KAND and Spasticity

Jennifer Bain, MD PhD
Assistant Professor of Neurology and Pediatrics
Child Neurology Division

Jacqueline Montes, PT, EdD
Associate Professor of Rehabilitation and Regenerative Medicine
Programs in Physical Therapy
Outline

• Approach to Management
• Types of Movement Disorders
• Cerebral palsy (CP) versus KAND
• Treatment of spasticity
  – Medications
  – Surgeries
  – Therapies
Approach to management

- What is the phenomenology of the movement disorder?
  - Most common patient has a mixed generalized movement disorder
  - Generalized condition, focal difficulties

- What impairs function for the patient? What matters to the patient and what is their goal?
  - Treatments to alleviate generalized spasticity and dystonia
  - Treatments to target focal areas of dysfunction

- Multidisciplinary approach
  - Collaboration between neurology, orthopedics, rehab medicine, physical/occupational/speech therapy, social work, psychology/psychiatry
  - CP Center?
What is spasticity?

• Increased tone
  – Tone = passive/continuous contraction of muscle (helps keep posture)
  – dependent on how quickly a part of the body is moved passively

• Unwanted posturing and muscle tightening

• Can lead to contractures (shortening/tightening of the soft tissue)

• Sometimes spasticity can be helpful to provide strength for example when weak.
Other important abnormal movements...Dystonia

- Involuntary movement
- Unwanted posturing and twisting
- Can be focal or generalized
- Usually increases when attempting to move
- Relaxes during sleep
  - does not lead to contractures
Choreoathetosis

- Chorea – derived from Latin “choreus” meaning “dance”
  - Involuntary brief, random, irregular muscle movements
  - can look like restlessness (but patient does NOT feel restless)
  - No pattern and moves between parts of the body

- Athetosis
  - Slower, writhing movements
  - Some consider this on the continuum with chorea and others with dystonia

- Choreoathetosis
  - used when there is both chorea and athetosis
Ataxia

• Incoordination
  – Clumsy, unsteady walking, slurred speech

• Due to dysfunction in the cerebellum
Complications of Movement Disorders

• Limiting functional ability
  – Walking, feeding, cleaning, writing, typing

• Weight loss
  – due to high energy expenditure (plus difficulty with feeding, decreased food intake, difficulty swallowing)

• Contractures (tightening/shortening of soft tissue)
  – Seen with spasticity, not dystonia or choreoathetosis or ataxia

• Pain

• Injuries – fractures, dislocations, cuts/bruises/stitches
What is cerebral palsy?

- Motor disturbance (movement, posture, tone)
- “Injury” or “alteration” to the developing brain (<3yrs)
- Non-progressive injury
- Impaired function
IS KAND cerebral palsy?

Probably not....

CP is static while KAND is progressive.

We will be speaking on next few slides about spasticity from CP studies...NOT from KAND
Treating Movement Disorders

• Do we need to?
  – Yes if the movements are affecting quality of life

• How:
  – Identify the correct type of movement disorder
  – Physical therapy
  – Oral medications
  – Procedures
    > Botulinum toxin injections
    > Baclofen pump
    > Deep Brain Stimulation (DBS)
    > Selective dorsal rhizotomy (SDR)

Important to know what each can do AND cannot do, and what risks/side effects each has
DISCLAIMER***This is CP, NOT KAND!

BTX = BoNT = Botulinum NeuroToxin (type A)

DBS = Deep Brain Stimulation

ITB = IntraThecal Baclofen

SDR = Selective Dorsal Rhizotomy

Novak et al. DMCN, 2013
## Pharmacological Treatment for Generalized Movement Disorders

