

Botox treatment in abnormal movement disorders



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BOTOX Clinic in SMC (2010.3 ~ 2012.5)

Type of Patients	Number of Patients
Hemifacial spasm	244
Blepharospasm (+ AEO)	86
Facial synkinesis	20
Meige syndrome	23
Dystonia	
Cervical dystonia	70
Oromandibular dystonia	9
Other focal dystonia	36
Segmental dystonia	7
Generalized dystonia	2
Eyelid flutter	12
 Total	540

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Selection of Botulinum toxin

Unique Origin
Unique Future

- ◆ Available in Korea
 - Botulinum toxin type A
 - BOTOX®
 - DYSPORT®
 - Meditox®
- ◆ Not-available in Korea
 - Botulinum toxin type B
 - Myobloc®



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Clinical study in Korea- BOTOX® vs Dysport

Unique Origin
Unique Future

Dysport and Botox at a Ratio of 2.5:1 Units in Cervical Dystonia: A Double-Blind, Randomized Study

MDS 2015

We aimed to compare Dysport (abobotulinumtoxinA, Ipsen Biopharm, Slough, UK) and Botox (onabotulinumtoxinA, Allergan, Irvine, CA, USA) at a 2.5:1 ratio in the treatment of cervical dystonia (CD). A Dysport/Botox ratio of lower than 3:1 was suggested as a more appropriate conversion ratio, considering its higher efficacy and more frequent incidence of adverse effects not only in the treatment of CD but also in other focal movement disorders. A randomized, double-blind, multicenter, non-inferiority, two-period crossover study was done in CD, with a duration of at least 18 months. Patients were randomly assigned to treatment for the first period with Dysport or Botox, and they were followed up for 16 weeks after the injection. After a 4-week washout period, they were switched to the other formulation and then followed up for 16 weeks. The primary outcome was the changes in the Tsui scale between the baseline value and that at 1 month after each injection. A total of 103 patients were enrolled, and 94 completed the study. Mean changes in the Tsui scale between baseline and 4 weeks after each injection tended to favor Botox; however, this was not statistically significant (4.0 ± 3.9 points for the Dysport treatment vs. 4.8 ± 4.1 points for Botox; 95% confidence interval, -0.1-1.7; $P = 0.091$). The mean change of the Toronto western spasmodic torticollis rating scale score, the proportion of improvement in clinical global impression and patient global impression, and the incidences of adverse events were not significantly different between the two treatments. With regard to safety and efficacy, Dysport was not inferior to Botox in patients with CD at a conversion factor of 2.5:1 [clinicaltrial.gov: NCT00950664]

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Clinical study in Korea

Unique Origin
Unique Future

◆ BOTOX® vs Medytox®

A Randomised, Double-blind, Multi-centre, Multi-National, Phase II, Dose Parallel Study to Determine the Safety and Efficacy of MT10109 (Clostridium Botulinum Toxin Type A) in Subjects with Cervical Dystonia in Comparison to BOTOX®

일차적 목적 :

1. 경부 근 긴장 이상 증상을 가진 피험자들에 대해서 피험자별 BOTOX® 기 투여량의 100% 용량으로 BOTOX®를 근육 주사 1회 치료했을 때와 비교하여, 여러 용량 범위 (피험자별 BOTOX® 기 투여량의 50%, 75% 및 100%)로 MT10109 를 근육 주사 1회 치료하였을 때의 안전성을 확인하기 위함.
2. 경부 근 긴장 이상 증상을 가진 피험자에 대해서, Day 30에서의 Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-사경 중증도 점수를 근거로 하여, 피험자 별 BOTOX® 기 투여량의 100% 용량으로 BOTOX®를 근육 주사 1회 치료했을 때와 비교하여, 여러 용량 범위 (피험자별 BOTOX® 기 투여량의 50%, 75% 및 100%)로 MT10109 를 근육 주사 1회 치료하였을 때의 유효성을 확인하기 위함.



Selection of Botulinum toxin

Unique Origin
Unique Future

	Botox type A	Botox type B
Clinical effect	Longer duration	Shorter
Adverse effect	slightly lower	slightly higher

→ Botox type A : front-line treatment

→ Botox type B : when developing resistance to Botox type A

❖ BOTOX® = DYSPORT®

Converting ratio 1:2 ~ 1:5 (usually 1:3)

❖ Preparation of Botox in our Clinic

BOTOX®

100U/2cc Normal saline (5U/0.1cc)

DYSPORT®

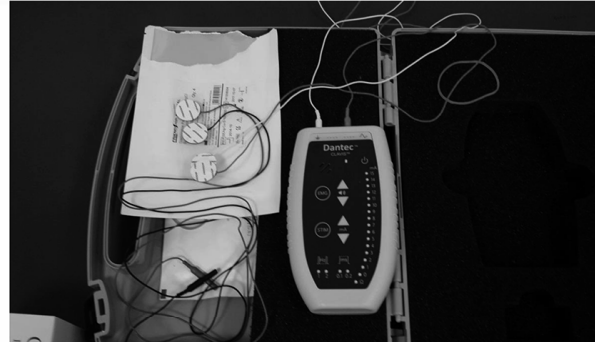
500U/3.3cc Normal saline (15U/0.1cc)



