Icahn School of Medicine at Mount Sinai

Other Neurological Uses of Neurotoxin

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9th Annual Comprehensive Neurotoxin Course for Neurological Conditions
10/24/2020

Agenda

- Sialorrhea
- Focal hyperhidrosis
- Tremor disorders
- Tics
- Camptocormia
- (gait freezing)

Sialorrhea

Sialorrhea

- A 68 year-old gentleman with PD for 7 years has developed a marked excess of salivation in the past year. He drools excessively when awake, and has resorted to carrying a towel at all times to keep his mouth and shirt dry.

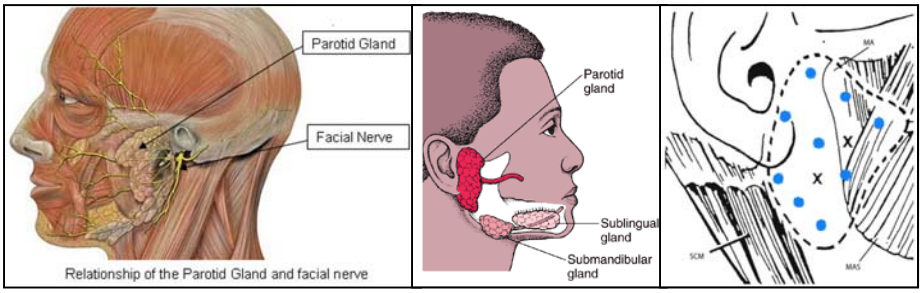
Treatment options for sialorrhea

- Anticholinergic agents
  - glycopyrrolate,
  - trihexyphenidyl,
  - benztropine,
  - sublingual atropine drops
- Radiotherapy
- Surgical removal of salivary glands

- Patient population:
  - Parkinson's disease/atypical parkinsonism
  - Cerebral palsy
  - Amyotrophic lateral sclerosis/motor neuron disease

- Mechanism = swallowing dysfunction (not excess saliva production)

Salivary glands



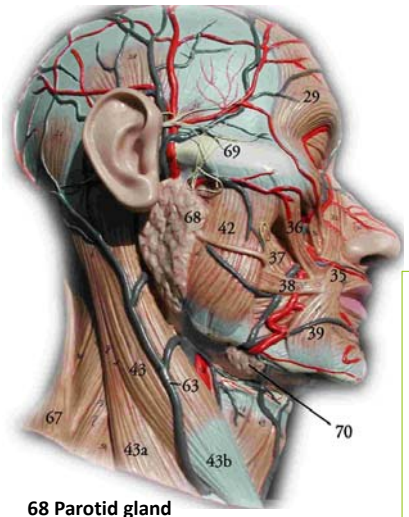
Minor salivary glands
- Throughout mouth

Major salivary glands
- Parotid gland
- Submandibular gland
- Sublingual gland

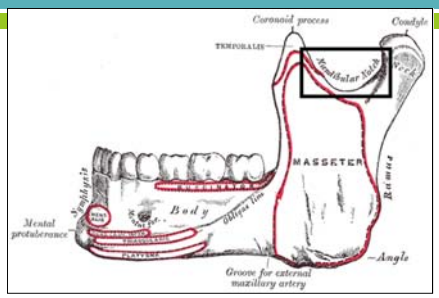
90% of saliva is produced by the submandibular and parotid glands
- Submandibular: 60–70% of baseline salivary flow
- Parotids become more active during eating or drinking
- Innervated by parasympathetic nerve terminals (chorda tympani of CN VII)

http://daphne.palomar.edu/ccarpenter/Models/head%20model_new.htm By File:Gray176.png, Gray's Anatomy plate., Public Domain

Injection technique: sialorrhea



68 Parotid gland
70 Submandibular gland



Parotid gland:

- Palpate posterior border of masseter and insert needle in the pre-auricular space and below

Submandibular gland:

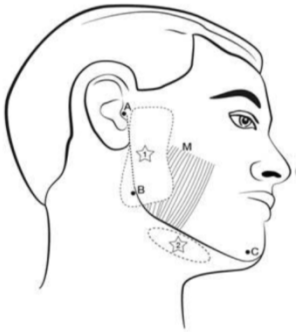
- Palpate the groove for the external maxillary artery
- Insert needle deep to that and slide up the ramus of the mandible

IncobotulinumtoxinA for Chronic Troublesome Sialorrhea in Various Neurological Conditions

- Population: Chronic troublesome sialorrhea, PD, Post-CVA, TBI
- N= 173 completed randomized study and enrolled into OLE
- Randomized to placebo / inco-BoNT-A 75u / inco-BoNT-A 100u
  - All subjects received bilateral parotid and submandibular injections
- Primary outcome measures:
  - Change From Baseline in Unstimulated Salivary Flow (uSFR) Rate (g/min) at Week 4
  - Participant's Global Impression of Change Scale (GICS) at Week 4
- Main findings: only the 100u dose met statistically significant reductions in both primary endpoints

Source: clinicaltrials.gov, NCT02091739

IncobotulinumtoxinA dosing for sialorrhea



- To inject the **parotid** gland: one fingerbreadth anterior to the midpoint of a line connecting the tragus and mandible angle.
- To inject the **submandibular** gland: one fingerbreadth medial to the interior surface of mandible at the midpoint of a line connecting the angle of the mandible and the tip of the chin

Gland	Units per side	Total
Parotid	30u	60u
Submandibular	20u	40u
Total	**50u**	**100u**

Most common side effects:

