Dystonias

Last updated: April 17, 2019

**Etiological Classification Of Dystonia**

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**Major differential diagnoses**

**X-linked dystonia-parkinsonism**

**ETIOLOGICAL CLASSIFICATION OF DYSTONIA**

**I. IDIOPATHIC (PRIMARY) DYSTONIA**

**A. Sporadic (idiopathic torsion dystonia, ITD)**

**B. Inherited (hereditary torsion dystonia)**

1. **CLASSIC autosomal dominant ITD (DYT1 gene; 9q34)**

2. **NONCLASSIC autosomal dominant ITD (not DYT1 gene)**

3. **Autosomal recessive dystonia tyrosine hydroxylase deficiency**

**II. SECONDARY DYSTONIA - known pathological cause**

**A. Dystonia-plus syndromes - forms of primary dystonia associated with additional neurological deficits**

1. **Myoclonic dystonia (not DYT1 gene)**

2. **Dopa-responsive dystonia - DRD**

3. **Rapid-onset dystonia-parkinsonism - RDP**

4. **Early-onset parkinsonism with dystonia - EPD**

5. **Paroxysmal dystonia-chorioptis lateralis**

**B. Associated with neurodegenerative disorders**

1. **Sporadic**

PARKIN'S disease

Progressive supranuclear palsy

Multiple system atrophy

Corticobasal ganglionic degeneration

Multiple sclerosis

Central pontine myelopathy

2. **Inherited**

Wilson's disease

Huntington's disease

Juvenile parkinsonism-dystonia

Progressive pallidal degeneration

Hallett-von Spatz disease

Hypereleptinoproteinoemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration (HARP syndrome)

Joseph's disease

Aisha trilateralis

Neuroacanthocytosis

Rek's syndrome (?)

Intracranial inclusion disease

Infantile bilateral stratal necrosis

Familial basal ganglia calcifications

Spinocerebellar degeneration

 Olivopontocerebellar atrophy

Hereditary spastic paraplegia with dystonia X-linked dystonia-parkinsonism or Lubag (pericentromeric)

Deletion of 18q

**C. Associated with metabolic disorders**

1. **Amino acid disorders**

Glutaric acidemia

Methylmalonic acidemia

Homocystinuria

Hartnag's disease

Tyrosinemia

2. **Lipid disorders**

Mitochondrial leukodystrophy

Cerebral lipidosis

Dystonic lipidoses ("sea blue" histiocytosis)

Gangliosidoses GM1, GM2 variants

Hexitosaminidase A and B deficiencies

3. **Miscellaneous metabolic disorders**

Wilson's disease

Mitochondrial encephalopathies: Leigh's disease, Leber's disease

Lesch-Nyhan syndrome

Trisomie phosphate isomerase deficiency

Vitamin E deficiency

Biotin deficiency

**D. Due to known specific cause**

Drugs: antipsychotics (tardive dyskinesia), levodopa, bromocriptine, metoclopromide, flunarizine, felbamate, reboxetine, anticonvulsants, certain calcium channel blockers

Perinatal cerebral injury and kernicterus: athetoid cerebral palsy, delayed onset dystonia

Infection: viral encephalitis, echinococcus leharia, Reye's syndrome, subacute sarcoenic encephalopathy, Creutzfeld-Jakob disease, AIDS

Other: tuberculoses, syphilis, acute infectious torticollis

Paraparetic brain stem encephalitis

Cerebral vascular and ischemic injury

Brain tumors

Atherosclerosis malformation

Head trauma and brain surgery

Peripheral trauma (→ focal dystonia in afflicted region)

Toxins: MN, CO, CS, methanol, disulfiram, wasp sting

**III. OTHER HYPERKINETIC SYNDROMES ASSOCIATED WITH DYSTONIA**

A. Tic disorders with dystonic spikes
B. Paroxysmal dystonias:

1. Paroxysmal kinesigenic choreoathetosis
2. Paroxysmal dystonic choreoathetosis
3. Intermediate paroxysmal dyskinesia
4. Benign infantile paroxysmal dyskinesia

IV. PSYCHOGENIC

V. PSEUDODYSTONIA

- Atlantoaxial subluxation
- Syringomyelia
- Arnold-Chiari malformation
- CN4 palsy
- Vestibular torticollis
- Posterior fossa mass
- Soft tissue neck mass
- Congenital postural torticollis
- Congenital Klippel-Feil syndrome
- Isaac’s syndrome
- Sandler’s syndrome
- Satoyoshi syndrome (s. Komuragari syndrome)
- Stiff person syndrome

