Using tone-reducing medications in children and youth with Cerebral Palsy

Dr Ted Prince
Dr Matt Hicks
Oct 28, 2014 on behalf of SCP
Objectives

- review the motor patterns likely to be encountered in children with Cerebral Palsy
- features that distinguish spasticity and dystonia
- goals of medical interventions
- oral medications used to manage spasticity
- oral medications used to manage dystonia
- medication algorithms
Cerebral Palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occur in the developing fetal or infant brain.

The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems.
Cerebral Palsy

- CP is not an etiologic diagnosis, but a clinical descriptive term
- the diagnosis relies essentially on clinical aspects, based on phenomenology
Cerebral Palsy

- ‘group’ – the singular Cerebral Palsy is preferred even though it may describe several groupings that serve different purposes, but may overlap
- ‘developmental’ nature of CP almost always implies impacts on the developmental trajectories of people who have CP
- ‘movement and posture’ abnormalities are core features
caused by abnormal development of, or damage to, motor control centers of the brain
caused by events before, during, or after birth
  ◦ origins may start as early as brain formation and early development but may extend to acquired brain injury in children and youth
abnormalities of muscle control that define CP are often accompanied by other neurological and physical abnormalities

the presence of other abnormalities should be considered the “norm” for CP, so must always be borne in mind
CP types

- CP is often defined based on topography of involved limbs, or type of motor disorder (or both)
Topography

- Hemiplegia (generally spastic but rare forms of hemiplegic dystonia exist)
- Diplegia
- Quadriplegia (Tetraplegia)
Descriptive terms

- spastic 75–80%, (upper motor neuron lesions)
  - hemiplegia 20–30%
  - diplegia 30–40%
  - quadriplegia 10–15%

- “non–spastic” – 15–20%,
  - dyskinetic – 10–15% (basal ganglia)
    - ataxic – <5%, (cerebellar lesions)
    - Hypotonic – <5%
Motor Control System

- Cerebral motor cortex
  - initiates the “command to move”
- Basal ganglia
  - starts and stops movement: “accelerator and “brake”;
  - organizes collaboration between agonist/antagonist muscles, especially for postural control
- Cerebellum
  - coordinates movement: the “steering wheel”
This classification may provide guidance for the selection of treatment modalities. (Note: Mixed CP is common, with variable combinations of neurological findings.)
Examination – Imaging Correlations

Spasticity: White matter lesions
Rigidity: Diffuse cortical lesions
Dyskinesia: Basal ganglia/thalamic lesions
Ataxia: Cerebellar lesions
Pyramidal system

Lesions to the pyramidal system may present as spasticity
Spasticity

- velocity-dependent increased resistance to passive stretch
- rapid increase in movement leads to ‘catch’ with subsequent release
- continuous and passive partial muscle contraction
- clonus (a series of rapid muscle contractions)
- exaggerated deep tendon reflexes,
- muscle spasms,
Spasticity

- ranges from mild muscle stiffness to severe, painful, and uncontrollable muscle spasms
- postural changes include scissoring (involuntary crossing of the legs), equinus posturing, fisting, and loss of wrist supination
- fixed joints (contractures = fixed high resistance to passive stretch of a muscle due to fibrosis)
Extra-pyramidal System

Lesions to the extra-pyramidal system may present as ‘dyskinesia’
Dyskinetic

- Dyskinetic or Extra-pyramidal
  - athetosis
  - chorea
  - choreoathetosis
  - ataxia
  - Hypotonia
  - dystonia
Dyskinesia

Movements

Chorea

Choreo-athetosis

Athetosis

Dystonia

hypotonia

hypertonia
Chorea

- from the Latin word choreia – dance
- ceaseless occurrence of a variety of jerky, but well coordinated involuntary movements
- movements may involve the limbs, trunk, or facial muscles
Athetosis

- continuous stream of slow, sinuous, writhing movements, typically of the hands and feet.
- movements typical to athetosis are sometimes called athetoid movements.
- often caused by damage to the corpus striatum of the brain, but can also be caused by a lesion of the motor thalamus.
Choreoathetosis