- Needing to have a tooth extracted
- Dry mouth
- Diarrhea
- High blood pressure

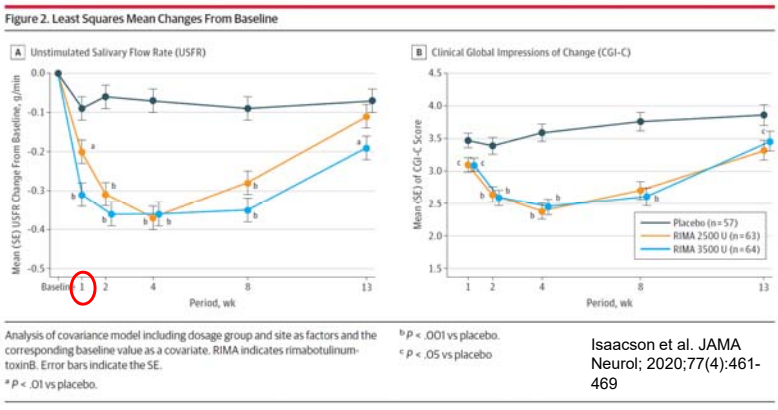
Source: Xeomin package insert

Safety and Efficacy of RimabotulinumtoxinB for Treatment of Sialorrhea in Adults: A Randomized Clinical Trial

Gland	2500u group	3500u group
Parotid	1000u	1500u
Submandibular	250u	250u

Most common side effects:

- Dry mouth
- Dysphagia
- Caries



Isaacson et al. JAMA Neurol; 2020;77(4):461-469

Recommendations for treatment selection

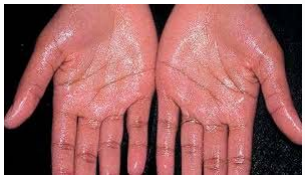
- No clear treatment guidelines with respect to choice of toxin, injection technique.
  - Type B may be preferred:
    - more regional as well as systemic anticholinergic adverse effects (Dressler and Eleopra, 2006)
  - Based on trials: follow dosing and distribution, use of anatomic landmarks
- Ultrasound-guided injections can be used if limited benefit
- Side effects: modification of saliva (viscous, with dry mouth), dysphagia, jaw dislocation, difficulty chewing, choking, aspiration pneumonia, transient paresis of facial nerve
- Suggested starting doses:

	onabotulinumtoxinA (Botox®)	abobotulinumtoxinA (Dysport®)
Parotid	20	50
Sub-mandibular	5	12.5

Focal primary hyperhidrosis and Frey syndrome

Hyperhidrosis

- A 28-year old male police officer presents for evaluation of excessive sweating. He drenches several shirts per day with sweat during routine activities. He does not like shaking hands due to palmar sweating, and this has led to some difficult interactions at work.



Primary hyperhidrosis

- Typically occurs focally in consequence to emotional stimuli
- Predominantly affects regions with a high density of eccrine glands,
  - Axillae > hands > feet > face/scalp > groin
- Exact mechanism of excessive sweating in primary focal hyperhidrosis is unknown.
- Familial/genetic association

Botulinum toxin for hyperhidrosis of areas other than the axillae and palms/soles.

(Glaser DA, Galperin TA. Dermatol Clin. 2014 Oct;32(4):517-25.)

Table 1
Most common body sites of hyperhidrosis in a North American population

Body Site	Percentage of Patients
Axilla	73.0
Palms	45.9
Soles	41.1
Face or scalp	22.8
Groin	9.3
Other[a]	9.6

[a] Other includes sites such as the chest, back, abdomen, arms, or legs.

Data from Lear W, Kessler E, Solish N, et al. An epidemiological study of hyperhidrosis. Dermatol Surg 2007;33(s1): S69–75.

The Treatment of Primary Focal Hyperhidrosis

(Wechter T, Feldman SR, Taylor SL. Skin Therapy Lett. 2019 Jan;24(1):1-7.)

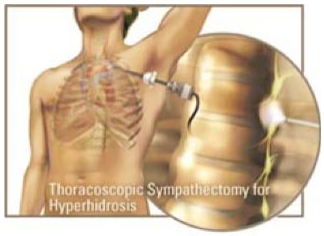
Type	Treatment	Mech. of Action	Summary	Side effects
Topical	Aluminum chloride antiperspirants	Precipitates and blocks sweat gland ducts	An effective initial option, although many patients require additional forms of treatment. Requires continued use.	Local skin irritation.
	Topical anticholinergics	Competitive inhibition of acetylcholine	Can be used as an alternative topical option. Studies of topical anticholinergic medications have been promising, although additional research is needed.	General anticholinergic effects.Possible cognitive impairment with long-term use.
Local Non-Surgical Therapies	Iontophoresis	Unknown	A great treatment option for palmoplantar disease with minimal side effects. Can also be used to deliver other medications through the skin.	Local skin irritation and burns.
	Botulinum toxin A	Prevents acetylcholine release into the synapse	An extremely effective treatment option for all disease locations.Requires multiple treatments, although symptomatic relief may be prolonged with repeated injection sessions. Less painful delivery methods are being investigated.	Pain at injection site, phantom sweating, reversible muscle weakness.
Surgical Manage-ment	Local surgical treatment (suction curettage, local excision)	Destroys and/or removes sweat glands	Generally effective, although very invasive treatment options.	Pain, bruising, bleeding, swelling, scarring, infection.
	Sympathectomy	Interrupts sympathetic outflow to sweat glands	An effective but invasive surgical treatment that provides long-term symptomatic relief. More effective for palmar disease than axillary disease. Compensatory sweating is its major limitation.	Pneumothorax, Horner's syndrome, neuropathy, subcutaneous emphysema, bradycardia and other surgical risks.
Systemic Therapy	Oral anticholinergics	Competitive inhibition of acetylcholine	Generally effective treatment options with reasonable side effect profiles.	General anticholinergic effects (i.e. dry mouth, vision changes, acute closed angle glaucoma, decreased intestinal motility, urinary retention). Possible cognitive impairment with long-term use.