Injection technique

Unique Origin
Unique Future

- Clinical observation
- Palpation technique
- EMG guided : not use in face
- Ultrasound-guided



- Frontalis test : 10-15U in unilateral corrugator muscle
- Re-injection interval
every 3-6 months



Hemifacial spasm

Unique Origin
Unique Future

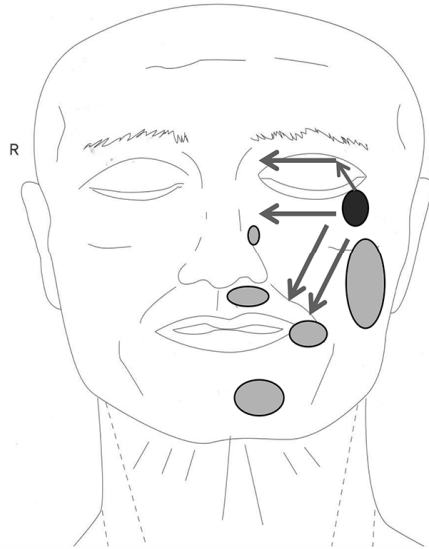
- Brief, stereotyped, but not synkinetic facial spasm
- Facial muscle spasm caused by heperexcitability of the 7th Cranial nerve
- Orbicularis oculi, zygomaticus, orbicularis oris, Levator labii, Levator angulii, mentalis, platysma
- DDx: blepharospasm, facial tics, myokimia, post-paralysis facial spasm



hemifacial spasm : Tip 1

Unique Origin
Unique Future

- Unilateral facial twitching
- Lower lateral eyelid → Medial side or upper eyelid → Lower face
- Orbicularis oculi, orbicularis oris, zygomaticus, Levator labii, Levator angulii, mentalis, platysma



Hemifacial spasm- Tip 2

The Babinski-2 Sign in Hemifacial Spasm

Matthias Pawlowski, MD,* Burkhard Gess, MD, and Stefan Evers, MD, PhD

Mov Disord 2013

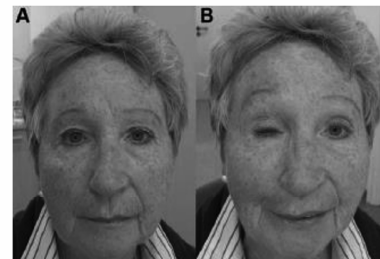


TABLE 1. The Babinski-2 sign for differential diagnosis of HFS and blepharospasm

Sensitivity	86%
Specificity	100%
Positive predictive value	100%
Interrater reliability	92% ^a

^aThis was 100% after repeated examination.

"the Other Babinski Sign"

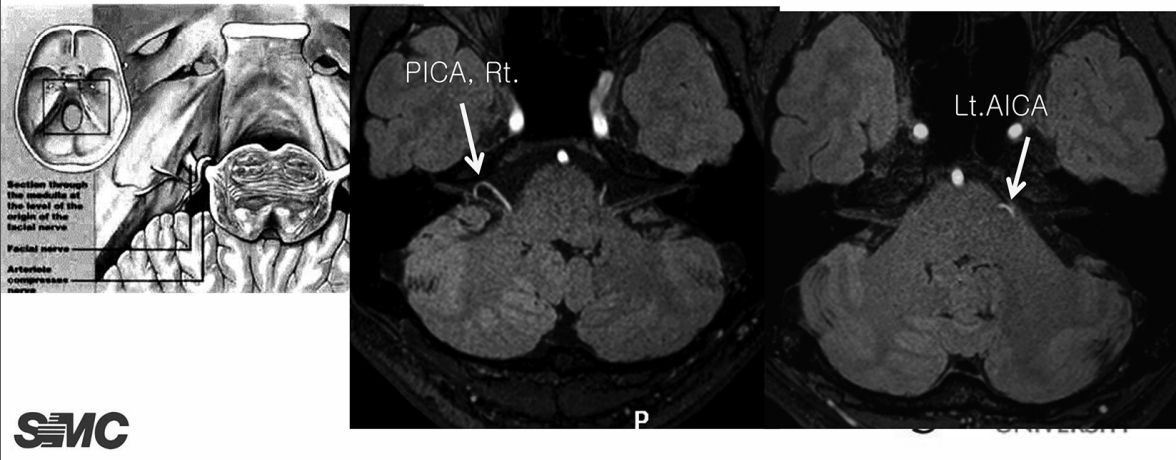


Hemifacial spasm

Unique Origin
Unique Future

■ Etiology

: Compression of the 7th nerve by an aberrant arterial loop
(Anterior inferior cerebellar artery > PICA)



Hemifacial spasm

Unique Origin
Unique Future

■ Treatment

Oral drugs

Micovascular decompression

Botulinum toxin injection ; Treatment of choice

Hemifacial spasm

Unique Origin
Unique Future

■ Which dose of toxin?

