SYLLABUS

WS05: Therapeutic Use of Botulinum Toxin

Wednesday, November 16, 2011 09:00 - 18:00 Hall 3

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY

XXth WCN 2011 MARRAKESH
World Congress of Neurology

WFN

SMN
SOCIETE MAROCAINE DE NEUROLOGIE

WCN Education Program

Wednesday, 16 November, 2011

09:00-18:00

THERAPEUTIC USE OF BOTULINUM TOXIN

Chairperson: **Christophe Vial**, *France*

09:00-10:30 **PART I: PHARMACOLOGY - CERVICAL DYSTONIA**

PHARMACOLOGY OF BOTULINUM TOXIN
THE USE OF BT IN TREATMENT OF CERVICAL DYSTONIA

10:30-11:00 *Coffee Break*

11:00-12:30 **PART II: CRANIO-FACIAL, LARYNGEAL AND OTHERS FOCAL DYSTONIA**

THE USE OF BOTULINUM TOXIN IN TREATMENT OF HEMI FACIAL SPASM, BLEPHAROSPASM AND EYELID APRAXIA, OROMANDIBULAR DYSTONIA, SPASMODIC DYSPHONIA

THE USE OF BOTULINUM TOXIN IN TREATMENT OF OTHERS FOCAL DYSTONIA: WRITER'S CRAMPS, DYSTONIA AND PARKINSON

12:30-14:30 *Lunch Break*

14:30-16:00 **PART III: SPASTICITY, MISCELLANEOUS**

SPASTICITY IN ADULTS
SPASTICITY IN CHILDREN: SPECIFICITY
MISCELLANEOUS: TREMOR, TICS, HYPERHYDROSIS, FREY SYNDROME EMERGING USE: HEADACHE, PAIN, SPASTIC BLADDER

16:00-16:30 *Coffee Break*

16:30-18:00 **PART IV: VIDEOS AND PRACTICE**

VIDEO CASES: PRACTICAL CASES, CHOICE OF INJECTION SITES, DOSAGES

DEMONSTRATION SESSIONS USING ELECTRONIC VIRTUAL INJECTION STIMULATOR (ELVIS) MANNEQUINS

Advisory Panel:
Christophe Vial, *France*
Ouafae Messouak, *Morocco*
Marie-Hélène Marion, *UK*
Pierre Krystkoviak, *France*

Pharmacology of Botulinum Toxin

Dr Marie-Helene Marion
Consultant neurologist
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Botulinum toxin (BoNT)

- Neurotoxin produced by Clostridium Botulinum, *a gram-positive anaerobic bacterium.*
- The clinical syndrome of botulism:
  - Following ingestion of contaminated food,
  - from colonization of the infant gastrointestinal tract,
  - from a wound infection.

BoNT

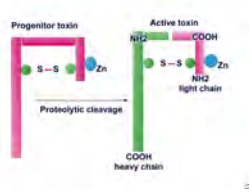
- A, B, C (trial) and E type : for therapeutic use
- Inhibits the release of acetylcholine at the neuromuscular junction and at the gland nerve terminal.
- Muscular paralytic effect
- Inhibits glands secretion :
  - Salivary, Sweat and Lacrymal glands

BoNT

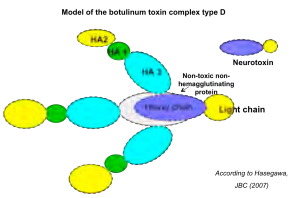
- 7 neurotoxins (labeled as types A, B, C [C1, C2], D, E, F, and G), which are antigenically and serologically distinct but structurally similar.

BoNT structure

The BoNT molecule is synthesized as a single chain (150 kD) and then cleaved to form the dichain molecule with a disulfide bridge

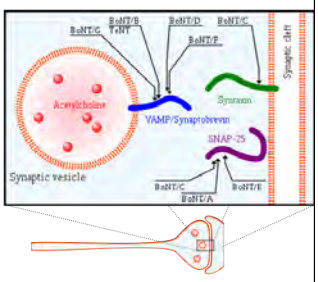


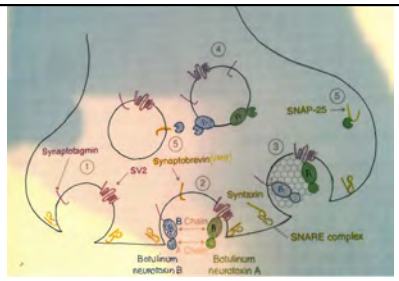
BoNT complex



- Hemaglutinin protein
- Non-hemaglutinin protein

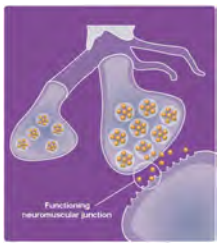
- Vesicle-associated membrane protein (VAMP)
  - Synaptobrevin (target BTX-B).
- Inner plasma membrane of the nerve terminal
  - Syntaxin (target BTX-C)
  - SNAP-25 (target BTX-A) synaptosomal protein





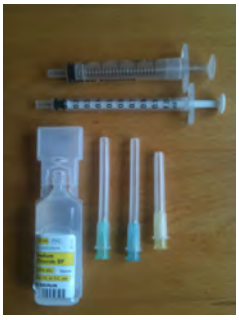
1-Exposition of intra luminal domains of SV2 and Synapto-tagmin
2-Binding of the heavy chain to SV2 and synapto-tagmin
3-Internalisation into the endocytotic membrane
4-Activation of the light chain (ph change)
5-Cleavage of the SNARE protein and loss of exocytocic ability

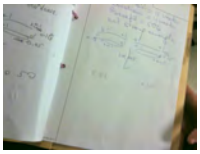
Sprouting



- Recovery of nerve activity occurs in newly formed sprouts
- Eventually the new nerve sprouts retract and the original nerve ending regain his function.

BoNT clinic





-Rating scale
-Video
-Functional anatomy atlas
-Database

BoNT-A

Ona-botulinum toxinA

Allergan: Botox
100, 200
Fridge 4C

Abo-botulinum toxinA

Ipsen: Dysport
500, 300
Fridge 4C

Inco-botulinum toxinA

Merz:Xeomin
100
Room temp

Key Characteristics of Different BoNT- Preparations

	BOTOX	DYSPORT	XEOMIN
Container	Glass vial with rubber stopper	Glass vial with rubber stopper	Septum bottle with rubber stopper
Vial size/protein content	100U vial, (50U vial) 5ng protein/100U	500U vial 0.87ng protein/100U	100U vial 0.6ng protein/100U
Excipients	Human albumin (500mg) Sodium chloride (0.9mg)	Human albumin (125mg) Lactose (2.5mg)	Human albumin (1000mg) Sucrose
Storage conditions	Store in a refrigerator (2°C-8°C) Store in a freezer (at or below -5°C)	Store in a refrigerator (2°C-8°C)	Store at 25°C
Shelf life prior to opening	36 months at 2-8°C	15-24 months at 2-8 °C	36 months at 25° C
Post reconstitution shelf-life	24 hours at 2°C – 8°C	8 hours at 2°C-8°C	24 hours at 2-8°C

Sources: Dysport/Botox:SPC-UK / Xeomin:SPC-Germany

U.S. Food and Drug Administration

- FDA notified healthcare professionals of changes to the established drug names for Botox/Botox Cosmetic, Dysport and Myobloc to reinforce individual potencies and prevent medication errors.08/03/2009

No dose standardisation between different preparations of BoNT

- BoNT-A:
  - Botox-100 units
  - Dysport- 500 units
  - Xeomin- 100 units
- BoNT-B:
  - Neurobloc -5000, 10000 and 15000 units

BoNT injections

- Injection of hyperactive muscles in order to weaken the muscle and relieve the abnormal movement.
- Benefit of the injection is limited in time

"Customise" BoNT injections

- Injection repeated at regular intervals
  - Wearing off effect (patient, condition)
- Duration effect depends
  - Doses injected
  - Condition
  - Minimum intervals of 9 weeks (avoid booster)
- Optimum dose:
  - Size of the muscles
  - Severity of spasms
  - Age of the patient
  - Potential local side effects

Short term side effects of BoNT

- Always transient, 4 to 6 weeks
- Due to the diffusion to the BoNT to adjacent muscles:
  - Ptosis, diplopia following injection of the orbicularis oculi.
  - Dysphagia +++
    - Following injection of SCM, suprahyoids, longus colli or lateral pterygoidians muscles.
    - Risk of aspiration +++
      - Dosages, techniques
      - Contact number given to the patient
      - Admission and Nasogastric tube

U.S. Food and Drug Administration

- A black boxed warning regarding the risk of adverse events when the effects of the toxin spread beyond the site where it was injected
- **Cerebral palsy children**
- reported cases of spread of botulinum toxin effect beyond the site of injection were described as **botulism,**
- or involved symptoms including **difficulty breathing, difficulty swallowing**, muscular weakness, drooping eyelids, constipation, aspiration pneumonia, speech disorder, facial drooping, double vision, or respiratory depression.
- Serious case reports described hospitalizations involving ventilatory support and reports of **death**.

U.S. Food and Drug Administration

- **Understand that dosage strength (potency) expressed in "Units" or "U" are different among the botulinum toxin produ**cts; clinical doses expressed in units are not interchangeable from one botulinum toxin product to another.
- **Be alert to and educate patients and caregivers about potential adverse events** due to distant spread of botulinum toxin effects following local injections including:
  - unexpected loss of strength or muscle weakness, hoarseness or trouble talking (dysphonia), trouble saying words clearly (dysarthria), loss of bladder control, trouble breathing, trouble swallowing, double vision, blurred vision and drooping eyelids.
- Understand that these adverse events have been reported **as early as several hours and as late as several weeks after treatment.**
- **Advise patients to seek immediate medical attention** if they develop any of these symptoms.

Long-term BoNT-A efficacy and safety

- 45 pts treated with BoNT-A for at least 12 years (mean: 15.8 years).
- Focal dystonias (CD,Cranial, BSP) and HFS
- Mean response rating after last injection: 3.7(scale from 0 : no effect and 4: marked improvement)
- Mean total duration of response to BoNT-A: 15.4 weeks
- 22 pts with poor response(rating 0 to 1) on 2 sessions
  - 4 (8.8%) Antibodies +
  - 16 (Ab -) responded after protocol adjustements
  - 2 (Ab-) persisted non-responders

NI Mejia, KD Vuong, J Jankovic,Mov Disorders 2005; 20:592-597

Long-term BoNT-A efficacy and safety

TABLE 2. *Long-term follow up of 45 patients treated with BTX for more than 12 years: Botulinum toxin response*

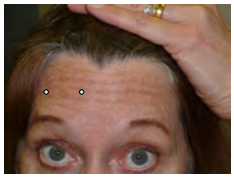
Parameter	First injection	Most recent injection	P
Botulinum toxin (units)	154.3 ± 98.9	221.2 ± 129.4	<0.0001
Response latency (days)	5.9 ± 5.8	4.0 ± 5.3	NS
Response duration (weeks)			
Maximum	9.3 ± 6.8	13.9 ± 5	<0.005
Total	11.6 ± 7.1	15.4 ± 3.4	NS
Efficacy, 0–4			
Global rating	2.5 ± 1.5	3.4 ± 0.9	<0.02
Peak effect	2.9 ± 1.5	3.7 ± 0.6	<0.05
Complications, n (%)	20 in 16/45 (35.6)	11 in 10/45 (22.2)	NS
Immunogenicity*			
Positive MPA, n (%)	4/45 (8.8)	—	—
Negative, nonresponder	2/45 (4.4)	—	—

Data presented as mean ± standard deviation unless noted otherwise.
*22 patients had Ab testing; 6 persisted as nonresponders.
MPA, mouse protection assay; NS, not significant.

