

Movement Disorders in Children

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Objectives After completing this article, readers should be able to:

1. Describe the prevalence of tic disorder.
2. Characterize the treatment of tic disorder.
3. Explain how movement disorders can differ from autism and mental retardation.
4. Describe the use of stimulant medication in the treatment of attention-deficit/hyperactivity disorder associated with a tic disorder.
5. Compare and contrast dopa-responsive dystonia and cerebral palsy.

Introduction

Supreme Court Justice Potter Stewart, in 1964, while trying to define “obscenity,” articulated the now well-known “I shall not today attempt to define the kinds of material I understand to be embraced . . . [b]ut I know it when I see it” In some respects, a similar comment can be made about movement disorders. A movement disorder typically is defined as dysfunction in the implementation of appropriate targeting and velocity of intended movements, dysfunction of posture, the presence of abnormal involuntary movements, or the performance of normal-appearing movements at inappropriate or unintended times. The movement abnormalities are not due to weakness or abnormal muscle tone, but may be accompanied by weakness or abnormal tone.

By convention, movement disorders are divided into two major categories. The first is hyperkinetic movement disorders, sometimes referred to as dyskinesias. This term refers to abnormal, repetitive involuntary movements and encompasses most of the childhood

movement disorders, including tics, chorea/ballismus, dystonia, myoclonus, stereotypies, and tremor. The second category is hypokinetic movement disorders, sometimes referred to as akinetic/rigid disorders. The primary movement disorder in this category is parkinsonism, manifested primarily in adulthood as Parkinson disease or one of many forms of secondary parkinsonism. Hypokinetic disorders are relatively uncommon in children. Although ataxia, weakness, and spasticity are characterized by motor dysfunction, by common convention these entities are not included among “movement disorders.” This review focuses on dyskinesias because they represent the bulk of movement disorders in children.

The components of the central nervous system typically implicated in disorders of movement are the basal ganglia (caudate, putamen, globus pallidus, subthalamic nucleus, substantia nigra) and frontal cortex. The accomplishment of smooth, coordinated movement requires a multifaceted network of brain regions, including basal ganglia and frontal cortex, but also thalamus, cerebellum, spinal cord, peripheral

Abbreviations

ADHD:	attention-deficit/hyperactivity disorder
ARF:	acute rheumatic fever
DRD:	dopa-responsive dystonia
GABHS:	group A beta-hemolytic streptococcal
IVIG:	intravenous immunoglobulin
NIH:	National Institutes of Health
OCD:	obsessive compulsive disorder
PANDAS:	pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection
SC:	Sydenham chorea
SLE:	systemic lupus erythematosus
SSRI:	selective serotonin reuptake inhibitor
TD:	tardive dyskinesia
TS:	Tourette syndrome

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Table 1. Phenomenologic Classification of Movement Disorders

Movement Disorder	Brief Description
Tics	Stereotyped intermittent, sudden, discrete, repetitive, nonrhythmic movements, most frequently involving head and upper body.
Chorea/ballismus	Chaotic, random, repetitive, brief, purposeless movements. Rapid, but not as rapid as myoclonus. When of very large amplitude, choreic limb movements often are called ballismus.
Dystonia	Repetitive, sustained, abnormal postures and movements. Abnormal postures typically have a twisting quality.
Myoclonus	Sudden, brief, shocklike movements that may be repetitive or rhythmic.
Stereotypy	Patterned, episodic, repetitive, purposeless, rhythmic movements.
Tremor	Rhythmic oscillation about a central point or position involving one or more body parts.
Parkinsonism	Hypokinetic syndrome characterized by rest tremor, slow movement (bradykinesia), rigidity, and postural instability.

nerve, and muscle. It is important to recognize the multiple components of the nervous system involved in motor control because determining the cause often depends on localization.

When faced with a movement disorder, the following key questions need to be asked:

- Is the pattern of movements normal or abnormal?
- Is the number of movements excessive or diminished?
- Is the movement paroxysmal (sudden onset and offset), continual (repeated again and again), or continuous (without stop)?
- Has the movement disorder changed over time?
- Do environmental stimuli or emotional states modulate the movement disorder?
- Can the movements be suppressed voluntarily?
- Is the abnormal movement heralded by a premonitory sensation or urge?
- Are there findings on the examination suggestive of focal neurologic deficit or systemic disease?
- Is there a family history of a similar or related condition?
- Does the movement disorder abate with sleep?

