BMJ Best Practice

Dystonias

Straight to the point of care

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Summary

Dystonia is a movement disorder characterised by sustained involuntary muscle contractions and abnormal postures of the trunk, neck, face, or extremities.

The involuntary movements are associated with simultaneous contraction of agonist and antagonist muscles, with unwanted 'overflow' contraction of adjacent muscles.

In some cases, pain in the affected muscles can be a prominent feature.

Dystonia may improve with simple 'sensory tricks' such as lightly touching the affected body part (geste antagoniste).

Can be generalised or focal, idiopathic (with no other neurological abnormalities), inherited, or acquired.

Dopa-responsive dystonias, although rare, should always be considered if the dystonia is generalised, as levodopa is dramatically effective in these situations.

Treatment is symptomatic. Agents include anticholinergics, antispasmodics, and botulinum toxin. Deep brain stimulation may be used in severe, refractory cases. Physiotherapy is recommended.

Definition

Dystonia is a movement disorder characterised by sustained involuntary contractions of agonist and antagonist muscles, often leading to repetitive twisting movements and abnormal postures of the trunk, neck, face, or extremities. It is often associated with unwanted 'overflow' contraction of adjacent muscles.

Epidemiology

Estimates from population studies of the prevalence of early-onset dystonia vary widely, ranging from as low as 7 per 100,000 to as high as 500 per 100,000.[3] [4] [5] [6] [7] Meta-analyses have calculated the prevalence of idiopathic ('primary') dystonia as 16-30 per 100,000, although this is likely to be an underestimate.[8] [9] [10]

The prevalence is higher in specific subgroups, such as Ashkenazi Jews where it is estimated at 1110 per 100,000. When late-onset cases are included, estimates of the prevalence of dystonia range from 300 per 100,000 to as high as 732 per 100,000.[4] [5] [11]

Aetiology

Dystonias may be idiopathic, inherited, or acquired.[1]

In idiopathic dystonia there is no identified gene, structural lesion or exposure responsible for the dystonia.[1] [12]

Several genes have been identified in association with inherited dystonia. These include autosomal-dominant (often with incomplete penetrance), autosomal-recessive, X-linked, and mitochondrial genetic causes.[12] A family history is not uniformly present in genetic forms of dystonia due to reduced penetrance.

Mutations in the TOR1A gene (also known as the DYT1 gene) that encodes TorsinA can be found in patients with early-onset dystonia (usually beginning before 26 years of age) that typically begins focally in one limb and subsequently generalises.[13] [14] Other isolated dystonias can be associated with genetic mutations, including a predominantly neck and upper limb dystonia with onset in the second and third decades of life that is characterised by mutations in the THAP1 gene (also known as the DYT6 locus).[15]

Mutations in the CGH1 gene are associated with an autosomal dominant, levodopa responsive dystonia.[16] [17]

Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT1	Primary torsion dystonia; idiopathic torsion dystonia; Oppenheim dystonia; dystonia musculorum deformans 1; TOR1A	Childhood or early adult (usually before 26 years of age)	Often starts as focal limb dystonia (commonly action dystonia of 1 foot); often generalises	9q34	TorsinA (GAG deletion); ATPase family; chaperone-like functions	AD	30% to 40%
DYT2	AR primary torsion dystonia	Childhood	Segmental or generalised dystonia	Unknown	Unknown	AR	Unknown
DYT3	X-linked dystonia; parkinsonism; Lubag	12-52 years (mean: 37.9)	Males with focal, then segmental or generalised dystonia; parkinsonism develops later in 50% of cases; endemic in Panay, Philippines	Xq13.1	TAF1/DYT3 multiple transcript system	X-linked	100% by 5th decade
DYT4	Torsion dystonia 4; non-DYT1 primary torsion dystonia; whispering dysphonia	13-37 years	Primarily laryngeal ("whispering") dysphonia; sometimes cervical; often generalises; ± psychiatric symptoms; reported in 1 large Australian family	19p13.3	TUBB4A; tubulin beta 4A	AD	Unknown (40% of patients' offspring older than age 40 are affected)
AD, autosomal dominant; AR, autosomal recessive.							

Genetics and dystonia

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Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT5a/DYT14 GCH1	Dopa-responsive dystonia; Segawa syndrome; hereditary progressive dystonia with marked diurnal variation	Usually childhood	Dystonia; parkinsonism; may mimic cerebral palsy; diurnal variation; dramatic response to levodopa	14q22.1-14q22.2	GTP cyclohydrolase; biopterin synthesis (cofactor for dopamine synthesis)	AD	30% (possibly higher in females)
DYT5b	Dopa-responsive dystonia; Segawa syndrome; hereditary progressive dystonia with marked diurnal variation		Dystonia; parkinsonism; may mimic cerebral palsy; diurnal variation; dramatic response to levodopa	11p15.5	Tyrosine hydroxylase	AR	
DYT6	Adolescent-onset primary torsion dystonia of mixed type	Average age of 16 years (range: 5-62)	Focal (arm, cranial, or cervical); may become generalized	8p21-8p22	THAP1 (thanatos-associated protein domain-containing apoptosis-associated protein 1); represses TOR1A expression	AD	30-60%
DYT7	Adult-onset focal primary torsion dystonia	Adult (28-70)	Focal dystonia (cervical, writer's cramp, laryngeal); hand tremors; does not generalize; reported in German families	18p	Unknown	AD	(incomplete 40%)
AD, autosomal dominant; AR, autosomal recessive.							

Genetics and dystonia

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Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT8	Paroxysmal dystonic choreoathetosis (PDC); paroxysmal nonkinesigenic dyskinesia (PNKD); Mount-Reback syndrome	Variable (childhood-early adulthood)	Episodes lasting 2 minutes to 4 hours of dystonia and chorea/dyskinesias triggered by stress, alcohol, caffeine, nicotine	2q33-2q36	Myofibrillogenesis regulator 1 (MR-1) gene	AD	Incomplete
DYT9 / DYT18	Paroxysmal choreoathetosis with episodic ataxia and spasticity; choreoathetosis, spasticity, and episodic ataxia	Childhood (2-15 years)	Chronic spastic paraplegia plus episodes of dystonia, choreoathetosis, paraesthesias, and diplopia triggered by exercise, stress, alcohol	1p13.3-1p21	Glucose transporter type 1 (GLUT1), also known as solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1)	AD	Unknown
DYT10	Paroxysmal kinesogenic choreoathetosis (PKC) ; paroxysmal kinesogenic dyskinesias (PKD); periodic dystonia	Childhood (6-16 years)	Episodes of dystonia and choreoathetosis triggered by sudden movements	16p11.2-16q12.1	Proline-rich transmembrane protein 2 (PRRT2)	AD	Incomplete
DYT11	Myoclonus-dystonia; alcohol-responsive dystonia	Variable; can be early childhood	Myoclonus plus dystonia; improves with alcohol	7q21-7q31; 18p11; (11q23 for D2 receptor?)	Epsilon-sarcoglycan; (SGCE); also possibly dopamine D2 receptor gene	AD	Incomplete; higher when inherited paternally (imprinting)
AD, autosomal dominant.							

Genetics and dystonia

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Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT12	Rapid-onset dystonia-parkinsonism	Variable (childhood-adult)	Acute or subacute onset of generalised dystonia plus parkinsonism	19q13	Na^+/K^+ ATPase α3 subunit (ATP1A3); sodium pump	AD	Incomplete
DYT13	Focal dystonia with cranial-cervical features	Variable (5 years-adult; average = 15 years)	Focal or segmental dystonia (cranial, cervical, or upper limb); mild in severity; rarely generalised; reported in an Italian family	1p36.13-1p36.32	Unknown	AD	58%
DYT14	Withdrawn: now known to be the same as DYT5a						
DYT15	Myoclonus-dystonia; alcohol-responsive dystonia		Jerky movements of upper limbs, hands, and axial muscles with alcohol-responsive myoclonus-dystonia	18p11	Unknown	AD	Incomplete
DYT16	Dystonia-parkinsonism	Childhood	Brazilian cases and a German case. Focal (limb) dystonia with progression to generalised, sometimes with bradykinesia	2q31	Protein kinase, interferon-inducible double-stranded RNA-dependent activator (PRKRA); cellular stress response	AR	
AD, autosomal dominant; AR, autosomal recessive.							

Genetics and dystonia

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Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT17	AR primary torsion dystonia	Teens	Lebanese family with primary focal torsion dystonia; torticollis plus dysphonia	20p11.2-q13.12	Unknown	AR	
DYT19	Episodic kinesogenic dyskinesia 2	Childhood	Indian family with brief episodes (up to 2 minutes) of dystonia or chorea induced by sudden movement; 120 episodes per day; ± seizures; ± sensory aura of paraesthesias; may have spontaneous remission	16q13-q22.1	Unknown	AD	75%
DYT20	Paroxysmal nonkinesigenic dyskinesia 2	Variable (childhood to 50)	Canadian family with episodes lasting 2-10 minutes of dyskinesias occurring daily or a few times per month; ± migraines; ± seizures	2q31	Unknown	AD	89%
DYT23	Cervical dystonia	Adult	Adult-onset cervical dystonia	9q	CIZ1	AD	
DYT24	Craniocervical dystonia	Variable	Craniocervical dystonia	11p	ANO3	AD	
DYT25	Cervical dystonia	Usually adult (range 7-54 years)	Adult-onset cervical dystonia	18p	GNAL	AD	
DFN-1/MTS (DDP)	Deafness-dystonia syndrome 1; Mohr-Tranebjaerg syndrome; XL dystonia optic atrophy	Childhood	Dystonia, sensorineural hearing loss, spasticity, mental retardation, cortical blindness; female carriers may present with adult-onset focal dystonia without deafness	Xq22	Dystonia-deafness peptide (DDP); mitochondrial protein import	X-inked	Incomplete in female carriers (incompletely skewed X-inactivation)
LHON-dystonia (mtDNA)	Leber hereditary optic neuropathy plus dystonia	Variable	Dystonia, optic atrophy, or both	mtDNA	ND6 (complex I subunit); mitochondrial function	Maternal	Incomplete
AD, autosomal dominant; AR, autosomal recessive.							

Genetics and dystonia

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Acquired dystonias may be due to the following factors:

- A structural lesion involving the basal ganglia (stroke, tumour, infection); also reported with lesions of the thalamus, brainstem, cortex, or cerebellum.
- An association with other neurological deficits (e.g., Parkinson's disease, Wilson's disease, cerebral palsy). Perinatal cerebral injury along with absence of normal early development is more suggestive of an acquired dystonia (cerebral palsy) rather than a idiopathic dystonia.
- Acute or chronic exposure to both typical and atypical antipsychotic agents and dopamine-receptor blocker anti-emetics such as metoclopramide and prochlorperazine are strongly associated with medication-induced dystonias. These can either be acute dystonic reactions or tardive dystonias.
- Trauma; post-traumatic dystonia is usually accompanied by other neurological signs including tremor, weakness, and spasticity if head trauma is the cause. A relatively rapid-onset fixed dystonia accompanied by signs of complex regional pain syndrome is thought to comprise another form of post-traumatic dystonia, usually a focal limb dystonia.[18] This form of dystonia is usually poorly responsive to the treatments used for primary dystonia. There are many reports of patients who have developed what appears to be focal dystonia of a body part that had been traumatically injured days

or weeks earlier, although the precise aetiological relationship between trauma and dystonia remains controversial.[19] [20] [21]

- Activity; there is strong anecdotal evidence suggesting that people who frequently use fine motor skills (e.g., musicians) are at increased risk of developing focal dystonia.

Dystonia also can be a feature of a more complex widespread neurodegenerative disorder, sometimes referred to as 'heredodegenerative' dystonia.[3] [22] [23] [24] [25] Functional dystonia and paroxysmal dystonia are also recognised subtypes of dystonia.[2] [26]

Pathophysiology

The pathophysiology is complex, with distinct factors contributing to the development of dystonia in different conditions. The precise pathophysiology of idiopathic dystonias remains unknown. Dopamine is likely to be involved in some types of dystonia, as suggested by the dopamine deficiency and dramatic responsiveness to dopaminergic agents in dopa-responsive dystonia. The frequent association of dystonia with parkinsonism and the induction of dystonia by dopamine-blocking antipsychotic medications provide further evidence of a role for dopamine in dystonia.[3] [23]

It is increasingly clear that both focal and generalised forms of dystonia are brain network disorders that may result in loss of normal surround inhibition of motor areas, abnormal sensorimotor integration, and maladaptive plasticity.[27] Multiple neuroimaging studies have demonstrated abnormal patterns of metabolic activity and microstructural changes in the basal ganglia, thalamus, cerebellum, and sensorimotor and premotor cortices.[27] [28] Fluoro-deoxyglucose positron-emission tomography and functional magnetic resonance imaging studies have generally shown increased resting glucose metabolism in premotor cortex and lentiform nucleus as well as possibly abnormal activity in premotor and primary motor cortex. It should be noted that these brain scans are not used to confirm a clinical diagnosis of dystonia. Electrophysiological studies indicate impaired central nervous system inhibitory activity. Impaired surround inhibition may contribute to spread of neural activity to regions adjacent to activated neural circuits, potentially accounting for inappropriate overflow of movement into adjacent muscles. Sensorimotor representations of affected body parts in focal dystonia are enlarged in the cerebral cortex. However, it remains unclear if these changes are primary or secondary.[23] [29]

Classification

Dystonia classification: clinical characteristics and aetiology[1]

New information concerning aetiology, and problems with older terminology, has led to the development and publication of an updated classification of dystonias by a consensus committee of experts. The dystonias are now classified according to two main axes: clinical manifestations and biological causes.

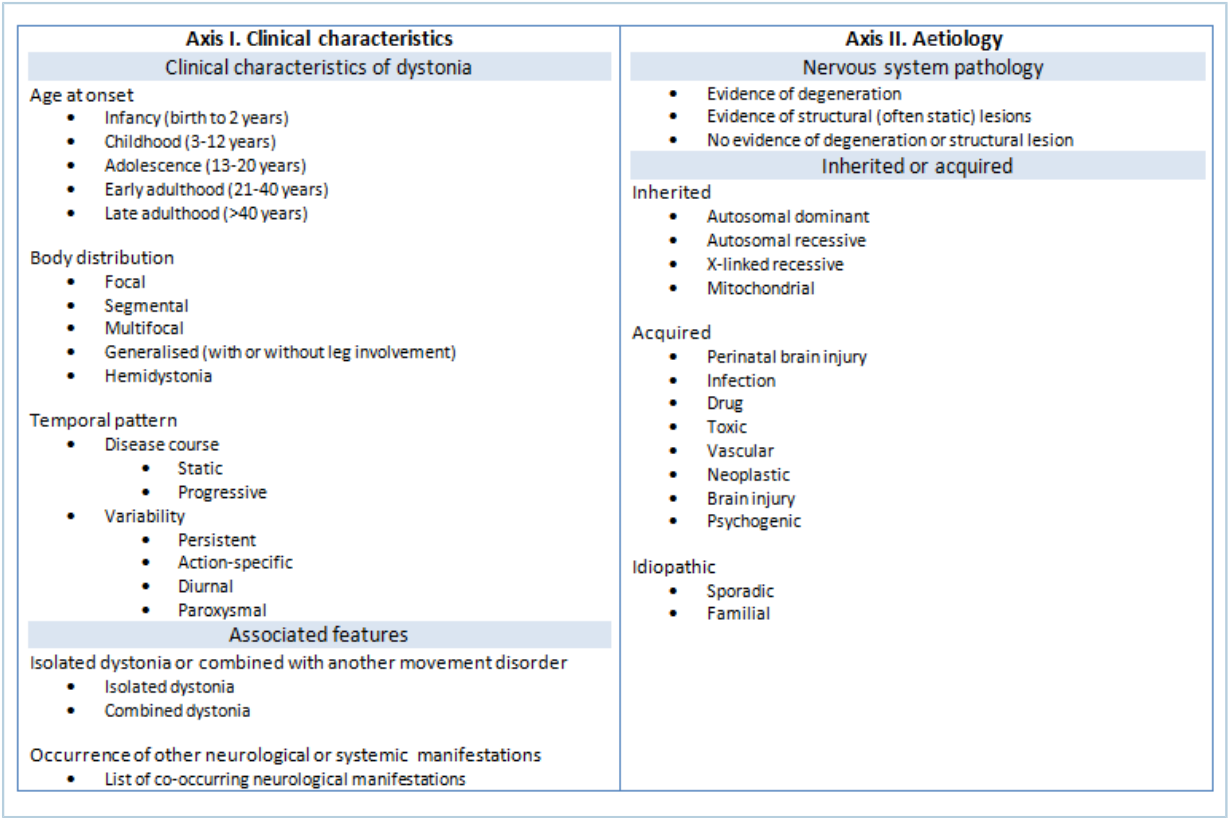
Axis I. Clinical characteristics

- Dichotomous classification of dystonia syndromes (childhood- or adult-onset) has been replaced by a scheme that classifies dystonias into five age ranges (infancy, childhood, adolescence, early adulthood, and late adulthood).
- Affected body distribution includes focal, segmental, multifocal, generalised, and hemidystonia.
- Temporal patterns exhibited in the dystonias. The disease course may be static or progressive, while disease variability includes persistent, action-specific, diurnal, and paroxysmal patterns.

- Associated features are important. Dystonia may occur in isolation, or there may be additional movement disorders. Isolated dystonia includes dystonias previously called 'primary' dystonia where, with the exception of tremor, dystonia is the only motor abnormality. Combined dystonia includes dystonias associated with other movement disorders such as parkinsonism or myoclonus. In addition, there may be other neurological or systemic manifestations that are associated with the dystonia.
- In the 2013 consensus classification, 'isolated' refers to phenomenology and not aetiology. In 'combined' forms, dystonia is not necessarily the predominant movement disorder.

Axis II. Aetiology

- Includes inherited and acquired disorders in which there are degenerative brain pathologies, acquired structural brain lesions, or disorders without identifiable brain abnormalities.
- Inherited disorders include autosomal-dominant, autosomal-recessive, X-linked, and mitochondrial diseases.
- The inherited dystonias include a mixed group of both isolated and combined dystonic syndromes, some of which are very rare.
- Dystonia may be due to an acquired disorder, such as a traumatic, infectious, drug-induced, toxic, vascular, or neoplastic cause, perinatal brain injury, or a functional (psychogenic) movement disorder.[2]
- Idiopathic adult-onset focal or segmental dystonias with either sporadic or familial distribution are also included in Axis II.