NI Mejia, KD Vuong, J Jankovic 2005; 20:592-597

Frontalis test

4 weeks after 40 units Dysport x 2 in right frontalis



Resistant to BoNT-A

Responsive to BoNT-A

BoNT-A exposure and immunogenicity results based on 12 treatment sessions

- 1.2% of resistance
- 4 MPA positive
  - 1 respond to 300 units Botox, but no response to 100,100, and 200
  - 3 lost clinical response:
    - 1 clinically resistant at frontalis test
    - 1 clinically resistant at corregator test
    - 1 was no tested

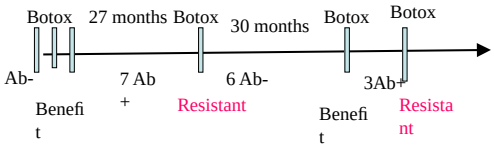
Brin et al, 08

Variability of the Immunologic and Clinical Response

- 7 dystonic patients (6 women, 1 man)
- Average dose/ visit: 207 units Botox
- Resistant to BoNT-A after 27 months (15-43)
  - Unresponsive to BoNT-A
  - AB+ in mouse bioassay
- Seroconversion 30 months later in AB-
  - 6/7 reinjected and responsive again to BoNT-A
- 3/6 lost initial second response and become again AB+

Sankhla et al, Mov Dis. 98

Variability of the Immunologic and Clinical Response



Sankhla et al, Mov Dis,. 98

Biological and clinical resistance

- Variability of the immunologic and clinical response to BoNT-A
  - Early diagnostic of resistance
  - Wait for 1 year if possible before reinjection
- Partial resistance ?
  - Difficult to diagnose
  - MPA high specificity but low sensitivity
  - Frontalis test: not quantitative
  - EDB test: quantitative but large variability

Conclusion

- BTX injections is an efficient treatment of muscle spasms (dystonia, spasticity, hemifacial spasms) and autonomic dysfunction
- Guidelines for dosage, site of injection and interval between injections are essential to follow.
- Be aware of potential side effects,
  - in particular dysphgia,
  - in vulnerable population

Cervical dystonia
Treatment with Botulinum toxin injections

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BTX- A in cervical dystonia

- "Highly effective and safe" (The Cochrane Review –2005)
- Efficient in 80% patients (62% -90%)
- Onset of clinical response in 5 to 7 days
- Duration of benefit : 10 to 12 weeks
- Side effects : dysphagia, cervical muscles weakness

BTX for spasmodic torticollis

- Large clinical spectrum with often mixed posture
  - Torticollis: head rotated to one side
  - Laterocollis: head tilted towards the contralateral shoulder
  - Retrocollis : extension of the head
- Antecollis is rare

Analysis of the dystonic posture

Functional anatomy of the cervical muscles

Cervical muscles

1-Trapezius
2-Levator scapulae
3-Sterno-Mastoid
4-Finger points to splenius

From S.Tixa, Ed Masson, 2001

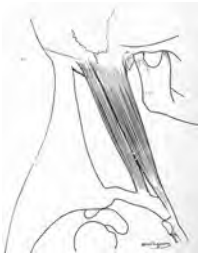
Sternomastoid muscle

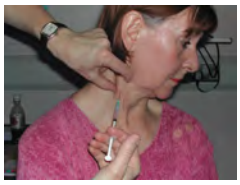
1-sternal
2-occipital
3-clavicular

Sterno-cleido-”occipito”-mastoid muscle

- Unilateral contraction:
  - Rotate the head to the opposite side, tilt the head to the same side, and extension.
- Bilateral contraction
  - If the neck is relax, hyperlordosis of the cervical spine and extension of the head.
  - If the neck is straight (contraction of anterior vertebral muscles), flexion of the neck.

Sternomastoid muscle





Lateral vertebral muscles

- Scalenus anterior
- Scalenus medius
- Scalenus posterior
  - From the transverse process of cervical vertebrae to the 1st and 2nd ribs.Between anterior and medius, brachial plexus.
  - Unilateral contraction:ipsilateral tilt and rotation of the neck.

Nuchal muscles: 4 layers

- 1-deep muscles; suboccipital muscles
- 2-semispinalis capitis
- 3- splenius capitis and levator scapulae
- 4- trapezius and a part of the SCM

Splenius capitis

- From the nuchal line and the spinous process of C7, T1-3 to the mastoid process.
- Unilateral contraction:rotation, tilt and extension of the head to the ipsilateral side of the contraction.
- Bilateral contraction: extension of the head and the neck with hyperlordosis.

Splenius capitis

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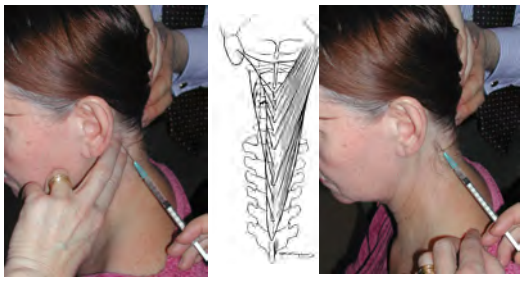
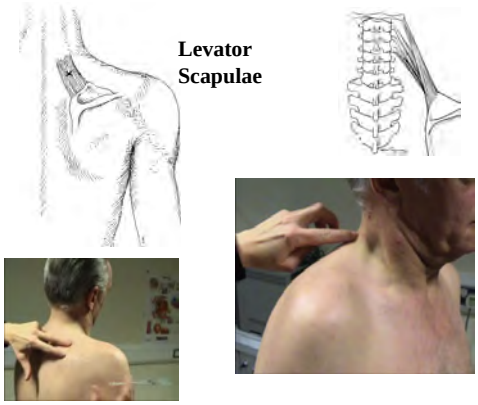
Splenius capitis



Levator scapulae

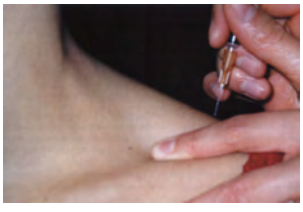
- From the anterior aspect of the scapulae to the mastoid process.
- Elevation of the ipsilateral shoulder.
- With scapulae fixed: rotation, tilt and extension of the head to the ipsilateral side of the contraction.

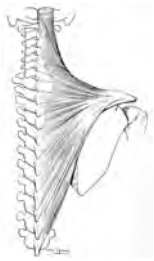


Trapezius (upper portion)

- From the occipital protuberance, the ligamentum nuchae, and the spinous process of C7 and the upper thoracic vertebrae to lateral third of the clavicle.
- Elevation of the ipsilateral shoulder.
- If shoulder fixed:extension of cervical spine with hyperlordosis, ipsilateral tilt of the head and contralateral rotation of the head.

Trapezius





From D. Ranoux, Ed Solal,2002

BTX muscle injections

- Injection of hyperactive muscles in order to weaken the muscle and relieve the abnormal movement.

"Customise" BTX injections

- Injection repeated at regular intervals
  - Wearing off effect (patient, condition)
  - Minimum intervals of 9 weeks (avoid booster)
- Optimum dose:
  - Size of the muscles
  - Severity of spasms
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No dose standardisation between different preparations of BTX

- BTX-A
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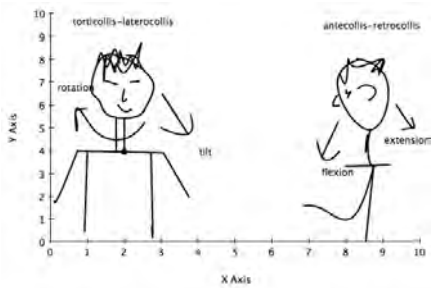
Analysis of the posture



Examination of ST

- Muscle selection based on clinical examination of neck and shoulders.
- Inspection of the patient standing eyes closed, walking, writing, reading…
- Assessment of the abnormal and compensatory posture.
- Amplitude of neck movements.
- Muscle palpation:pain, spasm,hypertrophy.

	Head posture	Cervical muscles
torticollis	-rotation +shoulder elevation	•Controlateral SCM •Ipsilateral splenuis + ipsilateral levator scapulae + controlateral trapezius
laterocollis	tilt	Ipsilateral SCM Ipsilateral splenuis Ipsilateral levator scapulae Ipsilateral trapezius
retrocolls	extension	Both splenii
antecollis	flexion	Longus colli Both SCM

Cervical muscles dosages (BOTOX units)

SCM	30-50 U Botox
Splenius	60-100 U Botox
Levator scapulae	25-60 U Botox
Trapezius	25-100 U Botox
Scalene complex	15-50 U Botox
Hyoid muscles	5-10 U Botox
Semispinalis	30-60 U Botox

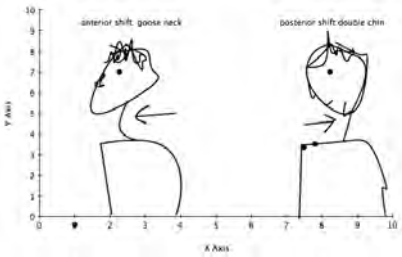
Dysphagia

- Major side effect after injection of cervical muscles
- Mainly the SCM muscle
  - Minimum initial dose (100 units dysport)
  - Upper third of the SCM
  - Higher concentration and only 1 site of injection
  - Careful with bilateral injection of SCM

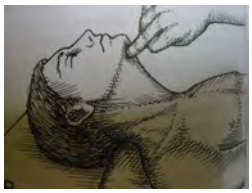
Reasons for failure in cervical dystonia

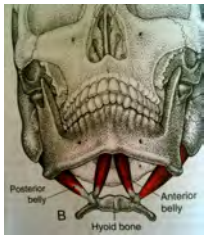
- Compensatory posture
- Saggital shift
- Antecollis
- Associated head tremor
- Technically difficult (short fat neck)
- Craniocervical dystonia with jaw spasms
- Limitation of the dosage by the the side effects
- Resistance to BTX-A

Saggital shift



Supra-hyoids muscles





Longus colli

Resistance to BTX-A

- Diagnostic+++. Frontalis test or EDB test
- If absence of resistance, review the protocol of injection (Dose, muscle selection, technique)
- If resistance, injection of BTX-B
  - 150 Botox, 500 units Dysport,10 000units Neurobloc
  - Dysautonomic side effects
  - after 1 year, majority of patients develop resistance to BTX-B

Conclusion

- BTX injections are the most effective treatment for cervical and jaw dystonia
- Success of BTX injections depends:
  - Careful clinical examination before each injection treatment .
  - Precise assessment of the effect (benefit, side effect) of the previous injection.
  - Good knowledge of the anatomy and functional anatomy of the muscles.