Oral medications to treat: 
- Spasticity
- Dystonia
- Dyskinesia

<table>
<thead>
<tr>
<th>Oral Medications</th>
<th>Mechanism of action</th>
<th>Dystonia</th>
<th>Chorea</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine agonists (levodopa)</strong>&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Enhances the activity of dopamine</td>
<td>Used</td>
<td>–</td>
<td>Nausea, orthostatic hypotension, and constipation</td>
</tr>
<tr>
<td><strong>Dopaminergic antagonist</strong>&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Blocks acetylcholine muscarinic receptors</td>
<td>Used</td>
<td>–</td>
<td>Drowsiness, confusion, memory difficulty, blurred vision, hallucinations, urinary retention, and worsening chorea</td>
</tr>
<tr>
<td><strong>Benzodiazepine receptor agonists (diazepam, clonazepam)</strong>&lt;sup&gt;15,16&lt;/sup&gt;</td>
<td>Enhances GABA-A inhibition</td>
<td>Used</td>
<td>Used</td>
<td>Sedation, confusion, depression, ataxia, and dependence</td>
</tr>
<tr>
<td><strong>GABA-B receptor antagonist</strong>&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Enhances the activity of GABA-B receptor</td>
<td>Used</td>
<td>–</td>
<td>Worsening chorea, incontinence, sedation, dizziness, dry mouth, and increased blood glucose</td>
</tr>
<tr>
<td><strong>Dopamine and serotonin antagonist (clozapine)</strong>&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Binds to serotonin and dopamine receptors and prevents release</td>
<td>Used</td>
<td>–</td>
<td>Decreased white blood cell count, sedation, hypotension, myocarditis, cardiomyopathy, drooling, arrhythmia, seizures, and diabetes mellitus</td>
</tr>
<tr>
<td><strong>Pre-synaptic α2 receptor agonist (clonidine)</strong>&lt;sup&gt;28&lt;/sup&gt;</td>
<td>Enhances the activity of pre-synaptic α2 receptor</td>
<td>Used</td>
<td>–</td>
<td>Orthostatic hypotension, bradycardia, sedation, fatigue, and headache</td>
</tr>
<tr>
<td><strong>Dopamine antagonists (piribedil, haloperidol)</strong>&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Antagonist of the D2, D3, and D4 dopamine receptors and the 5-HT&lt;sub&gt;1&lt;/sub&gt; receptor</td>
<td>–</td>
<td>Used</td>
<td>Hypotension, sedation, QT interval prolongation, and ventricular arrhythmias (including torsades de pointes); overdose causes severe extrapyramidal symptoms</td>
</tr>
<tr>
<td><strong>Monoamine blockers (tetrabenazine)</strong>&lt;sup&gt;31,33,36&lt;/sup&gt;</td>
<td>Inhibits vesicular monoamine transporter 2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine storage</td>
<td>Used</td>
<td>Used</td>
<td>Drowsiness, parkinsonism, depression, insomnia, anxiety, and akathisia</td>
</tr>
<tr>
<td><strong>Monoamine depleters (reserpine)</strong>&lt;sup&gt;35&lt;/sup&gt;</td>
<td>Blocks the vesicular monoamine transporter</td>
<td>–</td>
<td>Used</td>
<td>Nasal congestion, nausea, vomiting, weight gain, gastric intolerance, gastric ulceration, stomach cramps and diarrhoea, hypotension, bradycardia, and worsening of asthma</td>
</tr>
<tr>
<td><strong>Voltage-gated sodium and calcium channel blocker (carbamazepine)</strong>&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Blocks voltage-sensitive sodium channels</td>
<td>Used</td>
<td>–</td>
<td>Decreased white blood cell count and platelets; increased risk of suicide</td>
</tr>
<tr>
<td><strong>Calcium channel blocker (levetiracetam)</strong>&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Binds to a synaptic vesicle glycoprotein and inhibits presynaptic calcium channels, reducing neurotransmitter release and acting as a neuromodulator</td>
<td>–</td>
<td>Used</td>
<td>Somnolence, decreased energy, headache, dizziness, and (mild) ataxia</td>
</tr>
<tr>
<td><strong>Muscle tone reducer (dantrolene)</strong>&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Reduces skeletal muscle tone at the muscle fibre level</td>
<td>–</td>
<td>Used</td>
<td>Speech and visual disturbances; depression and confusion; hallucinations; headache; insomnia and exacerbation or precipitation of seizures, and increased nervousness</td>
</tr>
<tr>
<td><strong>Voltage-gated calcium channel blocker (gabapentin)</strong>&lt;sup&gt;45&lt;/sup&gt;</td>
<td>Antagonises binding of thrombospondin to voltage-gated calcium channel α2δ-1 receptors and inhibits synthesis of glutamnergic excitatory synapses</td>
<td>Used</td>
<td>–</td>
<td>Dizziness, drowsiness, sedation, fever, fatigue, viral infection, ataxia, and myasthenia</td>
</tr>
</tbody>
</table>

*Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinetic cerebral palsy*

Source: Monbaliu et al. Lancet Neurology 2017
Benzodiazepines

- Clonazepam (Klonopin)
- Diazepam (Valium)

- Treats dystonia, choreoathetosis, and spasticity

Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinetic cerebral palsy

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Dystonia</th>
<th>Chorea</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists (levodopa)</td>
<td>Used</td>
<td>--</td>
<td>Nausea, orthostatic hypotension, and constipation</td>
</tr>
<tr>
<td>Anticholinergic (trihexyphenidyl, benztropine)</td>
<td>Blocks acetylcholine muscarinic receptor</td>
<td>Used</td>
<td>Drowsiness, confusion, memory difficulty, blurred vision, hallucinations, urinary retention, and worsening chorea</td>
</tr>
<tr>
<td>GABA-B receptor agonist (bacoside)</td>
<td>Enhances GABA-A inhibition</td>
<td>Used</td>
<td>Sedation, confusion, depression, ataxia, and independence</td>
</tr>
<tr>
<td>Dopamine and serotonin antagonist (cilazapine)</td>
<td>Enhances the activity of GABA-B receptor</td>
<td>Used</td>
<td>Worsening chorea, incontinence, sedation, dizziness, dry mouth, and increased blood glucose</td>
</tr>
<tr>
<td>Pre-synaptic a2 receptor agonist (clonidine)</td>
<td>Enhances the activity of pre-synaptic a2 receptor</td>
<td>Used</td>
<td>Orthostatic hypotension, bradycardia, sedation, fatigue, and headache</td>
</tr>
<tr>
<td>Dopamine antagonists (pimozide, haloperidol)</td>
<td>Antagonist of the D2, D3, and D4 dopamine receptors, and the 5-HT, receptor</td>
<td>Used</td>
<td>Hypotension, sedation, QT interval prolongation, and ventricular arrhythmias (including torsades de pointes); overdose causes severe extrapyramidal symptoms</td>
</tr>
<tr>
<td>Monoamine blockers (tetrahydrozine)</td>
<td>Inhibits vesicular monoamine transporter 2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine storage</td>
<td>Used</td>
<td>Drowsiness, parkinsonism, depression, insomnia, anxiety, and akathisia</td>
</tr>
<tr>
<td>Monoamine depleters (reserpine)</td>
<td>Blocks the vesicular monoamine transporter</td>
<td>Used</td>
<td>Nasal congestion, nausea, vomiting, weight gain, gastric intolerance, gastric ulceration, stomach cramps and diarrhoea, hypotension, bradycardia, and worsening of asthma</td>
</tr>
<tr>
<td>Voltage-gated sodium and calcium channel blocker (carbamazepine)</td>
<td>Blocks voltage-sensitive sodium channels</td>
<td>Used</td>
<td>Decreased white blood cell count and platelets; increased risk of suicide</td>
</tr>
<tr>
<td>Calcium channel blocker (levetiracetam)</td>
<td>Binds to a synaptic vesicle glycoprotein and inhibits presynaptic calcium channels, reducing neurotransmitter release and acting as a neuromodulator</td>
<td>Used</td>
<td>Somnolence, decreased energy, headache, dizziness, and (mild) ataxia</td>
</tr>
<tr>
<td>Muscle tone reducer (dantrolene)</td>
<td>Reduces skeletal muscle tone at the muscle fibre level</td>
<td>Used</td>
<td>Speech and visual disturbances; depression and confusion; hallucinations; headache; insomnia and exacerbation or precipitation of seizures, and increased nervousness</td>
</tr>
<tr>
<td>Voltage-gated calcium channel blocker (gabapentin)</td>
<td>Antagonises binding of thromboxane to voltage-gated calcium channel a2a-1 receptors and inhibits synthesis of glutaminergic excitatory synapses</td>
<td>Used</td>
<td>Dizziness, drowsiness, sedation, fever, fatigue, viral infection, ataxia, and myasthenia</td>
</tr>
</tbody>
</table>