Axis I. Clinical characteristics

Clinical characteristics of dystonia

Age at onset
- Infancy (birth to 2 years)
- Childhood (3-12 years)
- Adolescence (13-20 years)
- Early adulthood (21-40 years)
- Late adulthood (>40 years)

Body distribution
- Focal
- Segmental
- Multifocal
- Generalised (with or without leg involvement)
- Hemidystonia

Temporal pattern
- Disease course
  - Static
  - Progressive
- Variability
  - Persistent
  - Action-specific
  - Diurnal
  - Paroxysmal

Associated features

Isolated dystonia or combined with another movement disorder
- Isolated dystonia
- Combined dystonia

Occurrence of other neurological or systemic manifestations
- List of co-occurring neurological manifestations

Axis II. Aetiology

Nervous system pathology
- Evidence of degeneration
- Evidence of structural (often static) lesions
- No evidence of degeneration or structural lesion

Inherited or acquired

Inherited
- Autosomal dominant
- Autosomal recessive
- X-linked recessive
- Mitochondrial

Acquired
- Perinatal brain injury
- Infection
- Drug
- Toxic
- Vascular
- Neoplastic
- Brain injury
- Psychogenic

Idiopathic
- Sporadic
- Familial

Consensus classification of dystonia

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THEORY

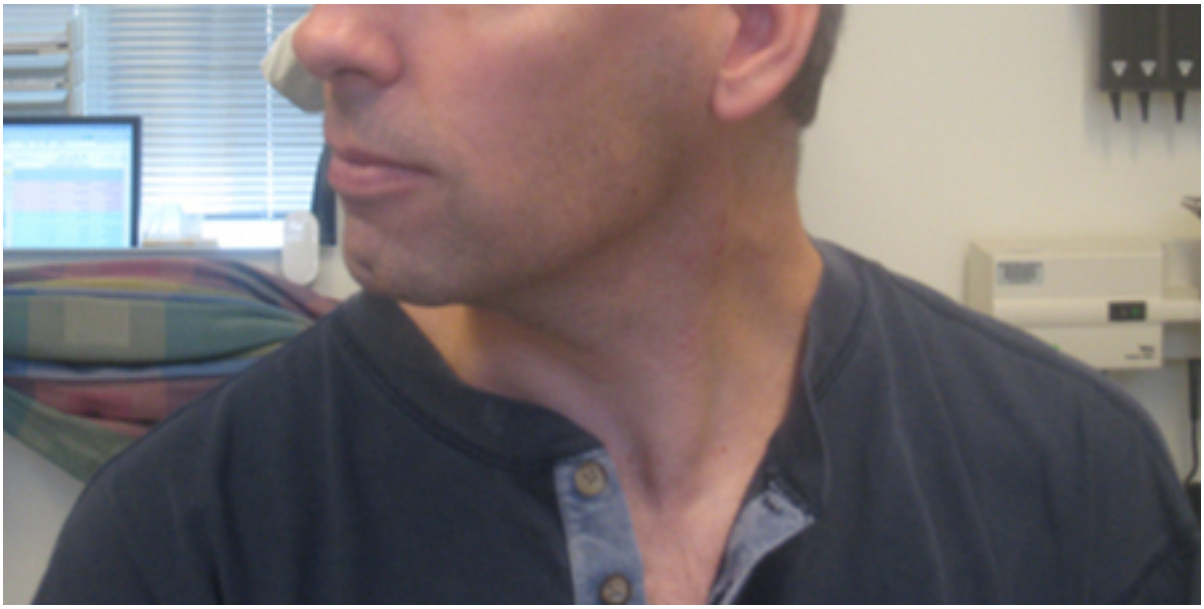
Case history

Case history #1

A 40-year-old man presents with a history of neck stiffness and limited head mobility with the tendency for his head to turn to the right and tilt to the left. He has also developed increasing neck discomfort and an irregular tremor of the head. After worsening over 1 year, the symptoms have stabilised but persisted. He reports that the abnormal head positioning, pain, and tremor are partially relieved if he gently touches his left cheek with his hand. No other family members are affected.

Other presentations

The diagnosis of dystonia is often missed, sometimes for several years. Some dystonias may be mistaken for a functional neurological disorder due to unusual features such as the irregular nature of the tremors or the sometimes surprising efficacy of a sensory trick ('geste antagoniste'). Early-onset generalised dystonia associated with TOR1A (also known as DYT1) mutations or dopa-responsive dystonia may mimic cerebral palsy, but early developmental milestones are usually normal.



Rotational torticollis

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The torticollis improves with a sensory trick: gently touching his chin

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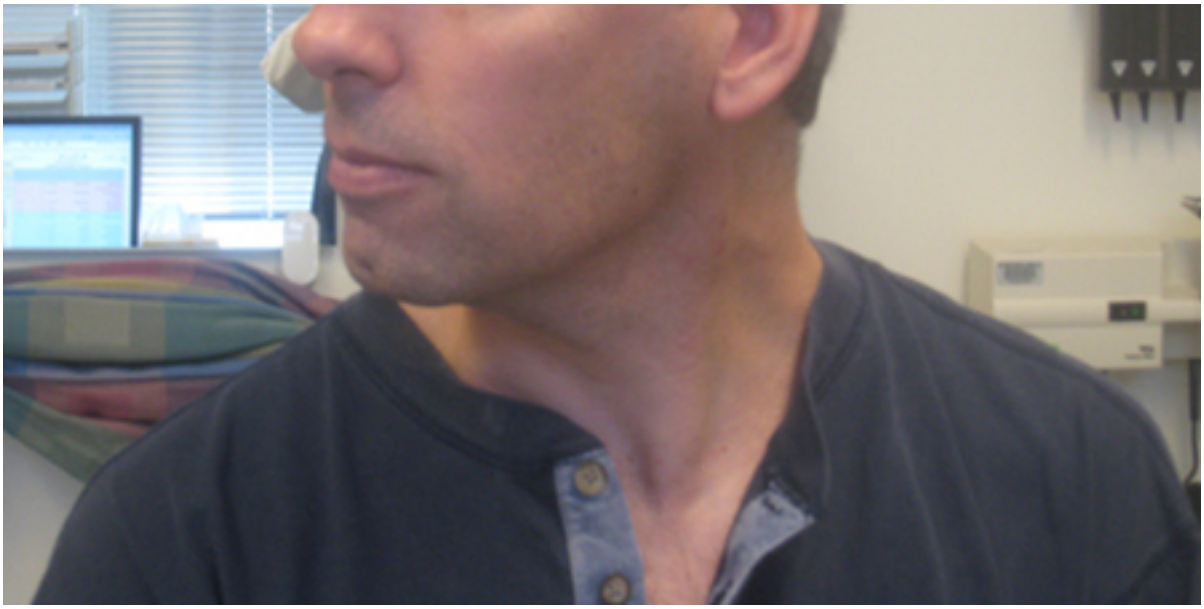
Approach

Diagnosis of dystonia is based on physical examination, and distinguishing it from other types of movement disorders is essential. The next step is to determine whether the dystonia is idiopathic, inherited, or acquired and identify an aetiological cause with selected investigations.

History

A history of abnormal muscle posture and movement, varying with different tasks, often worsening upon action of the same or a remote body part, is suggestive of dystonia. Pain in the affected muscles may be a prominent feature. Twisting of the dystonic body part frequently occurs if the limb, trunk, or neck is involved. Patients with dystonia are often able to temporarily suppress dystonic posturing or movements by touching the involved region or an adjacent body part. The sensory trick ('geste antagoniste') becomes less effective the more severe the dystonia.



Rotational torticollis

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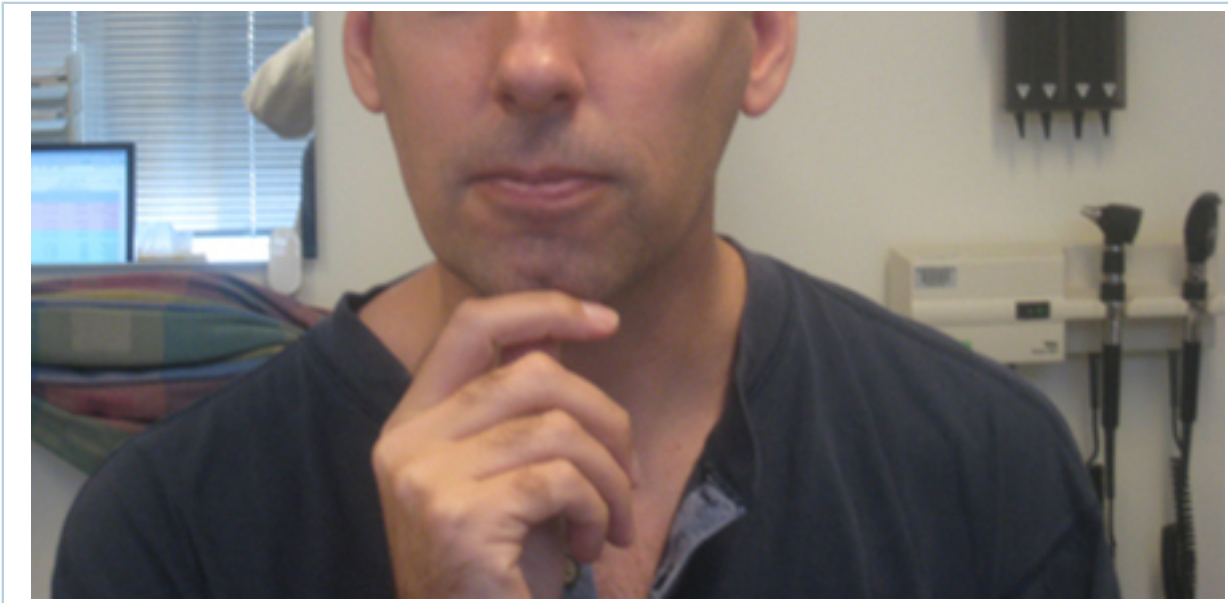

The torticollis improves with a sensory trick: gently touching his chin

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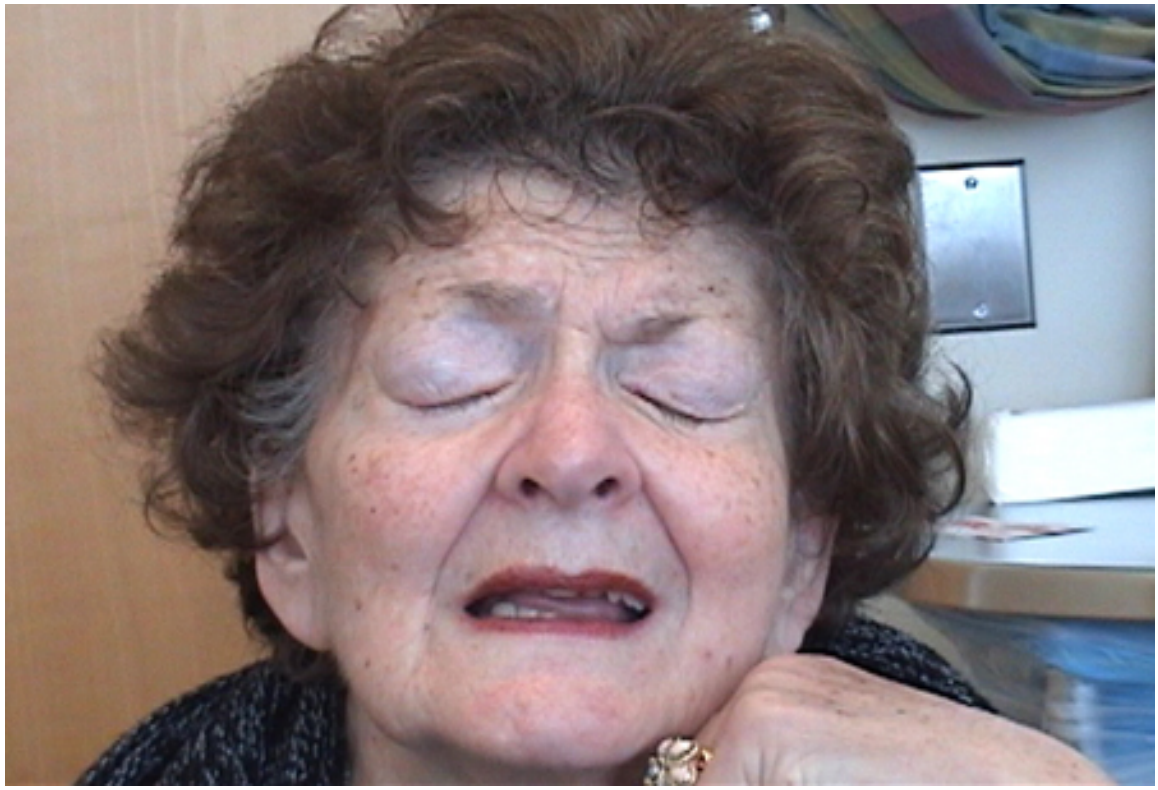
The dystonia may be focal (a single body part or region), multifocal (multiple non-adjacent regions), segmental (multiple adjacent regions), hemidystonia (multiple ipsilateral body parts, e.g., arm and leg), or generalised (one or both legs, the trunk, and at least one other body part). Focal dystonia may spread to adjacent body parts, becoming segmental or even generalising over time. This is particularly true with childhood-onset dystonia. Focal dystonias may be:

- Axial; blepharospasm; cervical (torticollis), usually a combination of rotational torticollis, anterocollis and/or laterocollis, and retrocollis



Blepharospasm

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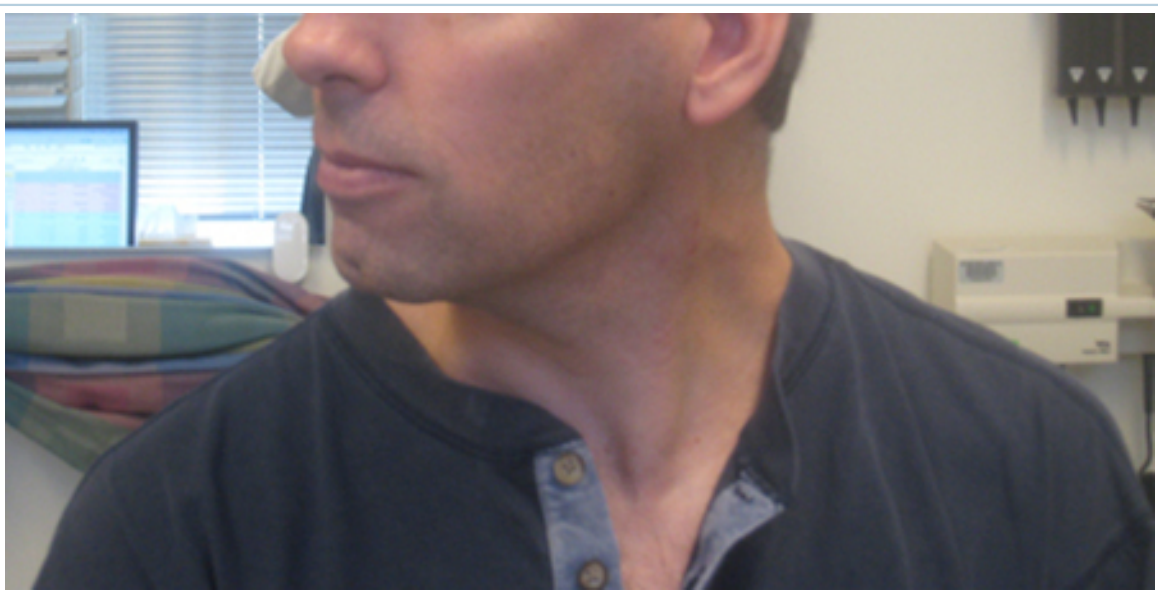

Rotational torticollis

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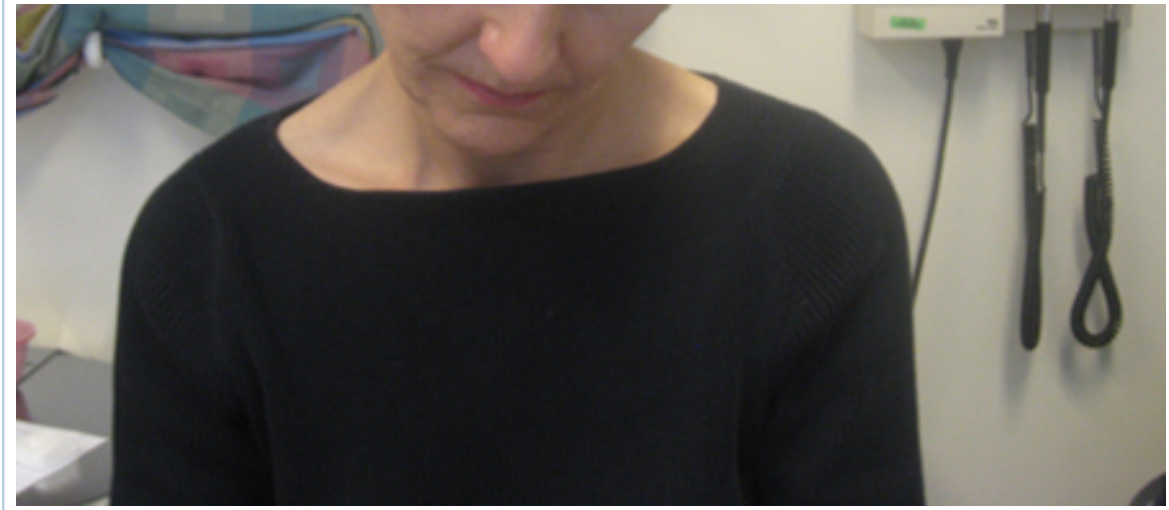

Cervical dystonia: anterolateralcollis

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Cervical dystonia: retrocollis

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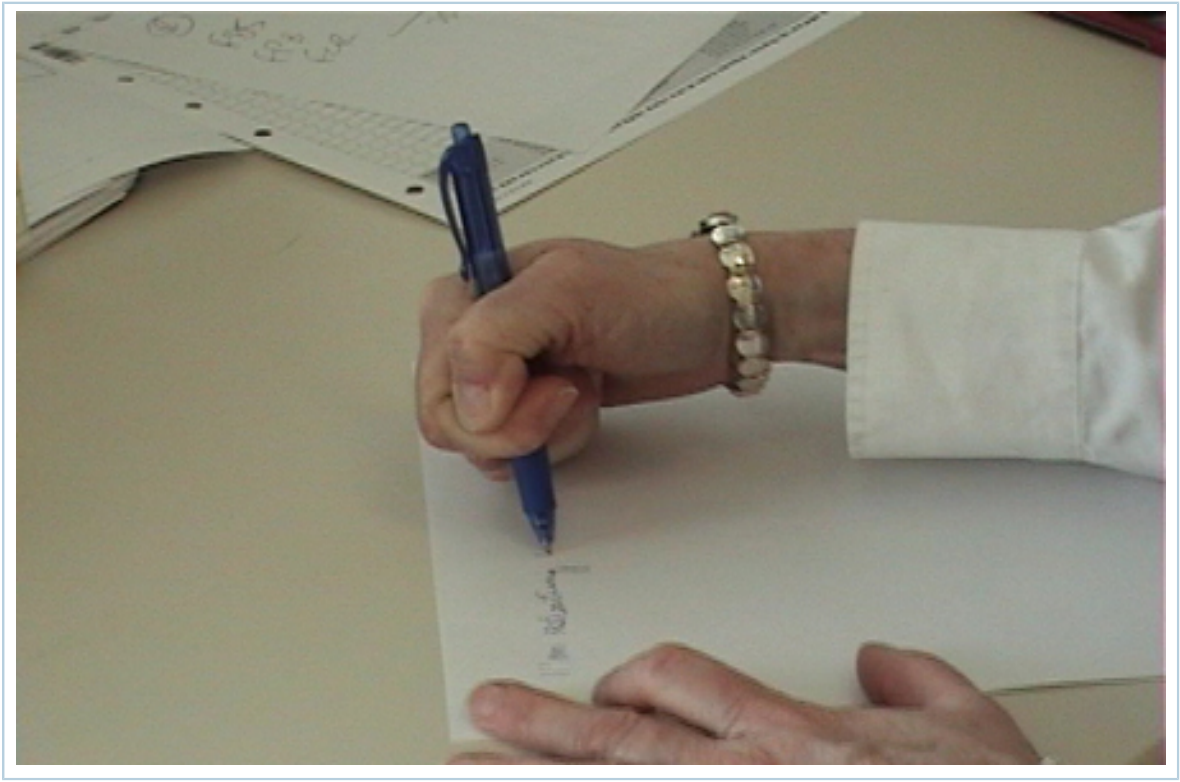
- Limb dystonia that can be task-related (e.g., writer's cramp); foot dystonia; orofacial dystonia; and oromandibular dystonia.



