Tone Management

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Disclosures

- I am involved with Ipsen research studies

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Outline

- Review abnormalities of tone and movement
- Overview of approach to management of tone (and movement) in cerebral palsy

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Motor problems affecting children with cerebral palsy

- **Tone** abnormalities (too high, too low)
- **Strength** – weakness
- **Movement** – too much (hyperkinetic), too little (hypokinetic)
- **Control**
- **Balance** – sensory deficits, ataxia
- **Orthopedic** – contractures, dislocations, scoliosis

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Muscle tone

something you feel

- Resting tension in the muscle
- Resistance to passive stretch, while the person is attempting to relax
- Strength - resistance to active movement

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Tone - classification

Normal tone

Hypotonia ↓

Hypertonia ↑

- **Spasticity**
- **Dystonia**
- **Rigidity**

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Spasticity

- *Velocity-dependent increase in tone*
- Tends to affect certain muscle groups more than others, e.g. adductors more than abductors
- Puts individuals at risk for contractures and other orthopedic complications

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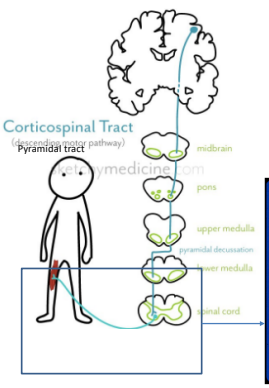
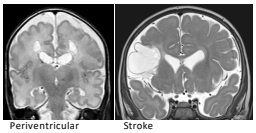
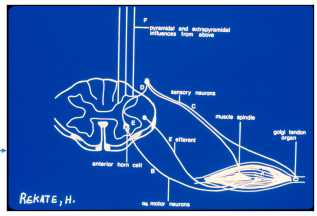
Where does spasticity come from?





Periventricular leukomalacia (PVL)

Stroke



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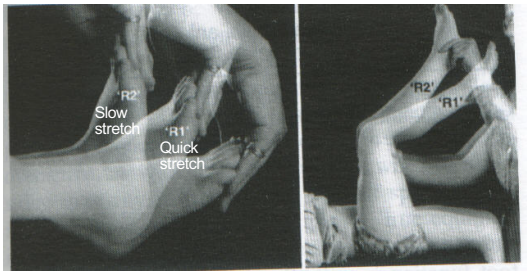
Measuring Spasticity



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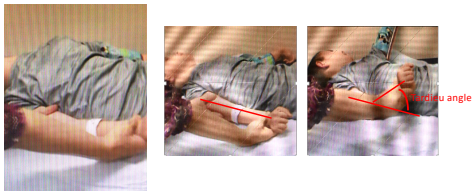
Measuring spasticity



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Tone - classification

Normal tone

Hypotonia ↓

Hypertonia ↑

- **Spasticity**
- **Dystonia**
- **Rigidity**

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Dystonia

Involuntary muscle contractions cause twisting and repetitive movements, abnormal postures or both

- Tone often normal at rest (and in sleep); abnormal postures triggered by movement
- Less likely to result in contractures or orthopedic complications

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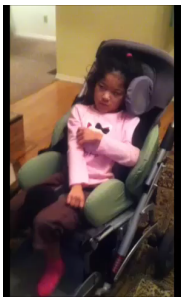

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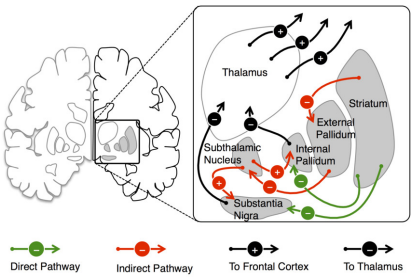
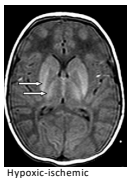
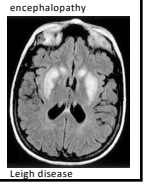
Where does dystonia come from?





Hypoxic-ischemic encephalopathy



Leigh disease

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Movement disorders

Neurologic syndromes in which there is either an excess of movement or a paucity of voluntary and automatic movements, unrelated to weakness or spasticity.