Botulinum Toxin *and* Laryngeal Dysphonia

Dr Christophe VIAL
Neurological Hospital - Lyon – France
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Laryngeal dystonia

- Rare disorder of the vocal function characterised by spasms of the larynx muscles modifying the voice or preventing a regular speech pattern
- 2 main presentations
  - Dysphonia in adduction : the larynx adductor muscles are affected. The voice is strained hoarse and interrupted by short pauses with respiratory spasms during inspiration or expiration
  - Dysphonia in abduction : the larynx abductor muscles are affected. The voice is whispered and not readily audible

Laryngeal dystonia diagnosis

- Acoustic examination of the voice : maximum phonation time of a vowel, vocal intensity,
- larynx video fibroscopy
  - normal morphology of the larynx
  - vocal fold normal at rest but sometimes abnormal abd/adduction movements. If there is inspiratory dyspnoea, the vocal cords are immobile in paramedian position
  - in adductor dysphonia : choppy and forced movements of the vocal cords
  - in abductor dysphonia : the vocal cords cannot be drawn together
- Electromyography : diagnosis and help for localization for BT injection
  - in adductor D : thyroarythenoid muscles at rest (permanent contraction) or during phonation (amplitude and recruitment of motor unit increased at the beginning and the end of contraction
  - in abductor D : posterior cricoarythenoid muscles

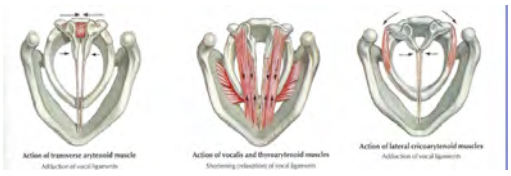
Laryngeal dystonia : Anatomy

The larynx muscles : 3 group based on their action of the larynx muscle

- Tension of the larynx folds on either side :
  - cricothyroideus
- Dilatation and abduction of the glottis on either side :
  - cricoarythenoidus posterior
- Constriction and adduction of the glottis
  - cricoarythenoidus lateral, lower thyroarythenoidus, upper thyroarythenoidus and arythenoidus muscles

Anatomy : Laryngeal motion

Adduction of vocal ligament



Laryngeal dystonia : Practical use of BT

- Material Dilution :
  - Intramuscular route
  - 1ml tuberculin syringe, 0,1 ml graduation
  - Botox and Xeomin : dilution 50 unit/ml
  - Dysport dilution 200 unit/ml
- Injection technique :
  - Transorally using a flexible endoscope
  - Percutaneously Under EMG guidance
  - Add D : thyroarythenoidus muscle : needle on the upper border of the cricoid cartilage, through the cricoïd membrane, rotate 45° upwards and 30° outwards on either side of the median line to penetrate into each thyroarythenoid muscle
  - Abd D : cricoarythenoid muscle posterior
- Uni or Bilaterally ??

Laryngeal dystonia

- Duration of action: 3 to 6 months
- Evaluation
  - Self evaluation by the patient and his relatives
  - Acoustic examination
  - Larynx video fibroscopy
- Side effects
  - Laryngospasm ? (in ADD D)
  - Hypophonia, hoarse and breathy voice
  - Swallowing disorders (liquids)
- Associated treatment
  - Relaxation
  - coaching for breathing movements by orthophonist

Clinical Context

- The evidence supporting BoNT use in laryngeal disorders is suboptimal.
- While most clinicians utilize EMG targeting for laryngeal injections, the utility of this technique is not established in comparative trials.
- Dramatic results in the initial open label studies and the lack of other effective therapy likely have discouraged efforts to study BoNT in larger and more properly controlled clinical trials.

Analysis of the Evidence

- Laryngeal Dystonia (continued)
  - One Class III study found that the addition of voice therapy following BoNT in ADSD prolonged benefit from BoNT treatment.
  - One Class III study of 15 patients with ABSD did not find a significant difference using either percutaneous or endoscopic injection technique.

Recommendations

- BoNT should be considered as a treatment option for adductor spasmodic dysphonia (Level B).
- There is insufficient evidence to support or refute the use of BoNT in abductor spasmodic dysphonia (Level U).

Botulinum Toxin *and* Oromandibular Dystonia

Hôpitaux de Lyon

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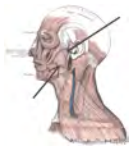
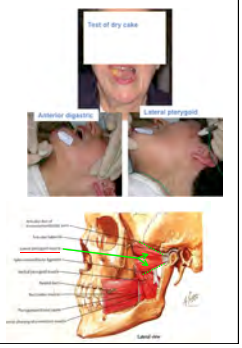
jaw-closure dystonia

- Permanent constriction of the jaws with limited mouth opening (slurred speech, difficulty feeding, dental care, ..
- Muscles to inject:
  - masseter,
  - temporalis,
  - internal pterygoid (EMG)
- Doses of BT: 50 to 100 u BT
- Side effects:
  - permanent opening of the mouth

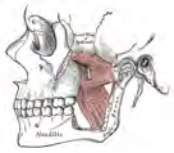


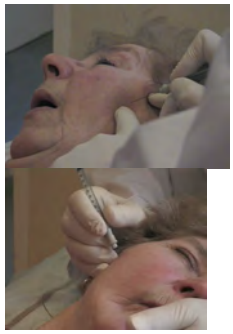
jaw-opening dystonia

- Incontinence mouth when taking food
- Major social handicap
- Weight loss
- Muscles to inject:
  - lateral pterygoid
  - anterior digastric
  - Submentalis complexus
- EMG guidance mandatory
- Doses of BT: 25 to 50 u BT
- Side effects:
  - Dysphagia

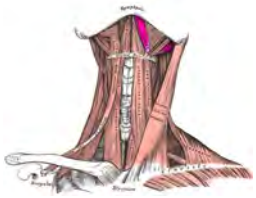


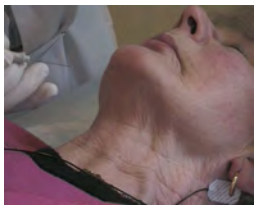
Lateral pterygoid muscle





Anterior digastric muscle





Botulinum toxin *and* Hemifacial Spasm

Hôpitaux de Lyon

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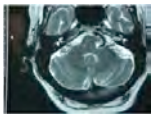
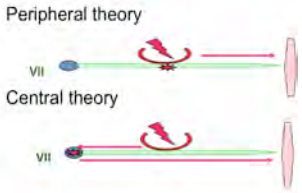
Facial spasms

- Primary Hemifacial Spasm
  - > 95% « essential » = neurovascular conflict
  - Pure and isolated
- Secondary Hemifacial Spasm
  - < 5% MS, posterior fossea tumour…
  - Other neurological signs associated
- Post-paralytic synkinesia

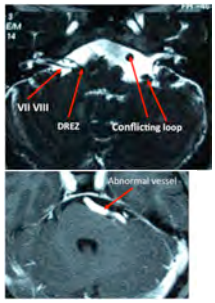
HFS Pathogenesis

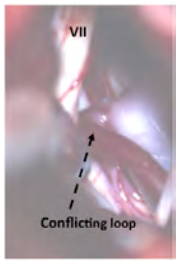
- Primary HFS is commonly attributed to vascular loops compressing the seventh cranial nerve at its exit zone from the brainstem producing abnormal ephaptic transmission.



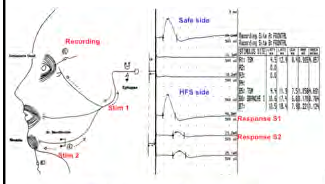


HFS MRI and operative aspects

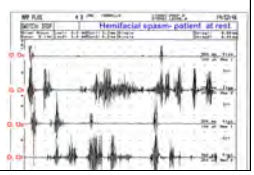




HFS electrophysiological pattern

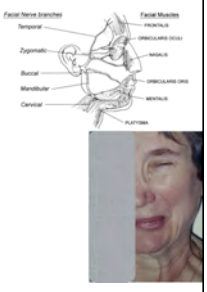


HFS- Late or spreading response

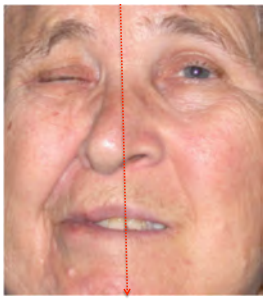


HFS – Clinical symptoms

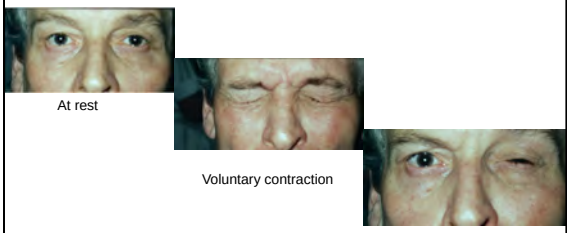
- muscles spasm in the ipsilateral hemiface
- Tonic-clonic contractions of the orbicularis oculi, extending progressively to the lower face (zygomaticus, orbicularis oris, mentalis and plathysma muscles.)
- Tonic form: forced closure of the eye, deviation of the nose on the spastic side: deforming tic of Babinski
- Synkinesia not always present
- Spasms persist during sleep



HFS « Full » hemiface contracture



HFS spasm induced by voluntary contraction



At rest

Voluntary contraction

Orbicularis oculi spasm

HFS treatment

- Symptomatic treatment by oral drugs:
  - benzodiazepine, carbamazepine,
  - Limited efficiency, side effects
- Curative treatment:
  - surgical neurovascular decompression
  - More than 85% full recovery
  - Operative risks
  - Permanent sequelae: facial palsy, deafness
- Symptomatic treatment with botulinum toxin injections

HFS- First injection

Where to inject ?

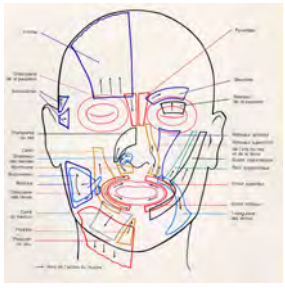
Explanation and choice of the patient

Clinical analysis:

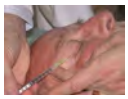
- If the spasm mainly affects the orbicularis oculi, inject only this territory: Risk of side effect is low
- Injections in the lower part of the facial territory are more difficult due to risk of mouth asymetry, except for the plathysma
- Sometimes injections in the upper facial territory improve the lower facial spasm in reducing the afferent way of the synkinesia

Technical aspects

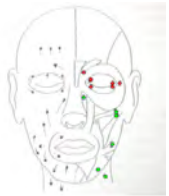
- Patient in supine position
- Injection without EMG guidance
- 1ml syringe and 25 Gauge Needle
- Subcutaneous injections
- For orbicularis oculi, pretarsal portion is better



HFS- First injection



Which injection sites?



which dose of BT

Doses of BT are often lower than in blepharospasm (specially in post paralytic facial synkinesia)

the dose depends on the severity of the spasm and the patient's own response

The dose injected into he orbicularis oculi: 1 to 5 points

- Botox: 7,5 to 15 U of Botox (dilution 50 U/ml)
- Dysport 30 to 50 U of Dysport (dilution 200 U/ml)

HFS repeat injections

- Patient satisfied:
  - repeat exactly the same treatment
- Patient experienced side effects
  - analysis of severity duration , consequences
  - decrease the dosage or avoid specific sites
- Patients not satisfied with the efficacy or duration:
  - increase the doses
- Patient satisfied in the orbicularis muscle but is greatly affected by spasm in the lower face
  - Inject the lower facial muscles

<u>The doses in the lower facial muscles</u>

- Risk of unsightly facial paralysis
- Specific dilution is better
  - (Botox dilution 12.5U/ml or Dysport dilution 50 U/ml)
  - Usually from 12.5 to 15 U Dysport in 5 or 6 sites
- The sites :
  - rizorius (2 sites above and below the angle of the mouth) zygomaticus major, mentalis, nasolabial fold
  - Avoid canine muscle
- Normal dilution for plathysma

HFS Results

Improvement

- Good to excellent in 76% to 100%
- Mean duration of action
  - ranged between 2.6 to 6 months.

