Clinical Guideline
DYSTONIA: IDENTIFICATION, INVESTIGATION AND MANAGEMENT IN CHILDREN

SETTING
Bristol Royal Hospital For Children (BRHC)

FOR STAFF
Medical Staff

PATIENTS
Paediatric patients with dystonia

GUIDANCE

Background

Dystonia is a symptom of an abnormally functioning motor system. It can occur singly as a result of a genetic mutation or as part of more complex motor disease in children with brain injury or neurodegenerative disease. When acquired it most commonly occurs in association with cerebral palsy.

The definition of dystonia, as updated in 2013 by an international consensus committee of movement disorder experts, is as follows:

- Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both
- Dystonic movements are typically patterned, twisting, and may be tremulous
- Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation

Status dystonicus is a medical emergency presenting with widespread intractable contractions. It can cause rhabdomyolysis leading to multiorgan failure and in severe cases death. It may be triggered by severe gut dysmotility, medication withdrawal, infection or disruption to deep brain stimulation.

The scope of this guideline is to outline the identification, history and initial investigation and management of children with dystonia including the management of status dystonicus.

Advanced therapies such as Deep Brain Stimulation or Intrathecal Baclofen are not discussed in any detail in this guideline.
History

When a child is having abnormal movements suspected of being dystonia, it is important to take a focused history to see if this helps establish a possible cause which can be further investigated. It is important at this point to rule out a dystonic medication reaction for example secondary to metoclopramide. See table below.

<table>
<thead>
<tr>
<th>Table 2: Focused History and Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
</tr>
<tr>
<td>Pregnancy/Delivery:</td>
</tr>
<tr>
<td>Previous Miscarriages; Infections during pregnancy; bleeding during pregnancy; gestation at delivery; need for resuscitation/Apgars/Cord Gases;</td>
</tr>
<tr>
<td>Neonatal Period:</td>
</tr>
<tr>
<td>Resuscitation/Admission to NICU; problems establishing breastfeeding; jaundice; concerns about weight loss; neonatal infection/sepsis; neonatal encephalopathy; neonatal seizures;</td>
</tr>
<tr>
<td>Development and Schooling:</td>
</tr>
<tr>
<td>Ages milestones achieved (if achieved); Developmental delay/plateauing/regression; extra support in school; visual/hearing difficulties</td>
</tr>
<tr>
<td>Movement Disorder/Dystonia:</td>
</tr>
<tr>
<td>At what age where concerns raised; body distribution at onset and with progression; cause of dystonia over time; other associated movement problems; fluctuating during day; exacerbating factors such as sudden motion</td>
</tr>
<tr>
<td>Family History:</td>
</tr>
<tr>
<td>Consanguinity; movement disorders (not just dystonia); psychiatric history;</td>
</tr>
<tr>
<td>Complications of Dystonia:</td>
</tr>
<tr>
<td>Feeding problems; mobility issues; communication issues; pain; gastroenterological issues; musculoskeletal deformities/Growth</td>
</tr>
<tr>
<td>Medication History:</td>
</tr>
<tr>
<td>Current medications; previous medications to treat dystonia (and why stopped); medications which have worsened dystonia</td>
</tr>
<tr>
<td><strong>Examination</strong></td>
</tr>
<tr>
<td>Growth Parameters:</td>
</tr>
<tr>
<td>Height; weight; head circumference</td>
</tr>
<tr>
<td>Motor Disorder:</td>
</tr>
<tr>
<td>Dystonia- regions body effected; other hyperkinetic movements; spasticity; rigidity; eye movements (including saccades); weakness; ataxia; selective motor control; dyspraxia</td>
</tr>
<tr>
<td>General Examination:</td>
</tr>
<tr>
<td>Neurocutaneous stigmata; organomegaly; musculoskeletal deformity/scoliosis; cardiovascular abnormalities; respiratory abnormalities</td>
</tr>
</tbody>
</table>
Categorisation or Grading of Dystonia (See Table)

Dystonia is usually a fluctuating state which at its most extreme can be life threatening. Identifying the point of entering this stage is challenging.