Something you see

Hypokinetic ↓

Hyperkinetic ↑

(Dyskinetic)

- **Athetosis**
- **Chorea**
- **Dystonia**

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Chorea and Athetosis

Athetosis: slow, continuous, involuntary writhing movement that prevents maintenance of a stable posture

Chorea: ongoing random-appearing sequence of one or more discrete involuntary movements or movement fragments

- Typically present at rest
- May occur during sleep
- Discrete postures not identifiable
- Unpredictable

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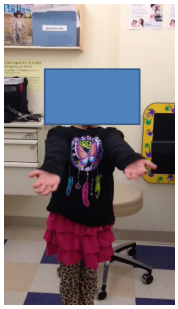

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Tone Management

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Why Treat Increased Tone?

- Pain – spasms, hip dislocation, pain with movement
- Function – gait/mobility, use of hand, ability to communicate/interact, play sports, independence, maximize learning potential etc.
- Other quality of life – dressing, bathing, diapering, maintaining hygiene
- Preventative –contractures, surgery
- Cosmetic

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Non-medical/surgical interventions

- Bracing/splinting
- Casting
- Other equipment/adaptations
- Stretching
- Therapy
- Complimentary/alternative approaches
  - Massage, craniosacral, patterning
  - Herbal/dietary
  - Other – biofeedback, magnetic therapies, stimulation therapies

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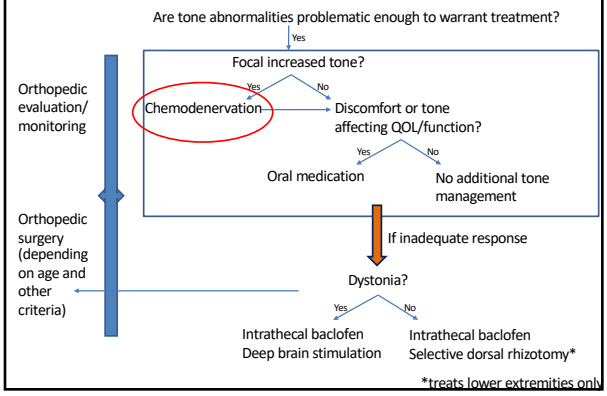
Approach to tone management



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Chemodenervation

- Botulinum toxin injections
- Phenol injections

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Botulinum Toxin

- Used to treat focal spasticity and dystonia since the 1990's
- Since 2016, FDA approval for botulinum toxin use in children with spasticity 2 years and older
- Given by injections into the muscles
- Onset days, peaks at 3 weeks, lasts 3-6 months
- Injections may be repeated, no more often than every 3 months

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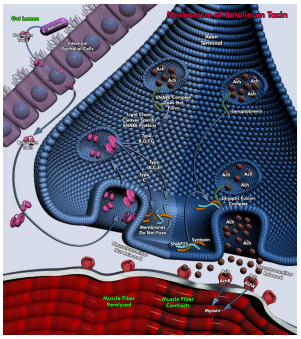
Botulinum toxin

- Neurotoxin produced by Clostridium botulinum
- Acts at the junction of the nerve and the muscle
- Weakens the muscle
- Over months, the nerve ending regenerates



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Botulinum toxins

	OnabotulinumtoxinA	AbobotulinumtoxinA	IncobotulinumtoxinA	RimabotulinumtoxinB
US Tradename	Botox®	Dysport®	Xeomin®	Myobloc®
Company	Allergan, Inc.	Ipsen Inc./Medicis	Merz Pharmaceuticals	Solstice Neurosciences Inc./Eisai Co., Ltd.
Active substance	BoNT-A complex	BoNT-A complex	BoNT-A free from complexing proteins	BoNT-B complex
Molecular weight	900 kDa	500–900 kDa	150 kDa	700 kDa
Target protein	SNAP-25	SNAP-25	SNAP-25	VAMP
Units per vial	50 or 100	300 or 500	100	2500, 5000, or 10000
Pharmaceutical form	Powder	Powder	Powder	Solution
US FDA-approved indications	Blepharospasm, cervical dystonia, glabellar lines, hyperhidrosis, chronic migraine	Blepharospasm, cervical dystonia, glabellar lines Pediatric lower limb spasticity	Blepharospasm, cervical dystonia, glabellar lines	Cervical dystonia