1 ~ 7.5 U of BOTOX[®] / 3~20U of DYSPORT[®] per each site

15 ~ 40 U of BOTOX[®] / 45~120U of DYSPORT[®] per session

■ Injection technique

subcutaneous, as superficial as possible (not intradermal)

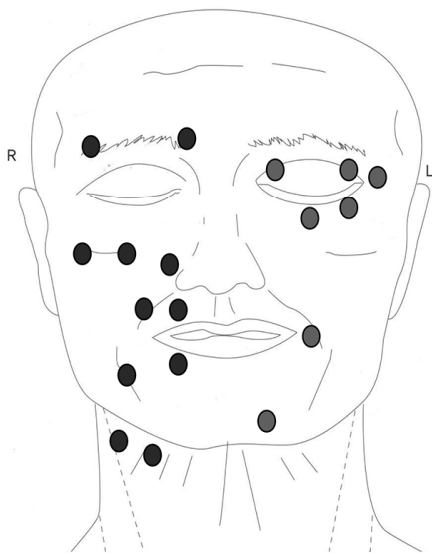
tip of the needle must directed outwards



hemifacial spasm

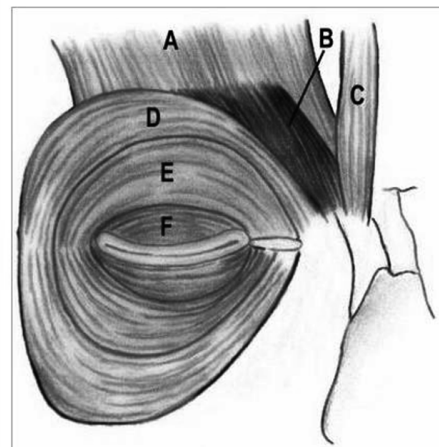
Unique Origin
Unique Future

Injection site



● Standard site in our clinic

● Additional site



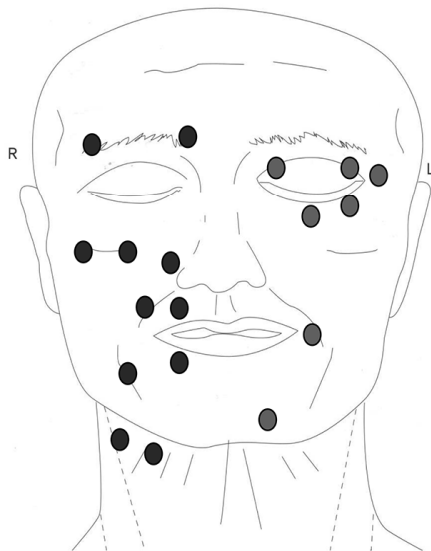
Orbicularis oculi muscle anatomy. (A) Frontalis, (B) corrugator superciliaris, (C) procerus, (D) orbital orbicularis, (E) preseptal orbicularis, (F) pretarsal orbicularis.



hemifacial spasm

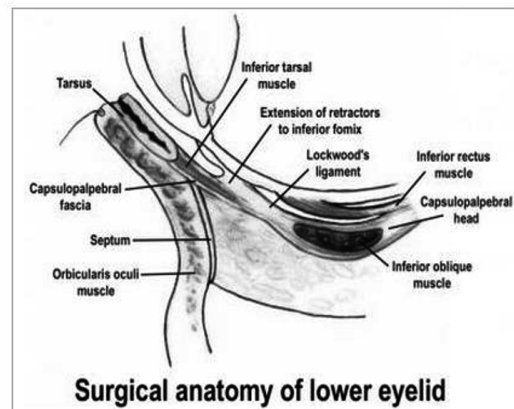
Unique Origin
Unique Future

Injection site



SMC

- Standard site in our clinic
- Additional site

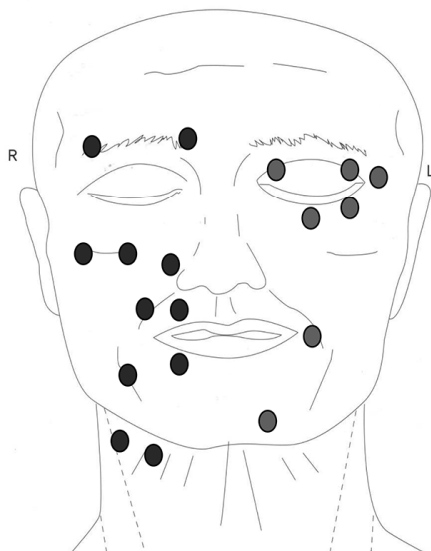


Lower eyelid anatomy.

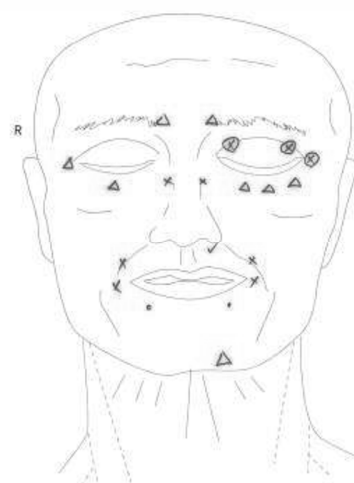
hemifacial spasm

Unique Origin
Unique Future

Injection site



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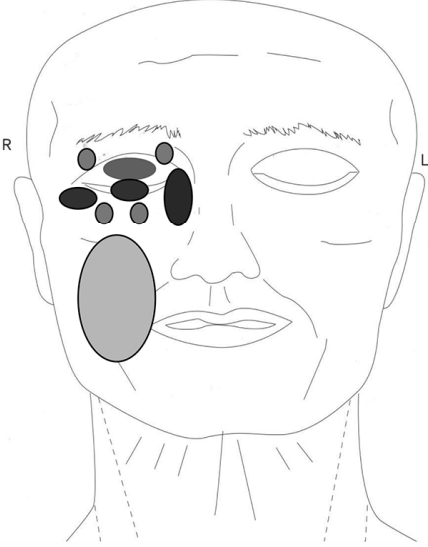
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0.75	▽
1	•
1.25	×
1.5	⊙
2	△
2.5	⊗
3.75	▲
5	●