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
</table>
| • Sits Comfortably  
• Regular Sleep  
• Stable on medication | • Irritable  
• Cannot Settle  
• Posturing interferes with sitting  
• Can only tolerate lying despite baseline medication | • Can’t tolerate lying  
• Sleep disturbed  
• No signs of metabolic or airway compromise | • Grade 3 plus metabolic disturbance: fever, dehydration, abnormal electrolytes, CK >1000 IU/L, myoglobinuria | • Severe generalised dystonia  
• Grade 4 with full metabolic decompensation (renal, metabolic) or respiratory-cardiovascular compromise: organ support required |
| • No assessment or change | • Assess in Days  
• Adjust dystonia plan | • Urgent assessment  
• Exclude metabolic decompensation  
• Escalate management may include hospital admission | • STATUS DYSTONICUS  
Manage in HDU or PICU | • STATUS DYSTONICUS  
Requires admission to PICU |

For a child with Grade 2-3 dystonia, on assessment it may be appropriate to escalate treatment.
Investigations in Dystonia

Investigation is dependent on the history and involves first excluding a dystonic medication reaction. There is a growing list of conditions giving rise to dystonia. Specific investigations should be sent if a diagnosis is suspected. If no diagnosis is suggested by history and examination first line investigations may include MRI brain with blood and urine tests. CSF is not routinely indicated unless a specific indication such as Glucose Transported Type 1 Deficiency is suspected. Investigation should be directed at the level of secondary or tertiary care.
Flow Chart 1: Initial Management of Dystonia

Is This Dystonia?

Yes

Exclude medication reaction- see appendix 1

No clear likely diagnosis

Focused history and Examination

Investigations specific to likely diagnosis (in some cases identification may be possible from history and examination alone)

MRI (consider CT if concern about hydrocephalus/space occupying lesion)

Blood Investigation:
- FBC + Blood film for acanthocytosis, LFT, Bone profile, CK, acylcarnitine, plasma amino acids, ammonia, lactate, DNA to save, copper, caeroplasmin, Vit B12, A,D+E, Folate, urate, TFT’s, homocysteine, white cell enzymes, Transferrin isoelectric focussing

Urine Investigations:
- Organic acids +/- toxicology

In light of results of 1st line investigations consider further testing
- Eg CSF +/- neurotransmitters, Genetic testing

Other forms of Hyperkinesia
- Chorea, Tics, Myoclonus

Other forms of Hypertonia:
- Spasticity, Rigidity

Other mimics of Dystonia
- Tonic Seizures, Sandifiers syndrome, torticollis, myotonia

Discontinue Medication
- Reassess need for further investigation
- Consider treatment with Promethazine or Diazepam (see table 4)

Differentiate from:

Drug related

Specific diagnosis

Other forms of Hyperkinesia
- Chorea, Tics, Myoclonus
Management of Dystonia

Once confirmed that a child has dystonia consideration may be given to management. This will depend upon type and grade of dystonia. In consideration of treating dystonia thought must be given both to the impact of the dystonia on the child and their family, the effect of removing the dystonia and side effects of the medication. For example medication may lead to drowsiness and a reduction in tone may lead to a loss of mobility. When deciding to treat dystonia the purpose of treatment and goal setting should be discussed with children and families. MDT involvement may be beneficial in goal setting. It may appropriate in the first instance to focus management not on treatment of the dystonia directly but on managing any exacerbating factors such as constipation, pain and reflux.

The flow charts 2 and 3 cover the initial management of dystonia in children.

Grade 1 Dystonia

This does not require change of current management or medication. If new diagnosis, consider whether child needs pharmacological treatment bearing in mind the contribution of dystonia to impairment, any potentially detrimental effects of reducing hypotonia- for example reducing mobility by reducing tone, and the side effects of medications.

If a cause has been found for dystonia which requires specific treatment eg glucose transporter receptor defects treat this. If dystonia is focal consider Botulinium toxin before systemic treatment.

Grade 2-3 Dystonia

For a child with Grade 2-3 dystonia, on assessment it may be appropriate to escalate treatment.

- In children not on medication, start Trihexyphenidyl in slow incremental doses or Gabapentin first
- Second line would include the least sedative dose of clonidine
- Baclofen may be added for spasticity
- Benzodiazepines and Chloral Hydrate may be used as add ons for their mild sedative effect
- Consider a Trial of Levodopa
- Children may require admission

Grade 4-5 Dystonia

This is a medical emergency and requires treatment as status dystonicus- see guidance below. Children should be managed in HDU and may require PICU.