(Wechter T, Feldman SR, Taylor SL. Skin Therapy Lett. 2019 Jan;24(1):1-7.)

Summary of treatment recommendations based on disease location and severity.

Disease Location	Recommendations	
	Mild to Moderate Disease	Severe Disease
Axillary	•1st line: Topical antiperspirant •2nd line: BTX-A injection •3rd line: Topical or oral anticholinergics	•1st line: Topical antiperspirant •2nd line: BTX-A injection •3rd line: Topical or oral anticholinergics •4th line: Microwave thermolysis, Nd:YAG laser or focused ultrasound •5th line: Suction curettage •6th line: Sympathectomy
Palmoplantar	•1st line: Topical antiperspirant •2nd line: Iontophoresis •3rd line: BTX-A injection •4th line: Topical or oral anticholinergics	•1st line: Topical antiperspirant •2nd line: Iontophoresis •3rd line: BTX-A injection •4th line: Topical or oral anticholinergics •5th line: Sympathectomy (only if palmar involvement)
Craniofacial	•1st line: Topical antiperspirant •2nd line: BTX-A injection •3rd line: Topical or oral anticholinergics	•1st line: Topical antiperspirant •2nd line: BTX-A injection •3rd line: Topical or oral anticholinergics •4th line: Sympathectomy

www.hidrex.usa.com



http://www.vascularpractice.org/Hyperhidrosis.html

Treatment of axillary hyperhidrosis with onaBoNT-A

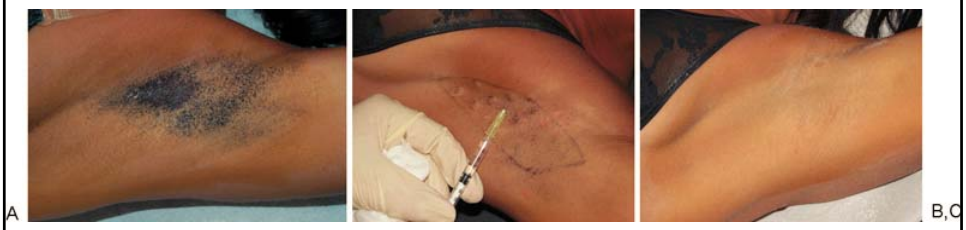


Fig. 1 Treatment of axillary hyperhidrosis with onabotulinumtoxinA (onaBoNT-A)**.**
(A) Demarcation of the sweating area in the left axilla by the iodine-starch test.
(B) Intradermal injections of 3 U onaBoNT-A 1.5 cm apart (1-ml syringe, 30-gauge needle).
(C) Negative iodine-starch test 4 weeks posttreatment.

Hosp C, Naumann MK, Hamm H. [Botulinum toxin in focal hyperhidrosis. An update]. Hautarzt 2012; 63 (6) 469-476

Randomized controlled trials of BTX in axillary hyperhidrosis

	50u	placebo
>50% Sweating reduction @ 4 weeks	94%	36%
Response rate at 16 weeks	82% in treatment group	21%
Mean duration of effect	7 months	

Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel group, double blind, placebo controlled trial. BMJ 2001; 323 (7313) 596-599

	50u	75u	Placebo
reduction of Hyperhidrosis Disease Severity Score (HDSS) of at least two grades	75%	75%	25%
>75% decrease in axillary sweat production @ week 4	80%	84%	21%
Duration of benefit	7mos	7mos	xx
Side effects: injection-site pain, injection-site bleeding, compensatory sweating			

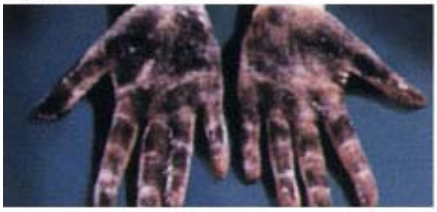
Lowe NJ, Glaser DA, Eadie N, Daggett S, Kowalski JW, Lai PY ; North American Botox in Primary Axillary Hyperhidrosis Clinical Study Group. Botulinum toxin type A in the treatment of primary axillary hyperhidrosis: a 52-week multicenter double-blind, randomized, placebo-controlled study of efficacy and safety. J Am Acad Dermatol 2007; 56 (4) 604-611

Recommendations for treatment of axillary hyperhidrosis

- Ona-BoNT-A
  - Start with 50 U onaBoNT-A per axilla
  - Onset of effect within 1 week
  - Duration of effect approx 6 to 7 months
  - large interindividual variation and substantial differences among trials
- Limited comparative studies to date suggest no major difference in effect between type A toxins
- Limited experience with BoNT-B

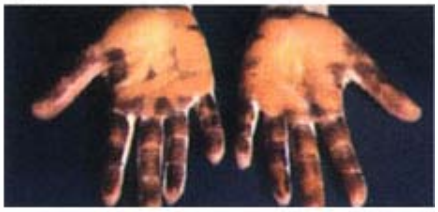
Palmar hyperhidrosis

Before



Localized sweating before shown by blackening of palms treated with STARCH-IODINE SOLUTION.