hemifacial spasm

Unique Origin
Unique Future

Injection site



Side effect:

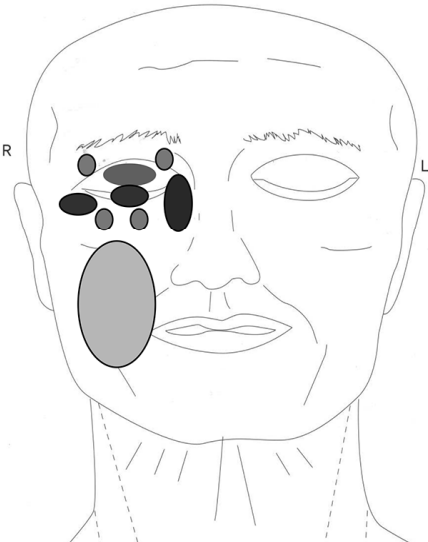
- ptosis
- facial weakness & asymmetry
- excessive or insufficient tearing
- incomplete eye closure
- bruise
- conjunctivitis due to reduced blinking
- diplopia (sup. rectus, inf oblique m)




hemifacial spasm

Unique Origin
Unique Future

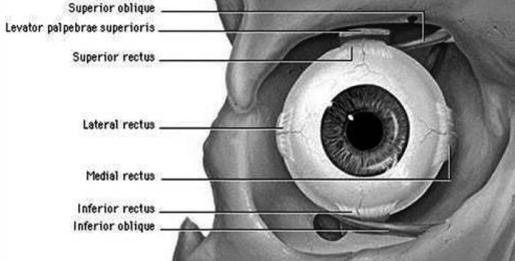
Injection site



Side effect:

- ptosis
- facial weakness & asymmetry
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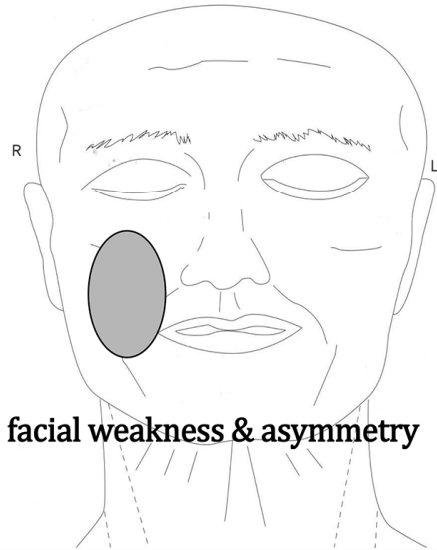




hemifacial spasm

Unique Origin
Unique Future

Injection site



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Study: Complication with Botox Tx in HFS

Unique Origin
Unique Future

- 대상
 - 3년이상 정기적으로 botox 치료중인 hemifacial spasm 환자
- 방법
 - 2015년 1월 ~ 2015년 4월 동안 botox clinic 에 hemifacial spasm 환자 내원시 PGI-Q 만족도 설문지 작성 및 HFS complication scale 확인
- Enrolled : 114 명
- Primary outcome: short-term & Long-term complication
- Secondary outcome: compare unilat. Inj & bilat. Inj
- Short-term complication
 - : Bruise, incomplete eye closure, facial discomfort, ptosis, diplopia
- Long-term complication
 - : facial asymmetry
 - : better with bilateral inj

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Case of hemifacial spasm injection

Unique Origin
Unique Future

- ❖ F/56
- ❖ Dx : HFS, Rt
- ❖ Onset: 2005
- ❖ Oral medication: no effect
- ❖ Initial BTX injection: 2007
- ❖ Response : Good
- ❖ Duration of effect : 3 months
- ❖ Complaint with BTX : facial asymmetry



Case 2 of hemifacial spasm

Unique Origin
Unique Future

- ❖ F/64
- ❖ Dx : HFS, Rt
- ❖ Onset: 1999
- ❖ Oral medication: no effect
- ❖ Initial BTX injection: 2009
- ❖ Response : Good
- ❖ Duration of effect : 5 months
- ❖ Side effect : none