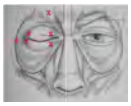
Side effects (transitory)

- dry eye 7-18%
- ptosis 3- 23%
- facial weakness : 18- 97%
- tearing : 5%
- diplopia : <1% up to 6%

HFS Side effects :

reasons and how to avoid them

Excessive weakness : 18-97%

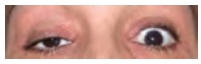


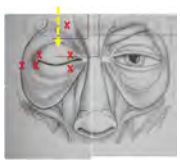
- Muscle weakness is an normal and intentional effect
- If excessive= side effect
- Orbicularis muscle:
  - From Souques's sign to Charles Bell sign
- In lower facial territory+++
- Decrease the doses
- Protection of the corneal
  - Conjonctivitis
  - Keratis
  - Corneal ulceration

HFS Side effects :

reasons and how to avoid them

ptosis 3% to 23%





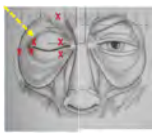
- Due to diffusion to the levator palpebrae muscle
- No treatment , awaiting the disappearance of the weakness
- Avoid injection in the middle part of the Superior lid

- *This side effect is sometimes used as a therapeutic effect : therapeutic ptosis to protect cornea in case of facial palsy*

HFS Side effects :

reasons and how to avoid them

dry eye 7% to 18%

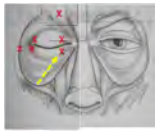


- Injection near the lacrimal gland induces a reduction of tears
- Injections far from the gland
- Local treatment with artificial tears
- *This side effect is sometimes used as a therapeutic effect for « crocodile tears syndrom »*

HFS Side effects :

reasons and how to avoid them

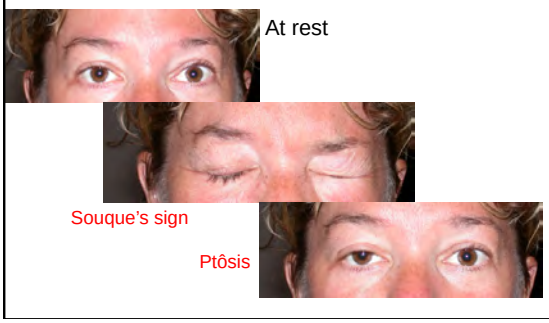
tearing : 5%



- Injection in the internal lower point can block the tear duct and induce an excessive tearing
- Avoid this point

- This side effect is sometimes used as a *therapeutic effect for treatment of drye eye*

HFS side effects post TB



Clinical Context

- The evidence supporting BoNT use in hemifacial spasm is suboptimal.
- The large magnitude of effects in the initial open label studies likely has discouraged efforts to study BoNT in properly controlled clinical trials.
- No studies have compared BoNT with the other major treatment alternatives, including oral pharmacologic and surgical therapy.

HFS Recommendations

- BoNT is possibly effective with minimal side effects for the treatment of hemifacial spasm (one Class II and one Class III study).
- Botox® and Dysport®, after dosage adjustment, are possibly equivalent in efficacy (one Class II study).
- **Recommendations**
- BoNT injection may be considered as a treatment option for hemifacial spasm (Level C).

Treatment of Blepharospasm and Meige syndrome with BTX injections

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Consultant neurologist
London BTX centre, UK
dr.mhmarion@londonbtxcentre.co.uk

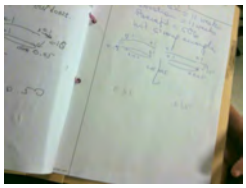
Blepharospasm

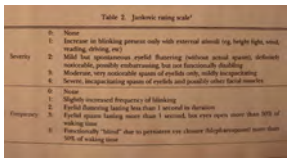
- Mean age of onset : 56 years
- Affects more woman than man
- Photophobia , dry eyes
- Major disability for watching TV, walking outdoors, driving.
- Bright light and looking up make it worst
- Can spread to lower part of the face in 31 % cases in the first 5 years.

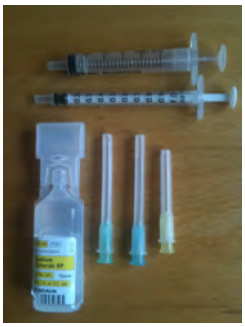
Treatment of BSP

- Anticholinergic drugs
- Clonazepam
- Proptosis
- BTX
- Orbicular myomectomy

BTX clinic







BTX clinic for Blepharospasm

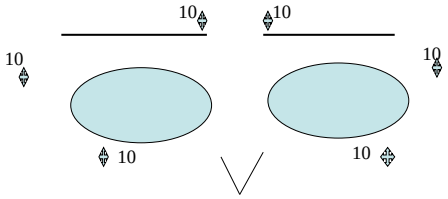
- Interval : 10 to 14 weeks
- Duration of effect: 10 weeks
- %Benefit (satisfaction patient):70% to 95%
- Side effects: ptosis, diplopia…
- Rating scale or picture taken

"Customise" BTX injections

- Injection repeated at regular intervals
  - Wearing off effect (patient, condition)
  - Minimum intervals of 9 weeks (avoid booster)
- Optimum dose:
  - Size of the muscles
  - Severity of spasms
  - Age of the patient

ential local side effects

Orbital sites for BTX injection
Botox units



BSP treatment failures

- **Clinical variant :Apraxia of eyelid opening**
- Severe BSP with Bell's phenomenon
- Severe Meige syndrome
- Sensitivity to side effects: ptosis, diplopia, inocclusion, excessive tears.

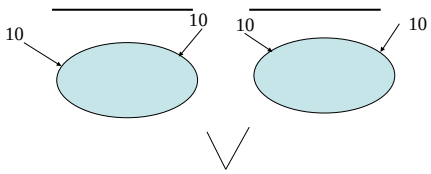
Apraxia of eyelid opening

- Apraxia of lid opening *(Goldstein-Cogan, 1965)*
- Inhibition of the levator palpebrae *(Lepore-Duvoisin, 1985)*
- Akinesia of eyelid opening *(Fahn, 1988)*
- Pretarsal Dystonia *(Elston, 1990)*
- Palpebral focal dystonia *(Krack-Marion,1994)*

Apraxia of Lid Opening : a focal eyelid dystonia

•Non-paralytic motor abnormality characterised by the patient's difficulty in initiating the act of lid elevation.

Pretarsal sites of injection
Botox units



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BSP treatment failures

- Clinical variant :Apraxia of eyelid opening
- Severe BSP with Bell's phenomenon
- **Severe Meige syndrome**
- Sensitivity to side effects: ptosis, diplopia, inocclusion, excessive tears.

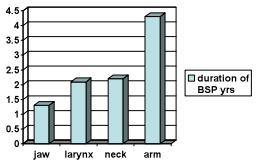
Henry Meige, 1866-1940

"In some cases, I have seen the facial contractions associated with;
- •laryngeal muscle contractions
- •jaw muscle contractions
- •mouth floor muscle contractions
- •even tongue muscle being involved."

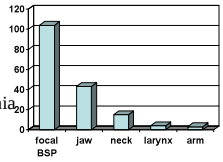
Les convulsions de la face,

Revue Neuro, 1910

Meige syndrome



Somatotopic progression of dystonia in BSP patients

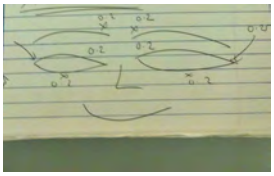


Pattern of spread of dystonia in BSP patients

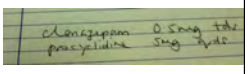
Defazio et al, J Neurol Neurosurg Psychiatry 1999;**67**:613–619

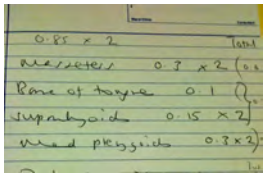
Therapeutic strategies: Dysport injections

- The most efficient treatment
- Careful clinical assessment of
  - the disability
  - the muscles involved in the spasms
  - Patient eating, speaking, drinking, walking
- Importance of unique session of injections when all the sites are treated.



Protocol of BTX injection of Robert C.

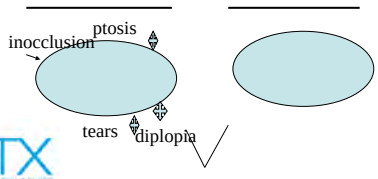




BSP treatment failures

- Clinical variant :Apraxia of eyelid opening
- Severe BSP with Bell's phenomenon
- Severe Meige syndrome
- **Sensitivity to side effects: ptosis, diplopia, inocclusion, excessive tears, scar tissue**.
- Biological resistance to BTX -A

Side effect sites after injection



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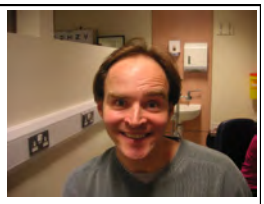
- Severe BSP with Bell's phenomenon
- Severe Meige syndrome
- Sensitivity to side effects: ptosis, diplopia, inocclusion, excessive tears.
- **Biological resistance to BTX -A**

Resistance to BTX-A



- Diagnostic+++. Frontalis test or EDB test
- If absence of resistance, review the protocol of injection (Dose, muscle selection, technique)
- If resistance, injection of BTX-B
  - 150 Botox, 500 units Dysport,10 000units Neurobloc
  - Dysautonomic side effects
  - after 1 year, majority of patients develop resistance to BTX-B

Conclusion

- BTX injections is an efficient treatment of Blepharospasm
- Good knowledge of functional anatomy is required
- Guidelines for dosage, site of injection and interval between injections are essential to

Spasticity of the lower limbs

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INTRODUCTION TO SPASTICITY

♦ Spasticity is a common feature of motor deficits associated with upper motor neuron syndromes.

♦ It is a significant cause of disability and handicap for people with stroke, multiple sclerosis, traumatic, non traumatic brain injuries, spinal cord injuries, cerebral palsy, and a variety of other neurological disorders.

DEFINITION:

♦ Spasticity is a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exagerated tendon jerks , resulting from hyperexcitability of the stretch reflex, as one of the component of the upper motor neuron syndrome

« Spastic Syndrome »

Upper Motor Neuron (UMN)Syndrome

The clinical features of UMN syndrome can be divided into two main groups:

➔Negative phenomenon : Weakness, paralysis, fatigue, incoordination and loss of dexterity

➔ positive phenomenon: Spasticity, clonus, rigidity, athetosis, extensor and flexor spasms.

CLINICAL FEATURES OF SPASTICITY

Tone and Power

♦ Voluntary control and power are usually reduced in spastic limbs but the force of the spastic contractions demonstrates that the muscles themselves are intrinsically normal.

♦ Sometimes, spasticity co-exists with apparently normal voluntary strength.

♦ When pyramidal weakness is more severe, spasticity may help to maintain posture.

♦ Abolishing spasticity may make standing more difficult

Posture

♦ Posture abnormalities are common in spasticity.