Dystonia is usually a fluctuating state which at its most extreme can be life threatening. Identifying the point of entering this stage is challenging.
Flow Chart 2: Management of Dystonia

**Urgent Assessment**

**Look for Precipitants:**
- GORD
- Infection
- Constipation
- Pain
- Hip subluxation/Musculoskeletal cause
- Review medication for triggers
- Check ITB pump function

**Look for Signs of Metabolic Decompensation:**
- Fever
- Dehydration
- Myoglobinuria
- Abnormal electrolytes
- CK >1000

**Managed precipitants but ongoing symptoms and no metabolic decompensation**

For Focal dystonia consider Botulinium Toxin first

Trihexyphenidyl or Gabapentin
Doses in Table 4

2nd line medications
Clonidine at least sedating dose

Baclofen for spasticity
Doses in Table 4

**If Additional Treatment Needed**

Add on Medications:
- Benzodiazepines
- Chloral Hydrate

Used for mild sedation- see Table 4

Consider Trial of Levodopa

Consider if admission needed

Treat as Grade 4-5 Dystonia and admit to HDU or PICU as required
Status Dystonicus

Children with Grade 4 or 5 Dystonia are on the spectrum of status dystonicus and require admission to either HDU or PICU for management.

Management of status dystonicus involves simultaneous management of 4 themes10:

- Treating Precipitants of Status
- Supportive Care
- Sedation
- Dystonia Specific Medication

Identifying and Treating Precipitants

In around two thirds of cases there will be an identifiable cause10.

- Treat for possible sepsis
- Discontinue any possible pharmacological precipitants
- Treat constipation or GORD
- Look for musculoskeletal riggers such as hip subluxation
- Review ITB drivers for possible interruption

Supportive Care6

This aims to both limit the effects of muscle spasm, and side effects of medications used in management.

- IV hydration
- Antipyretics +/- cooling blankets
- Promoting comfort and sleep
- Analgesia
- Monitoring of CK, electrolytes and liver function
- Consideration of:
  - Inotropes
  - Renal replacement therapy
  - Intubation (may be required)

Sedation6

Some sedatives may treat dystonia (benzodiazepines/clonidine)

- First line IV clonidine
- IV midazolam (tolerance may develop quickly)
- Consider Chloral Hydrate and Enteral Clonidine
- General anaesthesia may be required eg propofol +/- paralytic agents (non-depolarizing eg rocuronium, avoid suxamethonium as it is depolarising)

Dystonia6

- Once acute dystonic crisis managed, consideration can be given to longer term management- see treatment of dystonia flow chart.

Refractory Cases

May require progression to neurosurgical intervention including test dose intrathecal baclofen (prior to consideration of pump) or Deep Brain Stimulation. Patients should be rereferred to the Complex Movement Disorder clinic for consideration of ITB and DBS.
Flow Chart 4 Management of Status Dystonicus

Identify and Treat Precipitants

Supportive Care
Including normothermia, analgesia and maintenance IV fluids

Admit to HDU/PICU

Monitor bloods during acute phase
CK, U+E’s and LFT’s

IV Clonidine infusion
1-2 micrograms/kg/hr

IV Midazolam infusion
Slow iv injection of 50-200 microgram/kg then infusion of 30 microgram/kg/hr increase according to response

Consider Chloral hydrate and enteral clonidine

General anaesthesia
(propofol with non-depolarising paralytic agent eg rocuronium)

