

Dystonias

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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 *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-choreoathetosis

B. Associated with neurodegenerative disorders

1. Sporadic
 - Parkinson's disease
 - Progressive supranuclear palsy
 - Multiple system atrophy
 - Corticobasal ganglionic degeneration
 - Multiple sclerosis
 - Central pontine myelinolysis
2. Inherited
 - Wilson's disease
 - Huntington's disease
 - Juvenile parkinsonism-dystonia
 - Progressive pallidal degeneration
 - Hallervorden-Spatz disease
 - Hypoprebetalipoproteinemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration (HARP syndrome)
 - Joseph's disease
 - Ataxia telangiectasia
 - Neuroacanthocytosis
 - Rett's syndrome (?)
 - Intraneuronal inclusion disease
 - Infantile bilateral striatal 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
 - Hartnup's disease
 - Tyrosinosis
2. Lipid disorders
 - Metachromatic leukodystrophy
 - Ceroid lipofuscinosis
 - Dystonic lipidosis ("sea blue" histiocytosis)
 - Gangliosidoses GM₁, GM₂ variants
 - Hexosaminidase A and B deficiencies
3. Miscellaneous metabolic disorders
 - Wilson's disease
 - Mitochondrial encephalopathies: Leigh's disease, Leber's disease
 - Lesch-Nyhan syndrome
 - Triosephosphate isomerase deficiency
 - Vitamin E deficiency
 - Biopterin deficiency

D. Due to known specific cause

- Drugs: antipsychotics (tardive dystonia), levodopa, bromocriptine, metoclopramide, fenfluramine, flecainide, ergot, anticonvulsants, certain calcium channel blockers
- Perinatal cerebral injury and kernicterus: athetoid cerebral palsy, delayed onset dystonia
- Infection: viral encephalitis, encephalitis lethargica, Reye's syndrome; subacute sclerosing panencephalitis; Creutzfeldt-Jakob disease, AIDS
- Other: tuberculosis, syphilis, acute infectious torticollis
- Paraneoplastic brain stem encephalitis
- Cerebral vascular and ischemic injury
- Brain tumor
- Arteriovenous malformation
- Head trauma and brain surgery
- Peripheral trauma (→ focal dystonia in affected region)
- Toxins: MN, CO<CS₂, methanol, disulfiram, wasp sting

III. OTHER HYPERKINETIC SYNDROMES ASSOCIATED WITH DYSTONIA

A. Tic disorders with dystonic tics

B. Paroxysmal dyskinesias

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
- Sandifer's syndrome
- Satoyoshi syndrome (s. Komuragueri 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 **DYT1 gene** on 9q32-34 (coding for ATP-domain protein *torsin A*).
2. **NONCLASSIC** autosomal dominant ITD (not DYT1 gene)
3. Autosomal recessive **tyrosine 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 as 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. **Muscle 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 (BFMDRS)

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

DOPA-responsive dystonia *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).

- 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. **TRIHEXYPHENIDYL** [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).

Generalized 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) **thalamotomy** - useful in **unilateral** dystonia (most effective for **DISTAL** extremities dystonia); bilateral thalamotomy carries 20% risk of dysarthria!
- 3) cervical cord **stimulation**
- 4) **rhizotomy**, peripheral **nerve section** (denervation), **myotomy** – for **focal / segmental** dystonias.

MOST COMMON FORMS OF FOCAL DYSTONIA

CERVICAL DYSTONIA (s. SPASMODIC 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) **SANDIFER 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, traumas**
- 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

ABOBOTULINUMTOXINA A (DYSPORT®) – first choice for treatment of adults with cervical dystonia (both toxin-naïve and previously treated patients)

INCOBOTULINUMTOXIN A (XEOMIN®) - FDA approved botulinum toxin type A for treatment of adults with cervical dystonia or blepharospasm.

SURGICAL TREATMENT

DBS (BILATERAL GPI) – for botulinum toxin refractory cases. see p. Op360 >>

MICROVASCULAR DECOMPRESSION (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.

- 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 denervates posterior paraspinal muscles.
- sternocleidomastoid muscle is transected at midbelly.
 - 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-Negro.
- 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 Denervation for Cervical Dystonia: Modification of the Bertrand Procedure Thomas Operative Neurosurgery, opx147, <https://doi.org/10.1093/ons/opx147> Published: 06 July 2017

SELECTIVE MYOTOMY

- **scalene muscles** are transected in *anteflexional* or *lateroflexional 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.*

- etiology – unknown.
- women > men; usually > 50 yrs.
- may occur in isolation – FOCAL dystonia.
- **MEIGE syndrome** – association with *other cranial, cervical & laryngeal dystonias* – i.e. SEGMENTAL craniofacial dystonia.

CLINICAL FEATURES

- initiated / aggravated by emotion, stress, fatigue, drugs, bright light.
- preceded by exaggerated blinking.
- starts unilaterally, becoming *bilateral*.
- various tricks (*gestes antagonistes*) may reduce blepharospasm (e.g. touching just lateral to orbit, pulling eyelids).
- severe untreated cases result in **functional blindness**.



TREATMENT

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

INCOBOTULINUMTOXIN A (XEOMIN®) - FDA approved botulinum toxin type A for treatment of adults with cervical dystonia or blepharospasm.

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 (SPASMODIC) 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-q22.2) defect → defect in dihydrobiopterin synthesis.
- pathology - normal numbers of hypopigmented substantia nigra neurons, no Lewy bodies; reduced striatal dopamine.
- begins at age 6-16 yrs.
- **DYSTONIA + PARKINSONISM** without progression.
- hyperreflexia (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 DIAGNOSES

	Juvenile Parkinson Disease	DOPA-responsive Dystonia	Childhood Idiopathic Torsion Dystonia
Age at Onset	Rare < 8 yrs.	Infancy ÷ 12 yrs.	Uncommon < 6 yrs.
Gender	Predominantly male	Predominantly female	Equal
Initial Sign	Foot dystonia or PD	Foot and leg dystonia	Arm or leg dystonia
Dystonia	At onset	Throughout	Throughout
Diurnal variation	No	Yes	No
Bradykinesia	Yes	Yes	No
Pull Test	Abnormal	Abnormal	Normal
Gait	Abnormal	Abnormal	Abnormal if leg or trunk is affected
"Off" Episodes	Fluctuations	Stable	Unknown
Dyskinesias	Prominent	Uncommon	Unknown
Fluorodopa PET	Decreased	Slight decrease	Normal
DOPA Responsive (Dosage)	Yes (moderate to high)	Yes (very low)	No, or mild (high)
Anticholinergic Response	Yes		
Prognosis	Progressive	Plateaus	Usually worsens

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 >>](#)