Identification and management of movement disorders – the role of oral medication.

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**Definition and identification of movement disorders**

- **Movement disorders**: A group of neurological disorders that affect movement or posture. They can be divided into hyperkinesia and hypokinesia.

**Hyperkinesia** (Hyper-kinesis; -kinesis)

Characterized by involuntary movements or over- or part of voluntary movements.

**Hypokinesia** (Hypo-kinesis; -kinesis)

Characterized by a reduction or absence of normal movements. It can be caused by a primary neurological disorder or a side effect of medication.

**SPASTICITY**

Isokinetic movement disorder characterized by a velocity dependent increased resistance to passive muscle stretch. The resistance varies with the direction of joint movement and increase rapidly above a threshold speed or joint angle. Felt not seen.

**HYPERKINESIS**

Any unwanted or excess movements seen in children with neurologic disorders. Usually associated with injury to the basal ganglia, cerebral cortex, cerebellum or other motor pathways due to static or progressive injury.

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- **Achilles tendon**: A thick band of tissue that connects the calf muscles to the heel bone.

**DYSTONIA**

A slow, continuous, involuntary writhing movement that prevents maintenance of a stable posture. Continuous, smooth, repeated but not sustained.

- **Tics**: Repeated, individually recognizable intermittent movements or movement fragments that are almost always briefly suppressible and are usually associated with an awareness of an urge to perform the movement.

**MYOCLONUS**

A sequence of repeated, often non-rhythmic, brief, shock-like jerks due to sudden involuntary contraction of relaxation of one or more muscles.

**CHOREA**

Ongoing and random appearing sequence of one or more discrete involuntary movements, or movement fragments. Random due to variations in timing, duration, direction, anatomic location.

**STEREOTYPIES**

Repetitive, simple movements that can be voluntarily suppressed.

**TREMOR**

A rhythmic back-and-forth or oscillating involuntary movement about a joint axis.

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**SCHOOL**

A sequence of repeated, often non-rhythmic, brief, shock-like jerks due to sudden involuntary contraction of relaxation of one or more muscles.

**TREMOR**

A rhythmic back-and-forth or oscillating involuntary movement about a joint axis.

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### WHO?

**Physical Disability**

- Cerebral Palsy
  - Ex-premature
  - Hypoxia at birth
  - Other
- Neuropathological conditions
  - Pantothenate kinase-associated neurodegeneration
  - Wilson’s Disease
  - Alcardi-Goutieres
  - Other leukodystrophies
  - Pontocerebellar hypoplasia

### GENERAL HEALTH

#### Under-estimated
- Under-recognized
- Anxiety
- Mood
- Pain
- SE medications
- Insomnia
- Fear & guilt
- Social isolation
- Exhaustion
- Poor sleep

#### First line treatment
- Shared neurobiology

#### Mobilty
- Diet
- Drugs
- GUT

#### General Health
- Sleep
- Secretions
- Pain
- Mood
- Hunger
- OSA
- Habits
- GORD

#### Anxiety & Mood
- Epilepsy
- Medication SE
- Control

#### Epilepsy
- Breathing
- SLEEP
- Secretions
- GUT

#### Nutrition
- Anxiety
- Sleep

#### Nutrition
- GUT

- **Acquired Brain Injury**
  - Hypoxic Encephalopathy
  - Infection
  - Traumatic
  - Post-tumour

#### Spinal Cord Lesions
- Familial/hereditary
- Spastic paraparesis
- Spinal cord injury

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- GUT
Cerebral palsy

**TREATMENT OPPORTUNITY**

**CONTEXTUAL**

PSYCHO-COGNITIVE FUNCTION

MOVEMENT DISORDER

NEURO BIOLOGICAL

COMPLICATION OF Rx

**FIRST LINE Rx**

Rx MOOD ANXIETY

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**Cerebral palsy**

**CONTEXT**

**SHARED NEUROBIOLOGY**

**MEDICATIONS**

**MEASUREMENT TOOLS**

MD & MOOD

Understanding of symptom evolution

Predictive

Anticipatory

Timing of management

**Best agents**

Potential neurobiological consequences

**Efficacy**

---

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**GABA-active medications**

BACLOFEN

DIAZEPAM

**Anti-epileptics**

GABAPENTIN

LEVETIRACETAM

TOPIRAMATE

**Anti-cholinergic**

BENZHEXOL

**Neuroleptics**

TETRABENZAMINE

RESERPIE

**DOPA-active drugs**

LEVODOPA

BROMOCPRTINE

PERGOLIDE

**DOPA-antagonists depleters**

CHLORPROMAZINE

**A2-adrenergic Agonists**

CLONIDINE

TIZANIDINE

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**WHEN?**

**INDIVIDUALIZED**

Symptom driven

Personal care

Day to day function

Sleep

Pain

Age NOT a barrier

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**TONE MIGHT BE IMPORTANT**

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**FIRST LINE CHOICE**

BACLOFEN

Clinical population

Clinical experience

Local preference

BACLOFEN

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**BACLOFEN**

Binds to pre-synaptic GABA<sub>A</sub> receptors in the brain and dorsal horn spinal cord and other sites