In clinical practice, the diagnosis of a movement disorder requires a qualitative appreciation of the movement type and context. Abnormal movements can be difficult to define. To classify the disorder phenomenologically, one should describe the characteristics of the movements (Table 1), but even under the best circumstances, movement disorders may be difficult to characterize. Chorea can resemble myoclonus; dystonia can resemble spasticity; and paroxysmal movement disorders such as dystonia and tics may resemble other paroxysmal neurologic problems, namely, seizures. Movements in some contexts may be normal and in others may indicate

an underlying pathology. For example, frequent eye blinking can be normal and appropriate in one setting (a sand storm), but excessive in another (tic disorders). Movements that are worrisome for a degenerative disorder in adolescents (myoclonus) may be completely normal in an infant (benign neonatal myoclonus). In this article, we discuss most of the hyperkinetic movement disorders, but focus on tics, chorea, and dystonia. Drug-induced movement disorders, a common entity in childhood, fall under the same classification scheme as the other movement disorders (Table 1), but are considered in this discussion in a separate section.

Tics Definitions

Tics commonly are defined as stereotyped intermittent, sudden, discrete, repetitive movements. Movements that involve skeletal muscle are termed “motor” tics; those that involve the diaphragm or laryngeal-pharyngeal muscles, producing a sound, are termed “phonic” or “vocal” tics. Tics occur many times a day, nearly every day. They typically change anatomic location, frequency, type, complexity, and severity over time. Tics can be classified by mode of manifestation (motor or vocal) and complexity (simple or complex). Motor tics can be classified further by speed and quality as clonic (abrupt and fast) or dystonic/tonic (slow and sustained). Simple motor tics include blinking, nose twitching, grimacing, neck jerking, shoulder elevation, sustained eye closure, gaze shifts, bruxism, and abdominal tensing. Simple vocal tics include sniffing, throat clearing, grunting, squeaking, humming, coughing, blowing, and sucking sounds. Complex tics appear more “purposeful” than simple tics and may include combinations of movements of multiple body parts. Examples are head shaking, trunk flexion,

Table 2. Classification and Diagnosis of Tic Disorders

Transient Tic Disorder (<1 y duration; diagnosis made retrospectively)

- Motor
- Vocal
- Motor and vocal

Chronic Tic Disorder (>1 y duration)

- Motor (common)
- Vocal (rare)

Tourette Syndrome

- Motor and vocal (at some point, but not necessarily, concurrently)

scratching, touching, finger tapping, hitting, jumping, kicking, and gestures (obscene gestures are termed copropraxia). Complex vocal tics can encompass spoken syllables words or phrases; shouting of obscenities or profanities (coprolalia); repetition of the words of others (echolalia); and repetition of the final syllable, word, or phrase of one's own words (palillalia).

The definition of tic disorders can be guided by the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) classification scheme. The primary distinctions are between transient and chronic tic disorders and between chronic motor tic disorder and Tourette syndrome (TS) (Table 2). Transient tic disorder is a disorder of childhood in which one or several tics are indistinguishable from the tics of chronic tic disorder, but the condition lasts only several months. These frequently are interpreted as allergic manifestations. The most common chronic tic disorder is TS, manifested as chronic motor and vocal tics of greater than 1 year's duration with onset prior to age 18 years. Chronic motor tic disorder is characterized by motor tics for more than 1 year, but no vocal tics. Chronic vocal tic disorder is uncommon.

Epidemiology

Recent studies show the prevalence of tics to be approximately 20% of the population and the rate of chronic tic disorders to be about 3% among children. (The discrepancy between prevalence of tics and rate of chronic tic disorders is likely accounted for by transient tic disorders.) Thus, tics and tic disorders are at least one order of magnitude more common than was thought just 15 years ago. From the earliest descriptions, tic disorders have

been recognized as having a familial inheritance pattern and a greater prevalence among males. The specific genetic inheritance is being investigated in ongoing research, but a reasonable description of the pattern is autosomal dominant, with incomplete and gender-biased penetration (male:female ratio of 3:1).

Tics usually appear in the first decade of life, with a median age of onset of about 6 to 7 years. They have been reported at 2 years of age, but may occur earlier. In most children (96%), tics present before age 11. The most common presenting tic is eye blinking. Vocal tics are the presenting symptom in up to one third of individuals, with the most common initial tics being sniffing or throat clearing. Typically, vocal tics emerge later than motor tics, with a median onset of around 8 to 10 years of age. The most common course is for tics to worsen, with peak severity occurring around 10 to 12 years of age. By age 18 years, approximately 50% of chronic tic disorder patients are tic-free. Tic severity in childhood does not predict adult severity; tic severity rarely is greater in adulthood than in childhood.