Refractory cases
May require neurosurgical involvement
<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE</th>
<th>INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baclofen (GABA agonist enhancing central inhibitory neurotransmission)</td>
<td><strong>Orally:</strong> Initially 300 micrograms/kg daily in 4 divided doses; increased at weekly intervals. Maximum dose: 40 mg/day (less than 8 years of age) and 60 mg/day in older children.</td>
<td><strong>Side effects:</strong> Gastrointestinal (GI) disturbances, dry mouth, hypotension respiratory or cardiovascular depression, sedation or drowsiness, confusion. Severe withdrawal symptoms - wean gradually over 2 weeks.</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td><strong>Orally or rectally:</strong> 20-50 mg/kg (max 1g/dose) tds</td>
<td><strong>Side effects:</strong> Gastric irritant, rash, headache, ketonuria</td>
</tr>
<tr>
<td>Clonazepam</td>
<td><strong>Orally:</strong> 1-11 months: 250 micrograms nocte for 4 nights, increased over 2 weeks to 1 mg/day at night or in 3 divided doses 1-4 yrs: 250 micrograms nocte for 4 nights, increased over 2 weeks to 1-3 mg/day at night or in 3 divided doses 5-11 yrs: 500 micrograms nocte for 4 nights, increased over 2 weeks to 3-6 mg/day at night or in 3 divided doses 12-17 yrs: 1 mg nocte for 4 nights, increased over 2 weeks to 4-8 mg/day at night or in 3 to 4 divided doses</td>
<td><strong>Side effects:</strong> Anxiety, depression, or altered mood, ataxia, confusion, drowsiness, dizziness, dysarthria, fatigue, GI disorder, headache, hypotension, muscle weakness, nausea, sleep disruption, tremor, vertigo, visual disturbance, suicidal ideation, withdrawal symptoms.</td>
</tr>
<tr>
<td>Clonidine</td>
<td><strong>Orally:</strong> 1-5 micrograms/kg 8 hourly, total daily dose can be split to 4 hourly. <strong>IV infusion:</strong> (only use in HDU or PICU settings (In PICU consider loading dose first) 0.4 microgram/kg/hour up to 2 microgram/kg/hour. Total IV and oral daily doses are equivalent but consider if patient has been absorbing orally. <strong>Transdermal:</strong> (Consider for patients that aren’t absorbing oral clonidine). Calculate the total daily dose of oral/IV clonidine and round down to the nearest patch. Patch sizes 100, 200 or 300 micrograms/day. Patches to be replaced every 7 days.</td>
<td><strong>Side effects:</strong> Bradycardia, Hypotension. See Guideline Clonidine-administration of intravenous clonidine for status dystonicus on the high dependency unit (HDU) for further guidance (<a href="http://www.avon.nhs.uk/dms/Download.aspx?r=1&amp;did=23983&amp;f=ClonidineAdministrationOfIntravenousClonidineForSt-1.pdf">http://www.avon.nhs.uk/dms/Download.aspx?r=1&amp;did=23983&amp;f=ClonidineAdministrationOfIntravenousClonidineForSt-1.pdf</a>)</td>
</tr>
<tr>
<td><strong>Diazepam</strong></td>
<td><strong>Orally:</strong> Infants ≥ 6 months and children &lt;12 years: 0.12 to 0.8mg/kg/day in divided doses every 6 to 8 hours. Max 10mg/dose.</td>
<td><strong>Side effects:</strong> Drowsiness, irritability, respiratory depression.</td>
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<td></td>
<td>Children ≥12 years: 2 to 10mg 2-4 times a day</td>
<td><strong>Rectal:</strong> absorption via this route is slow, therefore repeated doses should be used in caution</td>
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<tr>
<td></td>
<td><strong>IV:</strong> Severe status dystonicus. &gt; 1 month to 11 years: 100-400 micrograms/kg repeated if necessary then every 1-4 hours to be given over 3-5 minutes.</td>
<td><em>Doses may be cumulative</em></td>
</tr>
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<td></td>
<td>12-17 years 5-10mg repeated if necessary, given over 3-5 minutes</td>
<td><strong>Tolerance may occur</strong></td>
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<tr>
<td><strong>Diazepam</strong></td>
<td><strong>Life Threatening Drug Induced Dystonic Reaction</strong></td>
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<td></td>
<td><strong>IV:</strong> 1 month - 11 years 100 micrograms/kg given over 3-5 minutes repeated if necessary</td>
<td><strong>Doses may be cumulative</strong></td>
</tr>
<tr>
<td></td>
<td>12-17 years 5-10mg given over 3-5 minutes repeated if necessary</td>
<td><strong>Tolerance may occur</strong></td>
</tr>
<tr>
<td><strong>Gabapentin</strong></td>
<td><strong>Orally:</strong> 15-90mg/kg/day in 3 divided doses, usual mean dose: 18mg/kg 8 hourly. Start with: 5mg/kg od on day 1, bd on day 2 and tds on day 3 (maximum starting dose 300mg)</td>
<td><strong>Start with 5mg/kg/dose once a day; increase weekly to 5mg/kg/dose BD then TDS, continue to increase by 5mg/kg/day, as tolerated, to a maximum of 30mg/kg 8 hourly; higher doses might occasionally be successful</strong></td>
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<tr>
<td></td>
<td>(maximum starting dose 300mg)</td>
<td><strong>Max dose 3.6 grams/day</strong></td>
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<td></td>
<td><strong>Rectal:</strong> As per oral dose, poor absorption rectally</td>
<td><strong>Side effects:</strong> sedation, GI upset</td>
</tr>
<tr>
<td><strong>Midazolam</strong></td>
<td><strong>Buccal:</strong> 300 microgram/kg (maximum of 10 mg)</td>
<td><strong>Side effects:</strong> Respiratory depression, cardiovascular depression (severe hypotension). Potentiated by erythromycin and other drugs. See use of midazolam in status guidance: <a href="http://nww.avon.nhs.uk/dms/Download.aspx?r=1&amp;did=13077&amp;f=StatusEpilepticusTreatment-1_1.pdf">http://nww.avon.nhs.uk/dms/Download.aspx?r=1&amp;did=13077&amp;f=StatusEpilepticusTreatment-1_1.pdf</a></td>
</tr>
<tr>
<td></td>
<td><strong>Oral:</strong> 500 microgram/kg (maximum of 20 mg)</td>
<td></td>
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<tr>
<td></td>
<td><strong>IV:</strong> Slow iv injection of 50- 200microgram/kg then infusion of 30microgram/kg/hr increasing according to response</td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>Acute dystonic reaction to be given with monitoring and resuscitation equipment available</td>
<td>Side effects: constipation, dry mouth, urinary retention, vision blurred, anxiety, cognitive impairment, confusion, dizziness, gingivitis, hallucination, memory loss, nausea, rash, vomiting</td>
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<td>--------------------------</td>
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<tr>
<td>Prochlorperazine</td>
<td>To be given IM or IV</td>
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<td></td>
<td>Child 1 month-1 year: 0.5-2mg for 1 dose (dose usually effective in 5-10 minutes but may take 30 minutes)</td>
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<td></td>
<td>Child 2-9 Years: 2-5mg for 1 dose (dose usually effective in 5-10 minutes but may take 30 minutes)</td>
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<tr>
<td></td>
<td>Child 10-17 Years: 5-10mg, occasionally, more than 10mg (dose usually effective in 5-10 minutes but may take 30 minutes)</td>
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<tr>
<td>Trihexyphenidyl (Centrally acting anti-cholinergic)</td>
<td>Orally: &gt;1 month starting dose 1-2mg daily in 1-2 divided doses, then increased in steps of 1mg every 3-7 days; dose to be adjusted according to response and side effects; maximum 2mg/kg/day(^7.8)</td>
<td>Side effects: Tachycardia, agitation, confusion, delusions, dizziness, drowsiness, constipation, urinary retention, blurred vision.</td>
</tr>
</tbody>
</table>
## Appendix 1