PRIMARY DYSTONIA (s. dystonia musculorum deformans, idiopathic torsion dystonia)

A. SPORADIC (idiopathic torsion dystonia, ITD)

B. INHERITED (hereditary torsion dystonia):

1. CLASSIC autosomal dominant ITD (DYT1 gene, 9q34) - most childhood- and adolescent-onset cases (formerly known as dystonia musculorum deformans).
   *three base pair deletion in DYTI gene on 9q2-a (coding for ATP-domain protein A).
2. NONCLASSIC autosomal dominant ITD (not DYTI gene)
3. Autosomal recessive tpyrine hydroxylase deficiency
4. X-linked recessive (Xq21.3).

PREVALENCE: 3.4-30 per 100,000 population;
- 2nd most commonly encountered movement disorder (after parkinsonism) in movement disorder clinics.
- among Ashkenazi Jews; prevalence is at least double!

PATHOLOGY, PATHOPHYSIOLOGY

- no reproducible morphological or biochemical abnormalities are identified!!
- altered physiological control of descending pathways from basal ganglia and brain stem.
- e.g. HEMIDYSTONIA results from lesion in contralateral striatum (particularly putamen).

CLINICAL FEATURES see p. Mov1 >>

1. Expression of gene is highly variable (even within families) – dystonia may be generalized (17%), segmental (33%) or only focal (50% of all cases).
2. Primary dystonia begins at FOCAL condition (and may sequentially progress to segmental – generalized).
   - in children-onset dystonia legs and feet are most commonly initially affected.
   - e.g. peculiar leg twisting and foot inversion when child walks forward, even though walking backward, running, or dancing may still be normal.
   - adult-onset dystonia usually begins in arms (writer’s cramp), neck (torticollis), face (blepharospasm), jaw (oromandibular dystonia), tongue (lingual dystonia), or vocal cords (spastic dysphonia); not in legs!
   - N.B. adult-onset dystonia is six times more common!
3. Younger age at onset, more likely dystonia is to become generalized and disabling (adult-onset primary dystonia is almost always focal or segmental).
   - rate of progression is extremely variable (usually greatest within first 5-10 years – static phase).
4. Environmental conditions affect dystonia; dystonic signs become prominent in later part of day.
5. During disorder progression: task-specific dystonia → action dystonia → overflow dystonia → continual dystonia (dystonia at rest) → fixed postures
6. Muscles tone & power are normal, but involuntary movements interfere with function and make voluntary activity extremely difficult.
7. Mental activity, sensations, tendon reflexes remain normal.

SCALES
Burke-Fahn-Marsden Dystonia Rating Scale (BFDMDRS)

DIAGNOSIS
- structural / functional imaging - no discernible abnormalities can be identified.
- abnormal results of blink, acoustic, vestibulo-ocular reflex testing - brain stem reflexes have enhanced excitability.
N.B. ceruloplasmin level should be obtained in all patients in whom dystonia occurs before age of 50!

DIFFERENTIAL DIAGNOSIS see below >>

- Symptomatic (secondary) dystonia - additional neurologic deficits, possible etiologic factors.
- Psychogenic dystonia - has suggestive clues:
  - abrupt onset as paroxysmal disorder with fixed posture.
  - inconsistent movements (changing characteristics over time).
CARBAMAZEPINE

- incongruous movements (do not fit with recognized patterns or with normal physiologic patterns)
- additional types of abnormal movements that are not consistent with basic abnormal movement pattern or are not congruous with known movement disorder.  
- movements disappear with distraction.
- response to placebo, suggestion, psychotherapy.
- spontaneous remissions.

N.B. because of fluctuations in severity, sometimes influenced by emotional state of patient. primary dystonia is often mistakenly attributed to psychogenic causes.

**TREATMENT**

1. High-dose ANTICHOLINERGICS  (e.g. TETRACYCLINES) [Artane®] up to 70 mg/d - most effective symptomatic relief, many patients are unable to tolerate such high doses.
2. High-dose BACLOFEN
3. BENZODIAZEPINES (CLONAZEPAM, LORAZEPAM, DIAZEPAM)
4. CARBAMAZEPINE
5. ANTIDOPAMINERGICS (reserpine, dopamine receptor blockers).

Childhood-onset dystonia → trial of LEVODOPA (aim is to not overlook DOPA-responsive dystonia).