Chorea
- intermittent irregular

Athetosis
- unsustained flowing

Dystonia
- sustained postures

Choreoathetosis
Dystonia

- sustained unwanted muscle contractions
- repetitive twisting movements
- abnormal postures of trunk, neck, face, limbs
- involuntary concomitant contraction of agonist and antagonist muscles
- overflow of unwanted muscle contractions to adjacent muscles
- tremor may be present
Primitive Reflexes

- Moro
  - evident at birth and disappears by 4–5 months
- Positive supporting reaction
  - generally disappears by 4 months
- Asymmetrical tonic neck
  - usually evident by 1 mo, and disappears by 4–6 months
- Parachute reflex
  - begins to emerge at 7–9 months
Mixed CP

- It is increasingly recognized that a number of individuals with cerebral palsy have a “mixed” disorder (including both spastic and non-spastic features)
Hypotonic CP is thought to be rare

- truncal and extremity hypotonia with hyperreflexia and persistent primitive reflexes
Ataxia

- ataxia = meaning "lack of order"
- signs and symptoms consisting of gross incoordination of muscle movements
- ataxia can be nonspecific; but implies dysfunction of areas such as the cerebellum
Spasticity

- More consistent
- Seen with upper motor neuron signs

Dystonia

- Resolves with sleep
- Increases with agitation or excitement
- Can be triggered by attempts at voluntary movement or a specific body position
Spastic vs Dystonic CP

**Spasticity**
- clasp-knife tone

**Dystonia**
- ‘rigid’ tone

<table>
<thead>
<tr>
<th></th>
<th>Spasticity</th>
<th>Dystonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>head</td>
<td>flexed</td>
<td>torticollis</td>
</tr>
<tr>
<td>elbows</td>
<td>flexed</td>
<td>extended</td>
</tr>
<tr>
<td>fingers</td>
<td>flexed</td>
<td>extended</td>
</tr>
<tr>
<td>hips</td>
<td>scissored</td>
<td>asymmetric</td>
</tr>
<tr>
<td>knees</td>
<td>flexed</td>
<td>often flexed</td>
</tr>
<tr>
<td>feet</td>
<td>equino–varus</td>
<td>often plano–valgus</td>
</tr>
</tbody>
</table>
HAT Tool

- Hypertonia Assessment Tool (HAT)

- Authors: Fehlings, D., Switzer, L., Jethwa, A., Mink, J., Macarthur, C., Knights, S., & Fehlings, T. (Bloorview Kids Rehab, Toronto)
<table>
<thead>
<tr>
<th>HAT ITEM</th>
<th>SCORING GUIDELINES (0=negative or 1=positive)</th>
<th>SCORE 0=negative 1=positive (circle score)</th>
<th>TYPE OF HYPERTONIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Increased involuntary movements/postures of the designated limb with tactile stimulus of a distal body part</td>
<td>0= No involuntary movements or postures observed &lt;br&gt; 1= Involuntary movements or postures observed</td>
<td>0</td>
<td>DYSTONIA</td>
</tr>
<tr>
<td>2. Increased involuntary movements/postures with purposeful movements of a distal body part</td>
<td>0= No involuntary movements or postures observed &lt;br&gt; 1= Involuntary movements or postures observed</td>
<td>0</td>
<td>DYSTONIA</td>
</tr>
<tr>
<td>3. Velocity dependent resistance to stretch</td>
<td>0= No increased resistance noticed during fast stretch compared to slow stretch &lt;br&gt; 1= Increased resistance noticed during fast stretch compared to slow stretch</td>
<td>0</td>
<td>SPASTICITY</td>
</tr>
<tr>
<td>4. Presence of a spastic catch</td>
<td>0= No spastic catch noted &lt;br&gt; 1= Spastic catch noted</td>
<td>0</td>
<td>SPASTICITY</td>
</tr>
<tr>
<td>5. Equal resistance to passive stretch during bi-directional movement of a joint</td>
<td>0= Equal resistance not noted with bi-directional movement &lt;br&gt; 1= Equal resistance noted with bi-directional movement</td>
<td>0</td>
<td>RIGIDITY</td>
</tr>
<tr>
<td>6. Increased tone with movement of a distal body part</td>
<td>0= No increased tone noted with purposeful movement &lt;br&gt; 1= Greater tone noted with purposeful movement</td>
<td>0</td>
<td>DYSTONIA</td>
</tr>
<tr>
<td>7. Maintenance of limb position after passive movement</td>
<td>0= Limb returns (partially or fully) to original position  &lt;br&gt; 1= Limb remains in final position of stretch</td>
<td>0</td>
<td>RIGIDITY</td>
</tr>
</tbody>
</table>
# Differential Diagnosis