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Botulinum Toxin

- Risks:
  - Over-weakening
  - Generalized weakness
  - Decrease in muscle bulk
  - Antibody production (loss of efficacy)

F.D.A. Orders Warning Label for Botox

By NATASHA SINGER APRIL 16, 2019

WARNING: DISTANT SPREAD OF TOXIN EFFECT
See full prescribing information for complete boxed warning.
The effects of BOTOX and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults, particularly in those patients who have an underlying condition that would predispose them to these symptoms. (5.2)

Botox and other similar antiwrinkle drugs must now carry the most stringent kind of warning label, the Food and Drug Administration said Thursday.

The F.D.A. issued that order the day after the agency approved a new drug, Dysport, that is expected to be the first real challenger to Botox in the United States. Like Botox, Dysport is an injectable drug derived from the paralytic agent botulinum toxin.

The F.D.A. said such drugs must carry warning labels explaining that the material has the potential to spread from the injection site to distant parts of the body — with the risk of serious difficulties, like problems with swallowing or breathing.

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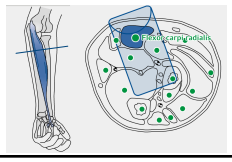
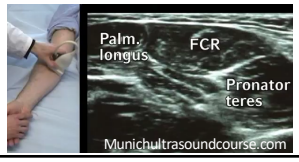
Botulinum toxin: procedure

- Decide on muscle targets and goals of injections
  - E.g. adductors – decrease scissoring
  - Thumb – easier grasp of objects
  - Hamstrings – help with sitting, better knee extension with walking
- Localization – EMG, nerve stimulator, ultrasound





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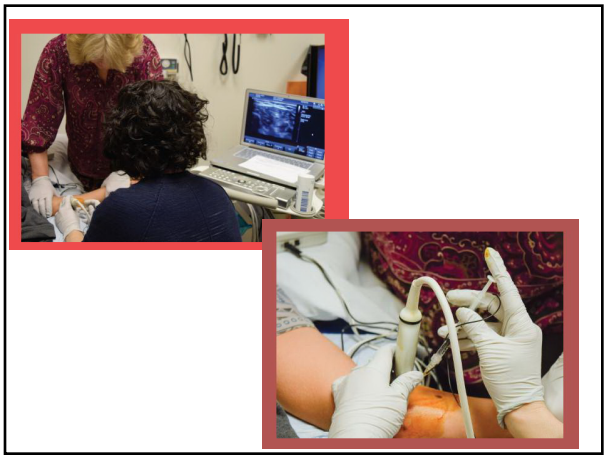

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Case

- 4 yo girl with right hemiplegic CP and toe walking
- Significant spasticity and contracture of the right ankle

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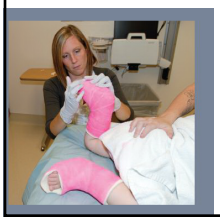
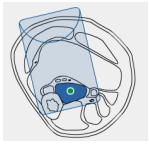
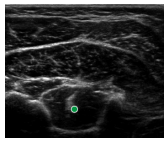
- Botox to the right gastrocnemius and posterior tibialis
- Serial casting for the contracture







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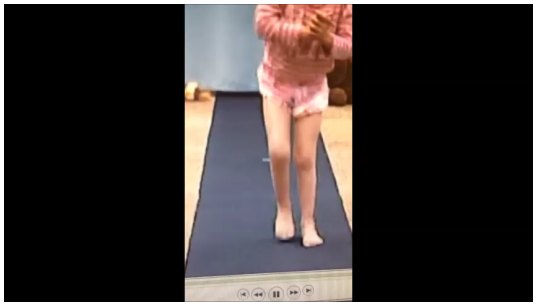

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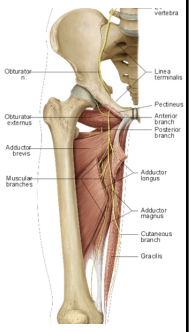
Phenol/alcohol injections

- Injections that target the nerves, decreasing the strength of the muscles
- Lasts 4-12 months
- Can be useful when multiple muscles need to be treated
- Painful – done under general anesthesia