**Genericized and axial dystonia → intrathecal BACLOFEN (controlled trials have not been published).**

Focal, segmental dystonia → intramuscular injections of BOTULINUM TOXIN TYPE A q 3-5 months.
- some clinicians perform with EMG guidance
- some patients develop resistance (antibodies to toxin).
- most efficient in CERVICAL DYSTONIA.
- also can be used for generalized dystonia (injections into most severely affected focal site).

**SURGICAL PROCEDURES**
- effective in majority but high rates of recurrence.

1. **pallidal DBS** (FDA approved; see p. Op360 >>)
2. **thaumatology** - useful in unilateral dystonia (most effective for distal extremities dystonia); bilateral thalamotomy carries 20% risk of dysthria!
3. **cervical cord stimulation**
4. **rhizotomy**.

**MOST COMMON FORMS OF FOCAL DYSTONIA**

CERVICAL DYSTONIA (s. SPASM DYSTONIC TORTICOLLIS)
- most common focal dystonia
- occurs at all ages (usually 20-60).

**CLINICAL FEATURES**
- any bilateral combination of neck muscles can be involved → sustained turning / tilting / flexing / extending neck, shifting head laterally or anteriorly (e.g. torticollis, laterocollis, anterocollis, retrocollis).
- shoulder is elevated and anteriorly displaced on side to which chin turns.

N.B. some neck muscles contract in compensation for movements of primary agonists (sometimes difficult to decide which muscles to inject with botulinum toxin).

- instead of sustained head deviation, some have jerking head movements (50% have associated head-neck tremor).
- neck pain (occurs in 2/3) - responds to botulinum toxin at site of pain or steroid injections (e.g. at greater occipital nerve; radiculopathy complicates cervical dystonia in ≈ 20%.
- common sensory trick may relieve cervical dystonia. (see p. Mov1)
- 10% have remission within year of onset → relapse years later.

Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS): >>
- Torticollis severity scale (max 35 points)
- Disability scale (max 30 points)
- Pain severity scale (max 20 points)

**DIFFERENTIAL DIAGNOSIS**

1) congenital contracture of sternocleidomastoid muscle; H: surgical release.
2) NANDLER syndrome - extreme head tilt caused by gastroesophageal reflux in young boys after full meal; H: plication surgery
3) CN-4 palsy
4) malformations - Arnold-Chiari; cervical spine (e.g. Klippel-Feil fusion, atlantoaxial subluxation)
5) cervical infections, trauma
6) tumor in posterior fossa
7) spasms from cervical muscle shortening.
8) BENIGN PAROXYSMAL TORTICOLLIS - recurrent attacks of head tilt associated with pallor, agitation, vomiting.

- onset at 2-8 months of age; spontaneous remission by 2-3 yr of age.
- during attack, child resists passive head movement.
- abnormalities in vestibular function (as in benign paroxysmal vertigo).

**MEDICAL TREATMENT**

- BADROTULINUMTOXIN A (Dysport®) - first choice for treatment of adults with cervical dystonia (both toxin-naive and previously treated patients)
- IMMITOTULINUMTOXIN A (Xeomin®) - FDA approved botulinum toxin type A for treatment of adults with cervical dystonia or blepharospasm.

**SURGICAL TREATMENT**

- DORSIFLEXOR GANGLIONotomy for botulinum toxin refractory cases. see p. Op360 >>

**MICROVASCULAR INCOMPRESSIBILITY (MVD)** of CN11 at cervicomedullary junction – for local vascular compression – manifests as horizontal rotary torticollis during upright or recumbent position.

**SELECTIVE CERVICAL ANTERIOR RHIZOTOMY**

1) Bilateral C1-C3 anterior rhizotomy
2) C4 anterior rhizotomy ipsilateral to side of head turning.

**DIAGNOSIS**

- cervical dystonia occurs in 2/3
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3) posterior rami of C5-7 roots on side of C1-4 anterior rhizotomy + posterior rami of C4-7 roots on opposite side, may be coagulated (where they pass around associated cervical facet joint) - further denerves posterior paraspinal muscles.

- sternocleidomastoid muscle is transected at midbello,
- branches of CN11 are stimulated to identify sternomastoid branch, which is then transected.
- high intradural CN11 transection will produce only partial denervation of sternomastoid and trapezius muscles.