<table>
<thead>
<tr>
<th>History</th>
<th>Exam</th>
<th>Neuroimaging</th>
<th>Workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>Spastic Diplegia</td>
<td>PWMI/PVL</td>
<td>None</td>
</tr>
<tr>
<td>Neonatal encephalopathy</td>
<td>Dystonia</td>
<td>Hi putamen, VL thalamus</td>
<td>Maternal/fetal risk factors</td>
</tr>
<tr>
<td>Severe developmental delays, no risk factors</td>
<td>Choreo-athetosis, hypotonia</td>
<td>Semi-lobar Holoprosencephaly</td>
<td>SNP array, HPE gene sequencing</td>
</tr>
<tr>
<td>Motor delay / abnormal gait</td>
<td>Dystonia</td>
<td>Normal</td>
<td>Trial of Sinemet, CSF Neurotransmitters</td>
</tr>
<tr>
<td>Normal development then CP</td>
<td>Dystonia</td>
<td>Hi Globus Pallidus</td>
<td>Metabolic disorders, including mitochondrial</td>
</tr>
</tbody>
</table>
Treating Hypertonia

- Spasticity
- Dystonia
- (Rigidity)
Goals of Treatment

Individualize medical-rehabilitative interventions based on goals of treatment:

- Improve/preserve function
- Improve ease of care/comfort
- Decrease pain/discomfort
- Decrease orthopedic deformities
- Promote general health and well-being
- Promote integration in school and community life
- Consider secondary morbidities
- Plan for long-term outcome
A systematic review of interventions for children with cerebral palsy: state of the evidence

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¹ Cerebral Palsy Alliance, Sydney; ² University of Notre Dame Australia, Sydney, Australia.

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E-mail: inovak@cerebralpalsy.org.au

This article is commented on by Msall on pages 877–878 of this issue.
Cerebral Palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occur in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems.

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The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems.

Green = Go: Effective, therefore do it

Yellow = Measure: Uncertain effect, therefore measure outcomes to determine if progress is made

Red = Stop: Ineffective, therefore don't do it

After seeing a patient...
Oral medications to address hypertonia


- After assessing for spasticity vs dystonia, considerations in choosing a medication
Recommendations

- Standardized and validated spasticity scales and clinically relevant measures should be used.
- Need for safety, efficacy and pharmokinetic data for oral medications.
- “There is an urgent need for studies to establish the efficacy of current therapies and find additional safe and effective treatments to help children affected by generalized spasticity due to CP.”
- The effects of both spasticity and the treatment of spasticity on activity and participation as defined by the ICF need to be studied in children with CP.
Goals of therapy

- Goal of therapy 3 fold
  - Ease burden of care due to abnormal tone/postures
  - Ease discomfort associated with daily stretches
  - Reduce painful muscle spasms
- Patients selected in our clinic are generally been more compromised (GMCS 4 and 5)
- Parents are informed of the limited role that medications play
<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Dosing</th>
<th>Evidence</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam (Valium)</td>
<td>GABA–A</td>
<td>1–2 mg/day up to 12 mg/day</td>
<td>Probably effective in short term</td>
<td>Ataxia, daytime somnolence, withdrawal</td>
</tr>
<tr>
<td>Oral Baclofen</td>
<td>GABA–B</td>
<td>10 – 60 mg/day</td>
<td>Conflicting evidence, insufficient evidence</td>
<td>Drowsiness, sedation, withdrawal</td>
</tr>
<tr>
<td>Dantrolene</td>
<td>Blocks Ca release from SR</td>
<td>0.5 – 12 mg/kg/day</td>
<td>Conflicting evidence</td>
<td>Weakness, drowsiness, irritability</td>
</tr>
<tr>
<td>Tizanidine</td>
<td>alpha2–noradrenergic agonist</td>
<td>0.05 mg/kg/day</td>
<td>Possibly effective</td>
<td>Hypotension, sedation, dry mouth, dizziness</td>
</tr>
<tr>
<td>Trihexyphenidyl (Artane)</td>
<td>Muscarinic receptor, ?Dopaminergic</td>
<td>0.1 to 0.75 mg/kg/day</td>
<td>No RCTs, observational studies</td>
<td>Anti-cholinergic</td>
</tr>
<tr>
<td>Levodopa / Carbidopa</td>
<td>Increases CNS dopamine levels</td>
<td>1–6 mg/kg/day</td>
<td>No RCTs, observations</td>
<td>Nausea, vomiting</td>
</tr>
</tbody>
</table>
Medication choices

