Dystonia

**Definition**

involuntary, sustained muscle contractions that result in twisting and repetitive movements or abnormal postures

may have overlying spasms that resemble tremor

dynamic disorder that changes in severity, depending upon activity and posture

sensory trick is a maneuver (eg, lightly touching the affected body part) that reduces or abolishes the dystonic symptoms (60%)

(REF: http://www.uptodate.com/contents/classification-and-evaluation-of-dystonia?source=search_result&selectedTitle=1%7E150)

**Pathophysiology**

Largely unknown

No degeneration

Can by associated with mutations of unclear function (DYT1A)

Abnormal cellular firing rates

Cholinergic and dopaminergic systems are implicated

**Clinical Features**

Is the movement dystonia?

Movements are repetitive and twisting, and postures may be sustained

The movement may vary with activity or over the course of the day

Presence of overflow, mirror movements or a geste antagoniste

Movements are not consistent with tics, chorea or myoclonus

Abnormal postures are not fixed

Is the dystonia episodic?

Consider inherited paroxysmal syndromes

Consider testing for glucose transporter type 1 deficiency and organic acids

What is the age of onset?

Investigate generalized and focal syndromes if symptoms appear outside the usual age ranges

What is the anatomical distribution?

Does the distribution match defined focal syndromes?

Presentation with orobulbar dystonia is likely to be due to tardive syndromes or neuroacanthocytosis; investigate for acanthocytes on blood film

If hemidystonia is suspected, image the brain to identify the causative lesion

Are other movements present?

Investigate for myoclonus and examine for parkinsonism and signs of pyramidal dysfunction

Is imaging required?

CT scan required to detect lesions and calcium deposition

MRI with T2* sequence may be required to detect iron deposition
a | The 'eye of the tiger' appearance of neurodegeneration in a patient with brain iron accumulation (axial fluid-attenuated inversion recovery MRI sequence). b | MRI showing caudate atrophy in a patient with neuroacanthocytosis (axial T1-weighted MRI). c,d | Enhanced signal in the putamen, globus pallidus and caudate in a patient with neuroferritinopathy, shown on coronal T2* MRI (c) and axial T2* MRI (d).

Could the syndrome be Wilson disease?
Examine for Kayser–Fleisher rings
Screen for serum ceruloplasmin and perform 24-h urinary copper quantification

Is screening for rare conditions required?
If the dystonia is of abrupt or young-onset, or if symptoms show progression over time, screening for organic and amino acidurias and neuroacanthocytosis is warranted


Classification
Age Early <26 (usually leg -> generalized >50%) < vs. Late 26 (neck/arm/face, stays focal/segmental)
Anatomic: focal, segmental (2 contiguous body areas), generalized (leg, trunk, +other body area), multifocal (2 noncontiguous body areas), hemidystonia (1 side of body)
Etiology: primary vs. secondary

Primary
Sustained involuntary movt
Sometimes +spasms
Consistent direction
Same body region(s)
Exacerbated by movt of involved area
Varies w/activity/posture/sensory tricks

No other neuro/lab/imaging abnormalities
gradual onset
usually without fixed postures, but can cause contractures
eg. primary torsion dystonia

Secondary
Known acquired cause or additional signs (weak, spastic, ataxia, ocular, retinal, cognitive, sz)
eg. perinatal asphyxia, dopamine antagonists

Etiology
1. Primary dystonia
   a. Genetic forms of dystonia (DYT1)
   b. Sporadic
2. Dystonia-plus syndromes
   a. Dopa-responsive dystonia
      i. GCH1 mutations (DYT5)
      ii. Tyrosine hydroxylase mutations
iii. Other biopterin deficient states

b. Dopamine agonist responsive dystonia due to decarboxylase deficiency

c. Myoclonus-dystonia

3. Other inherited (degenerative) disorders

a. Autosomal dominant

i. Rapid onset dystonia-parkinsonism

ii. Huntington disease

iii. Machado-Joseph disease (spinocerebellar ataxia type 3)