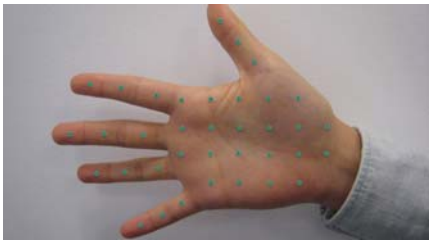
After

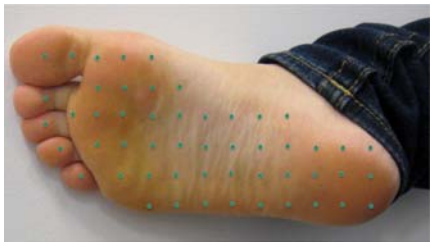


Absence or diminished blackening of palms after treatment.

http://www.caraderme.com/excessive-sweating-body-odor-prices.php

Injection grids for palmar and plantar hyperhidrosis





Anesthesia often required:

- Cryoanalgesia with ice packs or cooling spray
- Ulnar and median nerve blocks
- Topical lidocaine
- ?Reconstitute BoNT with lidocaine soln

Melissa A. Doft et al. Aesthet Surg J 2012;32:238-244

AESTHETIC SURGERY JOURNAL

Botulinum toxin for hyperhidrosis of areas other than the axillae and palms/soles.

(Glaser DA, Galperin TA. Dermatol Clin. 2014 Oct;32(4):517-25.)

Table 2
Craniofacial hyperhidrosis: typical doses of ona-BoNT-A

Facial Area	Units Per Injection	Spacing of Injections (cm)	Average Total Dose (units)	Average Duration of Effectiveness (mo)
Forehead and anterior scalp	2–3	2	100	4–6
Ophiasis scalp	2.5	2	100	4–6
Scalp and forehead	2–2.5	2	300	4–6
Nose	1–2	0.5–1	10–20	3–6
Upper lip	2	0.5–1	10	3–6
Chin	2	0.5–1	10	3–6

Botulinum toxin for hyperhidrosis of areas other than the axillae and palms/soles.

(Glaser DA, Galperin TA. Dermatol Clin. 2014 Oct;32(4):517-25.)

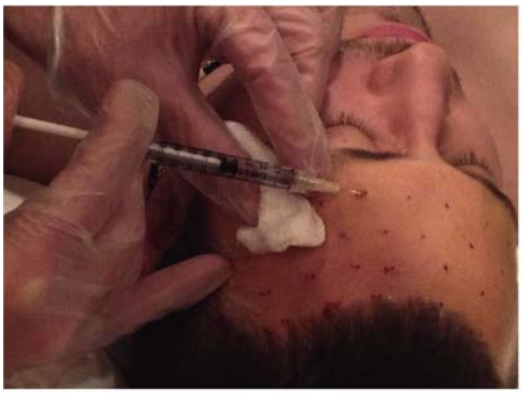
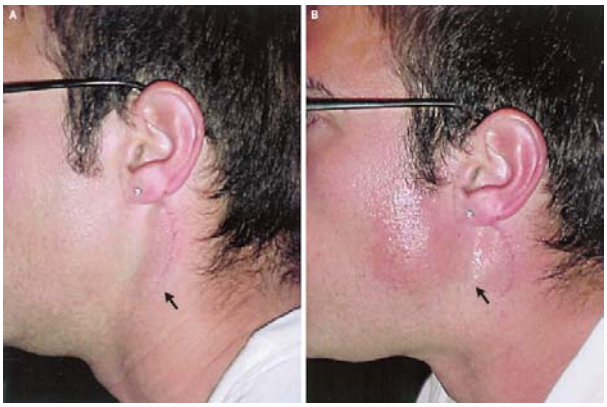


Fig. 3. Botulinum toxin injection technique into the forehead. (*Courtesy of* Albert Ganss, International Hyperhidrosis Society, Quakertown, PA; with permission.)

Frey Syndrome
(gustatory sweating)



Prattico and Perfetti, NEJM 2006

A 30-year-old man had a pleomorphic adenoma removed from his left parotid gland. His postoperative course was uncomplicated. Two months later, he noted that his left cheek became wet while he was eating. As soon as the patient ate a lemon wedge, his left auricular and parotic regions became flushed and sweaty (arrow, Panel B).

Tremor disorders

Tremor

- A 58-year old dentist has been increasingly embarrassed by comments from his patients about hand tremor that is obvious when holding cleaning and surgical instruments. He has not dropped or spilled anything, but desires treatment to stop his tremor. His handwriting is also noticeably tremulous when charting.

MDS Evidence-based review of treatments for Essential tremor (2019)

Pharmacologic class	Drug	Efficacy Conclusions	Implications for Clinical Practice	Safety Conclusions
				tardive dyskinesia
	Theophylline	Insufficient evidence	Investigational	Acceptable risk without specialized monitoring
	Trazodone	Unlikely efficacious	Unlikely useful	Acceptable risk without specialized monitoring
Botulinim toxin	Botulinum toxin type A	Likely efficacious	Possibly useful	Acceptable risk with specialized monitoring *Hand weakness was a frequent dose-related adverse event.*
Surgery	Unilateral Vim-DBS	Likely efficacious	Possibly useful	Acceptable risk with specialized monitoring
	Bilateral Vim-DBS	Insufficient evidence	Investigational	Acceptable risk with specialized monitoring
	Unilateral Radiofrequency thalamotomy	Likely efficacious	Possibly useful	Acceptable risk with specialized monitoring
	Unilateral Gamma-knife thalamotomy	Insufficient evidence	Investigational	Acceptable risk with specialized monitoring
	Unilateral MRI-focused ultrasound thalamotomy	Likely efficacious	Possibly useful	Acceptable risk with specialized monitoring

Ferreira JJ, et al; MDS Task Force on Tremor and the MDS Evidence Based Medicine Committee. MDS evidence-based review of treatments for essential tremor. Mov Disord. 2019 Jul;34(7):950-958.