Source: Monbaliu et al. Lancet Neurology 2017
Baclofen

- Treats dystonia and spasticity

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Dystonia</th>
<th>Chorea</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists (levodopa)</td>
<td>Enhances the activity of dopamine</td>
<td>Used</td>
<td>Used</td>
</tr>
<tr>
<td>Anticholinergic (trihexphenidyl, benztropine)</td>
<td>Blocks acetylcholine muscarinic receptor</td>
<td>Used</td>
<td>Used</td>
</tr>
<tr>
<td>Benzodiazepine receptor agonists (diazepam, clonazepam)</td>
<td>Enhances GABA-A inhibition</td>
<td>Used</td>
<td>Used</td>
</tr>
<tr>
<td>GABA-B receptor agonist (bacosene)</td>
<td>Enhances the activity of GABA-B receptor</td>
<td>Used</td>
<td>–</td>
</tr>
<tr>
<td>Dopamine and serotonin antagonist (clonazepam)</td>
<td>Binds to serotonin and dopamine receptors and prevents release</td>
<td>Used</td>
<td>–</td>
</tr>
<tr>
<td>Pre-synaptic α2 receptor agonist (clonidine)</td>
<td>Enhances the activity of pre-synaptic α2 receptor</td>
<td>Used</td>
<td>–</td>
</tr>
<tr>
<td>Dopamine antagonists (pimozide, haloperidol)</td>
<td>Antagonist of the D2, D3, and D4 dopamine receptors, and the 5-HT, receptor</td>
<td>–</td>
<td>Used</td>
</tr>
<tr>
<td>Monoamine blockers (tetrahydrozine)</td>
<td>Inhibits vesicular monoamine transporter 2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine storage</td>
<td>Used</td>
<td>Used</td>
</tr>
<tr>
<td>Monoamine depleters (reserpine)</td>
<td>Blocks the vesicular monoamine transporter</td>
<td>–</td>
<td>Used</td>
</tr>
<tr>
<td>Voltage-gated sodium and calcium channel blocker (carbamazepine)</td>
<td>Blocks voltage-sensitive sodium channels</td>
<td>Used</td>
<td>–</td>
</tr>
<tr>
<td>Calcium channel blocker (levetiracetam)</td>
<td>Binds to a synaptic vesicle glycoprotein and inhibits presynaptic calcium channels, reducing neurotransmitter release and acting as a neuromodulator</td>
<td>–</td>
<td>Used</td>
</tr>
<tr>
<td>Muscle tone reducer (dantrolene)</td>
<td>Reduces skeletal muscle tone at the muscle fibre level</td>
<td>Used</td>
<td>–</td>
</tr>
<tr>
<td>Voltage-gated calcium channel blocker (gabapentin)</td>
<td>Antagonises binding of thromboxane to voltage-gated calcium channel α2δ-1 receptors and inhibits synthesis of glutaminergic excitatory synapses</td>
<td>Used</td>
<td>–</td>
</tr>
</tbody>
</table>

Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinetic cerebral palsy

Source: Monbaliu et al. Lancet Neurology 2017
Levodopa
- always given as carbidopa/levodopa (Sinemet)
- Treats dystonia

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Dystonia</th>
<th>Chorea</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists (levodopa)(^{35})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticholinergic (trihexphenidyl, benzatropine)(^{25,35})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine receptor agonists (diazepam, clonazepam)(^{15,35})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABA-B receptor agonist (baclofen)(^{35,55,56})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine and serotonin antagonist (clozapine)(^{25})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-synaptic α2 receptor agonist (clonidine)(^{35})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine antagonists (pinazoxide, haloperidol)(^{4})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoamine blockers (tetrabenazine)(^{15,5,36})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoamine depleters (reserpine)(^{4})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voltage-gated sodium and calcium channel blocker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel blocker (levetiracetam)(^{35,36})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle tone reducer (dantrolene)(^{35})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voltage-gated calcium channel blocker (gabapentin)(^{35})</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinetic cerebral palsy

