulatory agencies deemed the products not interchangeable, and required unique chemical names

The screenshot shows the Health Canada website with a red maple leaf logo. The main navigation bar includes 'Recalls & alerts', 'Kids', 'Food', 'Your Health', 'Environment', and 'Consumer products'. The breadcrumb trail reads 'Home > Recalls & alerts'. The article title is 'New Labelling Information for all Botulinum Toxin Products: Botox / Botox Cosmetic, Dysport, Xeomin / Xeomin Cosmetic and Myobloc'. The text states: 'In order to help prevent medication errors with the use of botulinum toxin products currently available on the Canadian market, Health Canada will be requesting that all manufacturers of these products revise their product labels to reflect that each product has its own individual potency and as such, is not interchangeable with other botulinum products.' It further explains: 'The labelling changes are due to a risk evaluation of the active ingredients (Clostridium botulinum toxin type A and type B) within these products. Botulinum toxins are produced by different manufacturing processes, are obtained by different techniques and are derived from different Clostridium strains. As a result of these differences, these products cannot be interchanged as these changes can cause unexpected side-effects.'

New Labelling Information for All Botulinum Toxin Products: Botox/Botox Cosmetic, Dysport, Xeomin/Xeomin Cosmetic and Myobloc. Jan 2013.
http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/16787a-eng.php?_ga=1.42483045.1158135760.1472153358;
 Botox (onabotulinumtoxinA), Xeomin (incobotulinumtoxinA), Dysport (abobotulinumtoxinA)

Different Measures of Potency Between Botulinum Toxin A Products

	BOTOX ¹	XEOMIN ²	DYSPORT ³
Non-Proprietary Name	onabotulinumtoxinA	incobotulinumtoxinA	abobotulinumtoxinA
	1 Botox unit defined per Allergan potency assay	≠ 1 Xeomin unit defined per Mertz potency assay	≠ 1 Dysport unit defined per Ipsen assay

Health Canada and other regulatory agencies deemed the products not interchangeable, and required unique chemical names
All product monographs carry a warning regarding non-interchangeability of units

Botox

Serious Warnings and Precautions

- The term "Allergan unit" upon which dosing is based is a specific measurement of toxin activity that is unique to Allergan's formulation of botulinum toxin type A. Therefore, the "Allergan units" used to describe BOTOX[®] activity are different from those used to describe that of other botulinum toxin preparations and the units representing BOTOX[®] activity are not interchangeable with other products.
- BOTOX[®] should only be given by physicians with the appropriate qualifications and experience in the treatment and the use of required equipment.
- Follow the recommended dosage and frequency of administration for BOTOX[®] (See WARNINGS AND PRECAUTIONS, General and DOSAGE AND ADMINISTRATION).

Xeomin

Serious Warnings and Precautions

- The term "unit" or "U" upon which dosing is based, is a specific measurement of toxin activity that is unique to XEOMIN[®]. Therefore, the "unit" or "U" used to describe XEOMIN[®] activity are different from those used to describe that of other botulinum toxin preparations and the units representing XEOMIN[®] activity are not interchangeable with other products.
- Follow the recommended dosage and frequency of administration for XEOMIN[®] (See DOSAGE AND ADMINISTRATION).

Dysport

Serious Warnings and Precautions

- The term "Unit" upon which dosing is based, is a specific measurement of toxin activity that is unique to Ipsen's formulation of abobotulinumtoxinA. Therefore, the units used to describe DYSPORT[®] activity are different from those used to describe that of other botulinum toxin preparations and the units representing DYSPORT[®] activity are not interchangeable with other products.
- DYSPORT[®] should only be administered by physicians with the appropriate qualifications and experience in the treatment and the use of required equipment.
- Follow the recommended dosage and frequency of administration for DYSPORT[®] (See WARNINGS AND PRECAUTIONS, General and DOSAGE AND ADMINISTRATION).