- Spasticity:
  - Baclofen
  - Benzodiazepines
  - Dantrolene sodium
  - Tizanidine/Clonidine
  - Others

- Dystonia
  - Trihexyphenidyl
  - Levo-Dopa
Baclofen interferes with release of excitatory transmitters

Diazepam facilitates GABA-mediated presynaptic inhibition

Internuncial neuron

EPSP

IPSP

Initial segment

la
GABA-b agonist
- GABA and Glycine are principal inhibitory neurotransmitters in CNS) majority of GABA neurons are interneurons and constitute 30–40% of CNS neurons
- Mediates presynaptic inhibition of dorsal horn interneurons in spinal cord
- Decreases excitability of la afferent neurons, reducing output to motoneuron
Adverse effects

- Sedation
- Respiratory (bronchoconstriction)
- Reduced seizure thresholds
- Withdrawal syndrome
- Memory impairment
- Constipation
- Ataxia/Weakness/Fatigue
- Insomnia
  - Nausea/Constipation/Urinary frequency
  - Excessive sweating
  - Rash/Itch
Baclofen Adverse Effects

- **Cardiovascular:** Hypotension
- **Gastrointestinal:** Constipation, Nausea, Vomiting
- **Musculoskeletal:** Poor muscle tone
- **Neurologic:** Asthenia, Dizziness, Headache, Somnolence
- **Renal:** Urinary complication
- **Other:** Fatigue, Shivering
**Baclofen Dosing**

- **<2 years:** 10-20 mg daily ÷ tid; titrate dose every 3 days in increments of 5-15 mg/day to a maximum of 40 mg daily

- **2-7 years:** 20-30 mg daily ÷ tid; titrate dose every 3 days in increments of 5-15 mg/day to a maximum of 60 mg daily

- **≥8 years:** 30-40 mg daily ÷ tid; titrate dosage as above to a maximum of 120 mg daily
Benzodiazepines

- Diazepam (Nitrazepam/Clonazepam)
  - Diazepam Dosing: (minimal literature guidance)
    - 0.12-0.8 mg/kg/day ÷ tid

- Nitrazepam Dosing:
  - 0.3 to 1.5 mg/kg/day ÷ bid (based on anti-epileptic dosing)
Diazepam Adverse Effects

- **Cardiovascular:** Hypotension
- **Dermatologic:** Rash
- **Gastrointestinal:** Diarrhea
- **Musculoskeletal:** Muscle weakness
- **Neurologic:** Ataxia, Incoordination, Somnolence
- **Psychiatric:** Euphoria
- **Respiratory:** Respiratory depression
- **Other:** Fatigue
Tizanidine

- Alpha2–adrenergic agonist, (monoamine)
- Prevents release of excitatory neurotransmitters (glutamate/aspartate),
- may facilitate action of glycine,

- Dosing in children ‘not established’
  - 0.05 mg/kg/day ÷ bid
  - (adult max = 36 mg/d)
Tizanidine Adverse Effects

- Hypotension (less with tizanidine)
- Sedation (more common than baclofen)
- Weakness/dizziness
- Hallucinations/insomnia
- Elevated liver enzymes (tizanidine)
**Medication Options**