Blepharospasm

Unique Origin
Unique Future

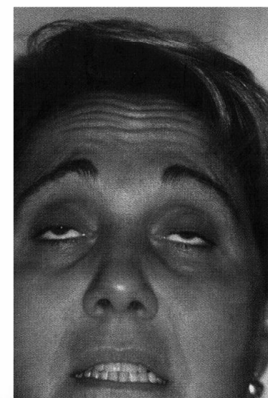
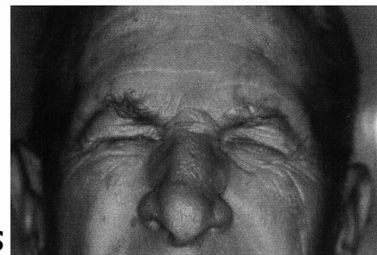
- Involuntary, tonic and spasmodic contraction of the orbicularis oculi, corrugator supercilii, and procerus muscles
- Adult-onset focal dystonia
- Begins insidiously in the 5th to 7th decade of life
- Excessive blinking, difficulty keeping eyes open → spasm
- Functional blindness in some patients
- Meige's syndrome
 - Combined with oromandibular dystonia, laryngeal or cervical dystonia



Blepharospasm – clinical forms

Unique Origin
Unique Future

- **Essential Blepharospasm**
 - Most common form
- **Apraxia of eyelid opening**
 - = focal dystonia of the pretarsal orbicularis oculi
 - = lid opening akinesia
 - Charcot's sign : raises eyebrows when eye opening
- **Meige's syndrome**
 - Combined with oromandibular, laryngeal or cervical dystonia



Blepharospasm – treatment option

- Medical treatment : Clonazepam, Baclofen....
- Surgical treatment
 - Resection of orbicularis oculi
 - Frontalis suspension
- Botulinum toxin injection
 - Treatment of choice

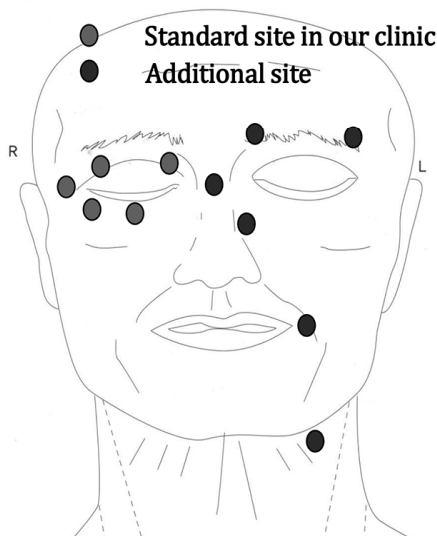


Blepharospasm

Unique Origin
Unique Future

Improvement (moderate to marked): 94%
 Average latency to improvement : 4.2 days
 Average duration for maximum benefit: 12.4 weeks
 Average duration for total benefit: 15.7 weeks

Jankovic et al 1990.



Injection Dose of Botox:

15 U~ 40 U per eye for Botox®

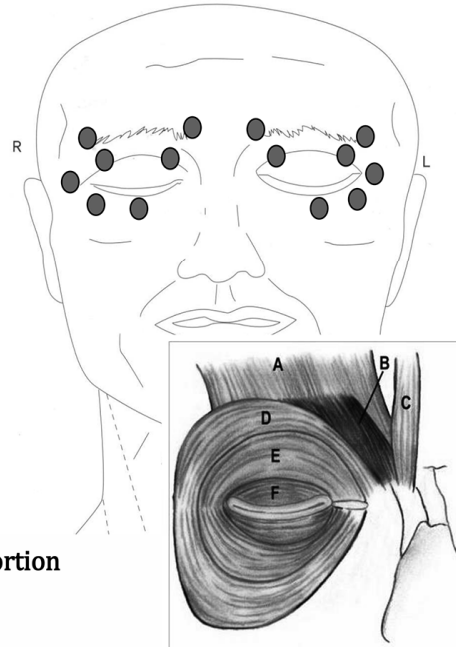
45 U~ 120 U per eye for Dysport®



Blepharospasm: injection site

Unique Origin
Unique Future

Essential blepharospasm



Preseptal Portion (tonic contraction) > Pretarsal Portion

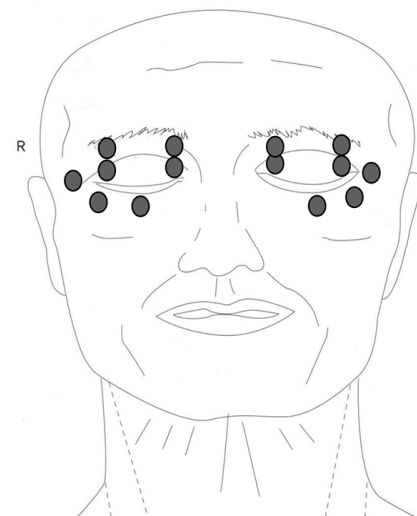


Orbicularis oculi muscle anatomy. (A) Frontalis, (B) corrugator supercilii, (C) procerus, (D) orbital orbicularis, (E) preseptal orbicularis, (F) pretarsal orbicularis.