Writer's cramp: a focal task

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Writer's cramp: a focal task

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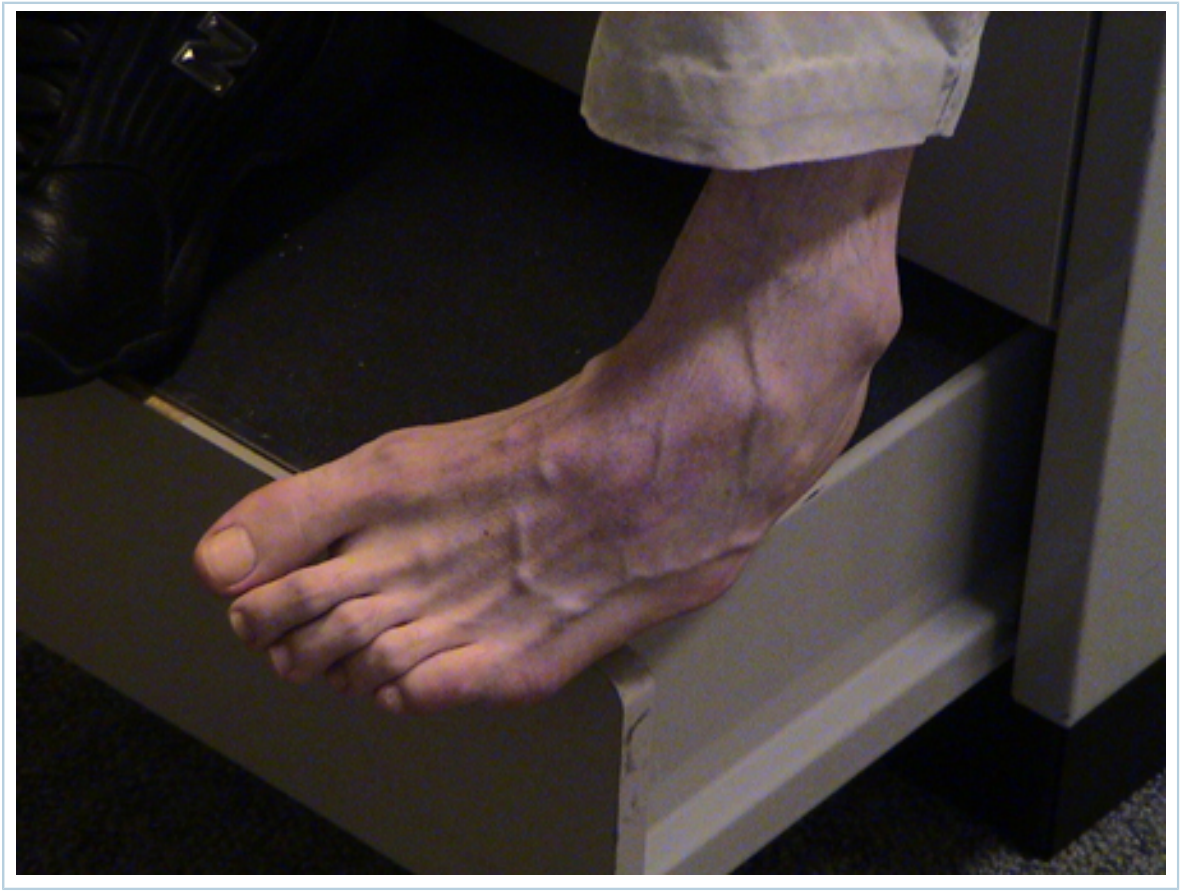

Foot dystonia with involuntary plantar flexion and foot inversion
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Other hyperkinetic movement disorders such as chorea, tremor, tics, and myoclonus should be distinguished, although these disorders can occur in association with dystonia. Dystonia is distinguishable from chorea in that movements are often sustained in postures rather than constantly moving. Myoclonus consists of a much briefer jerking movement, while tremor is a rhythmic oscillation of a body part.

In children, idiopathic dystonia often begins in a limb while in adults, idiopathic dystonia manifests almost exclusively in the head and neck region. A pattern of presentation deviating from this general rule may suggest the presence of an acquired dystonia.[35]

A thorough drug history is necessary to exclude the possibility of a dystonia induced by an antipsychotic or anti-emetic drug. Associated medications include both typical and atypical antipsychotic agents and dopamine-receptor blocker anti-emetics such as metoclopramide and prochlorperazine. These dystonias can either be acute dystonic reactions or a form of late-onset (tardive) dystonia.

Acute dystonic reactions, most commonly (but not exclusively) in younger male patients, may include torticollis, tongue or jaw dystonia, oculogyric crisis, or opisthotonus.[30] [31] [32] Patients presenting with an acute dystonic reaction typically provide history of current antipsychotics or anti-emetic use; typically dystonias are self-limiting and stop within hours after medication discontinuation. In tardive dystonia, history of concurrent or recent neuroleptic exposure is necessary for diagnosis; dystonia may initially present upon the first discontinuation of the agent.

Presence of dementia, seizures, spasticity, pyramidal weakness, and development delay raises the suspicion of an acquired dystonia, either a heredodegenerative dystonia or related to perinatal or birth injury.

Presence of parkinsonism may indicate Parkinson's disease (PD)-related dystonia or dystonia that occurs in several of the atypical parkinsonian syndromes.

A positive family history of dystonia is a significant risk factor, particularly for early-onset cases, and may signify an underlying genetic cause.[13]

There may be, in what appears to be a focal dystonia of a body part, a history of traumatic injury days or weeks earlier, although the precise aetiological relationship between trauma and dystonia remains controversial.[19] [20] [21]

An occupational history should also be taken as people who frequently use fine motor skills (e.g., musicians), are at increased risk of developing focal dystonia.

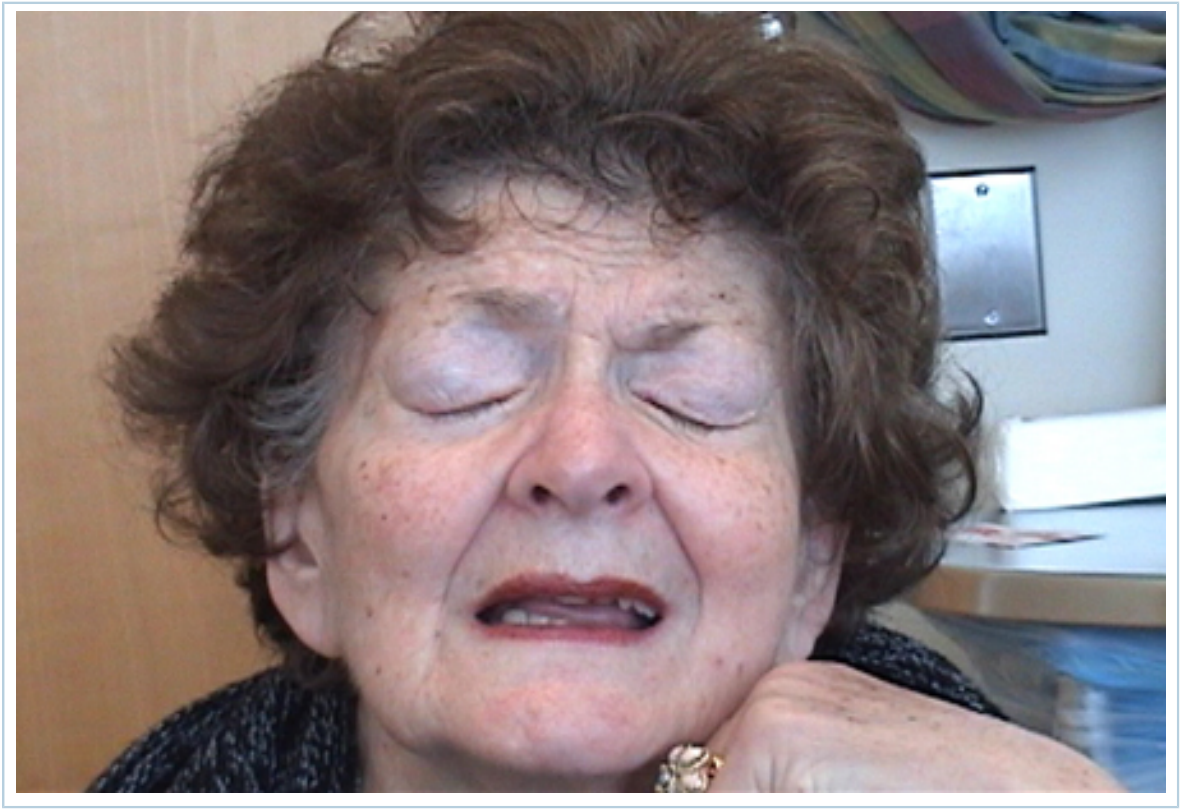
Physical examination

Observation

- Observing positions of trunk, neck, head, and limbs at rest and observing spontaneous movements are critical to making the diagnosis. Noting areas of hypertrophy and asymmetry are key aspects of the neurological examination.
- Palpating muscles may reveal more hypertrophy than simple observation.
- Watching patients walk may elicit some dystonia or subtle features of an underlying neurological process.
- Examining skin and nails may give a clue to the extent of dystonia. For example, toe flexion dystonia, often seen in Parkinson's disease, may cause calluses at the tips of the toes or thickened toenails.

Eliciting dystonia

- Simultaneous contraction of agonist and antagonist muscles is a hallmark of dystonia, but may be better appreciated by electromyography than by clinical examination.
- Action dystonia is a near-universal feature, and may be present only with specific tasks involving the dystonic body part or with activation of remote body parts. For example, certain dystonias can be triggered by playing a musical instrument or by writing. When more advanced, dystonia may appear at rest.
- Specific examination techniques of the affected region should be undertaken, as the dystonia may become more evident with certain tasks.
- Blepharospasm: forced eye closure, reading of text, bright light, watching television.



Blepharospasm

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- Spasmodic dysphonia: reading a passage, making a sustained 'eee' sound, and counting out loud.
- Orofacial and oromandibular dystonia: tongue protrusion, opening and closing the mouth repeatedly.
- Cervical dystonia: examine patient seated with eyes closed allowing head to move on its own, rotating head to extreme left and right, full flexion, and extension of the neck.

Cervical dystonia: retrocollis

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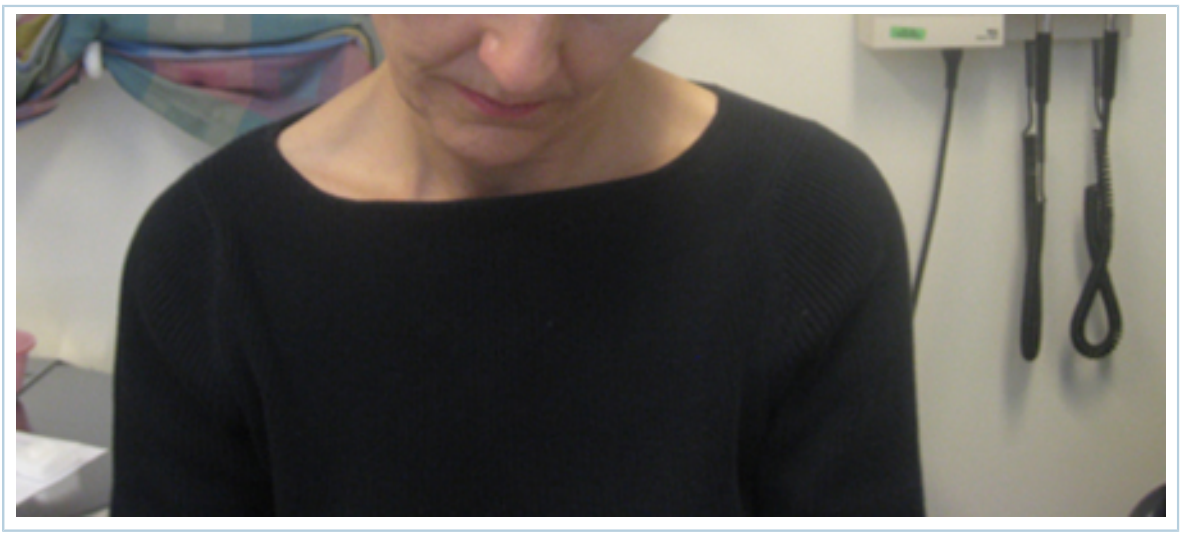

Cervical dystonia: anterolateralcollis

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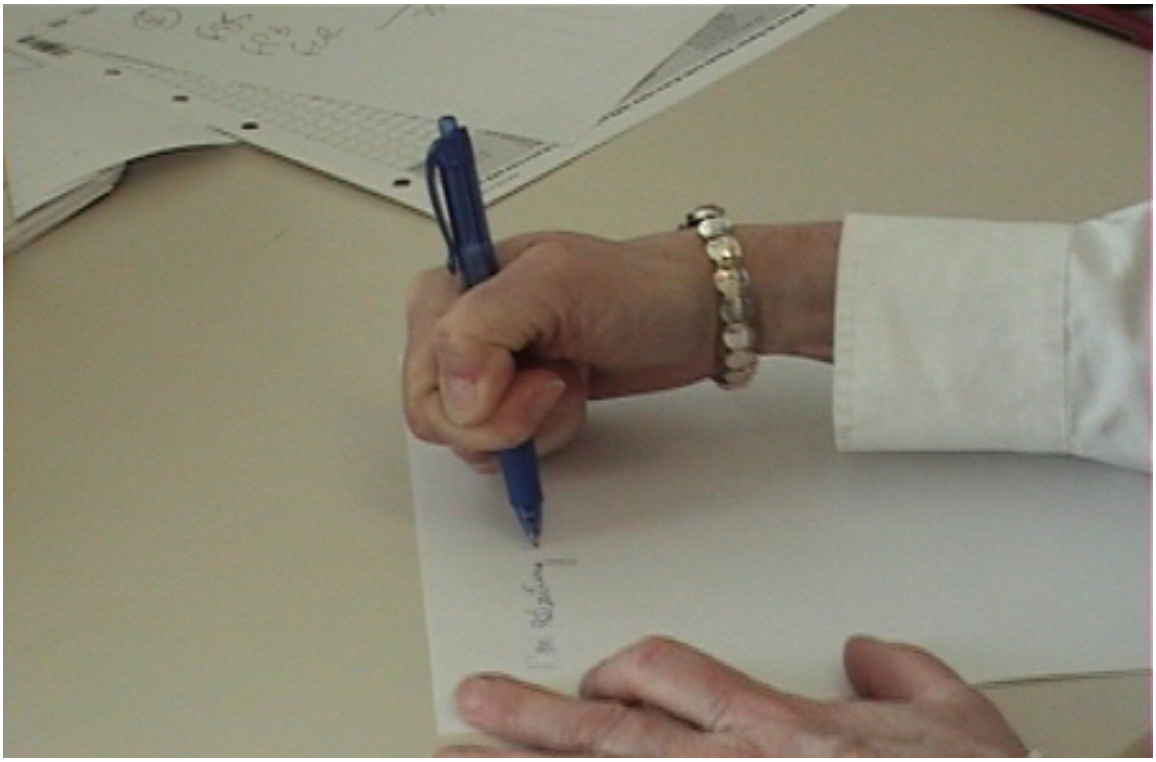
- Limb dystonia: arms extended supinated and pronated, finger to nose manoeuvre, finger tapping, handwriting, foot tapping, walking forwards and backwards; if appropriate, performing tasks related to the trigger of dystonia such as playing a musical instrument.