### Oral Baclofen
- **<2 years:** 10-20 mg daily ÷ tid; titrate dose every 3 days in increments of 5-15 mg/day to a maximum of 40 mg daily
- **2-7 years:** 20-30 mg daily ÷ tid; titrate dose every 3 days in increments of 5-15 mg/day to a maximum of 60 mg daily
- **≥8 years:** 30-40 mg daily ÷ tid; titrate dosage as above to a maximum of 120 mg daily

### Benzodiazepines: Diazepam or Nitrazepam
- **Diazepam:** 0.12-0.8 mg/kg/day ÷ tid
- **Nitrazepam:** 0.3 to 1.5 mg/kg/day ÷ bid

### Tizanidine
- **0.05 mg/kg/day ÷ bid**

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**Exclusions / Considerations**
- If seizures are not well controlled then Baclofen contraindicated (relative)
- Medications likely of greatest benefit in quadriplegia rather than diplegia or monoplegia given systemic effects
- Use benzodiazepines with caution in children with respiratory/OSA symptoms

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**Preparations**

**Baclofen**
- 10 and 20 mg regular release tablets; reliable recipe available to make into liquid

**Nitrazepam (Mogadon)**
- 5 and 10 mg regular release tablets & 1mg/mL liquid

**Diazepam (Valium)**
- 2, 5, 10 mg regular release tablets & 1 mg/mL liquid

**Tizanidine (Zanaflex)**
- 4 mg regular release tablets

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**Side Effects/Adverse Drug Reactions (ADRs)**

**Baclofen**
- Seizure exacerbation, somnolence, dizziness, cognitive effects, hypersalivation & swallowing difficulties

**Nitrazepam/ Diazepam**
- Somnolence, dizziness, cognitive effects, hypersalivation & swallowing difficulties

**Tizanidine**
- Hypotension, sedation, dry mouth, dizziness

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**Baseline Assessment**
- HAT
- CCQ
- COPM
- Adapted Tardieu
- Physical Exam

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**6 Week Assessment**
- HAT
- Screen for ADRs
- Physical Exam

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**Follow up Assessment**
- HAT
- CCQ
- Screen for ADRs
- Physical Exam

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**For suboptimal response or serious ADRs taper medication as follows:**

**Oral Baclofen**
- Wean 10% per week

**Benzodiazepines: Diazepam or Nitrazepam**
- Wean 10% per week
Dyskinesia

Movements

Chorea
Choreo-athetosis
Athetosis
Dystonia
Hypotonia
Hypertonia
## Medications for Treatment of Dyskinetic CP

<table>
<thead>
<tr>
<th>Medications for</th>
<th>Dystonia</th>
<th>Chorea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine agonists</strong>: levodopa/carbidopa, amantadine, bromocriptine, pergolide</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Dopamine antagonists</strong>: pimozide, haloperidol</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Monoamine depleters &amp; blockers</strong>: tetrabenazine</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Monamine depleter</strong>: reserpine</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Anticholinergics</strong>: trihexyphenidyl, benztropine</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong>: clonazepam, diazepam, lorazepam</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Other muscle relaxants</strong>: baclofen, cyclobenzaprine</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Antiepileptic drugs</strong>: primidone, carbamazepine</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Antiepileptic drugs</strong>: levetiracetam, valproic acid</td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>
Trihexyphenidyl

- Anticholinergic
  - Dose
    - Week 1 & 2: 0.1 mg/kg bid
    - Week 3 & 4: 0.1 mg/kg tid
    - Week 5 & 6: 0.15 mg/kg tid
    - Week 7 & 8: 0.20 mg/kg tid
    - Consider increase to 0.25 mg/kg tid if suboptimal response
    - Expected optimal response at 3 to 4 months post-medication initiation
**Trihexyphenidyl**

- **Dosing:**
  - one study found that younger children tolerated higher doses, and suggested the following mean dose/age:
    - 0–3yr – 0.76 mg/k/d
    - 4–6yr – 0.72 mg/k/d
    - 7–9yr – 0.51 mg/k/d
    - 10–12yr – 0.33 mg/k/d
    - 13–15yr – 0.4 mg/k/d
    - 16–18yr – 0.2 mg/k/d
Trihexyphenidyl