BoNT for limb essential tremor

Table 1 Botulinum toxin for essential tremor involving the upper limb

Study	Design	*N*	Injection (onabotulinumtoxinA)	Duration	Measures	Outcome	Comments
Jankovic et al, 1996[10]	R DB PC	25	Initial: 15 U–FCR and FCU 10 U–ECR and ECU Total: 50 U	16 wk	UTRA, functional rating scale, sickness impact profile, accelerometry	No statistically significant difference between 2 groups, but grade 1 improvement in 91.2% and grade 2 improvement in 75% of patients	Weakness was not functionally impairing and "customized dosing" may have shown better results.
			If no response at 4 wk 30 U–FCR and FCU 20 U–ECR and ECU Total: 100 U			Mild (50%) to moderate (42%) weakness at week 4 in extensor muscles	
Brin et al, 2001[11]	R DB PC Parallel group	133	Low-dose group 15 U–FCR and FCU 10 U–ECR and ECU Total: 50 U	16 wk	Severity rating, functional disability, QoL, grip strength	Significant improvement in postural tremor at week 6, 12, and 16 in low- and high-dose group and kinetic tremor improvement at 6 wk. Hand weakness mild in low-dose and pronounced in the high-dose group.	Modest benefits, but fixed protocol does not represent routine clinical practice
			High-dose group 30 U–FCR and FCU 20 U–ECR and ECU Total: 100 U				

Abbreviations: DB, double blind; ECR, extensor carpi radialis; ECU, extensor carpi ulnaris; FCR, flexor carpi radialis; FCU, flexor carpi ulnaris; PC, placebo controlled; QoL, quality of life; R, randomized; UTRA, Unified Tremor Rating and Assessment.

Notes:

- fixed dose – fixed muscle approach does not allow for individualization of therapy
- Weakness mostly in extensors - restricting dosing to flexor compartment can minimize this risk w/o compromising benefit
- Lesser response when proximal muscles are involved

Lotia M, Jankovic J. Botulinum Toxin for the Treatment of Tremor and Tics. Semin Neurol. 2016 Feb;36(1):54-63.

Injection technique - tremor

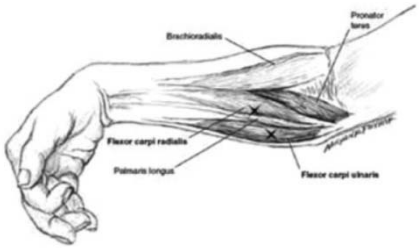
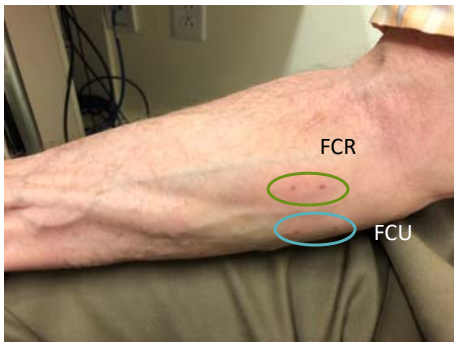
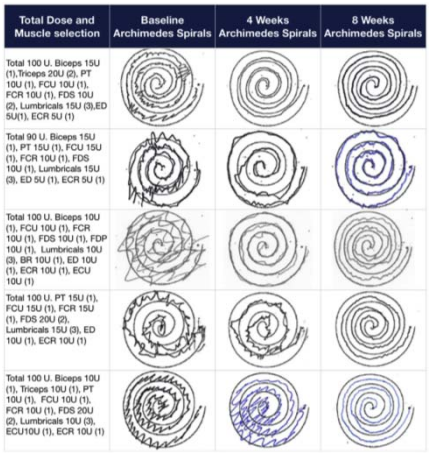


Fig. 1 Localization of flexor muscles for the injection of botulinum toxin for the treatment of essential tremor. Injections into the flexor group of muscles have provided marked benefits without causing severe arm weakness. (Reprinted with permission from Jankovic J. The use of botulinum toxin in tic disorders and essential hand and head tremor. In: Manual of Botulinum Toxin Therapy. 2nd ed. New York: Cambridge University Press; 2013:160–167.)



Botulinum toxin in essential hand tremor - A randomized double-blind placebo-controlled study with customized injection approach

- N=28 patients with ET treated with inco-BoNT-A
- Mean FTM tremor score = 3
- Clinical evaluation: ID muscles causing tremor at various joints:
  - fingers (PIP, DIP, MCP joints)
  - wrist (radial or ulnar flexion and extension)
  - elbow (flexion, extension, supination or pronation)
- EMG to confirm rhythmic burst potentials in these muscles
- Dose selection: based on activity and size of the muscle.
- # of injections: mean 9 injections/pt (range 8-14)
- Total dose of IncoA: mean 100u/patient (range 80-120)



Mean FTM tremor score improved to 2

Mittal, S.O., Parkinsonism and Related Disorders (2018), https://doi.org/10.1016/j.parkreldis.2018.06.019