Writer's cramp: a focal task

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Writer's cramp: a focal task

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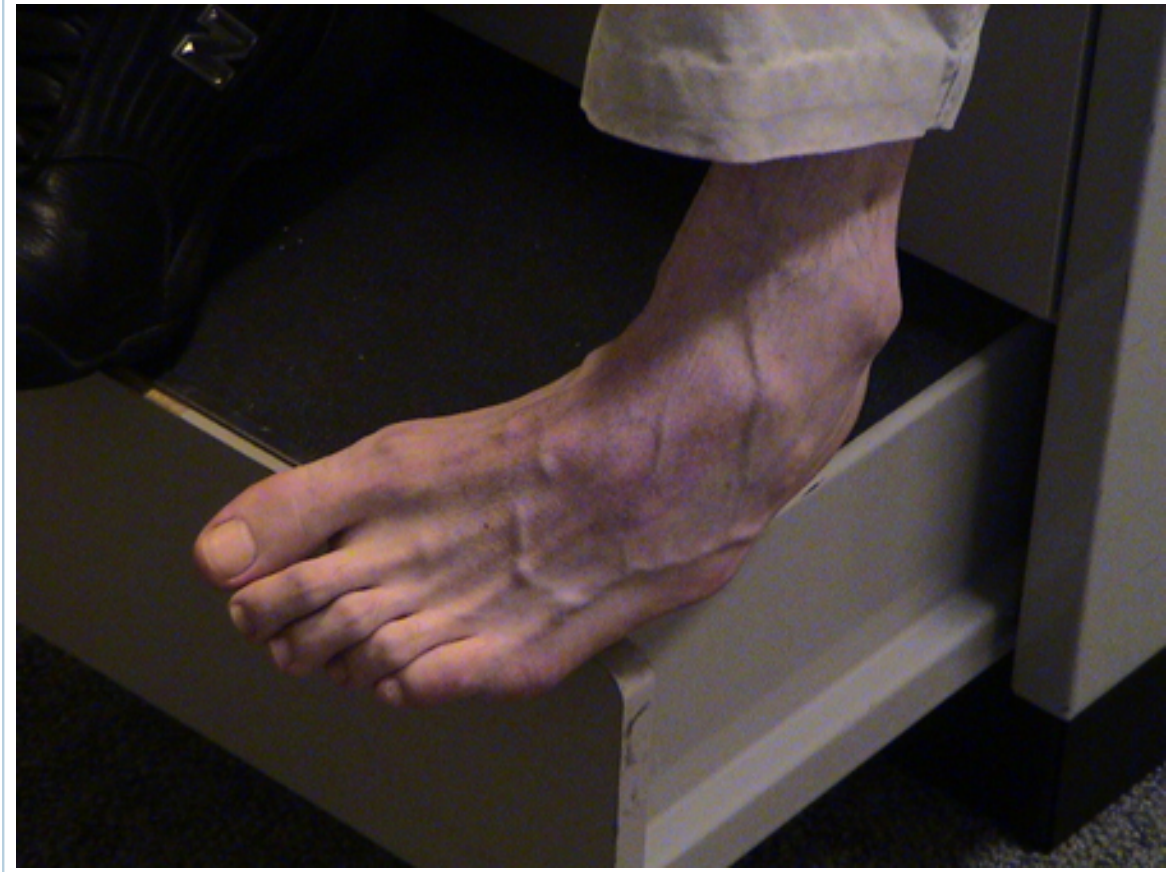

Foot dystonia with involuntary plantar flexion and foot inversion
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Signs of a cause of acquired dystonia

- Presence of other neurological signs should be carefully sought. Accompanying parkinsonism suggests the possibility of PD-related dystonia. This usually manifests as foot dystonia, blepharospasm, or cervical dystonia, and rarely as a lateral axial dystonia.[36]
- Dystonia can also occur in several of the atypical parkinsonism syndromes, such as multiple system atrophy (cranial, cervical, or axial dystonia), corticobasal degeneration (limb dystonia), or progressive supranuclear palsy (axial, limb, or hemidystonia).
- Presence of myoclonus may indicate a distinct genetic entity called myoclonus-dystonia syndrome.
- Post-traumatic dystonia is usually accompanied by other neurological signs including tremor, weakness, and spasticity if head trauma is the cause. A relatively rapid-onset fixed dystonia accompanied by signs of complex regional pain syndrome is thought to comprise another form of post-traumatic dystonia, usually a focal limb dystonia.[18]
- Ophthalmic examination may demonstrate the presence of Kayser-Fleischer rings in Wilson's disease.

Investigations

Laboratory testing is not usually necessary for typical adult-onset idiopathic focal dystonia. Genetic testing for the TOR1A (also known as DYT1) mutations is appropriate when a focal or generalised dystonia is present in a person younger than 26 years of age or in someone older with a family history of early-onset

dystonia. When available, referral to a genetic diagnostic testing service for testing of the other familial dystonias is advisable when features of a genetically identified dystonia syndrome are present (early onset, positive family history).

Investigations may also be indicated when Wilson's disease is suspected (serum ceruloplasmin, urinary copper analysis), although tremor is a more common movement disorder manifestation in this disease.[37]

In early-onset dystonia (<40 years), a trial dose of levodopa can be offered.[37] It needs to be given for 4 weeks to assess responsiveness.[38] In addition, GCH1 genetic testing can be considered in some cases to confirm the presence of some causes of dopa-responsive dystonia.[16] [17]

If an acquired dystonia is suspected, magnetic resonance imaging (MRI) of the brain is recommended.[39] It may be abnormal in the case of Wilson's disease, heredodegenerative diseases causing dystonia, and cerebral infarction causing hemidystonia. Conventional T1- and T2-weighted MRI do not show any significant abnormalities in primary dystonia.

Several diagnostic algorithms have been proposed to ensure the proper evaluation for dystonia in childhood and adolescence.[40] [41] The first step is to rule out mimics of dystonia in childhood and adolescence; the second, to rule out medication-induced dystonia; the third, to evaluate the likelihood of the presence of an acquired dystonia; and finally, biochemical and metabolic investigations are recommended before consideration of next-generation sequencing.

History and exam

Key diagnostic factors

presence of risk factors (common)

- Key risk factors include a positive family history of dystonia, repetitive activity of affected region, birth injury and delayed development in childhood, exposure to antidopaminergic agents, trauma, known genetic mutation, Ashkenazi Jewish ethnicity, structural lesions of the basal ganglia, and Parkinson's disease (PD) or other parkinsonian syndromes.[3] [13] [18] [19] [20] [21] [23] [30] [31] [32][33] [34]

simultaneous contraction of agonist and antagonist muscles (common)

- This is a hallmark of dystonia, but may be better appreciated by electromyography than by clinical examination.

muscle pain (common)

- In some cases, pain in the affected muscles may be a prominent feature.

appearance or worsening of dystonia with action (common)

- Action dystonia is a near-universal feature, and may be present only with specific tasks involving the dystonic body part or with activation of remote body parts. For example, certain dystonias can be triggered by playing a musical instrument or by writing. When more advanced, dystonia may appear at rest.

blepharospasm (common)

- Manifestation of focal dystonia.

cervical torticollis (common)

- Manifestation of focal dystonia.

hand spasms (common)

- Manifestation of focal dystonia. May be task related.

foot spasms (common)

- Manifestation of focal dystonia.

acute presentation (within 5 days of exposure to antidopaminergic agent) (uncommon)

- Strongly suggests an acute dystonic reaction, consisting of torticollis, tongue or jaw dystonia, oculogyric crisis, or opisthotonus.[30] [31] [32]

acute worsening of pre-existing generalised dystonia (uncommon)

- Some patients with poorly controlled generalised dystonia may develop acute worsening of their dystonia, which can be severe and life-threatening. Evidence for overlapping neuroleptic malignant syndrome, malignant hyperthermia, serotonin syndrome, or other acute infectious/metabolic/toxic derangement should be considered.[42]

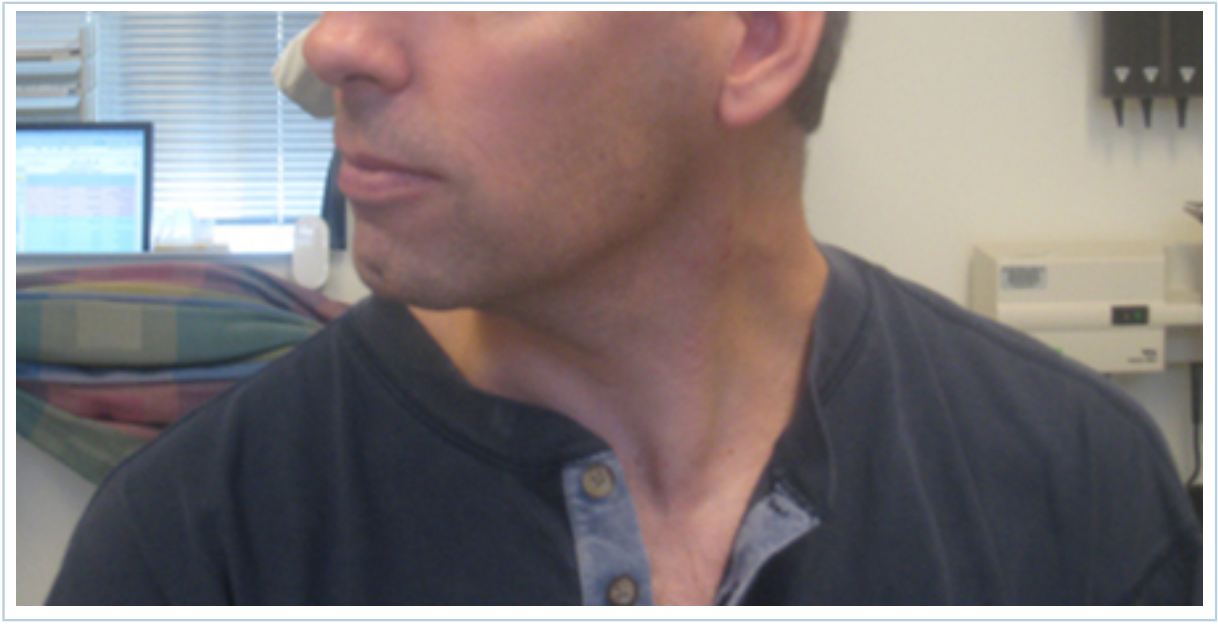
Other diagnostic factors

twisting of the affected body part (common)

- Twisting of the dystonic body part frequently occurs if the limb, trunk, or neck is involved.

geste antagoniste (sensory trick) (common)

- Patients with dystonia are often able to temporarily suppress dystonic posturing or movements by touching the involved region or an adjacent body part. The sensory trick becomes less effective the more severe the dystonia.



Rotational torticollis

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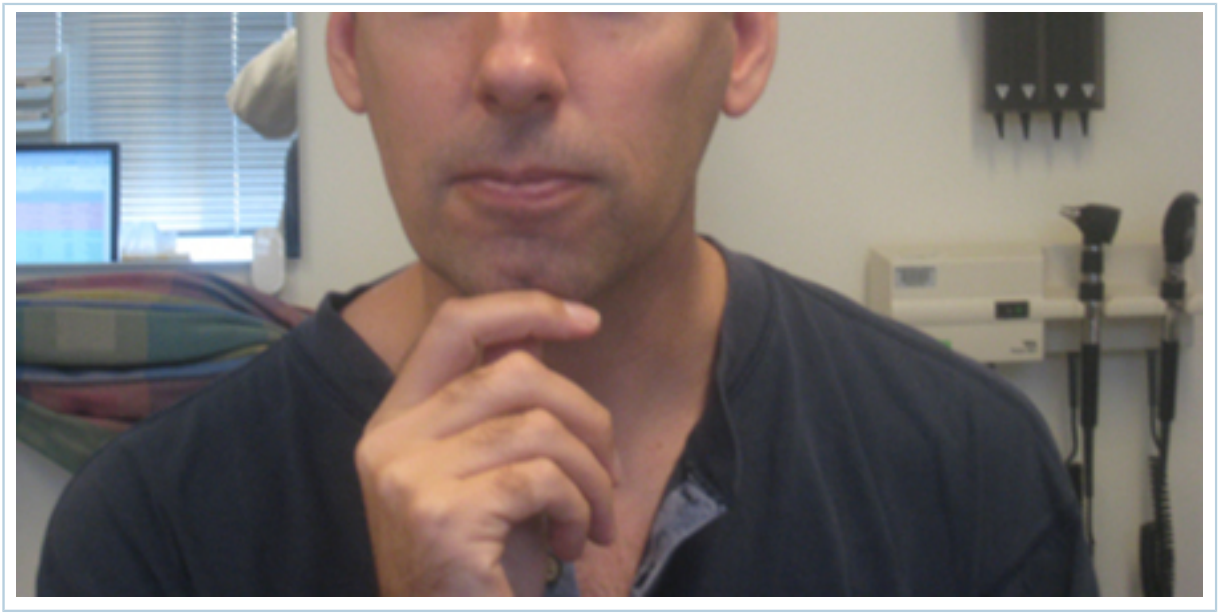

The torticollis improves with a sensory trick: gently touching his chin

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spread to another body part (uncommon)

- Focal dystonia may spread to adjacent body parts, becoming segmental or even generalising over time. This is particularly true with childhood-onset dystonia.

parkinsonism (uncommon)

- Accompanying parkinsonism suggests the possibility of Parkinson's disease-related dystonia. This usually manifests as foot dystonia, blepharospasm, or cervical dystonia, and rarely as lateral axial dystonia.[36]

myoclonus (uncommon)

- Presence of myoclonus as well may indicate a distinct genetic entity called myoclonus-dystonia syndrome.

tremor, weakness, or spasticity (uncommon)

- Post-traumatic dystonia is usually accompanied by other neurological signs including tremor, weakness, and spasticity if head trauma is the cause.

Kayser-Fleischer rings on slit-lamp examination (uncommon)

- Presence of Kayser-Fleischer rings suggests Wilson's disease.

Risk factors

Strong

family history of dystonia

- A positive family history of dystonia is a significant risk factor, particularly for early-onset cases, and may signify an underlying genetic cause.[13]
- A family history is not uniformly present in genetic forms of dystonia due to reduced penetrance.

repetitive activity of affected region

- Some forms of focal dystonia are referred to as task-specific dystonia. There is strong anecdotal evidence suggesting that people who frequently use fine motor skills (e.g., musicians), are at increased risk of developing focal dystonia.

birth injury and delayed development in childhood

- Documented history of perinatal cerebral injury along with absence of normal early development is more suggestive of an acquired dystonia (cerebral palsy) rather than an idiopathic dystonia.

exposure to antidopaminergic agents

- Acute or chronic exposure to both typical and atypical antipsychotic agents and dopamine-receptor blocker anti-emetics such as metoclopramide and prochlorperazine are strongly associated with medication-induced dystonias. These can either be acute dystonic reactions or a form of late-onset (tardive) dystonia.
- Acute dystonic reactions, most common (but not exclusively) in younger male patients, may include torticollis, tongue or jaw dystonia, oculogyric crisis, or opisthotonus.[30] [31] [32]

trauma

- Post-traumatic dystonia is usually accompanied by other neurological signs including tremor, weakness, and spasticity if head trauma is the cause. A relatively rapid-onset fixed dystonia accompanied by signs of complex regional pain syndrome is thought to comprise another form of post-traumatic dystonia, usually a focal limb dystonia.[18] This form of dystonia is usually poorly responsive to the treatments used for idiopathic dystonia. There are many reports of patients who have developed what appears to be focal dystonia of a body part that had been traumatically injured days or weeks earlier, although the precise aetiological relationship between trauma and dystonia remains controversial.[19] [20] [21]

genetic mutation

- Several genetic factors have been identified in association with dystonia. These include autosomal-dominant (often with incomplete penetrance), autosomal-recessive, X-linked, and mitochondrial genetic causes.
- Mutations in the TOR1A gene (also known as the DYT1 locus) that encodes TorsinA can be found in patients with early-onset dystonia (usually beginning before 26 years of age) that typically begins focally in one limb and subsequently generalises.[13] Other isolated dystonias can be associated with genetic mutations, including a predominantly neck and upper limb onset dystonia in the second and third decades of life, which is characterised by mutations in the THAP1 gene (also known as the DYT6 locus).[15]

Ashkenazi Jewish ethnicity

- The prevalence of dystonia is higher in Ashkenazi Jews, where it is estimated at 1110 per 100,000.[3]

structural lesion of the basal ganglia

- Although standard neuroimaging is normal in most patients with dystonia, structural lesions of the basal ganglia (particularly the putamen) and less commonly the thalamus, brainstem, parietal cortex, or cerebellum have been reported in association with dystonia.[3] [23] [33] [34]

parkinsonian syndrome

- Some patients with Parkinson's disease (PD) or other parkinsonian syndromes can develop dystonia as part of the disease. For example, PD may present with focal limb dystonia, or dystonia may occur in response to levodopa.[3]

Investigations

1st test to order

Test	Result
levodopa responsiveness • Dopa-responsive dystonia should be ruled out in early-onset dystonia cases (<40 years).[37] • Levodopa is given for at least 4 weeks to assess response.[38]	**positive if clinical improvement following administration**

Other tests to consider

Test	Result
cranial magnetic resonance imaging • Should be performed if an acquired cause of dystonia is suspected.[39] Consider if hemidystonia (multiple ipsilateral body parts, e.g., arm and leg) or other neurological signs are present in addition to dystonia. Can also consider if presentation is acute and there has been no exposure to antidopaminergic drugs. No evidence to support the yield of imaging in primary focal, segmental, or generalised dystonias.	**normal**
serum ceruloplasmin • Consider if Wilson's disease is suspected.[37] • Serum ceruloplasmin <20 mg/dL suggests dystonia due to Wilson's disease.	**normal**
24-hour urine copper • Consider if Wilson's disease is suspected. Levels >100 micrograms suggest Wilson's disease. • False positives may occur in patients with cholestasis, autoimmune conditions, or protein-losing enteropathy.	**normal**
TOR1A (also known as DYT1) gene testing • Consider testing in patients with any form of isolated dystonia younger than 26 years old or any patient with a relative with dystonia with onset before the age of 26 years.[39]	**variable; presence of GAG deletion in at least one allele of the TOR1A gene**
GCH1 gene testing • Can be considered in some cases to confirm the presence of some causes of dopa-responsive dystonia.[16][17]	**variable; GCH1 gene mutations usually result in a single amino acid change in the GTP cyclohydrolase 1 enzyme**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Athetoid or spastic cerebral palsy	• Patients typically present with other signs of developmental delay from birth.	• Cranial CT or MRI may reveal periventricular leukomalacia or evidence of cerebral anoxia or infarct.
Huntington's disease (HD)	• Typically present with psychosis or mood disorder. Cognitive impairment or dementia may be prominent and seizures may also be present. • Choreiform movements are more irregular and unsustained than dystonia, which is more sustained and stereotyped.	• HD gene >40 trinucleotide CAG repeats.
Parkinson's disease (PD) or atypical parkinsonism	• Typical features are bradykinesia, rigidity, and tremor.	• Diagnosis is clinical. • Functional neuroimaging may show reduced dopamine uptake. • MRI scan may show cerebral atrophy in advanced disease.
Wilson's disease	• Patients may present with a history of liver disease. • Detection of Kayser-Fleischer rings on slit-lamp examination, representing copper deposition on Descemet membrane on the cornea. This is virtually pathognomonic.	• Abnormal LFTs. • Serum ceruloplasmin is <20 mg/dL (<200 mg/L); 24-hour urinary copper is >100 micrograms.
Functional dystonia	• Patients may present with an unusual pattern of dystonia and discrepancy between patient's disability and objective signs. Psychological comorbidity may be present.[2]	• Diagnosis is clinical.
Non-dystonic torticollis	• A history or examination consistent with ocular motility problems, nuchal mass, atlantoaxial subluxation, or other structural cervical spine abnormality.	• Cervical spine imaging may show skeletal pathology (e.g., nuchal mass, atlantoaxial subluxation, or other structural cervical spine abnormality).