BOTOX[®] Product Monograph, Allergan, Inc., Markham, ON 2014; Xeomin[®] Product Monograph. Merz Pharma Canada Ltd. Burlington, ON 2015; Dysport[®] Product Monograph, Ipsen Biopharm Limited. Mississauga ON. June 2016; Botox (onabotulinumtoxinA), Xeomin (incobotulinumtoxinA), Dysport (abobotulinumtoxinA)

Botulinum Toxin A Product Indications Differ

Indications	Botox	Xeomin	Dysport
Blepharospasm	✓	✓	✗
Cervical dystonia	✓	✓	✓
Chronic Migraine	✓	✗	✗
Paediatric Cerebral Palsy patients ≥2 years old	✓	✗	✗
Focal spasticity, including Upper Limb Associated with Stroke	✓	✓	✓
Urinary incontinence in adults with neurogenic detrusor overactivity resulting from neurogenic bladder due to stable sub-cervical spinal cord injury, or multiple sclerosis.	✓	✗	✗
Idiopathic overactive bladder with symptoms of urinary incontinence, urgency and frequency in adult patients who have an inadequate response to, or are intolerant of, anticholinergic medication	✓	✗	✗

Botox® Product Monograph, Allergan, Inc., Markham, ON 2014

Xeomin® Product Monograph. Merz Pharma Canada Ltd. Burlington, ON 2015

Dysport® Product Monograph, Ipsen Biopharm Limited. Mississauga ON. June 2016

Botox (onabotulinumtoxinA), Xeomin (incobotulinumtoxinA), Dysport (abobotulinumtoxinA)



Understanding the Role of Botulinum Toxin A in Post Stroke Spasticity

Epidemiology of Stroke

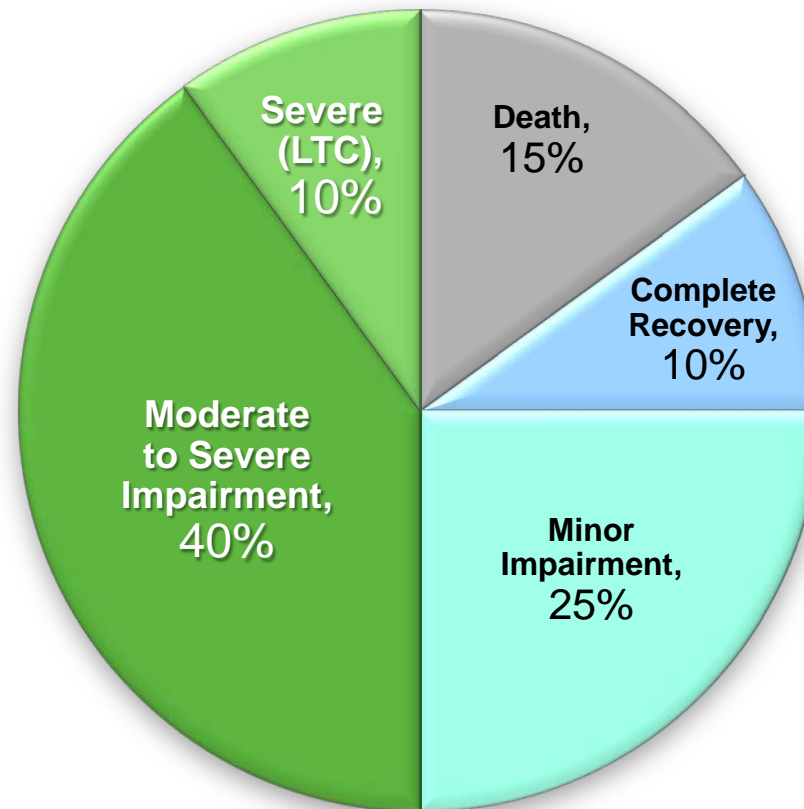
Stroke...

- Is the **leading** cause of adult disability in Canada
- Is the **third** leading cause of death in Canada
- ~ 426,000 Canadians are living with the effects of stroke
- Costs the Canadian economy more than \$3.6 billion / year

Over 50,000 new strokes annually in Canada...
that is **one stroke every 10 minutes**

What Happens After a Stroke?