⇒ Cerebral lesions affecting the leg tend to produce spasticity in extension:

- The hip: slightly extended and internally rotated.
- The knee: extended.
- The foot and ankle: flexed and inverted in equinovarus.

⇒ A different posture develops in spinal cord disease:

- The Hip: flexion, adduction and some internal rotation .
- The knee: flexed.
- The Foot: again platar flexed and inverted.

➡This abnormal posture results in many difficulties:

- Use of a wheelchair
- Difficulty with dressing,
- Positioning, hygiene,
- Sexual activity.

Spasms

♦ Third feature of spasticity:

- normally in the direction of the abnormal posture and tends to exagerate it.
- not usually spontaneous

Clonus

Spasticity patterns

♦ The most common pattern of spasticity in the lower limbs involves extension at the knee, plantar-flexion at the ankle, and sometimes inversion of the foot. (Mayer et al 2002)

♦ This pattern is seen : - unilaterally in stroke.
- bilaterally in cerebral palsy and some cord lesions

♦ Other patterns of the spasticity in the lower limbs include:

✓Scissoring adduction at the hip joints

✓Flexion or extension at the knees

✓Spastic extension of the great toe (Mayer et al 2002)

Common pattern of spasticity in lower limbs

CLINICAL CONSEQUENCES

Mobility

♦ Probably the most common consequence of the UMN syndrome is difficulty in walking:

- Gait can be clumsy and uncordinated.
- Falling can become a common event
- Walking may become impossible.

Pain

♦ Pain can be extremely great

Abnormal posture:

♦ increase risk of musculoskeletal problems and osteoarthritic change in the joints

Carers and nursing problems

♦ Advance spasticity➔ Difficulty to move

♦ Transfer from bed to toilet or bed to wheelchair

♦ Hygiene is a problem.

MEASURMENT OF SPASTICITY

♦ Before and after treatment, clinical rating of spasticity is essential

♦ Choosing the right muscles to inject depends on a good clinical evaluation.

♦ Evaluate passive range of motion at the ankle, knee and hip; measure spasticity using the modified Ashworth or the Tardieu scale and determine strength and selective motor control of different muscle groups of the lower limbs.

♦ Gait analysis using dynamic EMG may be helpful in complex Cases.

TREATMENT PLANNING

♦ Botulinum toxin (BoNT/A) is the most known potent neurotoxin.

♦ Clinical effects have been recognized since the end of the nineteenth century.

♦ The value of Botulinum neurotoxin type A (BoNT/A) in extrapyramidal disorders is well known.

♦ The paralytic effect of the toxin is due to blockade of neuromuscular transmission (Burgen et al 1949)

♦ Injection of (BoNT/A) in muscle causes irreversible chemodenervation and local paralysis.

♦ Two preparations of Botulinum toxine type A (BOTOX and DYSPORT) are commercially available.

The injection technique:

♦ Botulinum toxin:

- injected into the involved muscle for the treatement of spasticity
- The technique is relatively simple.
- Reconstitued in normal saline
- Injected intramusculary
- Into the affected area

Injection guidance

♦ Palpation and anatomical landmarks may be used to place injections.

♦ Guidance techniques:

- increases precision
- may improve safety,
- decrease side effects
- possibly increase efficacy.

♦ Some authorities would use electromyographic (EMG) guidance when injecting individual muscles.

♦ Other authorities feel that such EMG guidance is not required.

♦ The larger and easily identifiable and palpable muscles probably do not need EMG (Guidance)

♦ The smaller muscles with less clear landmarks, EMG guidance can be useful

♦ However, there are not clear studies indicating that EMG produces better efficacy than simple clinical palpation and injection.

♦Other guided injection techniques include ultra sound guidance ⟹ useful for iliopsoas injections for hip flexor spasticity (Westhoff et all 2003)

Injection placement

♦ Smaller muscles: generally require only one injection

♦ Larger, longer or wider muscles are best injected at two or four sites

♦ The total dose will not only depend on muscle size but also on the clinical state of the patient

♦ Total maximum dose administrated per visit = lesser of
10-20 u/Kg for Dysport.
3-6 u/ kg for Botox

♦ 1injection > 3 months

Dilutions and Maximum dose/ session of botulisme toxine

Neurotoxin	Dilution cc saline	Max dose
Botox	1-4	400U / limb 600U / session
Dysport	2,5 +	2000 U / limb 2000U / session
Neurobloc	pre-diluted	17500U / session

What are the advantages of BoNT/A?

- ♦ Reduce spastic muscle tone
- ♦ Normalize limb posture
- ♦ Ameliorate pain and spasms
- ♦ May improve motor fonction
- ♦ Prevent contracture
- ♦ No sensory disturbance
- ♦ No destructive
- ♦ Weakness resolves spontaneously
- ♦ Safe and well tolerated

What are the disadvantages of BoNT/A

- ♦ Biological effects last only 3-4 months.
- ♦ Effects are non reversible during period of action
- ♦ Limited max dose
- ♦ May require EMG guidance
- ♦ Develop antibodies
- ♦ Injection(painful)

Sides Effect of BoNT/A

♦ The injections are remarquably safe and free of side effects

- 1% Flu- like symptoms
- 1% Rash around the injections site
- Nausea 2%
- Excessive weakness with reduced function
- Pain at the injection
- Neuralgic amyotrophy-like illness
- Long term- secondary clinical resistance

WHEN USE TREATMENT WITH BoNT/A?

♦ Spasticity not General.

♦ The conventional treatment was inactif or insuffisant (phisiothérapie and oral drug treatment)

♦ Personnel objectif will be defined by patient and medical staff

♦ Multidisciplinar take in charge

♦ Spasticity will be not associated with fixed musculotendineuse retraction

Flexed hip

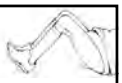
Muscle involved

- Iliopsoas
- Rectus femoris
- Adductor longus
- Adductor brevis
- Adductor maximus

Particularities and movements

- Always associated with thigh adductor
- The thigh flexum is better evaluated in ventral position, flexed knee and lie to different between rectus femoris action and iliopsoas.
- Gate and nursing will be difficult

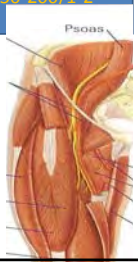
Flexed hip

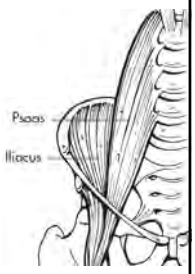


Injection technique

Iliopsoas: Below the inguinal ligament between the femoral artery and the anterior superior iliac spine 50-200/2-3
Psoas: Ultra sound or fluoscopi 50-200/1-2

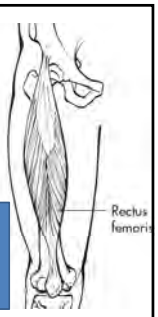
Iliacus



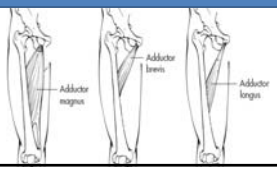


Flexed hip

Rectus femoris: The midbelly of the muscle is located at the midpoint between the anterior superior iliac spine and the patella 75-200/1-4



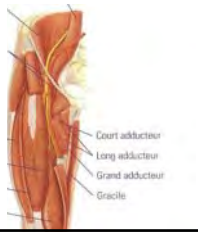
Adductor longus, brevis, maximus: Medial approch to the midbelly of the muscle located one- third of the distance from the public bone to the knee 75-300/2-6



Adducted Thigh

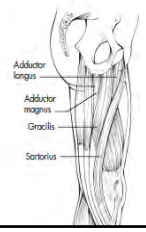
Muscle involved

- Adductor Magnus
- Adductor Longus
- Adductor Brevis



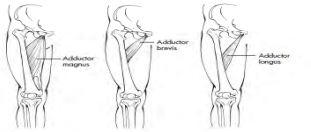
Particularities and movement

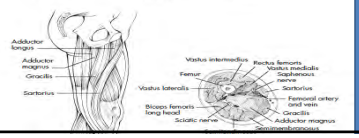
- Difficulty with personal hygiene and dressing
- Difficulty to walk (scissors)

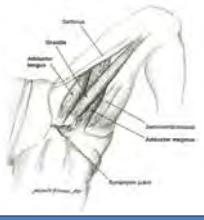


Adducted Thigh

Adductor Longus/Brevis/Magnus Medial: approch to the midbelly of the muscle located one-third of the distance from the public bone to the knee
Dose:75-300/2-6

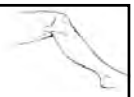






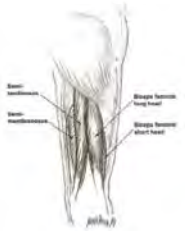
Iliopsoas:Below the inguinal ligament between the femoral artery and the anterior superior iliac spine
Dose: 50-200/2-3

Flexed Knee



Muscle possibly involved

- Medial Hamstrings
- Gastrocnemius
- Lateral hamstrings



Particularities and movement

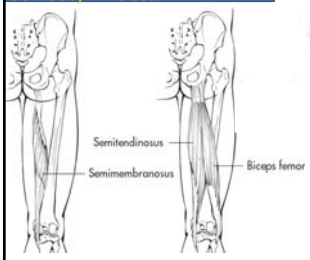
- Overactive hamstrings may present with pain

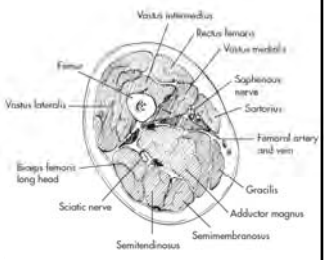
Difficulty in Bending the Knee

Difficulty with sitting and walking

Flexed knee

Medial Hamstring:
The midbelly of the muscle is located midway between the ischial tuberosity and the medial condyle of the tibia
50-200u/2-4 sites

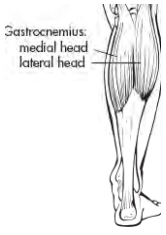




Lateral hamstring: The midbelly of the muscle is located midway between the lateral part of the ischial tuberosity and the fibular head. 75-200 u/2-4 sites

Flexed Knee

Gastrocnemius: The midbelly of the muscle is one –quarter the distance from the poplited fossa to the heel
50-150u/2-4 sites

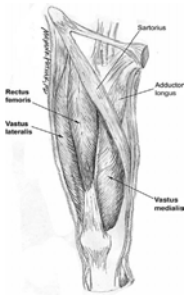


Extended(Stiff)Knee+++

Particularities and movement

Muscle involved

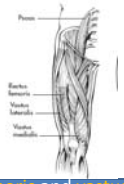
- Vastus intermedius
- Rectus femoris
- Vastus medialis
- Vastus lateralis

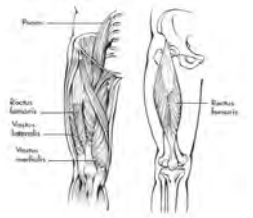


- Difficulty with relaxing the thig
- difficulty to maitain posture balance, walk or fit in wheelchair

Extended(Stiff)Knee

Vastus intermedius: the midbelly of the muscle is midway between the anterior superior iliac spine and the patella is often overlooked and can be a major contributor to knee extension