Criteria

Burke Fahn Marsden Dystonia Rating Scale (BFMDRS)[43]

The Burke Fahn Marsden Dystonia Rating Scale (BFMDRS) is a widely used rating scale to describe the severity and extent of the dystonia. The scale is weighted based on the product of provoking factors and severity factors in each of several body regions (eyes, mouth, speech and swallowing, neck, arm, trunk, and leg). A second component consists of a patient-reported scale to assess the impact of dystonia on activities of daily living.

Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)[44]

The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) is a validated clinical rating scale used by clinicians to rate the severity of spasmodic torticollis, taking into account the direction and the degrees of maximal displacement on objective examination as well as patient-reported impact of torticollis on activities of daily living and pain.

Approach

Treatment strategies for dystonias are highly dependent upon the age of onset and the affected body region.

For all patients, regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37] Patients with acquired dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

Acute dystonic reactions

Acute onset of dystonia is rare and, in most cases, is due to exposure to antidopaminergic agents. Initial evaluation in the emergency setting should include assessment of the airway.[45] If exposure to antidopaminergic agents is confirmed, give intravenous diphenhydramine or benzatropine and repeat if no effect is seen. Some patients with poorly controlled generalised dystonia may develop acute worsening of their dystonia which can be severe and life-threatening. If you suspect overlapping neuroleptic malignant syndrome, malignant hyperthermia, serotonin syndrome, or other acute infectious, metabolic, or toxic derangement as a cause for the acute worsening, treatment should be directed at these underlying aetiologies. See Neuroleptic malignant syndrome (Management approach) ; Malignant hyperthermia (Management approach) ; Serotonin syndrome (Management approach) .

Generalised dystonias

It is important to establish whether patients with generalised dystonia are responsive to dopaminergic therapy. A therapeutic trial of levodopa with a decarboxylase inhibitor (carbidopa) should be given, which will determine whether the patient has dopa-responsive dystonia (DRD).[37] Responsiveness should be apparent within a few days to weeks.[39] [46] DRD typically presents in childhood (DRD may comprise 5% to 10% of childhood-onset dystonia), but adults may also respond to treatment.[3] Some patients with other forms of dystonia may still respond to levodopa but usually less so and require higher doses than patients with DRD.

In a minority of patients, levodopa exacerbates dystonia.

If the dystonia does not improve with levodopa given for at least 4 weeks, the mainstay of oral symptomatic therapy consists of anticholinergic therapy. Trihexyphenidyl was shown in a double-blind, randomised, placebo-controlled study to produce a 50% improvement in dystonia ratings.[47] Anticholinergics in general are thought to be more effective in children than in adults, although this may be the result of higher doses being tolerated more easily by children.[48]

Antispasmodic medications may be given with levodopa or trihexyphenidyl. Oral baclofen has demonstrated efficacy in improving gait in some patients with TOR1A (also known as DYT1) mutations, although no randomised controlled trials investigating its use exist.[49] Clonazepam or zonisamide may also be helpful, particularly for myoclonic dystonia.[48] [50] Intrathecal baclofen has been proposed for use in cases of secondary dystonia when accompanied by spasticity, and may also be considered in children when dystonia is accompanied by cerebral palsy.[51] [52]

Although trihexyphenidyl, levodopa, and pallidal deep brain stimulation have been explored for dystonia related to cerebral palsy, there is little evidence supportive of overall benefit.[53] [54]

Focal dystonias

Most focal dystonias in adults and children do not respond to oral medications such as trihexyphenidyl and levodopa so botulinum toxin is usually the first line treatment.[39]

A number of randomised, placebo-controlled trials for various movement disorders have demonstrated efficacy of botulinum toxin in reducing the severity of the dystonia as well as pain and disability, and in improving quality of life measures.[55] [56] The best evidence exists for cervical dystonia.[57] [58] [59] [60] One Cochrane review found a significant and clinically relevant reduction in cervical dystonia-specific impairment and pain following a single treatment session of botulinum toxin type A.[60]

Botulinum toxin is available in two serotypes: type A and type B. Doses depend on the size of the muscle being injected and the serotype used.[61] Referral to a neurologist experienced in movement disorders and injection of botulinum toxin is strongly recommended when considering this treatment for cervical dystonia, blepharospasm, spasmodic dysphonia, writer's cramp, or focal lower limb dystonia.

Transcutaneous electrical nerve stimulation (TENS) has shown to be helpful for writer's cramp and speech therapy may be helpful as an adjunct to botulinum toxin for laryngeal dystonia.[62]

A trial of levodopa instead of botulinum toxin may be given for adults with isolated foot dystonia, especially if subtle signs of parkinsonism are present. Trihexyphenidyl (to a maximum tolerated dose) is a secondary option for isolated foot dystonia.

Treatment-refractory generalised, segmental, and focal dystonias

Deep brain stimulation (DBS) of the internal globus pallidus may be used in cases where oral medications or botulinum toxin have failed to improve dystonia.

DBS is approved by the US Food and Drug Administration under a humanitarian device exemption for treatment of primary generalised, segmental, cervical dystonia, or hemidystonia. DBS is thought to restore abnormal firing rates and patterns in the main outflow nucleus from the basal ganglia to the motor cortex. One Cochrane review found that DBS may improve functional capacity and reduce symptom severity in adults with cervical, segmental, or generalised moderate to severe dystonia, and may improve quality of life in adults with generalised or segmental dystonia, although the evidence was of low quality.[63] Subthalamic nucleus DBS has shown some benefit in patients with toe dystonia related to Parkinson’s disease.[64]

The following factors may have an affect on the success rate of DBS: the duration of dystonia before DBS, TOR1A (also known as DYT1) mutation status, the severity of disease, and whether the dystonia is idiopathic or acquired.[65] [66] Although data are equivocal, there are several case series indicating that idiopathic dystonias may be more likely than acquired dystonia to respond to a clinically meaningful degree, with the exception of tardive dystonias, which appear to respond very well to DBS of the internal globus pallidus.[67] [68] Consensus guidelines for patient selection suggest that there is currently not enough evidence to include or exclude candidates based on age, disease duration, or previous ablative procedures.[69]

Referral to a neurosurgery centre experienced in DBS implantation in dystonia is strongly recommended, especially in the case of children, for whom early referral may be a factor in a successful outcome.[70]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute		(summary)
acute dystonic reactions		
	1st	**diphenhydramine or benzatropine**

Ongoing		(summary)
generalised dystonia		
	1st	levodopa
	plus	physiotherapy
	adjunct	antispasmodic
	adjunct	treatment of underlying disease
	2nd	trihexyphenidyl
	plus	physiotherapy
	adjunct	antispasmodic
	adjunct	treatment of underlying disease
	3rd	deep brain stimulation (DBS)
	plus	physiotherapy
focal dystonia: other than adult isolated foot		
	1st	botulinum toxin
	plus	physiotherapy
	adjunct	transcutaneous electrical nerve stimulation
	adjunct	treatment of underlying disease
	adjunct	speech therapy
	2nd	deep brain stimulation (DBS)
	plus	physiotherapy
adult isolated foot dystonia		
	1st	levodopa
	plus	physiotherapy
	adjunct	treatment of underlying disease
	2nd	trihexyphenidyl
	plus	physiotherapy
	adjunct	treatment of underlying disease
	3rd	botulinum toxin
	plus	physiotherapy
	adjunct	treatment of underlying disease
	4th	deep brain stimulation (DBS)
	plus	physiotherapy

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

acute dystonic reactions

1st **diphenhydramine or benzatropine**

Primary options

» diphenhydramine: 50 mg intravenously as a single dose, may repeat in 20-30 minutes if necessary

OR

» benzatropine mesilate: 2 mg intravenously as a single dose

» Acute onset of dystonia is rare and, in most cases, is due to exposure to antidopaminergic agents. Initial evaluation in the emergent setting should include assessment of the airway.[45] If exposure to antidopaminergic agents is confirmed, give intravenous diphenhydramine or benzatropine and repeat if no effect is seen.

» Some patients with poorly controlled generalised dystonia may develop acute worsening of their dystonia, which can be severe and life-threatening.

» If you suspect overlapping neuroleptic malignant syndrome, malignant hyperthermia, serotonin syndrome, or other acute infectious, metabolic, or toxic derangement as a cause for the acute worsening, treatment should be directed at these underlying aetiologies. See Neuroleptic malignant syndrome (Management approach) ; Malignant hyperthermia (Management approach) ; Serotonin syndrome (Management approach) .

Ongoing

generalised dystonia

1st **levodopa**

Primary options

» carbidopa/levodopa: children: consult specialist for guidance on dose; adults: 25/100 mg orally (immediate-release) three times daily initially, increase dose gradually according to response

» It is important to establish whether patients with generalised dystonia are responsive to dopaminergic therapy. A therapeutic trial of levodopa with a decarboxylase inhibitor (carbidopa) should be given, which will determine whether the patient has dopa-responsive dystonia (DRD).[37] Responsiveness should be apparent within a few days to weeks.[38] [46] DRD typically presents in childhood (DRD may comprise 5% to 10% of childhood-onset dystonia), but adults may also respond to treatment.[3]

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

adjunct **antispasmodic**

Treatment recommended for SOME patients in selected patient group

Primary options

» baclofen: children: 2.5 mg/day orally initially, increase by 2.5 mg/dose increments every 3 days according to response, maximum 30 mg/day given in 3 divided doses; adults: 5 mg orally three times daily initially, increase by 5 mg/dose increments every 3 days according to response, maximum 80 mg/day

OR

» clonazepam: children: consult specialist for guidance on dose; adults: 0.5 mg/day orally initially, increase by 0.5 mg/dose increments according to response, maximum 4 mg/day

OR

Ongoing

» zonisamide: children and adults: consult specialist for guidance on dose

Secondary options

» baclofen intrathecal: children and adults: consult specialist for guidance on dose

» Oral baclofen has demonstrated efficacy in improving gait in some patients with TOR1A (also known as DYT1) mutations, although no randomised controlled trials investigating its use exist.[49]

» Clonazepam or zonisamide may also be helpful, particularly for myoclonic dystonia.[48] [50]

» Intrathecal baclofen has been proposed for use in cases of acquired dystonia when accompanied by spasticity. Intrathecal baclofen may also be considered in children when dystonia is accompanied by cerebral palsy.[51] [52]

adjunct **treatment of underlying disease**

Treatment recommended for SOME patients in selected patient group

» Patients with acquired dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

2nd **trihexyphenidyl**

Primary options

» trihexyphenidyl: children: consult specialist for guidance on dose; adults: 1-2 mg/day orally initially, increase according to response, maximum 15 mg/day given in 3-4 divided doses

» If the dystonia does not improve with levodopa given for at least 4 weeks, the mainstay of oral symptomatic therapy consists of anticholinergic therapy.

» Trihexyphenidyl was shown in a double-blind, randomised, placebo-controlled study to produce a 50% improvement in dystonia ratings.[47]

» Anticholinergics in general are thought to be more effective in children than in adults, although this may be the result of higher doses being tolerated more easily by children.[48]

Ongoing

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

adjunct **antispasmodic**

Treatment recommended for SOME patients in selected patient group

Primary options

» baclofen: children: 2.5 mg/day orally initially, increase by 2.5 mg/dose increments every 3 days according to response, maximum 30 mg/day given in 3 divided doses; adults: 5 mg orally three times daily initially, increase by 5 mg/dose increments every 3 days according to response, maximum 80 mg/day

OR

» clonazepam: children: consult specialist for guidance on dose; adults: 0.5 mg/day orally initially, increase by 0.5 mg/dose increments according to response, maximum 4 mg/day

OR

» zonisamide: children and adults: consult specialist for guidance on dose

Secondary options

» baclofen intrathecal: children and adults: consult specialist for guidance on dose

» Oral baclofen has demonstrated efficacy in improving gait in some patients with TOR1A (also known as DYT1) mutations, although no randomised controlled trials investigating its use exist.[49]

» Clonazepam or zonisamide may also be helpful, particularly for myoclonic dystonia.[48] [50]

» Intrathecal baclofen has been proposed for use in cases of secondary dystonia when accompanied by spasticity, and may also be considered in children when dystonia is accompanied by cerebral palsy.[51] [52]

Ongoing

adjunct **treatment of underlying disease**

Treatment recommended for SOME patients in selected patient group

» Patients with acquired dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

3rd **deep brain stimulation (DBS)**

» DBS of the internal globus pallidus is only used in patients who are refractory to medication. Referral to a neurosurgery centre experienced in DBS implantation in dystonia is strongly recommended, especially in the case of children, for whom early referral may be a factor in a successful outcome.[70]

» DBS is approved by the US Food and Drug Administration under a humanitarian device exemption for treatment of primary generalised, segmental, cervical dystonia, or hemidystonia. DBS is thought to restore abnormal firing rates and patterns in the main outflow nucleus from the basal ganglia to the motor cortex.

» One Cochrane review found that DBS may improve functional capacity and reduce symptom severity in adults with cervical, segmental, or generalised moderate to severe dystonia, and may improve quality of life in adults with generalised or segmental dystonia, although the evidence was of low quality.[63]

» Although data are equivocal, there are several case series indicating that primary dystonias may be more likely than secondary dystonias to respond to a clinically meaningful degree, with the exception of tardive dystonias, which appear to respond very well to DBS of the internal globus pallidus.[67] [68]

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

focal dystonia: other than adult
isolated foot

1st **botulinum toxin**

MANAGEMENT

Ongoing

Primary options

» botulinum toxin type A: consult specialist for guidance on dose

OR

» botulinum toxin type B: consult specialist for guidance on dose

» Most focal dystonias in adults and children do not respond to oral medications such as trihexyphenidyl and levodopa so botulinum toxin is usually the first line treatment.[39] A number of randomised, placebo-controlled trials for various movement disorders have demonstrated efficacy of botulinum toxin in reducing the severity of the dystonia as well as pain and disability, and in improving quality of life measures.[55] [56] The best evidence exists for cervical dystonia.[57] [58] [59] [60] One Cochrane review found a significant and clinically relevant reduction in cervical dystonia-specific impairment and pain following a single treatment session of botulinum toxin type A.[60]

» Botulinum toxin dosing depends upon the size of the muscle being injected and the serotype used (type A or type B).[61]

» Referral to a neurologist experienced in movement disorders and injection of botulinum toxin is strongly recommended when considering this treatment for cervical dystonia, blepharospasm, spasmodic dysphonia, writer's cramp, or focal lower limb dystonia.

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

adjunct **transcutaneous electrical nerve stimulation**

Treatment recommended for SOME patients in selected patient group

» Transcutaneous electrical nerve stimulation (TENS) has shown to be helpful for writer's cramp.[62]

adjunct **treatment of underlying disease**

Ongoing

Treatment recommended for SOME patients in selected patient group

» Patients with acquired dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

adjunct **speech therapy**

Treatment recommended for SOME patients in selected patient group

» Speech therapy may be helpful as an adjunct to botulinum toxin for laryngeal dystonia.[62]

2nd **deep brain stimulation (DBS)**

» DBS of the internal globus pallidus is only used in patients who are refractory to medication. Referral to a neurosurgery centre experienced in DBS implantation in dystonia is strongly recommended, especially in the case of children, for whom early referral may be a factor in a successful outcome.[70]

» DBS is approved by the US Food and Drug Administration under a humanitarian device exemption for treatment of primary generalised, segmental, cervical dystonia, or hemidystonia. DBS is thought to restore abnormal firing rates and patterns in the main outflow nucleus from the basal ganglia to the motor cortex. One Cochrane review found that DBS may improve functional capacity and reduce symptom severity in adults with cervical, segmental, or generalised moderate to severe dystonia, and may improve quality of life in adults with generalised or segmental dystonia, although the evidence was of very low quality.[63]

» Although data are equivocal, there are several case series indicating that primary dystonias may be more likely than secondary dystonias to respond to a clinically meaningful degree, with the exception of tardive dystonias, which appear to respond very well to DBS of the internal globus pallidus.[67] [68]

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

Ongoing

adult isolated foot dystonia

1st **levodopa**

Primary options

» carbidopa/levodopa: adults: 25/100 mg orally (immediate-release) three times daily initially, increase dose gradually according to response

» Focal dystonias are often poorly responsive to oral medications. However, a trial of levodopa is suggested in adult isolated foot dystonia, especially if subtle signs of parkinsonism are present.

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

adjunct **treatment of underlying disease**

Treatment recommended for SOME patients in selected patient group

» Patients with acquired dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

2nd **trihexyphenidyl**

Primary options

» trihexyphenidyl: adults: 1-2 mg/day orally initially, increase according to response, maximum 15 mg/day given in 3-4 divided doses

» Focal dystonias are often poorly responsive to oral medications. However, trihexyphenidyl may be tried to a maximum tolerated dose.

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

Ongoing

adjunct **treatment of underlying disease**

Treatment recommended for SOME patients in selected patient group

» Patients with secondary dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

3rd **botulinum toxin**

Primary options

» botulinum toxin type A: consult specialist for guidance on dose

OR

» botulinum toxin type B: consult specialist for guidance on dose

» Many of the focal dystonias respond well to botulinum toxin with reduction of dystonia severity and pain and disability scores.