50% of Patients Have Moderate to Severe Impairments Post-stroke¹



Impairment:
a functional and/
or physical deficit
caused by stroke
affecting ≥ 1
neurological
domains²

1. National Institute of Neurological Disorders and Stroke: Stroke Rehabilitation Information. Accessed Nov 28 2013

2. Kelly-Hayes et al. *Stroke* 1998; 29; 1274-1280



Motor Impairment in Chronic Post-stroke

- Weakness is one of the most common impairments in chronic post-stroke and a major factor in limiting motor performance¹
- In the first year following stroke:
 - Nearly 50% of stroke patients decline in mobility function²
 - Over 65% experience hemiparetic motor dysfunction¹
- Muscle strengthening and exercise is crucial in addition to pharmacotherapy to:
 - Promote functional improvement in strength/timing of muscle activation and cardiorespiratory fitness^{1,3}
 - Prevent additional long-term disability such as chronic post-stroke spasticity¹

1. Pak S & Patten *Top Stroke Rehab* 2008; 15; 177-199. 177C

2. Ivey et al. *J Amer Soc Exp Neurother* 2006;3:439-450 3. Gordon et al. *Stroke* 2004;35:1230-1240

What Is Post Stroke Spasticity?

Defined as:

- Velocity-dependent increase in muscle tone
- Exaggerated tendon jerks
- At times can be painful, interfere with functional recovery and slow rehabilitation efforts

But...

- Modifications to the definition occurred by experts, since tendency to classify all stiffness as spasticity



Chronic Spasticity in Stroke Survivors

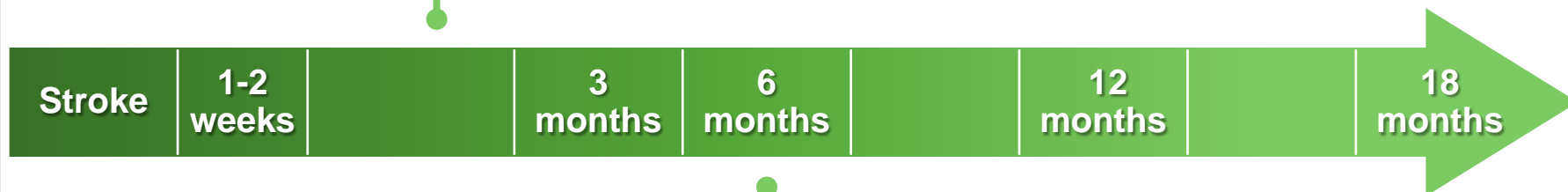
- Upwards of 40% of stroke survivors may develop spasticity¹⁻³
- Spasticity in stroke survivors may lead to reductions in⁴:
 - Ability to perform activities of daily living
 - Health-related quality of life (HRQoL)

Treatments that reduce spasticity and disability will likely increase functioning and improve HRQoL in stroke survivors⁴

Post-stroke Spasticity Symptoms Can Worsen When Left Untreated

- Post-stroke spasticity is a chronic problem and needs to be monitored over time¹

27% of post-stroke patients have signs of spasticity within 6 weeks²



52% of post-stroke patients develop contracture within 6 months in at least 1 joint (N=165)³

1. Sunnergan et al. *Neurology* 2013; 80(S2): S36-S44 2. Wissel J et al. *J Neurol* 2010;257:1067-1072

3. Kwah et al. *J Physiother* 2012; 58: 41-47

Spasticity Treatment Goals

When creating a treatment plan, discuss goals with patients and caregivers. It is important to make sure everyone is on the same page in terms of expectations.

Major classes of treatment goals and examples^{1,2}

Technical objectives	<ul style="list-style-type: none">• Increase range of motion• Reduce muscle tone• Reduce muscle spasms
Functional objectives	<ul style="list-style-type: none">• Improve activities of daily living (e.g. dressing, hygiene)• Reduce pain• Enhance ease of care• Improve limb position• Improve walking and other movements
Preventive objectives	<ul style="list-style-type: none">• Prevent immobility• Prevent pressure sores• Delay or prevent surgery

What Is the Place of the Toxins in Canadian Clinical Practice Guidelines?

Upper Limb Spasticity

Botulinum Toxin A: can be used to increase **range of motion** and decrease **pain** for focal and/or symptomatically distressing spasticity

Oral medications: Can be prescribed for disabling spasticity:

Tizanidine: Can be used for more generalized disabling spasticity

Baclofen: Can be used as a lower cost option, but not studied in this population

Benzodiazepines: Avoid due to sedating side effects, which may impair recovery

What Is the Place of the Toxins in Canadian Clinical Practice Guidelines?