Medications and Toxins which may cause dystonia in children

### Medications

<table>
<thead>
<tr>
<th>Medications</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Dopamine receptor blocking drugs</td>
<td>Including Neuroleptics, Antiemetics</td>
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<tr>
<td>Dopamine depleting drugs</td>
<td></td>
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<tr>
<td>Dopamine receptor stimulants</td>
<td>Eg Tetrabenazine</td>
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<tr>
<td>Antihistamines</td>
<td>L-Dopa, Dopamine receptor agonists</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td></td>
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<tr>
<td>Serotonin reuptake inhibitors</td>
<td></td>
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<tr>
<td>Cholinergic Agonists</td>
<td>Eg Trihexyphenidyl</td>
</tr>
<tr>
<td>Antiepileptic drugs</td>
<td>Particularly phenytoin and carbamazepine</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>Chloroquine, amodiaquine</td>
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<tr>
<td>Calcium channel blockers</td>
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<tr>
<td>Disulfiram</td>
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<tr>
<td>Lithium</td>
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<tr>
<td>Cocaine</td>
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</tbody>
</table>

### Toxins

<table>
<thead>
<tr>
<th>Toxins</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon Monoxide</td>
<td>Smoke inhalation, poorly functioning heating or fuel burning devices</td>
</tr>
<tr>
<td>Cyanide</td>
<td>Smoke inhalation, ingestion of toxic household or workplace substances or cyanogenic foods</td>
</tr>
<tr>
<td>Manganese</td>
<td>Long term TPN, drinking water with a high concentration of manganese</td>
</tr>
<tr>
<td>Methanol</td>
<td>Ingestion of anti-freeze products or cleaners</td>
</tr>
<tr>
<td>Organophosphate</td>
<td>Exposure to or ingestion of insecticides</td>
</tr>
</tbody>
</table>
References:


RELATED DOCUMENTS
Levodopa trial in children suspected to have dopamine responsive dystonia.
Administration of intravenous clonidine for status dystonicus on the high dependency unit (HDU)

AUTHORISING BODY
Paediatric Neurology Governance Group

SAFETY
None

QUERIES
Contact Paediatric Neurology Team Bleep 6734