Source: Monbaliu et al. Lancet Neurology 2017
<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Dystonia</th>
<th>Chorea</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists (levodopa)</td>
<td>Enhances the activity of dopamine</td>
<td>Used</td>
<td>Nausea, orthostatic hypotension, and constipation</td>
</tr>
<tr>
<td>Anticholinergic (trihexyphenidyl, benzatropine)</td>
<td>Blocks acetylcholine muscarinic receptor</td>
<td>Used</td>
<td>Drowsiness, confusion, memory difficulty, blurred vision, hallucinations, urinary retention, and worsening chorea</td>
</tr>
<tr>
<td>Benzodiazepine receptor agonists (diazepam, clonazepam)</td>
<td>Enhances GABA-A inhibition</td>
<td>Used</td>
<td>Sedation, confusion, depression, ataxia, and dependence</td>
</tr>
<tr>
<td>GABA-B receptor agonist (bacosides)</td>
<td>Enhances the activity of GABA-B receptor</td>
<td>Used</td>
<td>Worsening chorea, incontinence, sedation, dizziness, dry mouth, and increased blood glucose</td>
</tr>
<tr>
<td>Dopamine and serotonin antagonist (clozapine)</td>
<td>Blocks serotonin and dopamine receptors and prevents release</td>
<td>Used</td>
<td>Decreased white blood cell count, sedation, hypotension, myocarditis, cardiomyopathy, drooling, arrhythmia, seizures, and diabetes mellitus</td>
</tr>
<tr>
<td>Pre-synaptic α2 receptor agonist (clonidine)</td>
<td>Enhances the activity of pre-synaptic α2 receptor</td>
<td>Used</td>
<td>Orthostatic hypotension, bradycardia, sedation, fatigue, and headache</td>
</tr>
<tr>
<td>Dopamine antagonists (pimozide, haloperidol)</td>
<td>Antagonist of the D2, D3, and D4 dopamine receptors, and the 5-HT[1A] receptor</td>
<td>-</td>
<td>Hypotension, sedation, QT interval prolongation, and ventricular arrhythmias (including torsades de pointes); overdose causes severe extrapyramidal symptoms</td>
</tr>
<tr>
<td>Monoamine blockers (tetrabenazine)</td>
<td>Inhibits vesicular monoamine transporter 2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine storage</td>
<td>Used</td>
<td>Drowsiness, parkinsonism, depression, insomnia, anxiety, and akathisia</td>
</tr>
<tr>
<td>Monoamine depleters (reserpine)</td>
<td>Blocks the vesicular monoamine transporter</td>
<td>-</td>
<td>Nasal congestion, nausea, vomiting, weight gain, gastric intolerance, gastric ulceration, stomach cramps and diarrhoea, hypotension, bradycardia, and worsening of asthma</td>
</tr>
<tr>
<td>Voltage-gated sodium and calcium channel blocker (carbamazepine)</td>
<td>Blocks voltage-sensitive sodium channels</td>
<td>Used</td>
<td>Decreased white blood cell count and platelets, increased risk of suicide</td>
</tr>
<tr>
<td>Calcium channel blocker (levetiracetam)</td>
<td>Binds to a synaptic vesicle glycoprotein and inhibits presynaptic calcium channels, reducing neurotransmitter release and acting as a neuromodulator</td>
<td>-</td>
<td>Somnolence, decreased energy, headache, dizziness, and (mild) ataxia</td>
</tr>
<tr>
<td>Muscle tone reducer (dantrolene)</td>
<td>Reduces skeletal muscle tone at the muscle fibre level</td>
<td>Used</td>
<td>Speech and visual disturbances, depression and confusion, hallucinations, headache; insomnia and exacerbation or precipitation of seizures, and increased nervousness</td>
</tr>
<tr>
<td>Voltage-gated calcium channel blocker (gabapentin)</td>
<td>Antagonises binding of thromboplatin to voltage-gated calcium channel α2δ-1 receptors and inhibits synthesis of glutaminergic excitatory synapses</td>
<td>Used</td>
<td>Dizziness, drowsiness, sedation, fever, fatigue, viral infection, ataxia, and myasthenia</td>
</tr>
</tbody>
</table>

Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinetic cerebral palsy

Source: Monbaliu et al. Lancet Neurology 2017
Tetrabenazine

- Newer formulations:
  - Valbenazine
  - Deutetetabenazine

- Treats dystonia and choreoathetosis

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Dystonia</th>
<th>Chorea</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine agonists (levodopa)</td>
<td></td>
<td></td>
<td>Nausea, orthostatic hypotension, constipation</td>
</tr>
<tr>
<td>Anticholinergic (trihexyphenidyl, benztropine)</td>
<td></td>
<td></td>
<td>Drowsiness, confusion, memory difficulty, blurred vision, hallucinations,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>urinary retention, and worsening chorea</td>
</tr>
<tr>
<td>Benzodiazepine receptor agonists</td>
<td></td>
<td></td>
<td>Sedation, confusion, depression, ataxia, and dependence</td>
</tr>
<tr>
<td>(diazepam, clonazepam)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABA-B receptor agonist (baclofen)</td>
<td></td>
<td></td>
<td>Worsening chorea, incoordination, sedation, dizziness, dry mouth, and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>increased blood glucose</td>
</tr>
<tr>
<td>Dopamine and serotonin antagonist (clonazepine)</td>
<td></td>
<td></td>
<td>Decreased white blood cell count, sedation, hypotension, myocarditis,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>cardiomyopathy, drooling, arrhythmia, seizures, and diabetes mellitus</td>
</tr>
<tr>
<td>Pre-synaptic α2 receptor agonist (clonidine)</td>
<td></td>
<td></td>
<td>Orthostatic hypotension, bradycardia, sedation, fatigue, and headache</td>
</tr>
<tr>
<td>Dopamine antagonists (pimozide, haloperidol)</td>
<td></td>
<td></td>
<td>Hypotension, sedation, QT interval prolongation, and ventricular arrhythmias</td>
</tr>
<tr>
<td>(pimozide, haloperidol)</td>
<td></td>
<td></td>
<td>(including torsades de pointes); overdose causes severe extrapyramidal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>symptoms</td>
</tr>
<tr>
<td>Monoamine blockers (tetrabenazine)</td>
<td></td>
<td></td>
<td>Drowsiness, parkinsonism, depression, insomnia, anxiety, and akathisia</td>
</tr>
<tr>
<td>(pimozide, haloperidol)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoamine depleters (reserpine)</td>
<td></td>
<td></td>
<td>Nasal congestion, nausea, vomiting, weight gain, gastric intolerance,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>gastric ulceration, stomach cramps and diarrhea, hypotension, bradycardia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>and worsening of asthma</td>
</tr>
<tr>
<td>Voltage-gated sodium and calcium channel blocker (carbamazepine)</td>
<td></td>
<td></td>
<td>Decreased white blood cell count and platelets; increased risk of suicide</td>
</tr>
<tr>
<td>Calcium channel blocker (levetiracetam)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle tone reducer (dantrolene)</td>
<td></td>
<td></td>
<td>Speech and visual disturbances, depression and confusion; hallucinations;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>headache; insomnia and exacerbation or precipitation of seizures, and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>increased nervousness</td>
</tr>
<tr>
<td>Voltage-gated calcium channel blocker (gabapentin)</td>
<td></td>
<td></td>
<td>Dizziness, drowsiness, sedation, fever, fatigue, viral infection, ataxia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>and myasthenia</td>
</tr>
</tbody>
</table>

Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinetic cerebral palsy

Source: Monbaliu et al. Lancet Neurology 2017
Botulinum Toxin Injections

- Neurotoxin produced by bacterium Clostridium Botulinum
- Blocks communication between the nerve and the muscle
- Used in small doses to treat spasticity and dystonia (rehab, neurology, orthopedics)
- Benefit is a result of correct muscle target and dose
  - Trial and error
- Takes 2-7 days to work and can last on average about 12 weeks
- Used to treat focal spasticity and dystonia
  - Wide variety of indications in adults
  - Only approved in children for gastrocnemius spasticity; often used off label for other indications
- For spasticity the rehab specialists also use ethanol
- as noted above, may “worsen” strength before it gets better!