- Adverse effects reported in 6 articles:
  - agitation
  - dry mouth
  - blurred vision
  - urinary difficulty
  - drowsiness
  - forgetful, hallucinations
  - decreased seizure control
  - treatment emergent chorea
Trihexyphenidyl

- Side effects per Micromedex®
  - common
    - Gastrointestinal: Nausea (30% to 50%), Xerostomia (30% to 50%)
    - Neurologic: Dizziness (30% to 50%)
    - Ophthalmic: Blurred vision (30% to 50%)
    - Psychiatric: Feeling nervous (30% to 50%)
  - severe
    - Gastrointestinal: Paralytic ileus
    - Neurologic: Confusion
    - Ophthalmic: Angle-closure glaucoma, Raised intraocular pressure
    - Psychiatric: Disorientated
**Titrate medication as follows**

Week 1 & 2: 0.1 mg/kg bid  
Week 3 & 4: 0.1 mg/kg tid

**Exclusions / Considerations**
- Use with caution in hepatic impairment, glaucoma, GI obstruction and post-NEC/short gut  
- Consider a Sinemet trial for patients with prominent choreiform movements as these may be exacerbated by Artane

**Anticipated Responders**
- Preterm  
- Upper limb dystonia  
- Younger age at treatment initiation  
- Normal cognitive ability

**Preparation**
- Available as 2 and 5 mg regular release tablets  
- Suspension prepared as 0.4mg/mL

**Side Effects/Adverse Drug Reactions (ADRs)**
- Dry mouth  
- Constipation  
- Blurred vision  
- Drowsiness  
- Forgetfulness  
- Behaviour changes  
- Transient irritability  
- Rarely, worsening of dystonia  
- Hallucinations

**Baseline Assessment**
- HAT  
- CCQ  
- COPM  
- Adapted Tardieu  
- Physical Exam

**4-6 Wk Assessment**
- HAT  
- Screen for ADRs  
- Physical Exam

**Reassessment in clinic at 4-6 weeks**

**Continue medication titration as follows**

Week 5 & 6: 0.15 mg/kg tid  
Week 7 & 8: 0.20 mg/kg tid  
Continue at 0.20 mg/kg tid until reassessment at 3 months

**Reassessment in clinic at 3 months**

- Expected optimal response at 3 to 4 months post-medication initiation  
- Consider increase to 0.25 mg/kg tid if suboptimal response

**Reassess in clinic every 3 months for first year of trial then**

- Reassess in clinic every 6 months with a repeat Baseline Assessment annually

**Follow up Assessment**
- HAT  
- CCQ  
- Screen for ADRs  
- Physical Exam

For suboptimal response or serious ADRs taper medication slowly over 4 weeks
Dosing:

- There are no guidelines for treating CP with carbi-levo dopa, so we have been using the guidelines developed for Dopa Responsive Dystonia

- Week 1 & 2: 1 mg/kg/day of L-dopa ÷ bid
- Week 3 & 4: 2 mg/kg/day of L-dopa ÷ bid
- Week 5 & 6: 3 mg/kg/day of L-dopa ÷ bid
- Week 7 & 8: 4 mg/kg/day of L-dopa ÷ bid
- Week 9 & 10: 5 mg/kg/day of L-dopa ÷ bid
- Week 11 & 12: 6 mg/kg/day of L-dopa ÷ bid
Dopamine does not cross the blood–brain barrier, but levodopa does

A peripheral decarboxylase inhibitor such as carbidopa is combined with levodopa to reduce the incidence of nausea and vomiting by inhibiting the peripheral conversion of levodopa to dopamine
Carbi–Levo Dopa

- Adverse effects

  - Common
    - Gastrointestinal: Nausea (5.5% to 5.7%)
    - Neurologic: Confusion (2.3% to 3.7%), Dizziness (2.3% to 2.9%), Headache (1.9% to 2%)

  - Serious
    - Cardiovascular: Myocardial infarction
    - Dermatologic: Malignant melanoma
    - Neurologic: Dyskinesia (12.2% to 16.5%)
    - Psychiatric: Depression (1.3% to 2.2%), Hallucinations (3.2% to 3.9%), Suicidal thoughts
    - Other: Neuroleptic malignant syndrome
**DRAFT**
*Levodopa (L-dopa)/carbidopa (Sinemet) Guideline for Dystonia Management*