Lower Limb Spasticity

Botulinum Toxin A: can be used to reduce spasticity, increase **range of motion** and **improve gait** for focal and/or symptomatically distressing spasticity

Oral medications: Can be prescribed for disabling spasticity:

Tizanidine: Can be used for more generalized disabling spasticity

Baclofen: Can be used as a lower cost option to treat more generalized disability spasticity

Benzodiazepines: Avoid due to sedating side effects, which may impair recovery

Intrathecal Baclofen: For specific cases of severe, intractable and disabling / painful spasticity

How Does CADTH Position the Evidence on Toxins?

Evidence From:

- 8 systematic reviews (SRs)
- Plus 5 SRs with meta-analysis
- 15 RCTs
- 3 stroke guidelines

Guidelines Recommend Use In:

- Pain, interfering with physical function
- Maintenance of hand hygiene
- To improve gait
- To improve range of motion



Tools for Post Stroke Spasticity Screening

Global Stroke Assessment

POST-STROKE Checklist



Developed by the Global Stroke Community Advisory Panel [2012], endorsed by the World Stroke Organization, adapted by the Heart and Stroke Foundation Canadian Stroke Best Practice Recommendations development team [2014]

Patient Name: _____ Date Completed: _____
 COMPLETED BY: HEALTHCARE PROVIDER PATIENT FAMILY MEMBER OTHER

SINCE YOUR STROKE OR LAST ASSESSMENT

1 Secondary Prevention	<p>Have you received medical advice on health-related lifestyle changes or medications to prevent another stroke?</p> <p>NO <input type="radio"/> Refer patient to primary care providers for risk factor assessment and treatment if appropriate, or secondary stroke prevention services.</p> <p>YES <input type="radio"/> Continue to monitor progress</p>
2 Activities of Daily Living (ADL)	<p>Are you finding it more difficult to take care of yourself?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Do you have difficulty: <input type="radio"/> dressing, washing, or bathing? <input type="radio"/> preparing hot drinks or meals? <input type="radio"/> getting outside? If Yes to any, consider referral to home care services; appropriate therapist; secondary stroke prevention services.</p>
3 Mobility	<p>Are you finding it more difficult to walk or move safely (i.e., from bed to chair)?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Are you continuing to receive rehabilitation therapy? <input type="radio"/> No. Consider referral to home care services; appropriate therapist; secondary stroke prevention services. <input type="radio"/> Yes. Update patient record; review at next assessment.</p>
4 Spasticity	<p>Do you have increasing stiffness in your arms, hands, or legs?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Is this interfering with activities of daily living? <input type="radio"/> No. Update patient record; review at next assessment. <input type="radio"/> Yes. Consider referral to rehabilitation service; secondary stroke prevention services; physician with experience in post-stroke spasticity (e.g., physiatrist, neurologist).</p>
5 Pain	<p>Do you have any new pain?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Ensure there is adequate evaluation by a healthcare provider with expertise in pain management.</p>
6 Incontinence	<p>Are you having more problems controlling your bladder or bowels?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Consider referral to healthcare provider with experience in incontinence; secondary stroke prevention services.</p>