Clinical Features

Tics frequently are preceded by a premonitory sensation or urge, and performance of the tic usually is followed by a sense of relief. The common occurrence of eye blinking, sniffing, and throat clearing tics preceded by the sensation of an itch leads to the frequent misdiagnosis of tics as allergic symptoms. For some patients, the premonitory urge is manifested nonspecifically as a sense of anxiety. This sense of anxiety seems particularly true in younger children, perhaps because they are unable to characterize the feeling. Younger children are less likely to describe premonitory urges. For some patients, the premonitory urge may create greater morbidity than the tic itself and, therefore, represents the reason to treat. The premonitory urge has been compared with a compulsive urge, but the latter is believed to have a more cognitive component (ie, "If I don't wash my hands, I will get sick.").

Some individuals can suppress tics for limited periods of time. The ability to suppress tics sets tic disorders apart from most other movement disorders. However, younger children are less likely to be able to suppress tics, making this point of differentiation less useful in that population. Voluntary tic suppression often is at a cost of rising anxiety or discomfort and usually requires such active concentration that it may prevent the patient from attending to other tasks. Thus, voluntary suppression is not a useful strategy for managing tics.

A hallmark of tics is variable severity over time. Tics

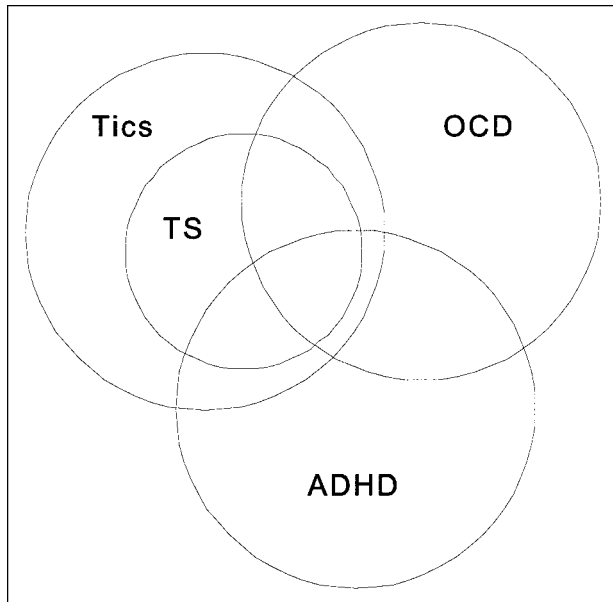


Figure. Potential comorbid conditions seen with tics. OCD=obsessive-compulsive disorder, TS=Tourette syndrome, ADHD=attention-deficit/hyperactivity disorder.

tend to occur in bouts, with interspersed periods of quiescence. Often a pre-existing tic abates as a new tic emerges. Tics tend to wax and wane over weeks to months. Tic severity seems to be modulated by environmental stimuli, stress, intercurrent infection, and poor sleep. Children commonly experience exacerbations of tics at the outset of the school year and at the time of return from school holidays. Tics also may increase during relaxation after a period of stress. Tics typically disappear with sleep, but in some individuals they persist during all stages of sleep.

In addition to tics, patients who have tic disorders may have a number of comorbid behavioral symptoms (Figure). These include symptoms of attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive behaviors or frank obsessive-compulsive disorder (OCD), anxiety disorders, mood disorders, learning disorders, sleep disorders, conduct and oppositional behavior, and self-injurious behavior. Zinner has discussed these conditions and their treatments in detail (see Suggested Reading). Recent evidence suggests that explosive outbursts or rage attacks are common among children who have TS, occurring in roughly 25%. When affected children have explosive outbursts, they also are more likely to have other comorbid features, such as ADHD, OCD, and oppositional defiant disorder. An important feature of comorbid symptomatology is that certain medications are effective for some symptoms but not for

Table 3. Causes of Secondary Tics

- Infections
- Drugs
- Toxins
- Developmental disorders
- Chromosomal disorders
- Stroke
- Heredodegenerative disorders
 - Huntington disease
 - Neuroacanthocytosis
 - Pantothenate kinase-associated neurodegeneration (PKAN)*
 - Wilson disease
- Neurocutaneous disorders
- Head trauma

*Also known as Hallervorden-Spatz syndrome

others. For example, selective serotonin reuptake inhibitors (SSRIs) may be beneficial for OCD or anxiety, but they are not effective for tics or ADHD and might be associated with worsened rage control.

Causes

When considering the differential diagnosis of tics, both cause and classification must be addressed. As noted previously, tics are protean in their manifestation. Clonic tics can resemble movements seen in myoclonus, chorea, and seizures. Dystonic tics can resemble the movements seen in primary dystonias. Tonic tics can resemble muscle spasms and cramps. Complex motor tics can be very difficult to discern from mannerisms, stereotypies, restless legs, complex partial or supplementary motor seizures, and akathisia (an inability to sit still due to an uncomfortable sensation of motor restlessness). Most individuals who have tics have a primary tic disorder. Transient tic disorder is the most common; TS is the second most common. Secondary tic disorders do exist, but they are uncommon. In secondary tic disorders, other signs and symptoms are present and distract from the consideration of a primary tic disorder (Table 3).