**SELECTIVE PERIPHERAL DENERVATION (BERTRAND PROCEDURE)**

- developed in the 1970s, Dr. Claude Bertrand, with the collaboration of Dr. Pedro Molina-Negra.
- Wilson et al. described modification - combination of C2-6 denervation, myectomy of the splenius capitis and/or semispinalis capitis, myotomy of the levator scapulae when indicated, and myotomy and selection denervation of the sternocleidomastoid. J. Wilson, MD Robert J. Spinner, MD. Selective Cervical Denerivation for Cervical Dystonia: Modification of the Bertrand Procedure Thunas Oppen Neurosurgery, opn147, https://doi.org/10.1093/ons/opx147 Published: 06 July 2017

**SELECTIVE MYOTOMY**

- **scalene muscles** are transected in anteflexional or introversal torticollis (scalene muscles are innervated by lower cervical roots which cannot be transected without producing paresis of upper extremity).
- **pure retrocollis** - unilateral resection of splenius and semispinalis muscles.

Aggressive physical therapy is necessary postoperatively.

**BLEPHAROSPASM**

- involuntary forceful spasmodic contraction of orbicularis oculi muscle leading to visual dysfunction.

**CLINICAL FEATURES**

- **unimated / aggravated** by emotion, stress, fatigue, drugs, bright light.
- **spontaneously** losing spasm. Bilateral involvement or if dystonia affects other cranial, cervical & laryngeal dystonias – i.e. SEGMENTAL CRANIOFACIAL DYSTONIAS.

**TREATMENT**

1) anticholinergics (e.g. BENZHEXOL),
2) orbicularis myotomy
3) BOTULINUM TOXIN TYPE A (BOTOX®) injections into orbicularis oculi muscle; repeated q 3 months.

**WRITER'S CRAMP**

- task-specific focal dystonia.
- may spread to other arm (cramp of adult onset usually remains limited to one limb).
- patient should learn to write with nondominant hand.
- bilateral involvement or if dystonia affects other activities (buttoning, shaving, playing musical instrument) → botulinum toxin injections.

Other task-specific dystonias: violinist's cramp, barber's cramp, telegrapher's cramp.

**DYSTONIA OF VOCAL CORDS**

1. **SPASTIC (SPASMIC) DYSPHONIA (more common type) - vocalis muscles** contract bringing vocal cords together → voice is restricted, strangled, coarse, often broken up with pauses.

   - often is associated with tremor of vocal cords.
   - H: botulinum toxin injections.

2. **Breathy (whispering) dysphonia** - contractions of posterior cricoarytenoids (abductors of vocal cords) → patient cannot talk in loud voice and tends to run out of air while trying to speak.

   - botulinum toxin injections are uncertain.

**DYSTONIA-PLUS SYNDROMES**

**DOPA-RESPONSIVE DYSTONIA**

- 10% cases of childhood-onset dystonia.
- autosomal dominant GTP cyclohydrolase 1 gene (14q22.1-1.q22.2) defect → defect in dihydrobiopterin synthesis.
- pathogenesis - normal numbers of hypopigmented substantia nigra neurons, no Lewy bodies; reduced striatal dopamine.
- begins at age 6-16 yrs.
- DYSTONIA + PARKINSONISM without progression.
- hyperseretions (particularly in legs, sometimes with extensor plantar responses).
• marked DIURNAL fluctuations: symptom-free in early-morning → worsening as day wears on → virtually crippled by evening.
• PET – normal.
• remarkable therapeutic response to low doses of LEVODOPA, dopamine agonist, or anticholinergic drug.
   N.B. all children with dystonia and adults with leg or trunk dystonia deserve trial of LEVODOPA!

MAJOR DIFFERENTIAL DIAGNOSIS

<table>
<thead>
<tr>
<th>Juvenile Parkinson Disease</th>
<th>Dopa-responsive Dystonia</th>
<th>Childhood Idiopathic/Torsion Dystonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Onset</td>
<td>Rare &lt; 8 yrs.</td>
<td>Infanty + 12 yrs.</td>
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<tr>
<td>Gender</td>
<td>Predominantly male</td>
<td>Predominantly female</td>
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<tr>
<td>Initial Sign</td>
<td>Foot dystonia or PD</td>
<td>Foot and leg dystonia</td>
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<tr>
<td>Dystonia</td>
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<td>Throughout</td>
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<td>Initial Sign</td>
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<td>Bradykinesia</td>
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<td>Abnormal</td>
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<td>Dyskinesias</td>
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<td>Fluorodopa PET</td>
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<tr>
<td>Prognosis</td>
<td>Progressive</td>
<td>Plateaus</td>
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</table>

X-LINKED DYSTONIA-PARKINSONISM

• confined largely to Philippines.
• patients, mostly men, develop severe axial dystonia and hunched parkinsonian posture.
• falls, dysphagia, and voice compromise are preludes to death.

BIBLIOGRAPHY for ch. “Movement disorders, Ataxias” → follow this LINK >>