» Botulinum toxin dosing depends upon the size of the muscle being injected and the serotype used (type A or type B).[61]

» Referral to a neurologist experienced in movement disorders and injection of botulinum toxin is strongly recommended when considering this treatment for focal lower limb dystonia.

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

adjunct **treatment of underlying disease**

Treatment recommended for SOME patients in selected patient group

» Patients with acquired dystonia (e.g., Wilson's disease, Parkinson's disease) and a treatable underlying cause should receive appropriate disease-specific treatment.

4th **deep brain stimulation (DBS)**

» DBS is only used in patients who are refractory to medication. Subthalamic nucleus DBS has shown some benefit in patients with toe

Ongoing

dystonia related to Parkinson's disease.[64] Referral to a neurosurgery centre experienced in DBS implantation in dystonia is strongly recommended.

» DBS is approved by the US Food and Drug Administration under a humanitarian device exemption for treatment of primary generalised, segmental, cervical dystonia, or hemidystonia. DBS is thought to restore abnormal firing rates and patterns in the main outflow nucleus from the basal ganglia to the motor cortex.

plus **physiotherapy**

Treatment recommended for ALL patients in selected patient group

» Regular physiotherapy, bracing, and stretching are recommended to alleviate pain and prevent contractures.[37]

» Stretching exercises are best provided by a physiotherapist.

Emerging

Vesicular monoamine transporter 2 (VMAT2) inhibitors

Tetrabenazine, deutetrabenazine, and valbenazine are VMAT2 inhibitors that deplete dopamine in the presynaptic terminal. They may have some efficacy in idiopathic dystonia and appear to be particularly effective for tardive dystonia. However, the numbers of patients studied in a controlled fashion are quite small, and further data are necessary for treatment recommendations to be made.[71] [72] [73] [74] One comprehensive review of tetrabenazine for use in dystonia, tardive dyskinesia, and tardive dystonia, suggests that tetrabenazine may be more useful in tardive dystonia than other forms of dystonia.[75]

Secondary prevention

Exercises and muscle stretching to prevent contractures may be helpful.[78]

Benzatropine may be considered as a prophylaxis against acute neuroleptic-induced dystonia reactions.[81]

Patient discussions

Some of the recommendations for patients include:[80]

- Regular exercise programme, including aerobic exercise
- Healthy diet
- Adequate hydration
- Good sleep habits
- Counselling if needed to address anxiety
- Relaxation techniques
- Physiotherapy to optimise balance and posture
- Attention to ergonomics at work and in activities outside of work.

A number of internet resources are available:

- Dystonia Medical Research Foundation [Dystonia Medical Research Foundation] (https://www.dystonia-foundation.org)
- National Institute of Neurological Disorders and Stroke [NINDS Dystonias Information Page] (https://www.ninds.nih.gov/Disorders/All-Disorders/Dystonias-Information-Page)
- National Spasmodic Torticollis Association [National Spasmodic Torticollis Association (NSTA)] (http://www.cdtorticollis.org)
- Bachmann-Strauss Dystonia & Parkinson Foundation [Bachmann-Strauss Dystonia & Parkinson Foundation (BSDPF)] (http://www.dystonia-parkinsons.org)
- Benign Essential Blepharospasm Research Foundation [Benign Essential Blepharospasm Research Foundation (BEBRF)] (http://www.blepharospasm.org)
- The Dystonia Society. [The Dystonia Society] (https://www.dystonia.org.uk)

Monitoring

Monitoring

For idiopathic dystonias, patients are generally seen every few months by a neurologist for repeat injections of botulinum toxin or for adjustment of medications. Loss of benefit from botulinum toxin following an initially beneficial response may signal the development of neutralising antibodies that inhibit therapeutic response. In one meta-analysis, neutralising antibodies were present in around 20% of patients who had been treated with botulinum toxin.[79]

For acquired dystonias, if amenable to therapy, treatment is directed against the underlying cause.

For patients who undergo deep brain stimulation, regular follow-ups for stimulator monitoring and programming are required.

Complications

Complications	Timeframe	Likelihood
degenerative cervical spine disease	**long term**	**medium**
Incidence of degenerative spine disease is uncertain. One group found 14 of 34 patients with cervical dystonia had clear degenerative changes, associated with the degree and direction of the torticollis.[76] Myelopathy or radiculopathy has been reported, but this is uncommon in either generalised or cervical dystonia. Degenerative changes may be detected on spinal x-rays, but if myelopathy is suspected, spinal magnetic resonance imaging is indicated.		
loss of benefit from botulinum toxin	**long term**	**medium**
Loss of benefit from botulinum toxin following an initially beneficial response may signal the development of neutralising antibodies that inhibit therapeutic response. In one meta-analysis, neutralising antibodies were present in around 20% of patients who had been treated with botulinum toxin.[79]		
contractures	**long term**	**low**
Although absolute data are lacking, the incidence of contractures is presumed to be greater with longer duration of disease. Contractures may be suspected by the presence of a palpable enlarged tendon across a joint but may be difficult to distinguish from extreme dystonia or spasticity. Electromyography may be helpful.[77] Regular physiotherapy, bracing, and stretching may reduce contractures, but no formal clinical trials have been carried out.[78]		

FOLLOW UP

Prognosis

The natural history of dystonias varies depending on the cause.

- For idiopathic focal dystonias, the disease may be insidious in onset and worsen in severity over a few months to a year, and then typically remains stable.
- Some forms of dystonia, such as dystonia associated with TOR1A (also known as DYT1) mutations, may start focally but then usually spread and become generalised; TOR1A-associated dystonia is variable in severity.
- Patients with dopa-responsive dystonia respond dramatically to dopaminergic agents such as levodopa or dopamine agonists, and also respond to anticholinergic agents. The response persists indefinitely, and (unlike patients with Parkinson's disease), these patients do not develop dyskinesias following dopaminergic treatment.

Treatment guidelines

United Kingdom

Long-term neurological conditions: management at the interface between neurology rehabilitation and palliative care (https://www.rcplondon.ac.uk/guidelines-policy/long-term-neurological-conditions)

Published by: Royal College of Physicians **Last published:** 2008

Deep brain stimulation for tremor and dystonia (excluding Parkinson's disease) (https://www.nice.org.uk/guidance/IPG188)

Published by: National Institute for Health and Care Excellence **Last published:** 2006

Europe

EFNS guidelines on diagnosis and treatment of primary dystonias (https://www.ean.org/research/ean-guidelines/guideline-reference-center)

Published by: European Federation of Neurological Societies **Last published:** 2011

North America

Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache (https://www.aan.com/practice/guidelines)

Published by: American Academy of Neurology **Last published:** 2016 (reaffirmed 2022)

Online resources

1. Dystonia Medical Research Foundation (https://www.dystonia-foundation.org) *(external link)*
2. NINDS Dystonias Information Page (https://www.ninds.nih.gov/Disorders/All-Disorders/Dystonias-Information-Page) *(external link)*
3. National Spasmodic Torticollis Association (NSTA) (http://www.cdtorticollis.org) *(external link)*
4. Bachmann-Strauss Dystonia & Parkinson Foundation (BSDPF) (http://www.dystonia-parkinsons.org) *(external link)*
5. Benign Essential Blepharospasm Research Foundation (BEBRF) (http://www.blepharospasm.org) *(external link)*
6. The Dystonia Society (https://www.dystonia.org.uk) *(external link)*

Key articles

- Lohmann K, Klein C. Update on the genetics of dystonia. Curr Neurol Neurosci Rep. 2017 Mar;17(3):26. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28283962?tool=bestpractice.bmj.com)
- Albanese A, Asmus F, Bhatia KP, et al. EFNS guidelines on diagnosis and treatment of primary dystonias. Eur J Neurol. 2011 Jan;18(1):5-18. Full text (https://onlinelibrary.wiley.com/doi/full/10.1111/j.1468-1331.2010.03042.x) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20482602?tool=bestpractice.bmj.com)
- Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016 Apr 18;86(19):1818-26. Full text (http://n.neurology.org/content/86/19/1818.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27164716?tool=bestpractice.bmj.com)

References

1. Albanese A, Bhatia K, Bressman SB, et al. Phenomenology and classification of dystonia: a consensus update. Mov Disord. 2013 Jun 15;28(7):863-73. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3729880) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23649720?tool=bestpractice.bmj.com)
2. Frucht L, Perez DL, Callahan J, et al. Functional dystonia: Differentiation from primary dystonia and multidisciplinary treatments. Front Neurol. 2021 Feb 4;11:605262. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7894256) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33613415?tool=bestpractice.bmj.com)
3. Tarsy D, Simon DK. Dystonia. N Engl J Med. 2006 Aug 24;355(8):818-29. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16928997?tool=bestpractice.bmj.com)
4. Defazio G, Abbruzzese G, Livrea P, et al. Epidemiology of primary dystonia. Lancet Neurol. 2004 Nov;3(11):673-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15488460?tool=bestpractice.bmj.com)
5. Liu X, Luo X, Hu W. Studies on the epidemiology and etiology of moldy sugarcane poisoning in China. Biomed Environ Sci. 1992 Jun;5(2):161-77. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/1642790?tool=bestpractice.bmj.com)
6. Muller J, Kiechl S, Wenning GK, et al. The prevalence of primary dystonia in the general community. Neurology. 2002 Sep 24;59(6):941-3. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12297587?tool=bestpractice.bmj.com)
7. Nutt JG, Muenter MD, Aronson A, et al. Epidemiology of focal and generalized dystonia in Rochester, Minnesota. Mov Disord. 1988;3(3):188-94. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3264051?tool=bestpractice.bmj.com)

REFERENCES

8. Steeves TD, Day L, Dykeman J, et al. The prevalence of primary dystonia: a systematic review and meta-analysis. Mov Disord. 2012 Dec;27(14):1789-96. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23114997?tool=bestpractice.bmj.com)

9. Medina A, Nilles C, Martino D, et al. The prevalence of idiopathic or inherited isolated dystonia: A systematic review and meta-analysis. Mov Disord Clin Pract. 2022 Oct;9(7):860-8. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9547134) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/36247920?tool=bestpractice.bmj.com)

10. Defazio G. The epidemiology of primary dystonia: current evidence and perspectives. Eur J Neurol. 2010 Jul;17(Suppl 1):9-14. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20590802?tool=bestpractice.bmj.com)

11. Epidemiological Study of Dystonia in Europe (ESDE) Collaborative Group. A prevalence study of primary dystonia in eight European countries. J Neurol. 2000 Oct;247(10):787-92. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11127535?tool=bestpractice.bmj.com)

12. Albanese A, Di Giovanni M, Lalli S. Dystonia: diagnosis and management. Eur J Neurol. 2019 Jan;26(1):5-17. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30035844?tool=bestpractice.bmj.com)

13. Lohmann K, Klein C. Update on the genetics of dystonia. Curr Neurol Neurosci Rep. 2017 Mar;17(3):26. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28283962?tool=bestpractice.bmj.com)

14. Bressman SB, Sabatti C, Raymond D, et al. The DYT1 phenotype and guidelines for diagnostic testing. Neurology. 2000 May 9;54(9):1746-52. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10802779?tool=bestpractice.bmj.com)

15. Fuchs T, Gavarini S, Saunders-Pullman R, et al. Mutations in the THAP1 gene are responsible for DYT6 primary torsion dystonia. Nat Genet. 2009 Mar;41(3):286-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19182804?tool=bestpractice.bmj.com)

16. Segawa M, Nomura Y, Nishiyama N. Autosomal dominant guanosine triphosphate cyclohydrolase I deficiency (Segawa disease). Ann Neurol. 2003;54(Suppl 6):S32-45. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12891652?tool=bestpractice.bmj.com)

17. Zirn B, Steinberger D, Troidl C, et al. Frequency of GCH1 deletions in Dopa-responsive dystonia. J Neurol Neurosurg Psychiatry. 2008 Feb;79(2):183-6. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17898029?tool=bestpractice.bmj.com)

18. Schrag A, Trimble M, Quinn N, et al. The syndrome of fixed dystonia: an evaluation of 103 patients. Brain. 2004 Oct;127(Pt 10):2360-72. Full text (https://academic.oup.com/brain/article/127/10/2360/404547) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15342362?tool=bestpractice.bmj.com)

19. Jankovic J. Can peripheral trauma induce dystonia and other movement disorders? Yes! Mov Disord. 2001 Jan;16(1):7-12. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11215595?tool=bestpractice.bmj.com)

20. van Hilten JJ, Geraedts EJ, Marinus J. Peripheral trauma and movement disorders. Parkinsonism Relat Disord. 2007;13 Suppl 3:S395-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18267271?tool=bestpractice.bmj.com)

21. Weiner WJ. Can peripheral trauma induce dystonia? No! Mov Disord. 2001 Jan;16(1):13-22. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11215572?tool=bestpractice.bmj.com)

22. Albanese A. Dystonia: clinical approach. Parkinsonism Relat Disord. 2007;13 Suppl 3:S356-61. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18267264?tool=bestpractice.bmj.com)

23. Breakefield XO, Blood AJ, Li Y, et al. The pathophysiological basis of dystonias. Nat Rev Neurosci. 2008 Mar;9(3):222-34. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18285800?tool=bestpractice.bmj.com)

24. Jankovic J. Dystonia: medical therapy and botulinum toxin. Adv Neurol. 2004;94:275-86. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/14509685?tool=bestpractice.bmj.com)

25. Ozelius LJ. Update on the genetics of primary torsion dystonia loci DYT6, DYT7, and DYT13 and the dystonia-plus locus DYT12. Adv Neurol. 2004;94:109-12. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/14509662?tool=bestpractice.bmj.com)

26. Latorre A, Bhatia KP. Treatment of paroxysmal dyskinesia. Neurol Clin. 2020 May;38(2):433-47. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32279719?tool=bestpractice.bmj.com)

27. Jinnah HA, Hess EJ. Evolving concepts in the pathogenesis of dystonia. Parkinsonism Relat Disord. 2018 Jan;46 Suppl 1:S62-5. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5696051) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28784298?tool=bestpractice.bmj.com)

28. Simonyan K. Neuroimaging applications in dystonia. Int Rev Neurobiol. 2018;143:1-30. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6331056) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30473192?tool=bestpractice.bmj.com)

29. Hallett M. Dystonia: abnormal movements result from loss of inhibition. Adv Neurol. 2004;94:1-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/14509648?tool=bestpractice.bmj.com)

30. Armstrong M, Daly AK, Blennerhassett R, et al. Antipsychotic drug-induced movement disorders in schizophrenics in relation to CYP2D6 genotype. Br J Psychiatry. 1997 Jan;170:23-6. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9068770?tool=bestpractice.bmj.com)

31. Dressler D, Benecke R. Diagnosis and management of acute movement disorders. J Neurol. 2005 Nov;252(11):1299-306. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16208529?tool=bestpractice.bmj.com)

32. Rodnitzky RL. Drug-induced movement disorders in children. Semin Pediatr Neurol. 2003 Mar;10(1):80-7. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12785751?tool=bestpractice.bmj.com)

33. Laihinen A, Halsband U. PET imaging of the basal ganglia. J Physiol Paris. 2006 Jun;99(4-6):406-13. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16723212?tool=bestpractice.bmj.com)

REFERENCES

34. Toma K, Nakai T. Functional MRI in human motor control studies and clinical applications. Magn Reson Med Sci. 2002 Jul 1;1(2):109-20. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16082132?tool=bestpractice.bmj.com)

35. Greene P, Kang UJ, Fahn S. Spread of symptoms in idiopathic torsion dystonia. Mov Disord. 1995 Mar;10(2):143-52. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7753056?tool=bestpractice.bmj.com)

36. Bonanni L, Thomas A, Varanese S, et al. Botulinum toxin treatment of lateral axial dystonia in Parkinsonism. Mov Disord. 2007 Oct 31;22(14):2097-103. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17685467?tool=bestpractice.bmj.com)

37. Sadnicka A, Meppelink AM, Kalinowski A, et al. Dystonia. BMJ. 2022 Apr 11;377:e062659. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9070304) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/35410890?tool=bestpractice.bmj.com)

38. Bragg DC, Sharma N. Update on treatments for dystonia. Curr Neurol Neurosci Rep. 2014 Jun;14(6):454. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4477531) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24744022?tool=bestpractice.bmj.com)

39. Albanese A, Asmus F, Bhatia KP, et al. EFNS guidelines on diagnosis and treatment of primary dystonias. Eur J Neurol. 2011 Jan;18(1):5-18. Full text (https://onlinelibrary.wiley.com/doi/full/10.1111/j.1468-1331.2010.03042.x) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20482602?tool=bestpractice.bmj.com)

40. van Egmond ME, Kuiper A, Eggink H, et al. Dystonia in children and adolescents: a systematic review and a new diagnostic algorithm. J Neurol Neurosurg Psychiatry. 2015 Jul;86(7):774-81. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25395479?tool=bestpractice.bmj.com)

41. Jinnah HA, Factor SA. Diagnosis and treatment of dystonia. Neurol Clin. 2015;33:77-100. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4248237) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25432724?tool=bestpractice.bmj.com)

42. Greene PE, Frucht SJ. Tardive and neuroleptic-induced emergencies. In: Frucht SJ, Fahn S, eds. Movement disorder emergencies. Totowa, NJ: Humana Press; 2005:117-22.

43. Burke RE, Fahn S, Marsden CD, et al. Validity and reliability of a rating scale for the primary torsion dystonias. Neurology. 1985 Jan;35(1):73-7. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3966004?tool=bestpractice.bmj.com)

44. Consky ES, Lang AE. Clinical assessments of patients with cervical dystonia. In: Jankovic J, Hallett M, eds. Therapy with botulinum toxin. New York, NY: Marcel Dekker, Inc.; 1994:211-37.