SINCE YOUR STROKE OR LAST ASSESSMENT

7 Communication	<p>Are you finding it more difficult to communicate?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Consider referral to speech language pathologist; rehabilitation service; secondary stroke prevention services.</p>
8 Mood	<p>Do you feel more anxious or depressed?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Consider referral to healthcare provider (e.g., psychologist, neuropsychologist, psychiatrist) with experience in post-stroke mood changes; secondary stroke prevention services.</p>
9 Cognition	<p>Are you finding it more difficult to think, concentrate, or remember things?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Is this interfering with your ability to participate in activities? <input type="radio"/> No. Update patient record; review at next assessment. <input type="radio"/> Yes. Consider referral to healthcare provider with experience in post-stroke cognition changes; secondary stroke prevention services; rehabilitation service; memory clinic.</p>
10 Life After Stroke	<p>Are you finding it more difficult to carry out leisure activities, hobbies, work, or engage in sexual activity?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Consider referral to stroke support organization (local/provincial support group, Heart and Stroke Foundation of Canada Living with Stroke program); leisure, vocational, or recreational therapist.</p>
11 Personal Relationships	<p>Have your personal relationships (with family, friends, or others) become more difficult or strained?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Schedule next primary care visit with patient and family member(s) to discuss difficulties. <input type="radio"/> Consider referral to stroke support organization (local/provincial support group, Heart and Stroke Foundation of Canada); healthcare provider (e.g., psychologist, counsellor, therapist) with experience in family relationships and stroke.</p>
12 Fatigue	<p>Are you experiencing fatigue that is interfering with your ability to do your exercises or other activities?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Discuss fatigue with Primary Care provider. <input type="radio"/> Consider referral to home care services for education and counselling.</p>
13 Other Challenges	<p>Do you have other challenges or concerns related to your stroke that are interfering with your recovery or causing you distress?</p> <p>NO <input type="radio"/> Continue to monitor progress</p> <p>YES <input type="radio"/> Schedule next primary care visit with patient and family member(s) to discuss challenges and concerns. <input type="radio"/> Consider referral to healthcare provider; stroke support organization (local or provincial support group, Heart and Stroke Foundation of Canada).</p>

For more information refer to www.heartandstroke.ca or www.strokebestpractices.ca

Spasticity Screening Tool

ORIGINAL RESEARCH ARTICLE

OPEN

A Screening Tool to Identify Spasticity in Need of Treatment

Richard D. Zorowitz, MD, Theodore H. Wein, MD, FRCPC, Kari Dunning, PT, PhD, Thierry Deltombe, MD, John H. Olver, MBBS, MD, FAFRM (RACP), Shashank J. Davé, DO, Michael A. Dimyan, MD, John Kelemen, MD, FAAN, Fernando L. Pagan, MD, Christopher J. Evans, PhD, MPH, Patrick J. Gillard, PharmD, MS, and Brett M. Kissela, MD, MS

Objective: To develop a clinically useful patient-reported screening tool for health care providers to identify patients with spasticity in need of treatment regardless of etiology.

Design: Eleven spasticity experts participated in a modified Delphi panel and reviewed and revised 2 iterations of a screening tool designed to identify spasticity symptoms and impact on daily function and sleep. Spasticity expert panelists evaluated items pooled from existing questionnaires to gain consensus on the screening tool content. The study also included cognitive interviews of 20 patients with varying spasticity etiologies to determine if the draft screening tool was understandable and relevant to patients with spasticity.

Results: The Delphi panel reached an initial consensus on 21 of 47 items for the screening tool and determined that the tool should have no more than 11 to 15 items and a 1-month recall period for symptom and impact items. After 2 rounds of review, 13 items were selected and modified by the expert panelists. Most patients (n = 16 [80%]) completed the cognitive interview and interpreted the items as intended.

Conclusions: Through the use of a Delphi panel and patient interviews, a 13-item spasticity screening tool was developed that will be practical and easy to use in routine clinical practice.

Key Words: Delphi Technique, Patient Outcome Assessment, Screening, Muscle Spasticity

(Am J Phys Med Rehabil 2016;00: 00–00)

Instructions: Please answer the following questions thinking about your muscle stiffness, tightness, or spasms over the past 1 month