iv. Other spinocerebellar ataxia subtypes

v. Dentatorubral pallidoluysian atrophy

vi. Familial basal ganglia calcification

b. Autosomal recessive

i. Wilson disease

ii. GM1 and GM2 gangliosidoses

iii. Metachromatic leukodystrophy

iv. Homocystinuria

v. Hartnup disease

vi. Glutaric acidemia

vii. Methylmalonic aciduria

viii. Pantothenate kinase-associated neurodegeneration (Hallervorden Spatz disease)

ix. Dystonic lipidosis

x. Neuronal ceroid lipofuscinosis

xi. Ataxia telangiectasia

xii. Neuroacanthocytosis

xiii. Intraneuronal inclusion disease

xiv. Juvenile parkinsonism (parkin)

c. X-linked recessive

i. Lubag (X linked dystonia-parkinsonism or DYT3)

ii. Lesch Nyhan syndrome

iii. X-linked deafness-dystonia

d. Mitochondrial

i. Myoclonic epilepsy with ragged red fibers (MERRF)

ii. Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS)

iii. Leber hereditary optic neuropathy (LHON) plus dystonia

4. Due to acquired/exogenous causes

a. Perinatal cerebral injury

b. Encephalitis, infectious and post-infectious

c. Head trauma

d. Pontine myelinolysis

e. Primary antiphospholipid syndrome
f. Stroke

5. Dystonia associated with parkinsonian disorders

a. Parkinson disease

b. Progressive supranuclear palsy

c. Multiple system atrophy

d. Corticobasal degeneration

**Workup**

Levodopa trial (e.g., carbidopa-levodopa 25/100 mg tid)

CT/MRI (esp BG)

Chem 7, LFT, CBC

ESR/CRP, ANA

Ceruloplasmin, serum Cu, and 24-hour urinary Cu (for Wilson disease)

Rapid plasma reagent

Genetic testing: for early onset or FH (DYT1, others possible, but not available)

**Management**

(REF: [http://www.uptodate.com/contents/treatment-of-dystonia?source=search_result&selectedTitle=2~150](http://www.uptodate.com/contents/treatment-of-dystonia?source=search_result&selectedTitle=2~150))

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<th>Efficacy and comment</th>
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<td>Dopamine agonists: Carbidopa /Levodopa</td>
<td>Dramatic response in the dopa responsive form of dystonia; effective in 10 to 15% of pts with other types of dystonia; more rapid upward titration possible</td>
<td>Nausea (especially at initiation of therapy); may worsen dystonia; rapid discontinuation possible</td>
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<td>Anticholinergic /antihistaminic: Trihexyphenidyl /Benztropine Procyclidine Diphenhydramine Ethopropazine</td>
<td>Effective in ~40% of pts, mainly children; benefit limited by side effects; requires slow upward titration</td>
<td>Dry mouth (may lead to dental caries); blurred vision; exacerbation of acute-angle glaucoma; urinary retention; memory problems; sedation; confusion; hallucinations; heat intolerance</td>
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**Baclofen**
- Effective in ~20% of pts; high doses tolerated in children; benefits limited by side effects; intrathecal baclofen minimally successful; withdrawal effects on sudden discontinuation
- Nausea; sedation; dysphoria; muscle weakness (in those with spasticity associated)

**Clonazepam**
- Effective in ~15% of pts; possibility for addiction; withdrawal effects on sudden discontinuation
- Sedation; depression; confusion; dependence

**Muscle relaxants:**
- **Tizanidine**
- **Cyclobenzaprine**
- Limited benefit in some pts; side effects frequent
- Sedaion; dysphoria

**Anticonvulsant medications:**
- **CBZ**, **GBP**
- Benefit <10% of pts
- Ataxia; sedation

**Dopamine-depleting agents:**
- **Tetrabenazine**
- **Reserpine**
- Requires a very slow upward titration (4 weeks between dose increases)
- Depression; dysphoria; parkinsonism

**Dopamine receptor blocking agents**
- Effective in up to 25% of pts; clozapine requires weekly blood counts and may cause life threatening agranulocytosis
- The possibility of tardive dyskinesia and the other adverse effects from this class of medications severely limits usefulness; not recommended for dystonia

**Surgery**
- DBS takes months to become effective (REF: Dr. Emad Eskandar, MGH Pediatric Neuro conf)