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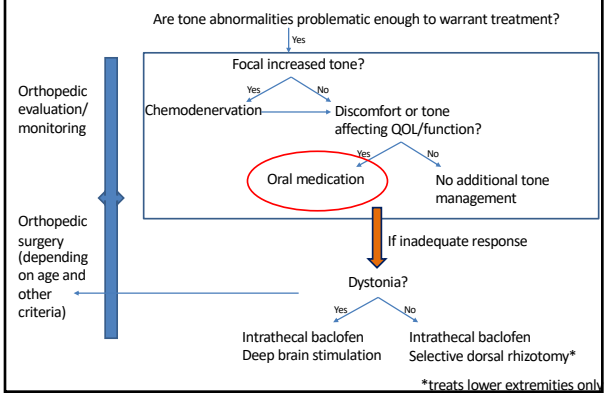
Approach to tone management



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Oral Medication: spasticity

- Baclofen
- Diazepam (valium)
- Tizanidine (Zaniflex)
- Dantrolene

- Useful when spasticity causes discomfort and is widespread
- **Sedation** is typically the limiting side effect

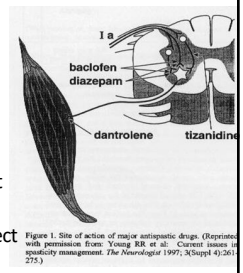

Figure 1. Site of action of major antispastic drugs. (Reprinted with permission from: Young RR et al. Current issues in spasticity management. *The Neurologist* 1997; 3(Suppl 4):261-275.)

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Oral Medication: dystonia

- Baclofen
- Trihexyphenidyl (Artane)
- Levodopa-carbidopa (Sinemet)
- Clonidine
- Benzodiazepines
- Gabapentin

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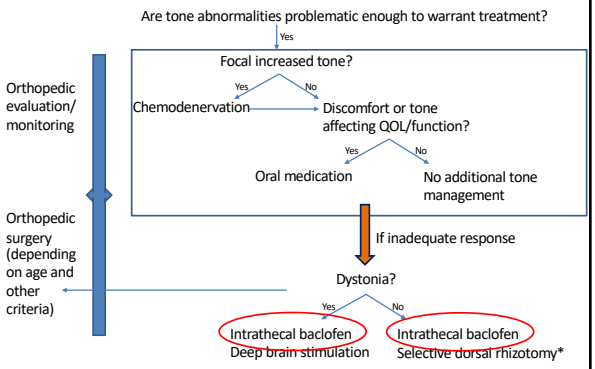
Approach to tone management



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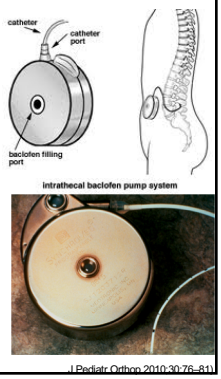
Intrathecal Baclofen Pump (ITB)

- Delivery of baclofen into the spinal fluid space, acts on spinal cord
- Greater effect with small doses
- Less sedation
- Indicated for severe spasticity, when patients fail oral medications.
- Used off-label for dystonia



J Pediatr Orthop 2010;30:76–81)

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Intrathecal Baclofen Pump (ITB)

- Cons:
  - Surgical complications
  - Having an implanted device
  - Intrathecal baclofen withdrawal is life-threatening
  - Needing refills every 1-6 months
  - Battery lasts 5-7 years
- Pros:
  - Very good tone management for most (high satisfaction rate (80%))
  - Can often stop tone medications and botulinum toxin injections

J Pediatr Orthop 2010;30:76–81)

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Intrathecal Baclofen Pump

- Baclofen trial: test dose of baclofen given as a one time dose through a spinal tap with a before and after assessment of tone
- Typically neurosurgery places the pump, and neurology, rehabilitation, neurosurgery, or pain medicine manages the pump
- Baclofen rate started very low, slowly titrated up over months to reach target dose