Item #	Question
1	How bad is the stiffness or tightness of your muscles, either at rest, when you move, or are being moved? <input type="checkbox"/> 0 I don't have stiffness or tightness <input type="checkbox"/> 1 A little stiff or tight <input type="checkbox"/> 2 Somewhat stiff or tight <input type="checkbox"/> 3 Very stiff or tight <input type="checkbox"/> 4 Extremely stiff or tight
2	How difficult is it for you to straighten, bend, or flex your limb(s) (leg[s] or arm[s]) due to stiffness or tightness in your muscles? <input type="checkbox"/> 0 Not difficult at all <input type="checkbox"/> 1 A little difficult <input type="checkbox"/> 2 Somewhat difficult <input type="checkbox"/> 3 Very difficult <input type="checkbox"/> 4 I am unable to straighten, bend, or flex my limbs
3	How bad are your spasms that occur unpredictably or are caused by movement? <input type="checkbox"/> 0 I don't have spasms <input type="checkbox"/> 1 A little bad <input type="checkbox"/> 2 Somewhat bad <input type="checkbox"/> 3 Very bad <input type="checkbox"/> 4 Extremely bad
4	Are any of the above stiffness, tightness, or spasms associated with pain? Please specify the location of the pain: _____ <input type="checkbox"/> 0 No, I don't have any pain <input type="checkbox"/> 1 Yes, a little bit of pain <input type="checkbox"/> 2 Yes, some pain <input type="checkbox"/> 3 Yes, quite a bit of pain <input type="checkbox"/> 4 Yes, a lot of pain
5	Over the past month, how often was your sleep disrupted because of stiffness, tightness, or spasms in your muscles? <input type="checkbox"/> 0 Never <input type="checkbox"/> 1 Rarely <input type="checkbox"/> 2 Sometimes <input type="checkbox"/> 3 Often <input type="checkbox"/> 4 Every night
6	Over the last month, how bothersome was your muscle stiffness, tightness, or spasms? <input type="checkbox"/> 0 Not bothersome at all <input type="checkbox"/> 1 A little bothersome <input type="checkbox"/> 2 Somewhat bothersome <input type="checkbox"/> 3 Very bothersome <input type="checkbox"/> 4 Extremely bothersome
Upper Limb Specific	
7	How bad is your hand clenching on its own? <input type="checkbox"/> 0 I don't have any hand clenching <input type="checkbox"/> 1 It clenches a little <input type="checkbox"/> 2 It clenches somewhat <input type="checkbox"/> 3 It clenches quite a bit <input type="checkbox"/> 4 It clenches all the way
8	How difficult is it for you or your caregiver to clean the <u>palm of your hand</u> or <u>between the fingers</u> due to the tightness or clenching of the thumb, fingers, or hand? <input type="checkbox"/> 0 Not difficult at all <input type="checkbox"/> 1 A little difficult <input type="checkbox"/> 2 Somewhat difficult <input type="checkbox"/> 3 Very difficult <input type="checkbox"/> 4 Extremely difficult
9	How difficult is it for you or your caregiver to clean your armpit due to stiffness or tightness in your arm? <input type="checkbox"/> 0 Not difficult at all <input type="checkbox"/> 1 A little difficult <input type="checkbox"/> 2 Somewhat difficult <input type="checkbox"/> 3 Very difficult <input type="checkbox"/> 4 Extremely difficult
10	How difficult is it for you or your caregiver to put your arm through the <u>sleeve of your coat</u> or <u>shirt</u> due to stiffness or tightness in your arm? <input type="checkbox"/> 0 Not difficult at all <input type="checkbox"/> 1 A little difficult <input type="checkbox"/> 2 Somewhat difficult <input type="checkbox"/> 3 Very difficult <input type="checkbox"/> 4 Extremely difficult
Lower Limb Specific	
11	How bad is your foot and/or toes <u>pulling in</u> , <u>curling</u> , <u>sticking up</u> , or otherwise <u>getting</u> stuck on their own when you try to move? <input type="checkbox"/> 0 My foot and/or toes do not pull in, curl, stick up, or otherwise get stuck on their own <input type="checkbox"/> 1 A little bad <input type="checkbox"/> 2 Somewhat bad <input type="checkbox"/> 3 Very bad <input type="checkbox"/> 4 Extremely bad
12	How difficult is it to walk or move your leg(s) due to stiffness or tightness in your leg(s)? <input type="checkbox"/> 0 Not difficult at all <input type="checkbox"/> 1 A little difficult <input type="checkbox"/> 2 Somewhat difficult <input type="checkbox"/> 3 Very difficult <input type="checkbox"/> 4 I am unable to walk or move my legs
13	How difficult is it for you or your caregiver to put on your pants or your shoes due to stiffness or tightness in your leg(s) or feet? <input type="checkbox"/> 0 Not difficult at all <input type="checkbox"/> 1 A little difficult <input type="checkbox"/> 2 Somewhat difficult <input type="checkbox"/> 3 Very difficult <input type="checkbox"/> 4 Extremely difficult

FIGURE 1. Spasticity screening tool items: final version.



Questions?