Nahm et al. CO Ped 2018
Goal of treatment:
- Improve function
- Prevent/minimize contractures (due to spasticity)
- Alleviate pain

Success is dependent on:
- correct dosage
- muscle target

Side effects/concerns:
- Short term: bleeding, bruising, local infection
- Weakness
- Long term: Muscle atrophy with long term use

Nahm et al. CO Ped 2018
Surgical Treatment Options:

- Baclofen Pump
  - Spasticity and dystonia

- Selective dorsal rhizotomy
  - Spasticity in legs

- Deep Brain Stimulation (DBS)
  - Dystonia
Intrathecal Baclofen in CP

- Treats **spasticity**, as well as dystonia

- Benefits of direct delivery to CNS:
  - Lower doses needed and avoids systemic side effects seen with oral baclofen
  - Continuous delivery of medication

Nahm et al. CO Ped 2018
Intrathecal Baclofen in CP

- Data shows ITB can:
  - improve tone
  - improve quality of life
  - Improve kinematic gait parameters

Nahm et al. CO Ped 2018

Intrathecal Baclofen (ITB) in CP

- Contraindications
  - baclofen sensitivity
  - body size cannot fit reservoir between ribs and iliac crest
  - poor compliance or inability to follow up regularly

- Complications
  - infection
  - wood dehiscence
  - CSF leaks
  - catheter clogs
  - abrupt interruption of baclofen can lead to life-threatening withdrawal (muscle spasms, dysesthesias, pruritis, agitation, rhabdomyolysis)

Nahm et al. CO Ped 2018
Selective Dorsal Rhizotomy (SDR) in CP

This is permanent! Discuss with a larger team as it is a big decision!
Deep Brain Stimulation (DBS) in CP

- Used to treat refractory dystonia
- Data has shown mixed results
  - Not permanent – on/off
  - Need more data
  - More difficult to identify target (Gpi or thalamus)
  - More difficult to quantify benefit?
- Complications:
  - Surgical: infection, hemorrhage
  - Hardware: device malfunction, lead migration, infection
  - Stimulation: improper placement, improper parameter settings
Orthopedic interventions

• Disclaimer….not orthopedic surgeons

• Many different procedures.

• Must be aware of progression of disease.

• Post operative regression and rehab course.

• Sometimes its okay to have imperfect hips!
Serial Casting

- Prolonged static positioning to promote soft tissue lengthening
- Typically done across 1 joint (ankles, knees, elbows)
- Casts are applied in series for long term passive stretching (4-6 weeks)
- Weekly cast changes:
  - assessments of skin integrity and range of motion
- Walking boots and weight bearing allowed for lower extremity casts
- Can be a stand-alone treatment or done with Botox injections
Physical Therapy

• School-based, outpatient, and/or home therapies

• Goals are to maximize function

• Flexibility, strengthening, and conditioning

• Mobility (home and community)

• Assistive devices and technology to enhance participation

  (from different providers)
Range of Motion / Stretching

- Orthoses and splints for upper and lower limbs
- Active-assisted and passive techniques
- Supported supine/standing frames
- Thoracic bracing – postural support
Strengthening

Exercise should be encouraged, incorporated into daily living, and age-appropriate

**Duration:** Minimum < 15 minutes (recovery time included), > 15 minutes optimal

**Frequency:** 2–3 times/week minimum, > 3 times/week optimal
Aerobic Exercise

Exercise should be encouraged, incorporated into daily living, and age-appropriate

- Swimming
- Active video game technology
- Hippotherapy
- Upper and/or lower-extremity ergometry
- Walking
- Yoga/Pilates
- Wheelchair sports

**Duration:** ≥ 30 minutes/session

**Frequency:** 2–3 times/week minimum, up to 5x times/week optimal
### Misconceptions?

- “Medications have one response in all patients”
  - Every patient is different
  - Trial and Error
  - Work together with doctor to see how you do (YOU know your body better than anyone)

- “More medication = more benefit”

- “One medication at a higher dose is better than two medications together”

- “One pill or surgery will fix everything”

- “One doctor can manage it all”
  - Collaboration in important

- Balance of different opinions (parents, providers, researchers)

- **WE DON’T KNOW THE RIGHT DECISION** for KAND! Natural History Study may be more telling.
Thank you