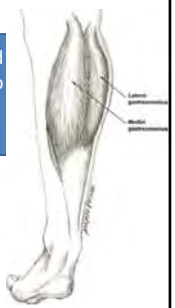


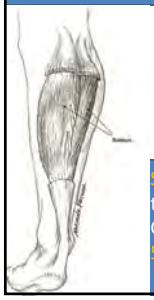


The Rectus femoris and vastus lateralis are injected halway between the patella and the groin fold
75-200u/4 sites
Vastus medialis : the midbelly of the muscle is located midway between the pubic synphysis and the medial part of the knee jointis best found more distally

Equinovarus Foot

Gastrocnemius: The midbelly of the muscle is located one-third to one-half of the distance from the heel to the popliteal fossa immediately posterior to the tibia
50-250u/2-4 sites

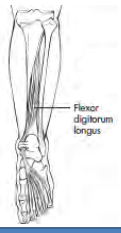


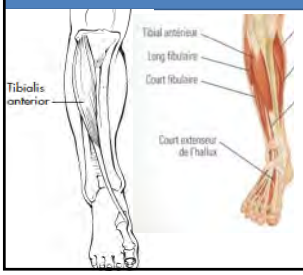


Soleus: Medial or lateral approach is midway to two-third the distance from the heel to the popliteal fossa. Can also be approached though the gastrocnemius
50-200u/1-3 sites

Equinovarus Foot

Flexor digitorum longus: The midbelly of the muscle is located one third to one-half of the distance from the heel to the popliteal fossa immediately posterior to the Tibia. 50-100u/1-2 sites

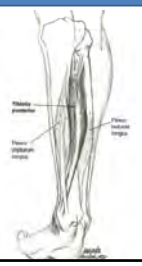


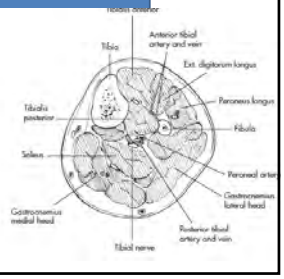


Tibialis anterior: The midbelly of the muscle is located at one third the distance from the patella to the ankle over the interosseus membrane and the fibula 50-150u/1-3 sites

Equinovarus Foot

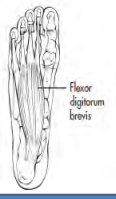
Tibialis posterior: Medial approch midway between the heel and the popliteal fossa. It lies posterior to the interosseus membrane. The medial approach will avoid nerves and vessels near the interosseus membrane. 50-150 u/1-3 sites

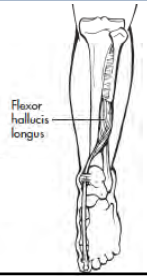




Equinovarus Foot

Flexor digitorum brevis: Midbelly of the muscle is located in the center of the sole. Shown in the equinovarus foot picture, but with no influence on ankle motion 20-40u /1-2 sites



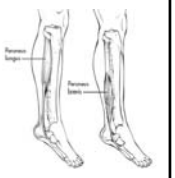


Flexor hallucis longus: Approach is lateral to the achilles tendon at one-third the distance from the heel to the popliteal fossa and over the fibula 25-75u/1-2 sites

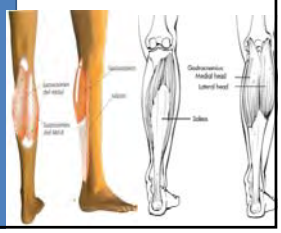
ValgusFoot

Muscles involved and Injection technique

Peroneus longus: The midbelly is located at the upper one- third of the lateral fibula. 35-85/1-2
Peroneus brevis: The midbelly is located at the lower one- third of the lateral fibula.40-70/1-2



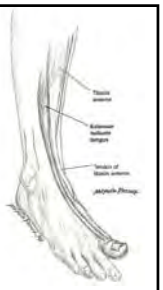
Gastrocnemius: The midbelly of the muscle is located one-quarter the distance from the popliteal to the heel 50-200/2-4
Soleus: Medial or lateral approach is midway to two-thirds the distance from the heel to the popliteal fossa. Can also approached through the gastrocnemius 50-200/1-3

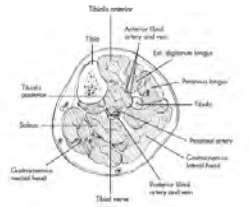


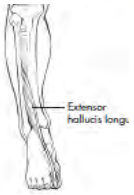
Striatal Toe

Muscles involved and Injection technique

Extensor hallucis longus: Anterior approach is at one-third the distance from the ankle to the patella over the interosseus membrane 20-100/1-2



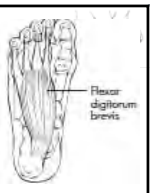




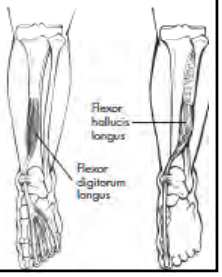
Flexed Toes

Muscles involved and Injection technique

Flexor digitorum brevis: Midbelly the muscle is located at the center of the sole. 20-40/1



Flexor digitorum longus: The midbelly of the muscle is located one-third to one-half of the distance from the heel to the popliteal fossa immediately posterior to the tibia: 50-100/ 1-3
Flexor halucis longus: Approach is lateral to the Achilien tendon at one-third the distance from the heel to the popliteal fossa and over the fibula 25-75/1-2



Conclusions

- BtxA reduces muscle hypertonia and the complications of spasticity & improves motor function.
- Clinical outcomes are improved by careful patient selection, clear treatment goals, use of correct dose of BtxA & injection technique.

Botulinum toxin and against-indications

No disease of the neuromuscular junction:
Myasthenia Gravis,
Lambert-Eaton syndrome

No motor neuron disease:

Peripheral neuropathy known
Pregnancy, lactation
No Association aminoglycoside discouraged

Botulinum Toxin *and* Upper Limb Spasticity

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When to use BT in adult spasticity

- If the spasticity is not generalised:
  - due to the dose distribution, BT must be used only to treat focal spasticity or focal objectives in case of generalised spasticity
- If standard treatments are inactive or insufficiently active
  - ? BT first treatment for spasticity ?
- If objectives are well defined by the patient and healthcare team
- If BT is performed as a part of a multidisciplinary management
- If the spasticity is not associated with fixed muscle and tendon retractions.

Special conditions (objectives)

- Helping daily activities (by the patient or the caregiver) :
  - putting on shoes, dressing, transfer
- Helping hygiene care (by the patient or the caregiver):
  - skin maceration of the hand, inability to cut nails
- Reducing muscle spasms and ankle clonus
- Reduce pain secondary to spasms and contractures
- Reduce cosmetically disturbing postures
  - which can be the main cause for poor quality of life
- Limit adverse compensatory postures: limp, scoliotic posture
- Improve motor function
  - either by revealing a residual motricity or by modifying the agonist/ antagonist balance
- Improve tolerance of ortheses, improve position in a wheel chair
- Evaluate and improve joint mobility:
- Therapeutic test prior to a neurotomy
- To delay surgery

Conditions modifying the use of BT

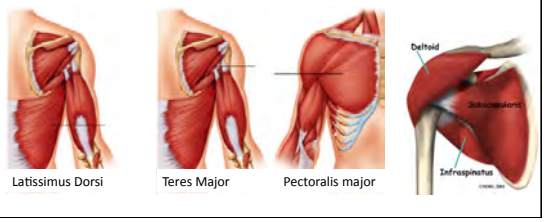
- Duration of the spasticity:
  - the use of BT in long lasting chronic spasticity must be based on precise objectives.
  - The early use of BT to prevent the onset of spasticity is debated
- The presence of residual motricity and function:
  - the beneficial effect on spasticity must not be overshadowed by greater discomfort created elsewhere
- The presence of associated disorders, whether sensory or neuropsychological (apraxia, anosognosia, orthopedic sequellae)

BT and upper limb spasticity: Shoulder

- Pain is the consequence of spasticity and sustained hemiplegic posture
- Frequent among patients with neglect following stroke
- Associated factors:
  - shoulder subluxation (glenohumeral), contractures, restricted shoulder range of motion
  - spasticity of pectoralis major and subscapularis muscle
  - sympathetic dystrophy
  - injury to the rotator cuff musculocutaneous unit
- Subscapularis muscle injection
  - reduces spastic shoulder pain or improve passive range of motion of the hemiplegic shoulder, more than injection of the pectoralis major muscle

BT and upper limb spasticity: Shoulder

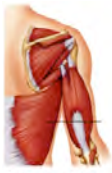
Posture	Muscles involved	Particularities and manoeuvres
Arm adducted Elbow flexed Internal rotation of shoulder	Latissimus dorsi Teres Major Pectoralis Major Subscapularis	The tendon of pectoralis is often palpable

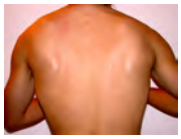


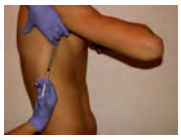
Latissimus Dorsi | Teres Major | Pectoralis major

Latissimus dorsi

- Origin:
  - thoracolumbar fascia
- Insertion:
  - intertubercular groove of the humerus
- Action:
  - extension, adduction, medially rotation of the arm
- Sites:
  - 1 or 2 on the upper part
- Technique:
  - posterior axillary line , 8 cm below the axillary fold
- Pitfalls:
  - Teres Major (if too medially)
- Dose:
  - 20-100 U Btx

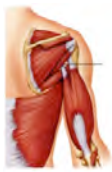


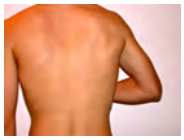




Teres major

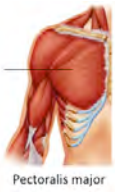
- Origin:
  - Inferior angle of the scapula
- Insertion:
  - Tubercule of humerus
- Action:
  - Adduction and medially rotation of the arm
- Sites: 1
- Technique:
  - 3-5 cm superior to the inferior angle of the scapula
- Pitfalls:
  - Latissimus dorsi (if too laterally) Serratus anterior (if too caudally)
- Dose:
  - 25-40 U Btx

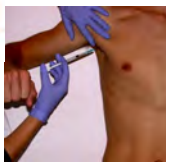




Pectoralis Major

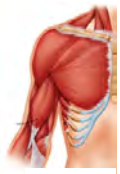
- Origin:
  - Clavicular, sternocostal, external oblique muscle
- Insertion:
  - Greater tubercule of humerus
- Action:
  - Adduction and medially rotation + anteversion
- Sites: 1-3
- Technique:
  - Muscle palpable, anterior axillary fold
- Pitfalls: coracobrachialis(if too deeply)
- Dose:
  - 20-100 U Btx

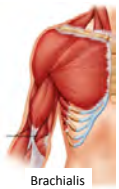


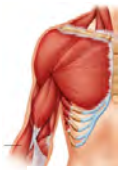


BT and upper limb spasticity: Elbow

Posture	Muscles involved	Doses	sites
Elbow flexion	Biceps Brachii	50-100	4
	Brachialis	50-100	2
	Brachioradialis	25-75	2

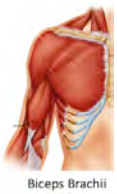


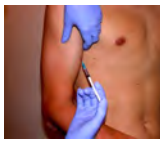




Biceps brachii

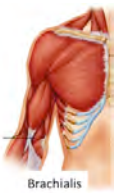
- Origin:
  - Supraglenoid an coracoid process of scapula
- Insertion:
  - Radial tuberosity
- Action:
  - Flexion and supination of the forearm
- Sites: 2-(4)
- Technique:
  - Inject long and short portion
- Pitfalls:
  - Brachialis (if too deeply)
- Dose: 20-100 U Btx