45. Queensland Ambulance Service. Medical/acute dystonic reaction. Apr 2016 [internet publication]. Full text (https://www.ambulance.qld.gov.au/docs/clinical/cpg/CPG_Acute%20dystonic%20reaction.pdf)

46. Nygaard TG, Marsden CD, Fahn S. Dopa-responsive dystonia: long-term treatment response and prognosis. Neurology. 1991 Feb;41(2 (Pt 1)):174-81. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/1899474?tool=bestpractice.bmj.com)

47. Burke RE, Fahn S, Marsden CD. Torsion dystonia: a double-blind, prospective trial of high-dosage trihexyphenidyl. Neurology. 1986 Feb;36(2):160-4. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3511401?tool=bestpractice.bmj.com)

48. Bhidayasiri R, Tarsy D. Treatment of dystonia. Exp Rev Neurotherap. 2006 Jun;6(6):863-86. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16784410?tool=bestpractice.bmj.com)

49. Greene P. Baclofen in the treatment of dystonia. Clin Neuropharmacol. 1992 Aug;15(4):276-88. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/1516073?tool=bestpractice.bmj.com)

50. Hainque E, Vidailhet M, Cozic N, et al. A randomized, controlled, double-blind, crossover trial of zonisamide in myoclonus-dystonia. Neurology. 2016 May 3;86(18):1729-35. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27053715?tool=bestpractice.bmj.com)

51. Roubertie A, Mariani LL, Fernandez-Alvarez E, et al. Treatment for dystonia in childhood. Eur J Neurol. 2012 Oct;19(10):1292-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22289078?tool=bestpractice.bmj.com)

52. Fehlings D, Brown L, Harvey A, et al. Pharmacological and neurosurgical interventions for managing dystonia in cerebral palsy: a systematic review. Dev Med Child Neurol. 2018 Apr;60(4):356-66. Full text (https://onlinelibrary.wiley.com/doi/10.1111/dmcn.13652) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29405267?tool=bestpractice.bmj.com)

53. National Institute for Health Care and Excellence. Cerebral palsy in adults. Jan 2019 [internet publication]. Full text (https://www.nice.org.uk/guidance/ng119)

54. Harvey AR, Baker LB, Reddihough DS, et al. Trihexyphenidyl for dystonia in cerebral palsy. Cochrane Database Syst Rev. 2018 May 15;5(5):CD012430. Full text (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012430.pub2/full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29763510?tool=bestpractice.bmj.com)

55. Zoons E, Dijkgraaf MG, Dijk JM, et al. Botulinum toxin as treatment for focal dystonia: a systematic review of the pharmaco-therapeutic and pharmaco-economic value. J Neurol. 2012 Dec;259(12):2519-26. Full text (https://link.springer.com/article/10.1007/s00415-012-6510-x) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22552527?tool=bestpractice.bmj.com)

56. Duarte GS, Rodrigues FB, Marques RE, et al. Botulinum toxin type A therapy for blepharospasm. Cochrane Database Syst Rev. 2020 Nov 19;11(11):CD004900. Full text (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004900.pub3/full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33211907?tool=bestpractice.bmj.com)

57. Charles D, Brashear A, Hauser RA, et al. Efficacy, tolerability, and immunogenicity of onabotulinumtoxina in a randomized, double-blind, placebo-controlled trial for cervical dystonia. Clinic Neuropharmacol. 2012 Sep-Oct;35(5):208-14. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22948497?tool=bestpractice.bmj.com)

REFERENCES

58. Colosimo C, Tiple D, Berardelli A. Efficacy and safety of long-term botulinum toxin treatment in craniocervical dystonia: a systematic review. Neurotox Res. 2012 Nov;22(4):265-73. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22359151?tool=bestpractice.bmj.com)

59. Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016 Apr 18;86(19):1818-26. Full text (http://n.neurology.org/content/86/19/1818.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27164716?tool=bestpractice.bmj.com)

60. Rodrigues FB, Duarte GS, Marques RE, et al. Botulinum toxin type A therapy for cervical dystonia. Cochrane Database Syst Rev. 2020 Nov 12;11(11):CD003633. Full text (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003633.pub4/full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33180963?tool=bestpractice.bmj.com)

61. Dressler D, Altavista MC, Altenmueller E, et al. Consensus guidelines for botulinum toxin therapy: general algorithms and dosing tables for dystonia and spasticity. J Neural Transm (Vienna). 2021 Mar;128(3):321-35. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7969540) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33635442?tool=bestpractice.bmj.com)

62. Delnooz CC, Horstink MW, Tijssen MA, et al. Paramedical treatment in primary dystonia: a systematic review. Mov Disord. 2009 Nov 15;24(15):2187-98. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19839012?tool=bestpractice.bmj.com)

63. Rodrigues FB, Duarte GS, Prescott D, et al. Deep brain stimulation for dystonia. Cochrane Database Syst Rev. 2019 Jan 10;1(1):CD012405. Full text (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012405.pub2/full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30629283?tool=bestpractice.bmj.com)

64. Laurencin C, Montaut S, Vial C, et al. Toe dystonia in Parkinson's disease: Impact of subthalamic nucleus deep brain stimulation. J Neurol Sci. 2018 Sep 15;392:65-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30025235?tool=bestpractice.bmj.com)

65. Isaias IU, Alterman RL, Tagliati M. Outcome predictors of pallidal stimulation in patients with primary dystonia: the role of disease duration. Brain. 2008 Jul;131(Pt 7):1895-902. Full text (https://academic.oup.com/brain/article/131/7/1895/389683) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18567622?tool=bestpractice.bmj.com)

66. Krauss JK, Loher TJ, Weigel R, et al. Chronic stimulation of the globus pallidus internus for treatment of non-dYT1 generalized dystonia and choreoathetosis: 2-year follow up. J Neurosurg. 2003 Apr;98(4):785-92. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12691403?tool=bestpractice.bmj.com)

67. Starr PA, Turner RS, Rau G, et al. Microelectrode-guided implantation of deep brain stimulators into the globus pallidus internus for dystonia: techniques, electrode locations, and outcomes. J Neurosurg. 2006 Apr;104(4):488-501. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16619651?tool=bestpractice.bmj.com)

68. Andrews C, Aviles-Olmos I, Hariz M, et al. Which patients with dystonia benefit from deep brain stimulation? A metaregression of individual patient outcomes. J Neurol Neurosurg Psychiatry. 2010 Dec;81(12):1383-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20841370?tool=bestpractice.bmj.com)

69. Bronte-Stewart H, Taira T, Valldeoriola F, et al. Inclusion and exclusion criteria for DBS in dystonia. Mov Disord. 2011 Jun;26 Suppl 1:S5-16. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21692112?tool=bestpractice.bmj.com)

70. DiFrancesco MF, Halpern CH, Hurtig HH, et al. Pediatric indications for deep brain stimulation. Childs Nerv Syst. 2012 Oct;28(10):1701-14. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22828866?tool=bestpractice.bmj.com)

71. Jankovic J. Treatment of hyperkinetic movement disorders with tetrabenazine: a double-blind crossover study. Ann Neurol. 1982 Jan;11(1):41-7. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/6460467?tool=bestpractice.bmj.com)

72. Paleacu D, Giladi N, Moore O, et al. Tetrabenazine treatment in movement disorders. Clin Neuropharmacol. 2004 Sep-Oct;27(5):230-3. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15602104?tool=bestpractice.bmj.com)

73. Fernandez HH, Factor SA, Hauser RA, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia: The ARM-TD study. Neurology. 2017 Apr 26;88(21):2003-10. Full text (http://n.neurology.org/content/88/21/2003.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28446646?tool=bestpractice.bmj.com)

74. Touma KT, Scarff JR. Valbenazine and deutetrabenazine for tardive dyskinesia. Innov Clin Neurosci. 2018 Jun 1;15(5-6):13-6. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30013814?tool=bestpractice.bmj.com)

75. Chen JJ. Tetrabenazine for the treatment of hyperkinetic movement disorders: a review of the literature. Clinical Therapeutics. 2012 Jul;34(7):1487-504. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22749259?tool=bestpractice.bmj.com)

76. Chawda SJ, Münchau A, Johnson D, et al. Pattern of premature degenerative changes of the cervical spine in patients with spasmodic torticollis and the impact on the outcome of selective peripheral denervation. J Neurol Neurosurg Psychiatry. 2000 Apr;68(4):465-71. Full text (https://jnnp.bmj.com/content/68/4/465.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10727482?tool=bestpractice.bmj.com)

77. Sanger TD. Use of surface electromyography (EMG) in the diagnosis of childhood hypertonia: a pilot study. J Child Neurol. 2008 Jun;23(6):644-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18344454?tool=bestpractice.bmj.com)

78. Jankovic J. Treatment of dystonia. Lancet Neurol. 2006 Oct;5(10):864-72. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16987733?tool=bestpractice.bmj.com)

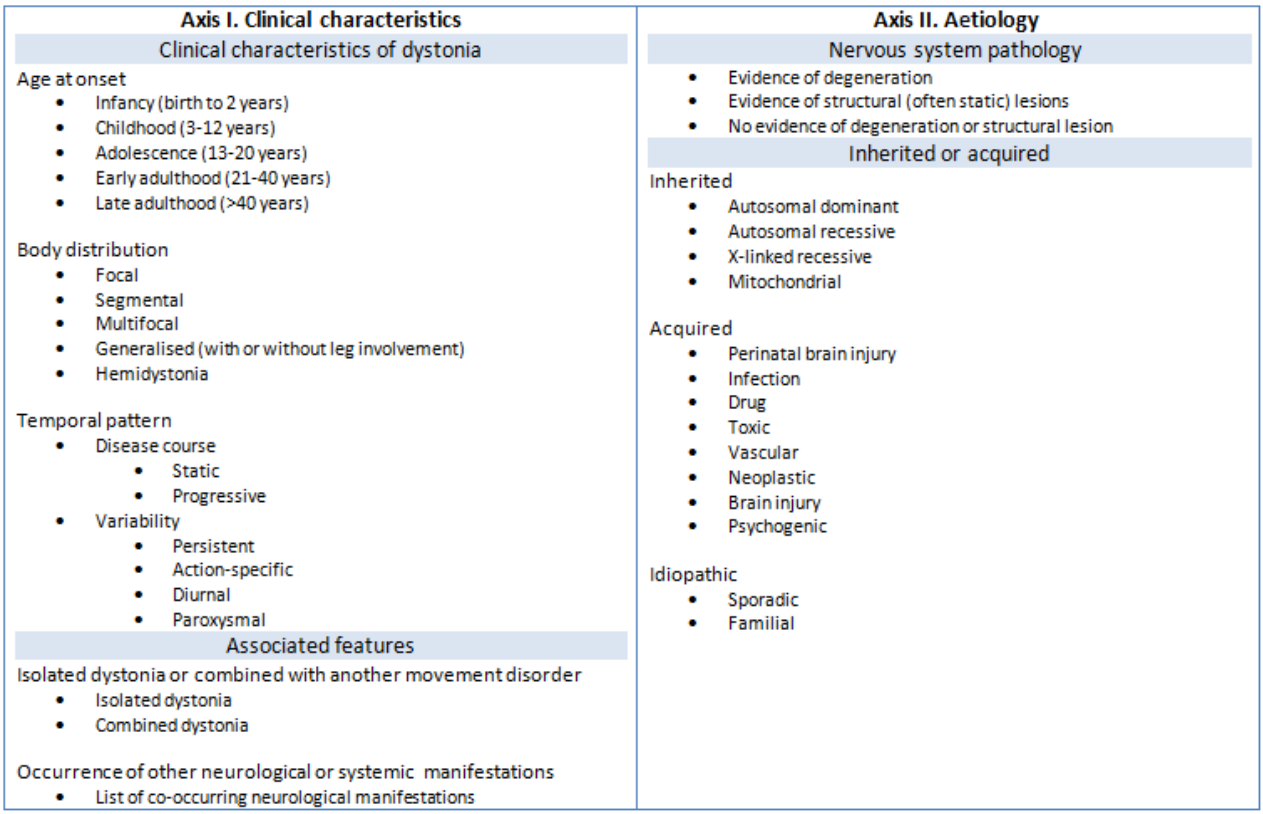
REFERENCES

79. Fabbri M, Leodori G, Fernandes RM, et al. Neutralizing antibody and botulinum toxin therapy: A systematic review and meta-analysis. Neurotox Res. 2016 Jan;29(1):105-17. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26467676?tool=bestpractice.bmj.com)

80. Brin MF, Comella C, Jankovic J. Dystonia: etiology, clinical features, and treatment. Philadelphia, PA: Lippincott Williams & Williams; 2004:45-9.

81. Goff DC, Arana GW, Greenblatt DJ, et al. The effect of benztropine on haloperidol-induced dystonia, clinical efficacy and pharmacokinetics: a prospective, double-blind trial. J Clin Psychopharmacol. 1991 Apr;11(2):106-12. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/2056136?tool=bestpractice.bmj.com)

Images



Axis I. Clinical characteristics

Clinical characteristics of dystonia

Age at onset
- Infancy (birth to 2 years)
- Childhood (3-12 years)
- Adolescence (13-20 years)
- Early adulthood (21-40 years)
- Late adulthood (>40 years)

Body distribution
- Focal
- Segmental
- Multifocal
- Generalised (with or without leg involvement)
- Hemidystonia

Temporal pattern
- Disease course
  - Static
  - Progressive
- Variability
  - Persistent
  - Action-specific
  - Diurnal
  - Paroxysmal

Associated features

Isolated dystonia or combined with another movement disorder
- Isolated dystonia
- Combined dystonia

Occurrence of other neurological or systemic manifestations
- List of co-occurring neurological manifestations

Axis II. Aetiology

Nervous system pathology
- Evidence of degeneration
- Evidence of structural (often static) lesions
- No evidence of degeneration or structural lesion

Inherited or acquired

Inherited
- Autosomal dominant
- Autosomal recessive
- X-linked recessive
- Mitochondrial

Acquired
- Perinatal brain injury
- Infection
- Drug
- Toxic
- Vascular
- Neoplastic
- Brain injury
- Psychogenic

Idiopathic
- Sporadic
- Familial

Figure 1: Consensus classification of dystonia

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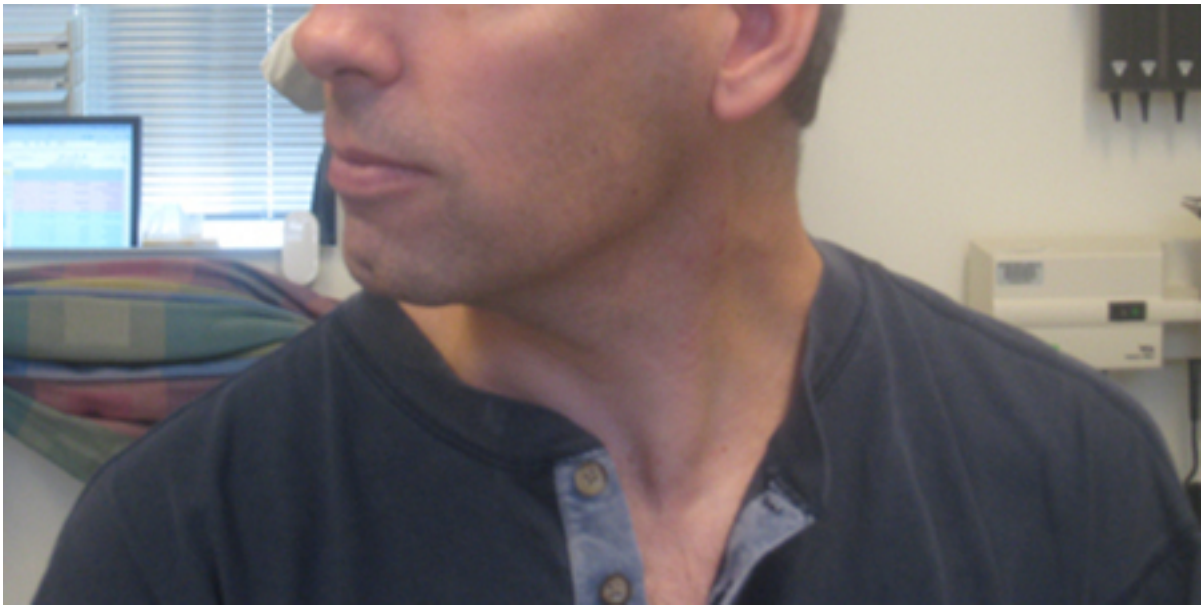

Figure 2: Rotational torticollis

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Figure 3: The torticollis improves with a sensory trick: gently touching his chin

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Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT1	Primary torsion dystonia; idiopathic torsion dystonia; Oppenheim dystonia; dystonia musculorum deformans 1; TOR1A	Childhood or early adult (usually before 26 years of age)	Often starts as focal limb dystonia (commonly action dystonia of 1 foot); often generalises	9q34	TorsinA (GAG deletion); ATPase family; chaperone-like functions	AD	30% to 40%
DYT2	AR primary torsion dystonia	Childhood	Segmental or generalised dystonia	Unknown	Unknown	AR	Unknown
DYT3	X-linked dystonia; parkinsonism; Lubag	12-52 years (mean: 37.9)	Males with focal, then segmental or generalised dystonia; parkinsonism develops later in 50% of cases; endemic in Panay, Philippines	Xq13.1	TAF1/DYT3 multiple transcript system	X-linked	100% by 5th decade
DYT4	Torsion dystonia 4; non-DYT1 primary torsion dystonia; whispering dysphonia	13-37 years	Primarily laryngeal ("whispering") dysphonia; sometimes cervical; often generalises; ± psychiatric symptoms; reported in 1 large Australian family	19p13.3	TUBB4A; tubulin beta 4A	AD	Unknown (40% of patients' offspring older than age 40 are affected)
AD, autosomal dominant; AR, autosomal recessive.							

Figure 4: Genetics and dystonia

Adapted from N Engl J Med. 2006 Aug 24;355(8):818-29; used with permission. Additional information Mov Disord. 2011 May;26(6):1106-26

Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT5a/DYT14 GCH1	Dopa-responsive dystonia; Segawa syndrome; hereditary progressive dystonia with marked diurnal variation	Usually childhood	Dystonia; parkinsonism; may mimic cerebral palsy; diurnal variation; dramatic response to levodopa	14q22.1-14q22.2	GTP cyclohydrolase; biopterin synthesis (cofactor for dopamine synthesis)	AD	30% (possibly higher in females)
DYT5b	Dopa-responsive dystonia; Segawa syndrome; hereditary progressive dystonia with marked diurnal variation		Dystonia; parkinsonism; may mimic cerebral palsy; diurnal variation; dramatic response to levodopa	11p15.5	Tyrosine hydroxylase	AR	
DYT6	Adolescent-onset primary torsion dystonia of mixed type	Average age of 16 years (range: 5-62)	Focal (arm, cranial, or cervical); may become generalized	8p21-8p22	THAP1 (thanatos-associated protein domain-containing apoptosis-associated protein 1); represses TOR1A expression	AD	30-60%
DYT7	Adult-onset focal primary torsion dystonia	Adult (28-70)	Focal dystonia (cervical, writer's cramp, laryngeal); hand tremors; does not generalize; reported in German families	18p	Unknown	AD	(incomplete 40%)
AD, autosomal dominant; AR, autosomal recessive.							