Inhibits release of excitatory NT from pre-synaptic membrane

Dampens effect of excitatory NT at post synaptic membrane

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**BACLOFEN**

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AusACPDM 2016 Current concepts in tone management, surgery & rehab for the ambulant child with CP
**BACLOFEN**

- Spasticity
- Dystonia
- Muscle spasm
- Muscle tone

Ease of care
- Improve sleep
- Pain
- Seating
- Personal care
- ? Functional gains

Tablet (only!)
- Given orally or via PEG
- Start low, go slow to avoid SE
- Start with night-time dosing
- 2.5-5.0mg nocte
- Maximum doses 2-3mg/kg per day
- Best given 3 to 4 times a day
- 10mg, 25mg tablets
- Easy to get & give

**DIAZEPAM**

Binds to γGABA<sub>A</sub> receptors
- At both spinal and supra spinal sites

Similar action to baclofen via different GABA receptor

Ease of care
- Improve sleep
- Pain
- Seating
- Personal care
- ? Functional gains

Tablet & oral liquid available
- Start low, go slow
- Start with night-time dosing
- Starting dose ≈ 0.03mg/kg/dose
- In practice 0.5mg
- Nocte dosing common
- Two to three times daily dosing
- 2mg, 5mg tablets
- Oral liquid 1mg/ml
- Available on PBS Authority
  “Disabling spasticity”

**SE**

Sedation
- Weakness
- Constipation
- Nausea
- Headache
- Low mood

Risk of withdrawal, gradually stop

Commonly used in post-operative care for spasm and dystonia management

- Small doses in combination with baclofen at night very effective

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GABAPENTIN

Exact action in the brain
Structurally related to GABA (γ-aminobutyric acid)
No evidence of capacity to bind to GABA_A or GABA_B receptors
Not converted into GABA or αGABA
Not an inhibitor of GABA uptake or degradation
MECHANISM OF ACTION UNCLEAR

Multiple reported actions
Anti-epileptic
Management of neuropathic pain
↓ Dystonia
↓ Anxiolytic
Management of dysautonomia
↓ Gut pain
↓ Food tolerance

GABAPENTIN

Multiple reported actions
NEUROPATHIC PAIN
- Pain-related responses in neuropathic pain models (including spinal injury)
ALLODYNA
- Pain-related behavior in response to a normally innocuous stimulus
HYPERALGESIA
- Exaggerated response to painful stimuli
INFLAMMATION
- Pain-related responses following peripheral inflammation

GABAPENTIN

Tablet (only)!
Orally or via PEG
Start with night-time dosing
Best given 3 times a day
Starting dose 10-15 mg/kg/day
< 5 years: 40 mg/kg/day
> 5 years: 25-35 mg/kg/day
Max doses 50-60mg/kg/day
100, 300, 400, 600, 800mg tablets
Wide therapeutic range
Peri-operative management
Palliative care
?EVIDENCE

GABAPENTIN

Sedation
Ataxia
Weakness
Dizziness
Emotional lability
Low mood
Agitation, aggression
Hyperactivity

Flu-like symptoms when starting
May exacerbate myoclonic epilepsy
**BENZHEXOL**

Acetylcholine agonist

Acts at muscarinic receptors both peripheral and centrally

**Trihexyphenidyl**

- Involuntary movements
- Muscle spasm
- Muscle stiffness
- Dystonia
- Saliva production

- Excessive movements
- Muscle stiffness may help with personal care?
  - Functional gains

Tablet (only!)

Orally or via PEG

Gradual increase to ↓ SE

Starting dose 0.5-1.0mg tds or qid

Higher doses tolerated in children cf adults

High doses often required

Up to 100mg/day in some studies

2mg, 5mg tablets

Potential interactions with other medications

Potential benefit in specific children

**SE**

- Involuntary movements
- Muscle spasm
- Muscle stiffness
- Dystonia
- Saliva production

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Agitation

Constipation

Behavioral changes

Hallucinations

Low mood

Aggression

Urinary retention

Dry mouth

Blurred vision

Reduced heat tolerance

Poor sleep

**LEVODOPA**

Dopamine is a catecholamine NT active in neurons of both the central and peripheral nervous systems

D1 receptor subtype - D1, D5

D2 receptor subtype - D2 D3 D4

Major transmitter in the extrapyramidal system of the brain, and important in regulating movement

Dopamine does not cross BBB, however, levodopa can and in converted centrally
LEVODOPA

- Muscle stiffness
- Muscle tremors
- Muscle spasms
- Poor muscle control
- Saliva production