Treatment of other tremors with botulinum toxin

Tremor type	Author / n	Dosing/distribution
Essential head tremor	Pahwa et al 1995 n=10	40u each SCM + 60u each splenius ona-BoNT-A
Primary writing tremor	Bain et al 1995 n=2	200u abo-BoNT-A to wrist flexors and extensors
	Papapetroulos et al 2006, n=5	10-12.5u each to FCU, ECU, ECR, APL, EDC
	Singer et al 2005, n=1	12.5u FCR
Jaw tremor	Schneider et al 2006, n=3	30-100u abo-BoNT-A to each masseter
Parkinsonian tremor	Rahimi et al 2015, n=28	75-390u inco-BoNT-A to wrist, elbow or shoulder muscles based on kinematic analysis at rest and during posture holding

- Lotia M, Jankovic J. Botulinum Toxin for the Treatment of Tremor and Tics. Semin Neurol. 2016 Feb;36(1):54-63.
- Rahimi F, Samotus O, Lee J, Jog M. Effective Management of Upper Limb Parkinsonian Tremor by IncobotulinumtoxinA Injections Using Sensor-based Biomechanical Patterns. Tremor Other Hyperkinet Mov (N Y). 2015 Oct 30;5:348. doi: 10.7916/D8BP0270.

Botulinum Toxin in Parkinson Disease Tremor: A Randomized, Double-Blind, Placebo-Controlled Study With a Customized Injection Approach

TABLE 1. Summary of the Muscles Injected and Their Doses

Muscle	Patients (No. [%]) (N=30)	IncobotulinumtoxinA (U)
Lumbricals	29 (97)	2.5-20
Flexor carpi radialis	27 (90)	10-15
Flexor digitorum superficialis	26 (87)	10-20
Flexor carpi ulnaris	25 (83)	10-20
Pronator	25 (83)	10
Biceps	25 (83)	10-20
Triceps	23 (77)	10-15
Extensor carpi radialis	19 (63)	5-10
Extensor digitorum	18 (60)	5-10
Flexor pollicis brevis	11 (37)	5-10
Extensor carpi ulnaris	10 (33)	5-10
Flexor digitorum profundus	7 (23)	10
Abductor pollicis brevis	6 (20)	5-10
Brachioradialis	5 (17)	10
Supinator	3 (10)	10
Opponens pollicis	1 (3)	5

N=30 completed a double-blind cross-over study of IncoA vs placebo

 # injections: mean 9 injections/pt (range 7-12)

Total dose of IncoA: mean 100u/patient (range 85-110 U)

Mittal et al. Mayo Clin Proc. September 2017;92(9):1359-1367; http://dx.doi.org/10.1016/j.mayocp.2017.06.010

Mittal SO, Lenka A, Jankovic J. Botulinum toxin for the treatment of tremor. Parkinsonism Relat Disord. 2019 Jun;63:31-41.

A practical approach to BoNT injection for hand tremor

- 1. Examine the tremor in different positions; with hands at rest, at different postures, and during action (e.g. drawing a spiral and writing). Observe for tremor not only in the affected fingers, metacarpophalangeal joint, and wrist but also at the elbow and shoulder.
- 2. Muscle selection should be individualized and customized to the patients' tremor. For the patients who also have proximal tremor that may contribute to the motor impairment, the arm (biceps, triceps) and even shoulder (deltoid, pectoralis) muscles may need to be injected. If the tremor involves specific fingers without compensatory contraction and contributes to the motor impairment, then lumbricals and other distal hand muscles should be considered for injection.
- 3. Depending on the response to the tremor movements, the dose can be adjusted and other muscles can be selected for injection based on the response to prior injection.
- 4. If possible, the extensor muscles should be avoided as these muscles are sensitive to BoNT and their injection frequently causes wrist and finger extension weakness. If needed absolutely, low dose of BoNT and close follow-ups should be done to assess for any weakness.
- 5. For the task-specific dystonia and primary writing tremor, precaution should be taken to avoid injection in the compensatory muscle rather than dystonic muscle. Having the patient to write (or perform a specific task) with the contralateral, unaffected, hand may elicit dystonic mirror movement in the involved hand which can lead to more appropriate selection of target muscles.
- 6. The complexity of tremor assessment and the need for individualization implies that at the current stage, these injections should be performed only by those who are highly skilled injectors.

Tic disorders

Tics

Patient Videos

Cervical dsytonic/whiplash

Studies of BoNT injections for tics

Table 5 Botulinum toxin for tics

Study	Design	N	Injection site	Duration	Measures	Outcome	Comments
Jankovic et al, 2000[20]	Case series	35	Upper and lower eyelid, eyebrow, paranasal muscles, masseters, SCM, submental complex, scalenes, trapezius, splenius, vocal cords	7 y at least one follow-up or phone interview	Global response rating scale, peak effect scale, premonitory sensation	29 patients with marked improvement. 78% overall improvement in global rating and 84% improvement in the premonitory sensation	Subjective scale Open-label study Improvement in the urge sensation
Marras et al, 2001[58]	R DB, PC Crossover case series	18	Blink, brow lift, head turn, neck extension, lower facial pull, shoulder shrug, neck flexion	2 wk, but followed over 12 wk	Subjective Urge Scale, Shapiro- Tourette Syndrome Scale tics/min	39% improvement in the BoNT group and improvement in urge sensation.	Small study and thus lacking power to show significance
					Video recording	50% reported weakness, but nondisabling	Milder tics
Porta et al, 2004[60]	Open-label case series	22	2.5 IU of onabotulinumtoxinA in bilateral vocal cords	2 wk phone call 2 follow- up in y	Hopkins Vocal Tic Scale, Global Impression of Scale, Interference In Life Scale	93% of patients with improvement in phonic tics with resolution in 50% Improvement in frequency Improved social life 80% improvement in premonitory urge	Open-label single study. 80% with hypophonia

Abbreviations: BoNT, botulinum toxin; DB, double blind; PC, placebo controlled; R, randomized; SCM, sternocleidomastoid.