Blepharospasm: injection site

Unique Origin
Unique Future

Apraxia of eyelid opening



Pretarsal Portion & Preseptal Portion



Blepharospasm: Side effect

Unique Origin
Unique Future

Side effect : less than 10%

Diplopia
: sup rectus m
inf oblique m

Excessive tear



Ptosis : Lev. palpebra

Incomplete eye
closure

Side effect:
Spontaneously improved within 30 days



Case 1 of Blepharospasm

Unique Origin
Unique Future

- ❖ F/62
- ❖ Dx : Meige syndrome
- ❖ Onset: 2011.3.
- ❖ Oral medication:
Trihexyphenidyl, baclofen,
clonazepam
- ❖ Initial BTX injection: 2012.3
- ❖ Response : Good
- ❖ Duration of effect : 4 months
- ❖ Side effect : none



Evaluation of Cervical dystonia

Unique Origin
Unique Future

Examination

Sitting

Talking

Writing

Walking

Lying down

Description

- Rotation in the vertical axis
- Flexion in the vertical axis
- Lateral tilting
- Shift of the vertical axis
- Limitation of movement
- associated movements
- Sensory trick
- Pain



TSUI score

A. 비정상적인 목운동의 진폭 (점수 = 1+2+3)

1. 목이 돌아간 정도(rotation)
- ☐ 0. 없다
 - ☐ 1. 15° 이하
 - ☐ 2. 15°~30°
 - ☐ 3. 30° 이상

2. 목의 경사(tilt)
- ☐ 0. 없다
 - ☐ 1. 15° 이하
 - ☐ 2. 15°~30°
 - ☐ 3. 30° 이상

3. 목의 앞으로 또는 뒤로 기울기
- ☐ 0. 없다
 - ☐ 1. 경미한 정도다
 - ☐ 2. 중간 정도다
 - ☐ 3. 심한 정도다

- B. 비정상적인 목운동의 기간
- ☐ 1. 간헐적으로 있다
 - ☐ 2. 항상 있다

- C. 어깨가 올라간 정도
- ☐ 0. 없다
 - ☐ 1. 조금 있으면서 간헐적으로 있다
 - ☐ 2. 조금 있으면서 항상 있거나 심하면서 간헐적으로 있다
 - ☐ 3. 심하면서 항상 있다