Excessive movements
Muscle stiffness may help with function and activity
Specific role in conditions where dopamine levels are low

LEVODOPA

- Muscle stiffness
- Muscle tremors
- Muscle spasms
- Poor muscle control
- Saliva production

Excessive movements
Muscle stiffness may help with function and activity
Specific role in conditions where dopamine levels are low

Increase very slowly
Dose too quickly can cause dyskinesia if underlying dopamine deficiency

Madopar® 62.5 Rapid contains 50mg L-dopa
Starting dose 0.3mg/kg/DOSE
Aim for 10mg/kg/DAY (not DOSE)
Stay at this dose for a few weeks
No response = no benefit in ↑ dose
May take > time to see an change

TETRABENAZINE

Inhibition of monoamine transporter
Weak D₂ receptor-antagonist
Results in depletion of dopamine, serotonin & noradrenaline
Hypermobility in extrapyramidal disorders
Chorea in Huntington's Disease

Monitor BP when starting Rx
Tablet
Twice daily dosing
25mg tablets
Available on PBS
Careful dose titration
Maximum dose 50mg
Must increase slowly

CONTRA-INDICATED if history of depressive illness
↑ Risk suicide risk

Dyskinesia
Chorea

Excessive movements
Primary role in adults management of focal dystonia

Safety not established in paediatric population

TETRABENAZINE

- Dyskinesia
- Chorea

Excessive movements
Primary role in adults management of focal dystonia

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Agitation
Anxiety
Hypotension
Sedation

Involuntary movements
Tremor
Mouth movements
Parkinsons-like symptoms
Drooling
Constipation
Depression
Weakness
Insomnia
Fatigue
PREGABALIN
Analogue of gamma-aminobutyric acid (GABA).
Pre-synaptic modulator of excitatory NT release by binding to alpha 2-delta protein part of voltage gated calcium channels
Neuropathic pain
Anxiety
Excessive movements
Pain management
Drug dependence and abuse
Alcohol dependence

Neuropathic pain ↓
Anxiety ↓
Excessive movements ↓
Pain management
Use in management of alcohol dependence and drug abuse
Baclofen has a similar role

PREGABALIN

PRE OPERATIVE MANAGEMENT

PRE-OPERATIVE ASSESSMENT
Part of routine care
Alert to physician of upcoming surgery
Plan available

DRUGS
Part of routine care
Additional Rx pre-op
Plan available

NUTRITION
PRE-OP TUNE UP
PRE-OP PLAN
(Two weeks prior)

Part of routine care
Alert to physician of upcoming surgery
Plan available

NUTRITION
Consider supplemental feeds
Management of reflux

Management of constipation
Oral aperients
Lactulose
Movicol®, Osmolax®
PR medications
Small or large volume enemas
Microlax®, Bisacodyl volume enema

FEVER
FERRITIN
B12, FOLATE
LIVER FUNCTION
ALBUMIN/PROTEIN
Nutritional markers
THYROID FUNCTION
VITAMIN D
ZINC
CO2

BLOOD WORK

RESPIRATORY
Baseline CO2
Overnight oximetry
Formal sleep study
Antibiotics
Nebulized saline
Hypertonic
Physiotherapy

Overnight respiratory support
CPAP
BIPAP
Supplemental oxygen

Atopy
Seasonal rhinitis
Allergic rhinitis
Intransal steroids

UA Secretion
management
Benzhexol, atropine
Botox®, Saliva control surgery
UA management
Dental health
**PRE OPERATIVE MANAGEMENT**

**CONSIDER PRE-SURGERY ADMISSION “TUNE-UP”**

**OPTIMIZE NUTRITION**
- Supplemental feeds
- Nasogastric/nasojejunal feeds short term

**OPTIMIZE RESPIRATORY FUNCTION**
- Intensive respiratory care
- Physiotherapy
- Antibiotics
- Nebulized saline
- Secretion management

**SECRETION MANAGEMENT**
- Benzhexol, glycopyrrolate, atropine
- Upper airway management
- Intranasal steroids
- Dental health

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**PRE OPERATIVE MANAGEMENT**

**TWO WEEKS PRIOR**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia</td>
<td>Gabapentin Aim for 200-300mg tds</td>
</tr>
<tr>
<td>GORD</td>
<td>Ranitidine 4-8mg/kg/day as bd dose</td>
</tr>
<tr>
<td>Constipation</td>
<td>Microlax® enema day prior</td>
</tr>
</tbody>
</table>

**ORAL FUNCTION POST-OP PERIOD**

- Borderline oral function
- Sedation, fasting, GORD, pain
- Unable to take usual medications
- Unable to manage nutrition, fluids, oral analgesics
- Dependence on IV access

**EVIDENCE**

↓ RISK = ↑ BENEFIT

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**www.akronchildrens.org**

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