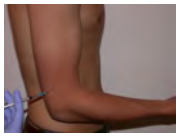




Brachialis

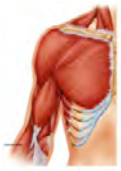
- Origin:
  - 2/3 distal anterior shaft of humerus
- Insertion:
  - Ulnar tuberosity
- Action:
  - The most powerful flexor of elbow
- Sites: 1-2
- Technique:
  - 3-4 cm proximal to the elbow fold, lateral to the tendon of the biceps
- Pitfalls
  - Biceps (if too medially)
- Dose: 20-60 U Btx

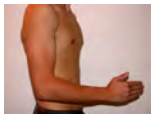




Brachioradialis

- Origin:
  - Supracondylar ridge of humerus
- Insertion:
  - Base of radial styloid process
- Action:
  - Flexion of the elbow, neutral position
- Sites: 1-2
- Technique:
  - 2-3 cm distal to the elbow fold
- Pitfalls
  - Extensor carpi radialis longus (if too laterally)
- Dose: 20-100 U Btx

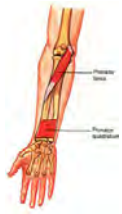




BT and upper limb spasticity: Forearm pronation

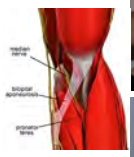
Posture	Muscles involved	Doses U Dysport	sites
Forearm pronation	Pronator terres	25-75	1
	Pronator quadratus	25-50	1

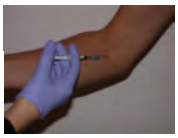
- Particularities and manœuvres
  - Supination is one of the last recovered movement in hemiplegia
  - The pronator teres is easily palpable



Pronator Teres

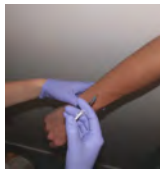
- Origin:
  - Medial epicondyle of humerus, coronoid process of ulna
- Insertion:
  - Middle lateral part of radius
- Action:
  - Pronation of the forearm
- Sites: 1
- Technique:
  - 1-2cm distal to the elbow fold, medially to the tendon of biceps
- Pitfalls:
  - flexor digitorum superficialis (if too deeply), flexor carpis radialis (if too ulnary)
- Dose: 10-30 U Btx





Pronator Quadratus

- Origin:
  - Distal ¼ of the anterior surface of ulna
- Insertion:
  - Distal ¼ of the anterior surface of radius
- Action:
  - pronation
- Sites: 1
- Technique:
  - Dorsal part of the wrist, 3 digits proximal , through the interosseus membrane
- Pitfalls:
  - flexor digitorum sublimis (if too deeply)
- Dose:
  - 10-20 U Btx



BT and upper limb spasticity: **Wrist**

Posture	Muscles involved	Doses	sites
Wrist flexion	Flexor carpis radialis	25-100	2
	Flexor carpis ulnaris	10-50	2
	Flexor digitorum superficialis	25-75	4
	Flexor digitorum profundus	25-100	2

Aim to intervention:

- to make dressing easier
- improve grasping and support
- improve fine motor skills
- reduce pain

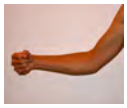
Adverse effects

- excessive weakness of the treated musculature increase the loss of function

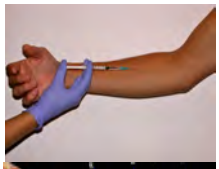
Practical aspect of treatment

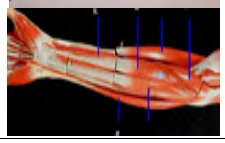
- rarely isolated
- association with cubito-ulnar deviation, pronation and digital motor disorders
- Dosage: take in consideration the ulnar/ radial deviation
- Take in consideration:
  - spontaneous position of fingers,
  - angular changes of metacarpophalangeal, interphalangeal joints during passive wrist movement

Flexor carpis radialis



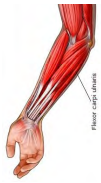
- Origin:
  - Epicondyle of humerus
- Insertion:
  - II and II metacarpal
- Action:
  - Flexion of the wrist with radial deviation
- Sites: 1-2
- Technique:
  - 6-8 cm distal from the elbow
- pitfalls
  - Flexor digitorum superficialis (if too deeply), pronator teres (if too laterally) palmaris longus (if too medially)
- Dose: 25-60 U Btx

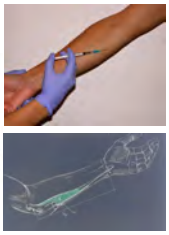




Flexor carpis ulnaris

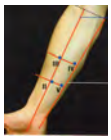
- Origin:
  - Medial Epicondyle of humerus, olecranon
- Insertion:
  - Hamate, pisiformis, Vth metacarpal
- Action:
  - flexion of the wrist with ulnar deviation
- Sites: 1-2
- Technique:
  - Muscle palpable, between the 1st and 2nd thirds
- pitfalls
  - Flexor digitorum profundis (if too deeply)
- Dose: 25-60 U Btx

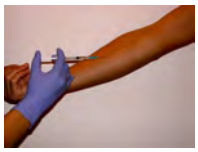


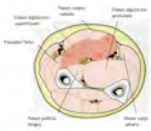


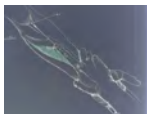
Flexor digitorum superficialis

- Origin:
  - Epicondyle of humerus, coronoid prodess of ulna, radius
- Insertion:
  - Bases of second phalanges of digits
- Action:
  - Flexion of metacarpophalangeal and proximal interphalangeal joints II-V
- Sites: 1-4
- Technique:
  - Middle of the ulnar side of the forearm, 10 to 20 mm deepth
- pitfalls
  - Flexor carpis radially (if too radially), flexor digitorum profundus (if too ulnary)
- Dose: 20-60 U Btx



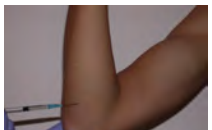


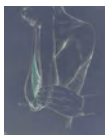




Flexor digitorum profundus

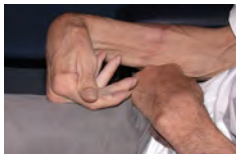
- Origin:
  - Upper ¾ of volar and medial surfaces of ulna
- Insertion:
  - Distal phalanges of four digits
- Action:
  - Flexion of metacarpophalangeal and proximal and distal interphalangeal joints II-V
- Sites: 1-4 (1 if medial way)
- Technique:
  - 4 fingersunder the olecranon, along the ventral surface of the ulna, 1-2 cm (lateral part) 3-5 cm (medial part)
- pitfalls
  - Flexor carpis ulnaris (if too volarly)
- Dose: 20-60 U Btx





BT and upper limb spasticity: Wrist

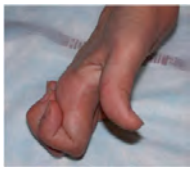
Before BT



After BT

BT and upper limb spasticity: **Fingers**

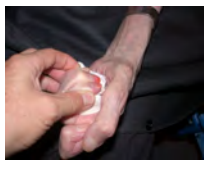
Posture	Muscles involved	Doses	sites
Closed fist, fingers flexed and locked in the palm	Flexor digitorum superficialis	25-75	4
	Flexor digitorum profundus	25-100	2



BT and upper limb spasticity: **Fingers**

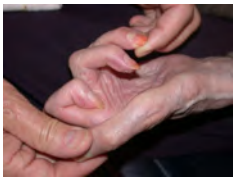
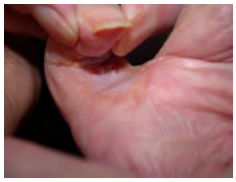
Before BT

Before TB



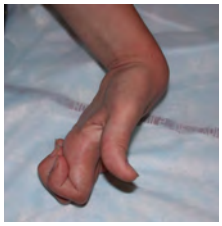
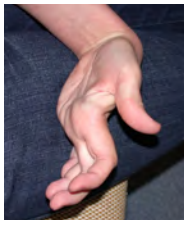
BT and upper limb spasticity: **Fingers**

After BT **After BT**

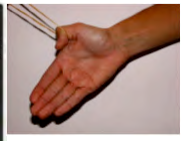
BT and upper limb spasticity: **Fingers**

Before BT **After BT**

BT and upper limb spasticity: Thumb

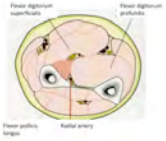
Posture	Muscles involved	Doses	sites
Thumb in palm	Flexor pollicis longus	5-25	1
	Adductor pollicis	5-25	1
	Flexor pollicis brevis	5-25	1




Flexor pollicis longus

- Origin:
  - Anterior shaft of radius, interosseus membrane
- Insertion:
  - Distal phalanx of the thumb
- Action:
  - Flexion of the distal phalanx of thumb
- Sites: 1
- Technique:
  - middle of the forearm, radial border, 1-2 cm depth. Avoid radial artery!
- pitfalls
  - Flexor digitorum sublimis (if too superficialis)
- Dose: 5-20 U Btx







Assessment: Botulinum neurotoxin for the treatment of spasticity (an evidence-based review)

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

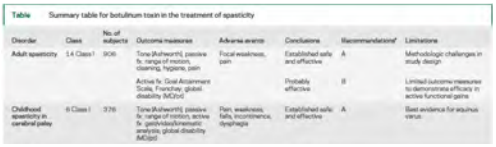


Table Summary table for botulinum toxin in the treatment of spasticity

Analysis of the Evidence

- Spasticity in adults
  - Most clinical trials concerned changes in resistance to passive movement (i.e., muscle tone).
  - Active functional improvement is rarely but frequently observed in clinical practice
  - BoNT has been approved for adult and childhood spasticity by regulatory agencies in many European countries, but has not yet in the United States by the FDA.

Analysis of the Evidence

- Upper extremity spasticity
  - 11 Class I efficacy trials in adult upper extremity spasticity
  - All but one used measurements of tone as the primary outcome measure.
  - All demonstrated that BoNT is safe and reduced tone in a dose dependent manner, but without correlation with active function (activities that the subject can voluntarily perform with the spastic limb).

Analysis of the Evidence

- Upper extremity spasticity
  - Functional assessment measures used as secondary outcome measures.
  - Global satisfaction scores reported by subjects, family members, or clinicians showed benefits of BoNT.
  - Class I studies incorporating subjective assessments of daily function by the patient or caregiver have shown functional improvement following BoNT injection in the spastic upper limb.

Analysis of the Evidence

- Upper extremity spasticity
  - One Class I study found that BoNT produced significant improvement in the Disability Assessment Score, which combines reports of passive and active function.
  - In this scale, the subject and the site investigator chose a target area of outcome assessment of personal hygiene, dressing, pain, or limb position.

Spasticity of children

Pr Messouak.O

Service de Neurologie CHU de Fès

DEFINITION(1)

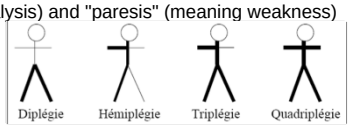
- Spasticity is a velocity-dependent increase in resistance to passive movement of a limb.
- Move the child's arm or leg, resistance increases as the speed of the movement is increased.
- In some cases, the increased tone due to spasticity is helpful to maintain the legs straight and thereby to support the child's weight against gravity.
- Spasticity is one symptom of the "upper motor neuron syndrome," a condition caused by damage to portions of the brain or spinal cord controlling movement.