D. 떨림 (점수 = 1+2)

1. 심한정도(severity)
- ☐ 1. 경미하다
 - ☐ 2. 심하다

2. 기간(duration)
- ☐ 1. 간혹 있다
 - ☐ 2. 항상 있다



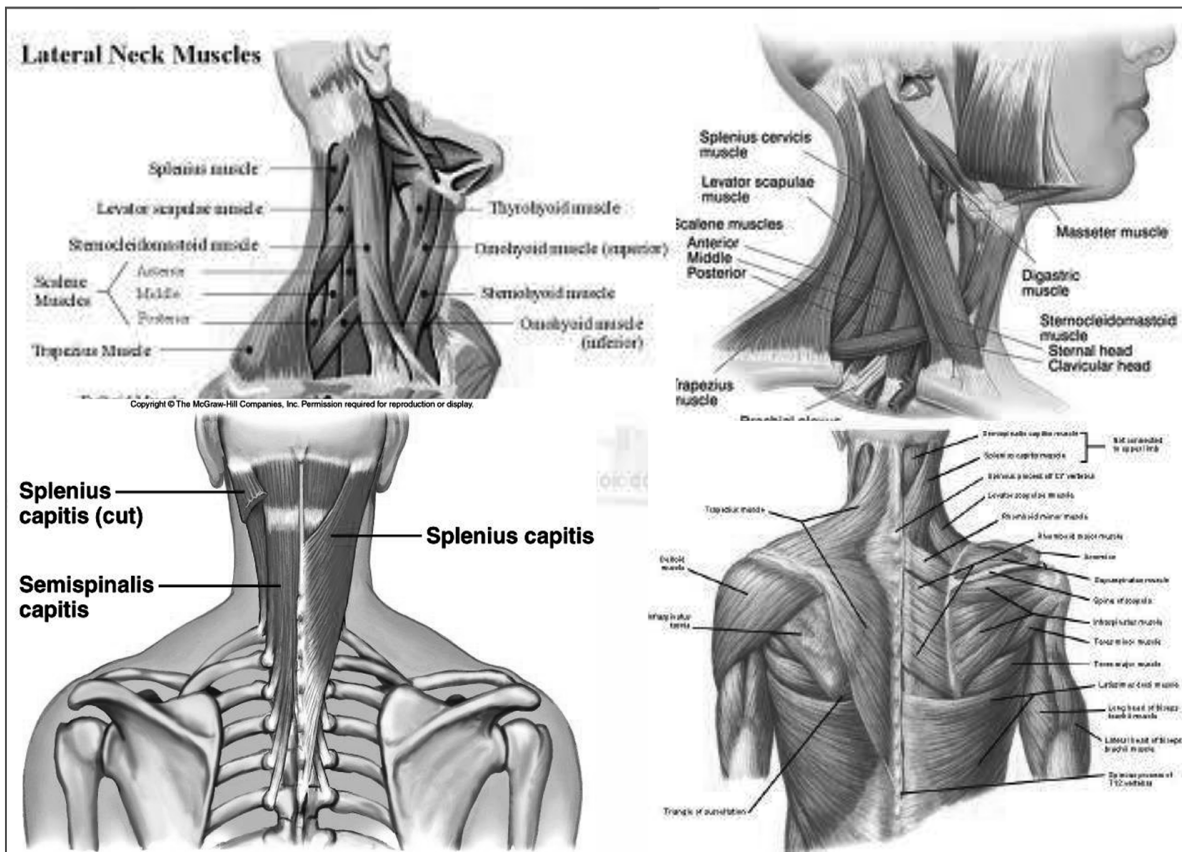
TWSTRS

I. 사지 운동도 측정 (최대 25)							
A. 최대로 기울어졌을 때 병위 (가장 나쁜 상태)							
1. 목에 돌아온 정도 (오른쪽 혹은 왼쪽)	0	1	2	3	4	5	
2. 목의 경사 (오른쪽 혹은 왼쪽, 어깨상부 경위)	0	1	2	3	4	5	
3. 앞/뒤 기울기							
a. 앞	0	1	2	3	4	5	
b. 뒤	0	1	2	3	4	5	
4. 몸의 측면이동 (오른쪽 혹은 왼쪽)	0	1	2	3	4	5	
5. 몸의 앞뒤이동 (앞 혹은 뒤)	0	1	2	3	4	5	
6. 회색시간 (점수 x 2)	0	10	20	30	40	50	
C. 감각적 자극수의 효과 (목을 받치거나 하는 것)	0	1	2	3	4	5	
D. 어파의 상하/앞뒤로 이동	0	1	2	3	4	5	
E. 목 움직임의 범위 (감각적 자극수의 도움 없이)	0	1	2	3	4	5	
F. 정상유지시간 (60초 이상, 2회 측정 평균값)	0	1	2	3	4	5	
II. 팔다리 측정 (최대 25)							
A. 앞 (직접 혹은 거사/가정관리)	0	1	2	3	4	5	
B. 일상생활수행	0	1	2	3	4	5	
C. 물건	0	1	2	3	4	5	
D. 걷기	0	1	2	3	4	5	
E. 물리비판	0	1	2	3	4	5	
F. 목외 활동	0	1	2	3	4	5	
III. 통증 측정 (최대 25)							
A. 통증 정도 (가장 고통을 더 + 가장 나쁜 더 + 평(0x2)/4)	Best	Worst	Usual				
B. 통증 회색시간	0	1	2	3	4	5	
C. 통증으로 인한 장애	0	1	2	3	4	5	

★ 점

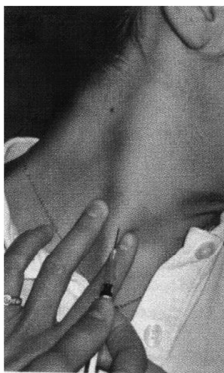
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Selection of Muscles in Cervical Dystonia				Unique Origin	Unique Future
Muscle	Action	Torticollis	Retrocollis	Laterocollis	Anterocollis
Sternocleidomastoid	Unilateral; ipsilateral flexion and contralateral rotation	•		•	•
Splenius capitis	Bilateral: head and flexion Unilateral: flexes and rotates the head to the same side Extension: lateral flexion and rotation of neck	•	•	•	
Semispinalis capitis	Extension: lateral flexion and rotation of neck		•		
Scalenes: anterior	Bilateral: elevate ribs during inhalation			•	•
Scalenes: medius	Unilateral: ipsilateral neck flexion, contralateral rotation				•
Scalenes: posterior	Anterior neck flexion				•
Levator scapulae	Elevates the superior angle of the scapula		•	•	
Trapezius upper	Elevates, retracts, and rotates scapula	•			
Torticollis	ipsilat splenius contralat SCM			ipsilat semispinalis levator scaulae...	
Laterocollis	splenius capitis, ipsilat scalene complex levator scapulae, longissimus, trapezius			splenius cervicalis	
Retrocollis	Bilat splenius capitis semispinalis capitis, trapezius				
Anterocollis	Bilat SCM			Splenius cervicalis scalene complex	



Selection of Muscles in Cervical Dystonia

Unique Origin
Unique Future



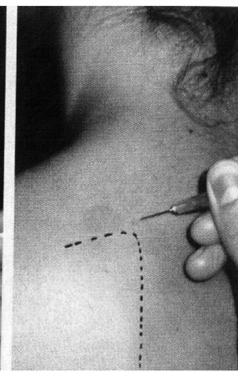
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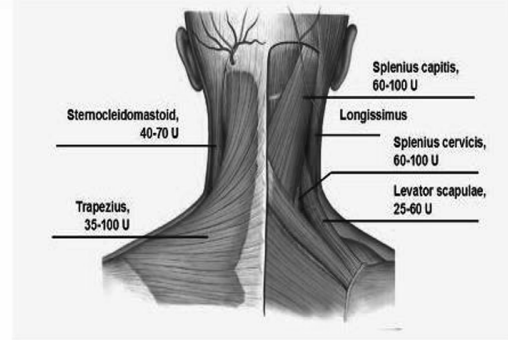
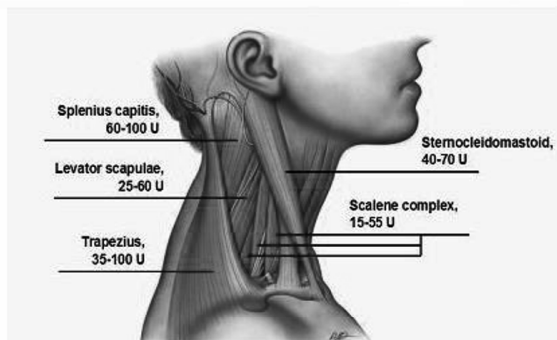