**Exclusions / Considerations**
- 1st line if patient has prominent choreiform movements
- Consider if diagnosis or etiology unclear to rule out Dopa-responsive dystonia
- History of psychosis, hypertension and melanoma are contraindications

**Anticipated Responders**
- Upper limb dystonia

**Preparation**
- Preferred tablets for kid available as Levodopa 100mg/ Carbidopa 25mg regular release tablets
- Liquid preparation made as 5mg/1.25mg per mL

**Side Effects/Adverse Drug Reactions (ADRs)**
- Nausea and vomiting
- Somnolence
- Dyskinesia

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**Titrate medication as follows**
- Week 1 & 2: 1 mg/kg/day of L-dopa + bid
- Week 3 & 4: 2 mg/kg/day of L-dopa + bid
- Week 5 & 6: 3 mg/kg/day of L-dopa + bid

**Reassessment in clinic at 6 weeks**

**Continue medication titration as follows**
- Week 7 & 8: 4 mg/kg/day of L-dopa + bid
- Week 9 & 10: 5 mg/kg/day of L-dopa + bid
- Week 11 & 12: 6 mg/kg/day of L-dopa + bid
- Continue 6 mg/kg/day of L-dopa + bid until reassessment at 3 months

**Reassessment in clinic every 3 months for first year of trial then Reassess in clinic every 6 months with a repeat Baseline Assessment annually**

For suboptimal response or serious ADRs taper medication slowly over 4 weeks

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**Baseline Assessment**
- HAT
- CCQ
- COPM
- Adapted Tardieu
- Physical Exam

**6 Wk Assessment**
- HAT
- Screen for ADRs
- Physical Exam

**Follow up Assessment**
- HAT
- CCQ
- Screen for ADRs
- Physical Exam
Treatment Planning Summary

- Standardized baseline and follow up assessments
- Standardized timing of assessments
- Standardized dose titration
- Ongoing contact with Nurse Clinician for Adverse Drug Reactions
Care and Comfort Questionnaire

- Please rate how easy or difficult it is for you or your child in the last two weeks to perform the following tasks relative to a cooperative individual without a disability (try to distinguish between motor control and abnormal tone as the explanation for the problem):

  - **Personal Care**
  - 1. Putting on pants (trousers)? Very easy 1 2 3 4 5 6 7 Impossible N/A
  - 2. Taking off pants (trousers)? Very easy 1 2 3 4 5 6 7 Impossible N/A
  - 3. Putting on a shirt? Very easy 1 2 3 4 5 6 7 Impossible N/A
  - 4. Changing diapers? Very easy 1 2 3 4 5 6 7 Impossible N/A
  - 5. Ease of sitting on a toilet seat? Very easy 1 2 3 4 5 6 7 Impossible N/A
  - 6. Ease of sitting in a bathtub, with or without adaptive equipment? Very easy 1 2 3 4 5 6 7 Impossible N/A
Assessing the impact of therapy using an adapted questionnaire

Care and Comfort Caregiver Questionnaire (CareQ)

Patient’s name: __________ Date of birth: __/__/__ Date of visit: __/__/__

Name of person completing form: ________________________________

Relationship to patient: Mom  Dad  Other relative  Other nonrelative

For the sections on personal care and positioning, please rate how easy or difficult it is for you (the caregiver) to perform the following tasks. In the right-hand column, please indicate how much of the task your child is able to do himself or herself, for example, 20%, 50%, 80%, or some other percent that you believe is appropriate.

Thank you very much for taking the time to complete this questionnaire.

<table>
<thead>
<tr>
<th>Personal Care</th>
<th>Very Easy</th>
<th>Impossible</th>
<th>Child Is Able To Do:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Performing oral-facial hygiene (e.g., brushing teeth, washing face, combing hair)</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Putting on shirts</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Taking off shirts</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Putting on pants</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Taking off pants</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Changing incontinence pads or briefs (underwear)</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Cleaning buttocks or perineum with toileting</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Washing upper body</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Washing lower body</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Questions???