DEFINITION(2)

- The spasticity of children is most commonly:
  - Cerebral palsy(cp).
  - Secondary to a disorder or trauma.
  - Spinal cord injury (SCI).
  - Brain injury.
  - Tumor
  - Stroke.
  - Multiple sclerosis (MS).
  - Peripheral nerve injury.

Spasticity syndromes or patterns

- This spasticity syndromes or patterns include:
  - Spastic diplegia (both legs involved greater than arms)
  - Hemiplegia (involves an arm and a leg on the same side of the body)
  - Double hemiplegia (both arms involved, more than legs)
  - Tetraplegia (all four limbs involved, usually severely)
- Some clinicians distinguish between "plegia" (meaning complete paralysis) and "paresis" (meaning weakness)



Measuring spasticity

- Spasticity is difficult to quantify, but clinically useful scales include the following:

  - Ashworth scale/Modified Ashworth - From 0-4 normal to rigid tone)
  - Physician's rating scale - Gait pattern and range of motion assessed
  - Spasm scale - From 0-4 (no spasms to >10/h)

Measuring spasticity

Ashworth scale/Modified Ashworth

0 No increase in muscle tone
1 Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end range of motion when the part is moved in flexion or extension/abduction or adduction, etc.
1+ Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2 More marked increase in muscle tone through most of the ROM, but the affected part is easily moved
3 Considerable increase in muscle tone, passive movement is difficult
4 Affected part is rigid in flexion or extension (abduction ,adduction, etc.)

Measuring spasticity

Tardieu scale

Quality of muscle reaction is measured as:

0: No resistance throughout the course of the passive movement

1: Slight resistance throughout the course of the passive movement

2: Clear catch at precise angle, interrupting the passive movement, followed by release

3: Unsustained clonus (less than 10 sec when maintaining the pressure)

occurring at a precise angle, followed by release

4: Sustained clonus (more than 10 sec when maintaining the pressure) occurring at a precise angle

The beneficial effects of spasticity

- Effects on posture & weight-bearing
- Prevents muscle atrophy (in animal models)
- Effects on bone density
- Effects on risk of DVT

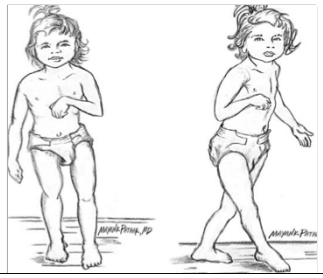
The negative effects of spasticity

- Interferes with motor function
- Causes pain, flexor & extensor spasms
- Increases the physiological cost of walking
- Predisposes to fixed contractures

Hemiplegia

♦ Hemiplegic children have involvement of the arm and leg on one side of the body.

♦ The upper extremity is more severely involved than the lower

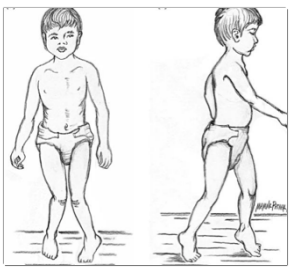


Musculoskeletal problems in hemiplegia

Upper extremity	*Lower extremity*
Shoulder	Hip
Internal rotation, Adduction	Flexion, Internal rotation
Elbow	Knee
Pronation,	Flexion Extension
Wrist	Ankle
Flexion	Plantar flexion
Hand	Foot
Flexion Thumb-in-palm	Varus

Diplegia

♦ With diplegia, the lower extremities are severely involved and the arms are mildly involved.



Musculoskeletal problems in diplegia

Musculoskeletal problems in diplegia

- Hip Flexion, internal rotation and adduction
- Knee Flexion or occasionally extension
- Ankle Equinus, valgus (rarely varus)

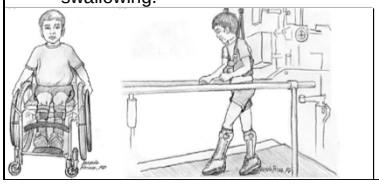
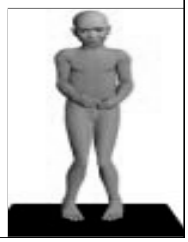


Quadriplegia

♦Quadriplegia is the involvement of neck, trunk and all four extremities.

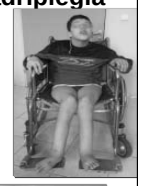
♦Quadriplegics have severe motor impairment and other signs and symptoms of CNS dysfunction:

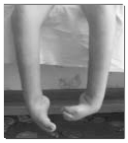
cognitive impairments
seizures.
speech.
swallowing.

Musculoskeletal problems in quadriplegia

Spine Scoliosis
Hyperkyphosis
Hip: Subluxation Dislocation
Knee: Flexion
Ankle: Plantar flexion






Elbow flexion-pronation contracture and wrist flexion in a quadriplegic child

Improper positioning results in equinovarus deformity.

Patient with a severe wrist flexion contracture

TREATMENT

♦ Treatment cannot eliminate all the problems associated with these disorders.

♦ Treatment do exist to minimize the impact these impairement, especially spasticity, can have on function.

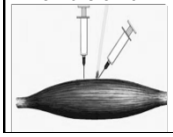
♦ Molar1992: the goal of treating children with CP, or TBI or other is to assist in acquiring skills and minimizing complication associated with the brain injury.

♦ Spasticity should not be treated because of its mere presence, but only if it adversly impacts some level of the patients functionning and if treatment would minimize this impact.

TREATMENT

Specific goals for botulinum toxin A treatment

♦ To improve walking in the spastic diplegic and hemiplegic child
♦ To minimise adductor tone in the child with early hip subluxation
♦ To decrease the spasms and pain in the spastic-athetoid patients
♦ To reduce tone in the psoas muscle in patients with back pain because of hyperlordosis
♦ As a simulation for orthopedic surgery, to have a general idea of how the child will be when spasticity is reduced.



Botulinum toxin injected into the muscle inhibits acetylcholine release at the neuromuscular junction and causes a chemical denervation for 3 - 6 months.

Evidence of efficacy

- Cosgrove et al, 1994
- Koman et al, 2000
- Massin & Allington, 1999
- Corry et al, 1998 - BtxA vs plaster casts
- Kirazli et al, 1998 -BtxA vs 5% phenol

TREATMENT

Botulinum toxin A Any age

- ♦ Age: 2-10 most common
- ♦ *Patient group:* All spastic types Focal spasticity
- ♦ *Indication:* too young for other interventions
- ♦ *Follow-up: care* Range of motion,stretching, strengthening,exercises
- ♦ *Result :* Effective for 3-6 months good results in walking and ADLs
- ♦ *Side-effect :*None obvious

EMG-Guided Botulinum Toxin Injections

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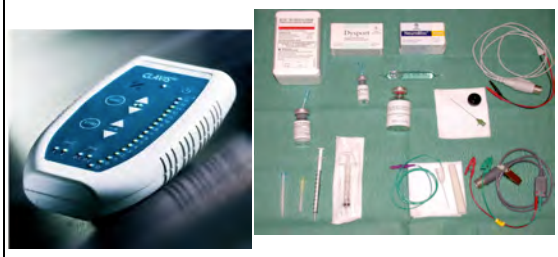
EMG and BT: When?

- Prior BT injection: evaluation
  - Blepharospasm: Orbicularis oculi/levator palpebrae muscle EMG to differenciate BSP from lid apraxia
  - Hemifacial spasm: late response to differenciate HFS from synkinesia
  - Cervical dystonia or writer's cramp: multi-channel analysis
  - EMG assessment prior to chemodenervation may also
- At the time of BT injection: EMG or stimulation guidance
  - to locate deep muscle
  - For some specific indications (spasmodic dysphonia, oromandibular dystonia in opening)
  - To improve accuracy, safety, and economy of toxin
  - help to plan toxin dosage (hypertonic muscles, muscles with persistent neuromuscular blockade, and muscles with possible contracture).
- After injections of BT
  - Immunization
  - Quantification of denervation

Specificity of BT injections

- Effective and safe chemodenervation requires identification of the appropriate hypertonic muscles
- The paralysis have to be selective
- Knowledge of anatomy and kinesiology is necessary
- Careful clinical observation of the abnormal movement and posture help to constitute a list of candidate muscles



BT injections : indications

- Blepharospasm:
  - the orbicularis oculii muscles solely responsible for involuntary forced eye closure.
- Limb dystonia
  - identification of candidate muscles generally straightforward
  - some movements may be assisted by several muscles.
    - wrist flexion flexor carpi ulnaris, palmaris longus, and flexor carpi radilis
- Cervical dystonia
  - identification of muscles involved may prove difficult.
  - complex anatomy of neck muscles
    - 26 muscle pairs link the skull, cervical spine, upper thorax, and shoulder girdles.
  - Many of these muscles serve redundant functions
  - the number of muscle activation patterns is nearly limitless.

General injection technique

- Injections should be performed at the endplate region to maximize the paralytic effect of BT
  - In neck muscles, the end plate regions are elongated, and there is less clustering of end-plates by comparison with limb muscles.
- EMG pattern
  - Motor unit action potentials with short rise time and without positive deflection are observed near the motor end-plate.
- Muscle fascia retards the spread of botulinum toxin by about 25%
- Diffusion
  - higher toxin doses and volumes increase the degree of toxin spread
  - Increased neuromuscular jitter in muscles distant from those injected with botulinum toxin confirms that botulinum toxin injected in neck or facial muscles becomes systemically distributed

EMG-guidance for chemodenervation

- EMG techniques
  - intramuscular injection using a cannulated monopolar needle,
  - Diagnostic needle examination prior to the injection of chemodenervating agents
  - motor point stimulation.

BT injections: EMG-guided

- Live EMG recordings are monitored in real time
  - spontaneous motor unit potential activity corresponding with the abnormal movement
  - Denervation in case of re-injection
- This provides
  - the tip of the needle is located in a ggod position in the muscle
  - the muscle is involved in the abnormal movement.
- Toxin is subsequently administered through the recording needle into the muscle.
- In the absence of EMG guidance, needle placement into dystonic neck muscles is often inaccurate.
  - sternocleidomastoid muscle 17%
  - levator scapulae 53%

Motor point stimulation techniques

- Injection as close as endplates
  - If the injection is located 0.5 cm from the motor point, the paralytic effect decreases by 50%
  - for the maximum effect
  - For the lowest-limited diffusion to adjacent territories.
  - For economy
- How to know the good position
  - EMG: based on the brightness of the sound to the speaker, the motor end plates potentials recordings, the size and rise time of motor unit potentials,
  - Stimulation: a maximal muscle twitch may be elicited using a minimum stimulus (approximately 0.25 to 0.50 mA)
- In spastic limb muscles
  - to administer toxin precisely at the endplate zones
  - to achieve a maximal paralytic effect at a minimal toxin dosage.

situations where the EMG-guided injection is required

- Spasmodic dysphonia
  - thyroarythenoidus muscle
- Oromandibular dystonia
  - Lateral pterygoïd muscle
- Writers cramps
  - Fexor digitorum muscle
- Spasmodic torticollis
  - Deep muscles