- May be particularly useful in focal dystonic tics such as blepharospastic tics and cervical dystonic tics; also coprolalia
- May reduce urge
- Injection technique and dosing are similar to what would be done for corresponding focal dystonias
- "Whiplash tics" may be considered a medical emergency and should prompt consideration of BoNT injections

Lotia M, Jankovic J. Botulinum Toxin for the Treatment of Tremor and Tics. Semin Neurol. 2016 Feb;36(1):54-63.

Truncal dystonia/camptocormia

Camptocormia in PD

- A 66 year old woman with PD for 7 years presented with camptocormia for two years associated with painful abdominal contractions that were worse during the “off” state. There were palpable abdominal contractions when standing and she could not lie completely flat on her back. She described a sensation of a “hard cramp” that was “pulling her down” when trying to stand and walk. Once medications kicked in, the abdominal contractions abated and she could stand more erect.

Truncal dystonia/camptocormia

- Types of camptocormia
  - Dystonic
    - Primary dystonias
    - PD
  - Neuromuscular
    - Myopathic – inflammatory, mitochondrial, MD
    - Neuropathic – eg CIDP
    - Motor neuron disease
  - Orthopedic
    - Osteoporosis
    - Lumbar spine disease

Camptocormia as a presentation of generalized inflammatory myopathy.

Kuo SH, Vullaganti M, Jimenez-Shahed J, Kwan JY. Muscle Nerve. 2009 Dec;40(6):1059-63.

FIGURE 2. The patient demonstrated flexed posture while standing **(A)** and was able to correct the posture with her hands 'climbing up' the wall **(B)**.

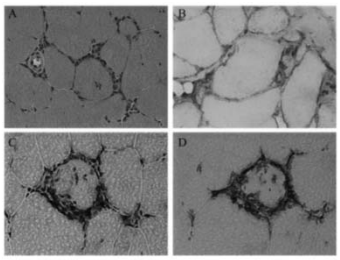


FIGURE 4. Muscle biopsy of the rectus femoris muscle in hematoxylin and eosin stain showed endomysial infiltration of lymphocytes **(A)** with increased MHC I expression on the muscle membrane **(B)**. CD8-positive cells **(C)** were more prominent than CD4-positive cells **(D)**, and the pathological findings are consistent with polymyositis.

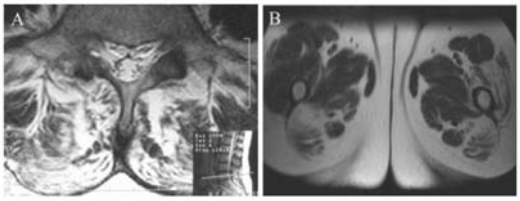


FIGURE 3. Axial lumbar spine MRI showed T2 hyperintensity in bilateral paraspinous muscles consistent with near complete fatty replacement of the muscles **(A)**. Axial MRI of thigh muscles revealed T2 hyperintensity of bilateral vastus lateralis and intermedius muscles **(B)**, indicating a generalized myopathic process.

Treatment options for camptocormia in PD

Treatment	Limitations
PT	Variable outcome
Bracing	Poorly tolerated
Backpack therapy	Beneficial in small Ns of patients
Optimize dopaminergic therapy	
Spinal surgery – laminectomy, fusion	Poor response, complications
Deep brain stimulation	Variable effect
Lidocaine injection to eternal oblique	In conjunction with PT, series of injections over 5 days

Bertram KL, Stirpe P, Colosimo C. Treatment of camptocormia with botulinum toxin. Toxicon. 2015 Dec 1;107(Pt A):148-53.

Case reports/series of BoNT for camptocormia

Table 1
Synopsis of reports on the use of Botulinum toxin A in camptocormia.

Author	Patients	Duration of camptocormia	Total toxin dose per injection cycle	Location of injection	Response
Von Coelln	4: – 3 PD –1 MSA	1–3 years	1000–3000 Mu Abobotulinum toxin A	2 Unilateral IL 2 Bilateral IL	1 improved upright posture for 2 weeks 1 improved upright posture for 6 weeks 1 no improvement 1 worsening of MSA, no improvement in posture
Wijemanne	1-PD	2 years	400 Mu Onabotulinum toxin A	Bilateral RA; Unilateral RA, contralateral EO	RA-Improved pain, minimal postural change: RA + EO-Improved from 45 to 15–20° forward flexion in the "on" motor state
Colosimo	2 –PD	Not stated	800 Mu Onabotulinum toxin A	Bilateral IL CT guided Bilateral RA	No response over 2 weeks
Fietzek	10 – PD	1.9 ± 0.2(IL) 3.0 ± 1.4(RA)	100–300 Mu Incobotulinum toxin A	5 Bilateral IL 5 Bilateral RA	No improvement in goal attainment scales incorporating pain relief, postural improvement, f unctional goals at 3 weeks
Azher	16 described (9 injected): 11 PD 5 other MD	4.5 ± 3.9 yrs	PD group 350–600 Mu Onabotulinum toxin A NON PD group 300–800 Mu Onabotulinum toxin A	RA ± PS	PD group- 3 no response; 3 good response; 5 not injected Other group- 2 no response; 1 partial response; 2 not injected

Abbreviations: PD- Parkinson's Disease; MSA- Multiple System Atrophy; MD-movement disorders; RA- Rectus Abdominis; IL- iliopsoas; EO- External Oblique; PS- paraspinal; Mu- Mouse units.