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Dose recommendations

Unique Origin
Unique Future



Injection site	BOTOX [®] Dose Units	Number of Injection Sites
Levator scapulae	25-100	1-3
Longissimus capitis	50-150	1-4
Scalene complex	15-50	1-3
Semispinalis capitis	50-150	1-4
Splenius capitis	50-150	2-4
Splenius cervicis	20-60	2
Sternocleidomastoid	15-75	1-2
Submental complex	5-25	1
Trapezius	50-100	3

Total dose:

BOTOX[®]

70~374U

Usually 100~150U

Dysport[®]

500U

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OMD with jaw closing/Bruxism

Unique Origin
Unique Future

- Masseter, &/or Temporalis m, &/or med pterygoid
- Masseter m Inj point:
 - Point of max muscle hypertrophy
 - 20mm below the lower border of zygomatic arch
- Dysport 100~160U/BOTOX 30~50U
(Temporalis 40~60U of Dysport)
- First effect: pain control → dec Bruxism (long lasting)
- Side effect:
 - bruising
 - "frozen" face
 - relative masticatory weakness (not impact on eating)

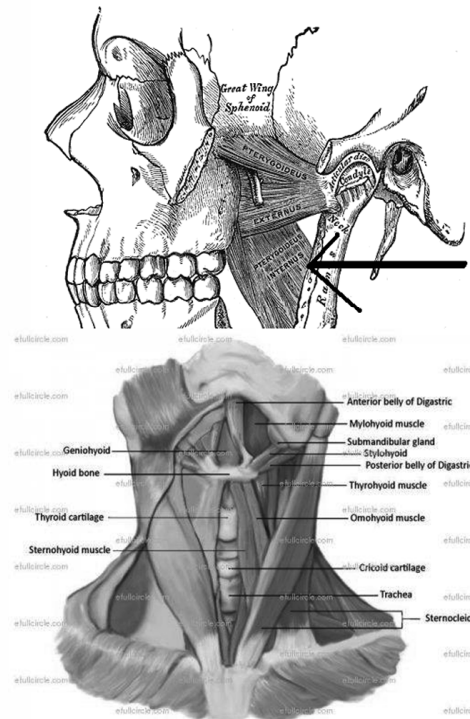
SMC

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OMD with forced Jaw Opening

Unique Origin
Unique Future

- Associated with BPS (71%)
 - Meige's syndrome
 - Sensory trick(+)
 - Difficulty in chewing and swallowing
- Target muscles
 - Lateral pterygoid
 - Diaphragm



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Writer's cramp

Unique Origin
Unique Future

- Muscles selection
 - Inspection: resting/writing /mirror study
 - Palpation
 - EMG recording
 - Video recording
 - Injection technique
 - EMG guided
 - 1~2 injection sites in one muscle
 - Small dose first (5~10U)
 - Recommending dose
 - Side effect: pain/bruising/weakness
- Flexor:
 - FCU/FCR (10-30U)
 - FDP (5-30U)
 - FD superficialis(5-20U)
 - FPL (5-20U)
 - pronator teres (10-20U)
 - Extensor
 - EPL (5-10U)
 - EI(indicis) (2.5-10U)
 - ECU (10-30U)
 - ECR (10-30U)
 - Intrinsic M : 2-5U

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Focal dystonia

Unique Origin
Unique Future

- Focal foot dystonia

video case

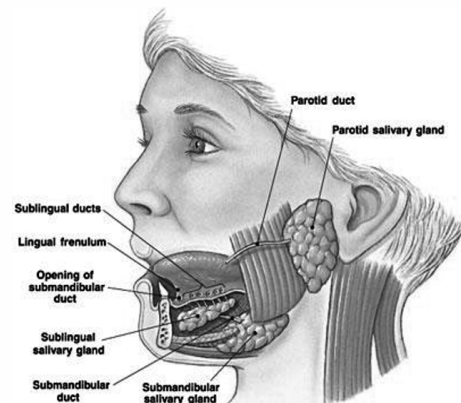
- Target muscles
 - Tibialis posterior
 - Gastrocnemius
 - Soleus



Hypersalivation

Unique Origin
Unique Future

- Hypersalivation
 - Salivary gland: parotid + sublingual + submandibular
 - Ultrasound guided
 - Injection site: 1cm from TM jt
 - 15U of Botox each side
 - side effect : careful to injury of facial N



Other neurological condition Unique Origin Unique Future

- Pain Control
 - effective Tx
- Segmental Myoclonus
- Spasm
- Spasticity
- Headache/vocal tremor/Hyperlacrimation/Hperhydrosis



How to inject Botox succesfully Unique Origin Unique Future



百聞不如一見 To See is to Believe.

百聞不如一行 The proof of the pudding is in the eating.



Movement clinic in SMC

Unique Origin
Unique Future

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