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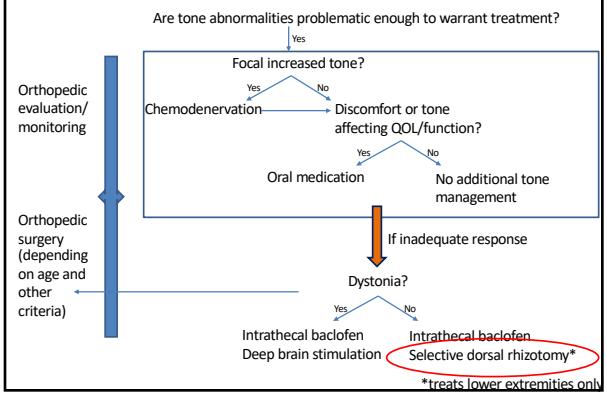
Approach to tone management



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Selective Dorsal Rhizotomy

- Some of the dorsal (sensory) nerve roots are selectively cut
- Interrupts the reflex arc, decreasing spasticity
- Typically used to spastic diplegia
- Children walking without a device, who have a history of prematurity, are most likely to benefit
- Less data, however children with spastic quadriplegia also tend to benefit

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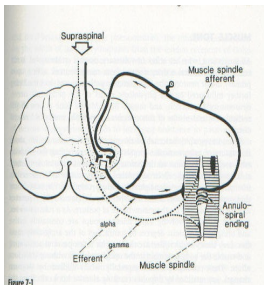
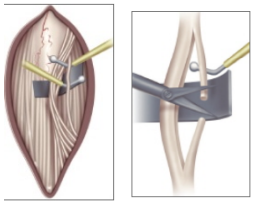
Selective Dorsal Rhizotomy





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Selective Dorsal Rhizotomy

- Pros:
  - Results in immediate decrease tone
  - One time treatment, no hardware
- Cons:
  - Weak patients may lose function – best for patients who walk independently
  - Irreversible
  - Does not treat dystonia
  - Ambulatory patients require significant rehabilitation

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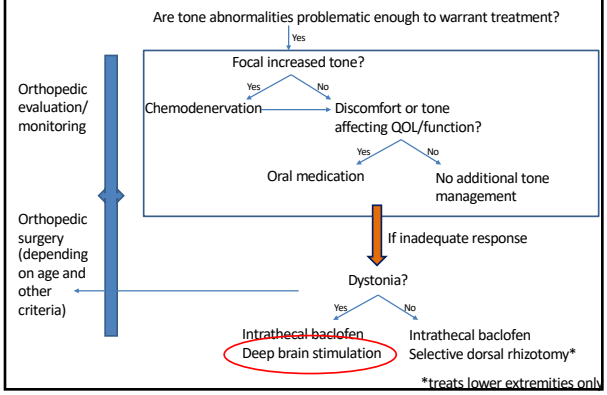
Approach to tone management



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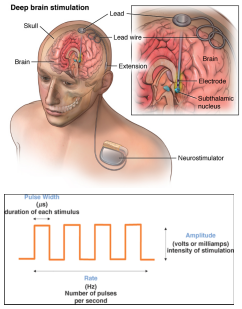
Deep Brain Stimulation: dystonia

- Stimulator implanted into the basal ganglia or thalami
- Changes in pattern of neuronal activity in the basal ganglia motor circuit



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Deep Brain Stimulation (DBS)

- Mostly used in adults for tremor, Parkinsons disease
- Very effective in certain genetic dystonias
- May have some benefit in dystonia due to CP, though limited numbers of patients
- One study showed 25% improvement in dystonia ratings

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Deep Brain Stimulation (DBS)

- Pros
  - Low-ish complication rate
  - Limited side effects, no sedation
  - Targeted therapy
- Cons:
  - Few centers with expertise in pediatric DBS
  - Knowledge about target sites, ideal programming still limited
  - Not all children respond, or response can be modest
  - No test ahead of time
  - Implanted device
  - Can takes months to a year to see full benefit
  - Frequent charging or need to surgically replace generator

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Summary

- Important to identify the types of tone/movement abnormalities
- Botulinum toxin for focal increased tone
- Oral meds for more generalized increased tone
- Selective dorsal rhizotomy for ambulatory children with spastic diplegic cerebral palsy
- Intrathecal baclofen pump, deep brain stimulator options for severe increased tone not managed by less invasive means

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