Muscles to consider:
- rectus abdominis
- Iliopsoas
- external oblique

Bertram KL, Stirpe P, Colosimo C. Treatment of camptocormia with botulinum toxin. Toxicon. 2015 Dec 1;107(Pt A):148-53.

Improvement in dystonic camptocormia following botulinum toxin injection to the external oblique muscle

Wijemanne S, Jimenez-Shahed J. Parkinsonism Relat Disord. 2014 Oct;20(10):1106-7

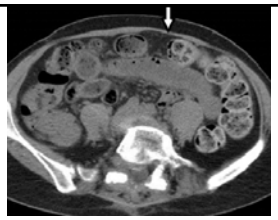


Fig. 2. CT Abdomen showing a thin left rectus abdominis muscle due to surgical excision.

Fig. 1. Camptocormia prior to carbidopa/levodopa and BTX injections (A) including difficulty in "climbing the wall" (a sensory trick) (B). After 4 sessions of BTX injections, the patient is able to "climb the wall" with ease (C) and stand much straighter with another sensory trick (D) by placing the palms on her thighs.

Neurol Ther
https://doi.org/10.1007/s40120-018-0108-x

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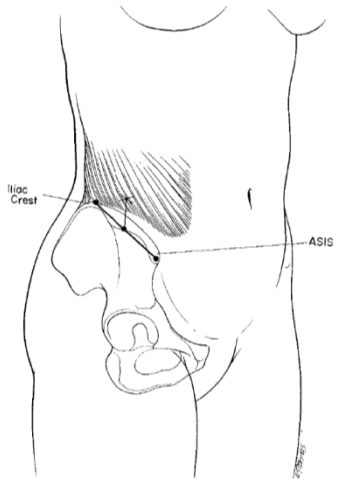
BRIEF REPORT

Injection of Onabotulinum Toxin A into the Bilateral External Oblique Muscle Attenuated Camptocormia: A Prospective Open-Label Study in Six Patients with Parkinson's Disease

Hiroyuki Todo · Hiroshi Yamasaki · Go Ogawa · Katsuya Nishida · Naonobu Futamura · Itaru Funakawa

Dose of BT (units per EO)	75	90	90	90	90	90
CA (degrees, before vs. 2 weeks after BT)	49 vs. 9	21 vs. 4	83 vs. 30	33 vs. 27	19 vs. 8	43 vs. 37

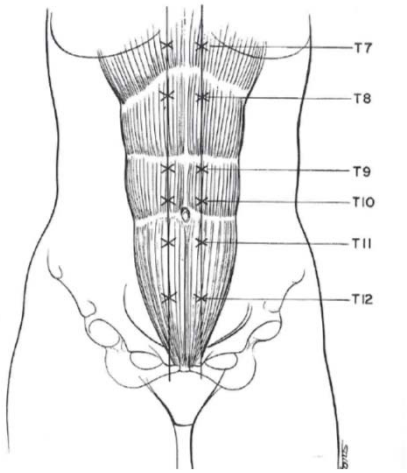
External oblique



- Identify the highest point of the iliac crest and the ASIS; insert needle midway along ASIS and just above the iliac crest
- Generally use EMG guidance to verify depth
- Ask patient to perform crunches in order to optimize your position

Perotto AO. Anatomical guide for the electromyographer, 4th Ed. Charles C. Thomas, Springfiled, IL (2005).

Rectus abdominis injection



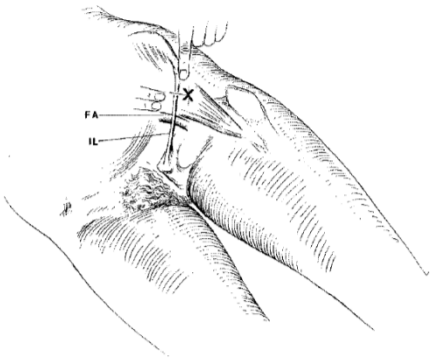
- Most PD patients describe abdominal contractions below the umbilicus, and these can be palpated when the patient stands
- Insert needle 2 fingerbreadths lateral to the abdominal midline
- Generally use EMG – to avoid piercing abdominal cavity and to verify appropriate depth of muscle
- Once needle is inserted, ask patient to perform crunches until you hear the EMG activity
- May be able to feel the needle piercing the anterior aponeurosis; avoid piercing the posterior aponeurosis

Perotto AO. Anatomical guide for the electromyographer, 4th Ed. Charles C. Thomas, Springfiled, IL (2005).

EMG-guided rectus abdominis injection

Patient Video

Iliopsoas injection



- Flexes the thigh at the hip – ask patient to flex the thigh with the knee flexed beyond 90°
- Locate femoral artery (FA)
- Insert needle two fingerbreadths lateral to the FA and one fingerbreadth below the inguinal ligament (IL)

Perotto AO. Anatomical guide for the electromyographer, 4th Ed. Charles C. Thomas, Springfiled, IL (2005).

Conclusions

- When treating sialorrhea
  - Inco-BoNT-A or rima-BoNT-B are injected to both parotid and submandibular glands at standard doses
- When treating hyperhidrosis
  - Iodine-starch test to identify problematic regions
  - Standard grid approach can also be used
- Treatment of tremor or tic disorders depends on correctly identifying muscles involved in the abnormal movement or postures
- Treatment of camptocormia involves identification of amenable etiology, followed by carefully selecting involved muscles including rectus abdominis, external oblique, and iliopsoas
- Regardless of indication, be wary of potential side effects, most notably weakness