IMAGES

Figure 5: Genetics and dystonia

Adapted from N Engl J Med. 2006 Aug 24;355(8):818-29; used with permission. Additional information Mov Disord. 2011 May;26(6):1106-26

Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT8	Paroxysmal dystonic choreoathetosis (PDC); paroxysmal nonkinesigenic dyskinesia (PNKD); Mount-Reback syndrome	Variable (childhood-early adulthood)	Episodes lasting 2 minutes to 4 hours of dystonia and chorea/dyskinesias triggered by stress, alcohol, caffeine, nicotine	2q33-2q36	Myofibrillogenesis regulator 1 (MR-1) gene	AD	Incomplete
DYT9 / DYT18	Paroxysmal choreoathetosis with episodic ataxia and spasticity; choreoathetosis, spasticity, and episodic ataxia	Childhood (2-15 years)	Chronic spastic paraplegia plus episodes of dystonia, choreoathetosis, paraesthesias, and diplopia triggered by exercise, stress, alcohol	1p13.3-1p21	Glucose transporter type 1 (GLUT1), also known as solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1)	AD	Unknown
DYT10	Paroxysmal kinesogenic choreoathetosis (PKC) ; paroxysmal kinesogenic dyskinesias (PKD); periodic dystonia	Childhood (6-16 years)	Episodes of dystonia and choreoathetosis triggered by sudden movements	16p11.2-16q12.1	Proline-rich transmembrane protein 2 (PRRT2)	AD	Incomplete
DYT11	Myoclonus-dystonia; alcohol-responsive dystonia	Variable; can be early childhood	Myoclonus plus dystonia; improves with alcohol	7q21-7q31; 18p11; (11q23 for D2 receptor?)	Epsilon-sarcoglycan; (SGCE); also possibly dopamine D2 receptor gene	AD	Incomplete; higher when inherited paternally (imprinting)
AD, autosomal dominant.							

Figure 6: Genetics and dystonia

Adapted from N Engl J Med. 2006 Aug 24;355(8):818-29; used with permission. Additional information from Mov Disord. 2011 May;26(6):1106-26 and Neuropath Applied Neurobiol. 2012 Oct;38(6):520-34

Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT12	Rapid-onset dystonia-parkinsonism	Variable (childhood-adult)	Acute or subacute onset of generalised dystonia plus parkinsonism	19q13	Na^+/K^+ ATPase α3 subunit (ATP1A3); sodium pump	AD	Incomplete
DYT13	Focal dystonia with cranial-cervical features	Variable (5 years-adult; average = 15 years)	Focal or segmental dystonia (cranial, cervical, or upper limb); mild in severity; rarely generalised; reported in an Italian family	1p36.13-1p36.32	Unknown	AD	58%
DYT14	Withdrawn: now known to be the same as DYT5a						
DYT15	Myoclonus-dystonia; alcohol-responsive dystonia		Jerky movements of upper limbs, hands, and axial muscles with alcohol-responsive myoclonus-dystonia	18p11	Unknown	AD	Incomplete
DYT16	Dystonia-parkinsonism	Childhood	Brazilian cases and a German case. Focal (limb) dystonia with progression to generalised, sometimes with bradykinesia	2q31	Protein kinase, interferon-inducible double-stranded RNA-dependent activator (PRKRA); cellular stress response	AR	
AD, autosomal dominant; AR, autosomal recessive.							

Figure 7: Genetics and dystonia

Adapted from N Engl J Med. 2006 Aug 24;355(8):818-29; used with permission. Additional information Mov Disord. 2011 May;26(6):1106-26

Gene	Dystonia type	Age of onset	Clinical features	Chromosome	Gene; function	Inheritance	Penetrance
DYT17	AR primary torsion dystonia	Teens	Lebanese family with primary focal torsion dystonia; torticollis plus dysphonia	20p11.2-q13.12	Unknown	AR	
DYT19	Episodic kinesogenic dyskinesia 2	Childhood	Indian family with brief episodes (up to 2 minutes) of dystonia or chorea induced by sudden movement; 120 episodes per day; ± seizures; ± sensory aura of paraesthesias; may have spontaneous remission	16q13-q22.1	Unknown	AD	75%
DYT20	Paroxysmal nonkinesigenic dyskinesia 2	Variable (childhood to 50)	Canadian family with episodes lasting 2-10 minutes of dyskinesias occurring daily or a few times per month; ± migraines; ± seizures	2q31	Unknown	AD	89%
DYT23	Cervical dystonia	Adult	Adult-onset cervical dystonia	9q	CIZ1	AD	
DYT24	Craniocervical dystonia	Variable	Craniocervical dystonia	11p	ANO3	AD	
DYT25	Cervical dystonia	Usually adult (range 7-54 years)	Adult-onset cervical dystonia	18p	GNAL	AD	
DFN-1/MTS (DDP)	Deafness-dystonia syndrome 1; Mohr-Tranebjaerg syndrome; XL dystonia optic atrophy	Childhood	Dystonia, sensorineural hearing loss, spasticity, mental retardation, cortical blindness; female carriers may present with adult-onset focal dystonia without deafness	Xq22	Dystonia-deafness peptide (DDP); mitochondrial protein import	X-inked	Incomplete in female carriers (incompletely skewed X-inactivation)
LHON-dystonia (mtDNA)	Leber hereditary optic neuropathy plus dystonia	Variable	Dystonia, optic atrophy, or both	mtDNA	ND6 (complex I subunit); mitochondrial function	Maternal	Incomplete
AD, autosomal dominant; AR, autosomal recessive.							

Figure 8: Genetics and dystonia

Adapted from N Engl J Med. 2006 Aug 24;355(8):818-29; used with permission. Additional information Mov Disord. 2011 May;26(6):1106-26 and Mov Disord. 2013 Jun 15;28(7):899-905

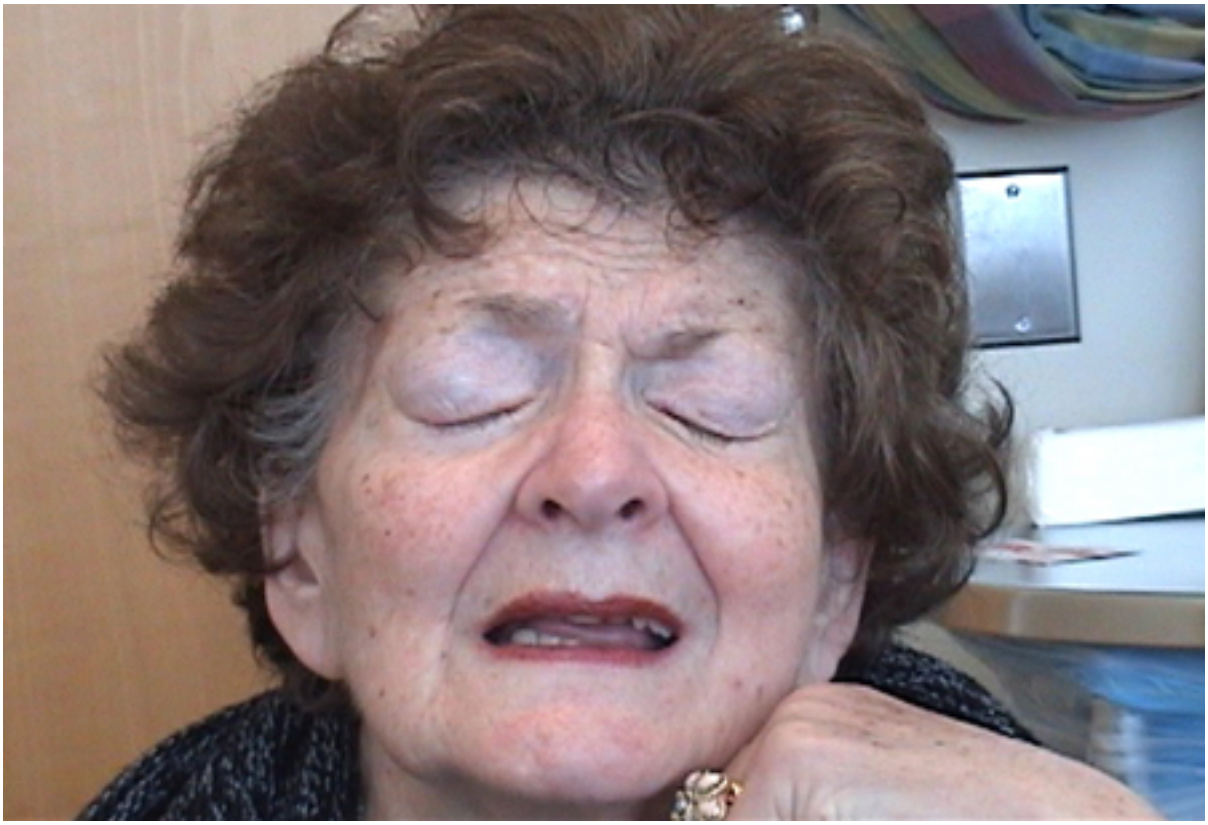

Figure 9: Blepharospasm

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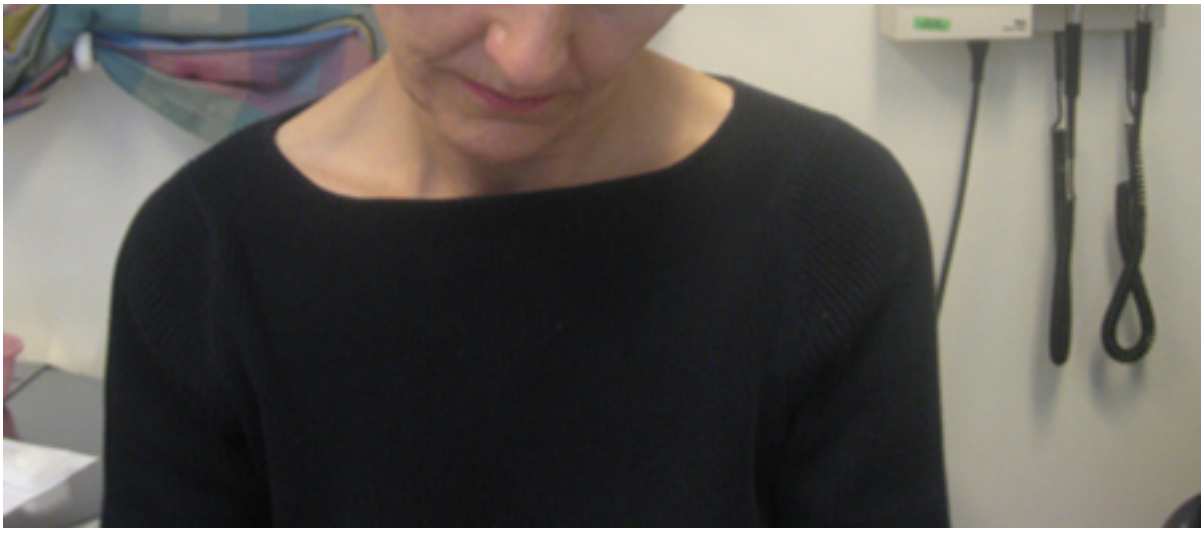

Figure 10: Cervical dystonia: anterolateralcollis

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Figure 11: Cervical dystonia: retrocollis

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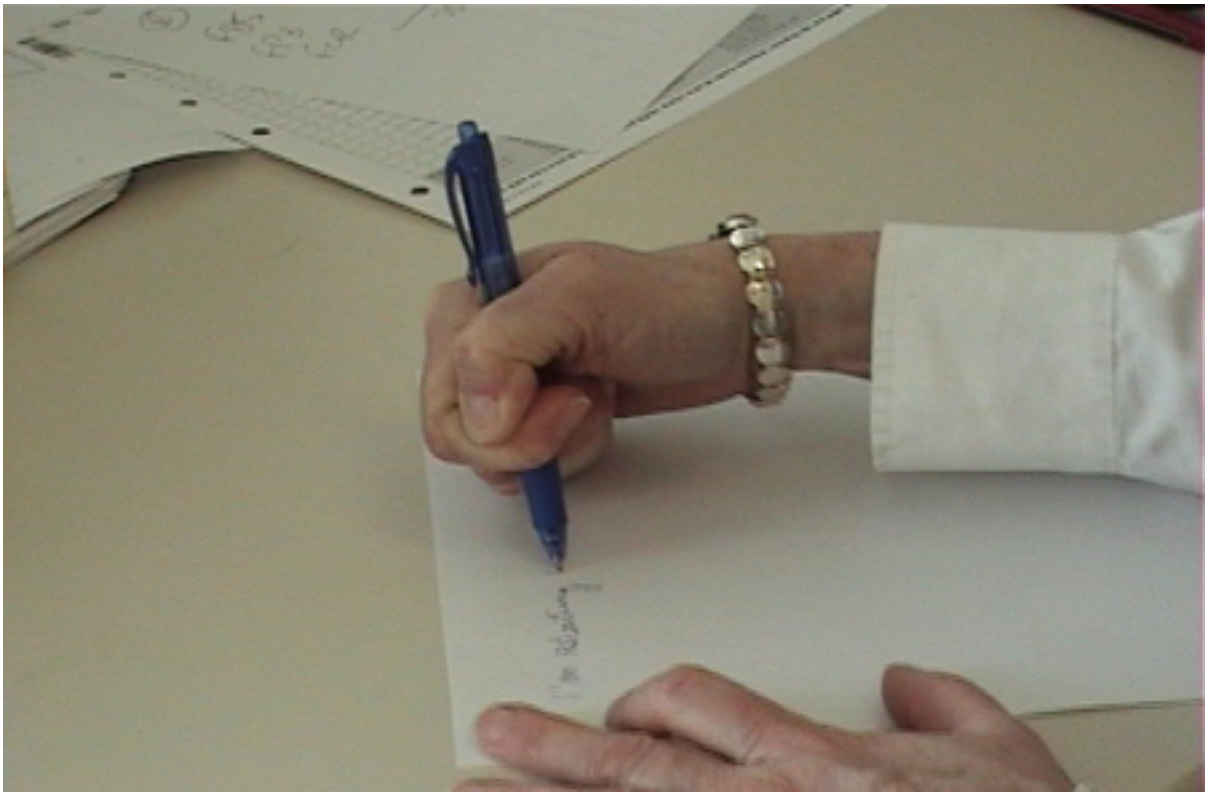

Figure 12: Writer's cramp: a focal task

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Figure 13: Writer's cramp: a focal task

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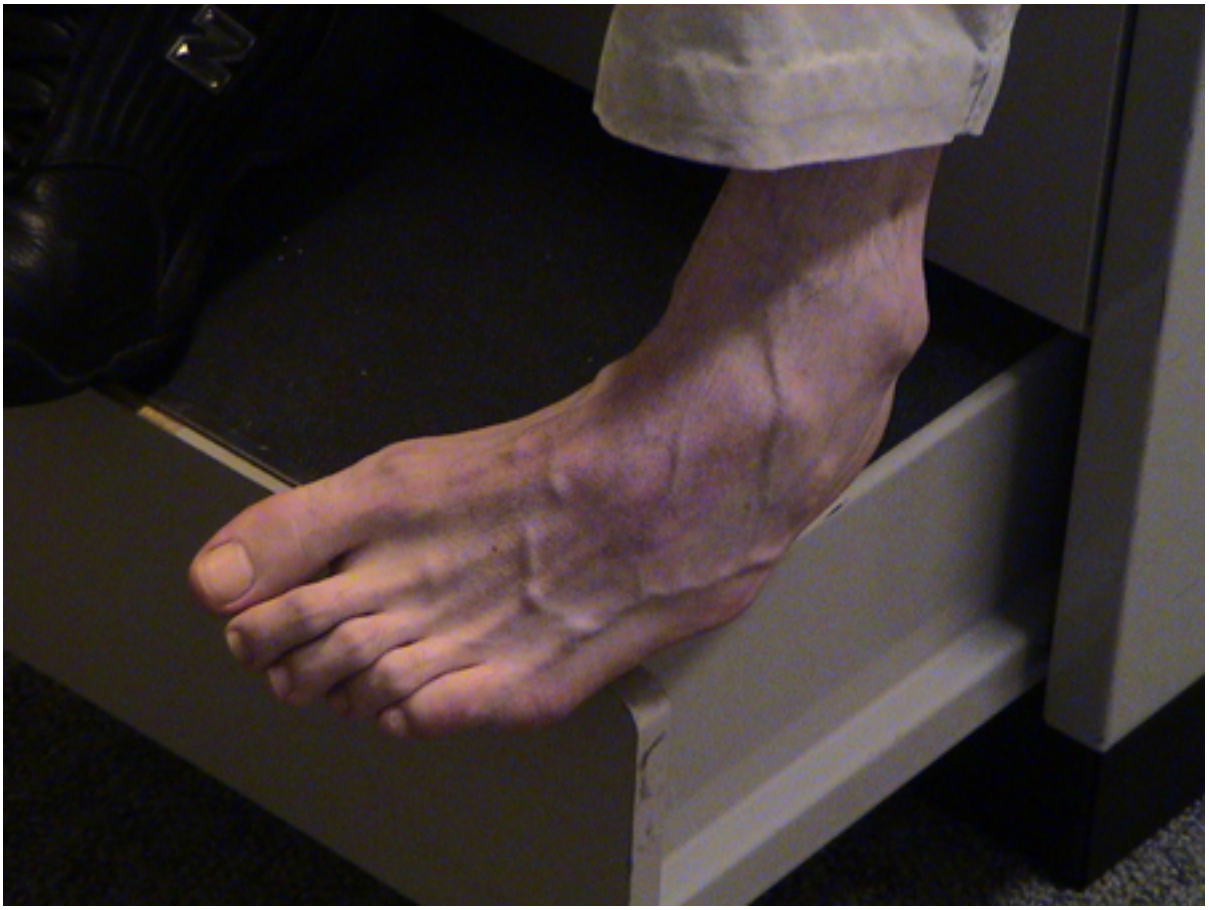

Figure 14: Foot dystonia with involuntary plantar flexion and foot inversion

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This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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