An interesting but unproven autoimmune mechanism for tics and TS (and OCD) has been postulated. The best-known concept is that of pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS). The hypothesis that an antecedent group A beta-hemolytic streptococcal (GABHS) infection could result in a neuropsychiatric manifestation such as TS, OCD, or both is conceptually based on Sydenham chorea, a recognized neuropsychiatric manifestation of acute rheumatic fever (ARF). The postulated PANDAS

subgroup has been described as having the following characteristics: presence of OCD/chronic tic disorder, prepubertal onset, episodic course with acute and severe onset and explosive exacerbations, neurologic abnormalities other than chorea during the exacerbations, and a documented temporal relationship between GABHS infections and the episodic exacerbations. Whether patients whose TS (and OCD) manifestations appear to be triggered by streptococcal infections can be distinguished clearly from the entire population remains unclear. For this reason, the National Institutes of Health

ratory studies, and measurement of antibodies to GABHS are not indicated. Individuals who have other neurologic abnormalities or developmental abnormalities deserve further evaluation and should be referred to a neurologist.

Treatment

The primary question when considering treatment of tics is whether the patient has sufficient morbidity to warrant pharmacologic treatment. Reassurance that tics are a common feature on the landscape of human behaviors that (typically) cause no injury and frequently are transient can successfully bypass the desire to start medication. Anticipatory guidance and education for parents, siblings, and teachers can aid immeasurably in preventing the initiation of medications. One important component of anticipatory guidance is recognition of the natural history of tic disorders. For example, for a significant

proportion of patients, tics peak in severity at ages 10 to 13 years and diminish substantially in the late teenage years. For many individuals, the tics become so mild by adulthood that they no longer are noticed or may abate completely. Most patients who have uncomplicated tic disorders do well without pharmacologic intervention. However, the symptoms cause sufficient morbidity for some patients to warrant consideration of medication.

Zinner recently reviewed therapeutic considerations of pharmacotherapy for this publication (see Suggested Reading). If the patient has tics alone, we recommend starting treatment with an alpha-2-adrenergic agonist such as clonidine or guanfacine. Guanfacine may be less sedating than clonidine, but it also may be less effective. Neuroleptics, both typical and atypical, are effective for tics. Good evidence supports the use of typical neuroleptics such as haloperidol and pimozide, but adverse effects frequently are limiting. Atypical neuroleptics such as risperidone appear to be effective for tics and impulsivity and are less likely to cause extrapyramidal adverse effects, but they still have significant morbidity in the form of weight gain and diabetes mellitus. A newer atypical neuroleptic, ziprasidone, shows promise as an anti-tic medication, and early experience suggests that it may not cause weight gain or diabetes mellitus. In addition to medications, behavioral therapies may be helpful. The clinician should determine the relative burden imposed by tics and any comorbidities. For example, if OCD is the primary problem and tics are mild, pharmacotherapy should target the OCD. The incidence of comorbidities

Most patients who have uncomplicated tic disorders do well without pharmacologic intervention.

(NIH) is sponsoring a prospective multicenter epidemiologic study to ascertain whether a PANDAS subgroup of TS and OCD patients exists.

Intense interest in the idea of PANDAS has led to small experimental trials of antibiotic prophylaxis and immunomodulation with intravenous immunoglobulin (IVIG) with or without plasma exchange. At present, these interventions have not been proven effective. Indeed, in July 2000, the National Institute of Mental Health released a statement (<http://www.nimh.nih.gov/events/pandaalert.cfm>) that treatment of PANDAS, TS, or OCD with IVIG or plasma exchange is considered experimental and that these interventions should be used only in NIH-approved research protocols. Therefore, for patients whose tics appear to be exacerbated by GABHS infections, we recommend that:

- Standard pharmacologic and nonpharmacologic approaches be used to treat tics and exacerbations.
- Until evidence supports their clinical implementation, the use of immune modulation, including plasma exchange and IVIG, be reserved for clinical studies.
- Antibiotics not be used to treat tic exacerbations.
- Antibiotic prophylaxis be reserved for patients who have ARF.

Diagnosis

Most children who have tics have a primary tic disorder, and diagnosis is based on history plus normal findings on neurologic examination aside from tics. Imaging, labo-

is significant. Across series, an average of approximately 50% of individuals who have TS have ADHD, 50% have OCD, 20% have a mood disorder, and 20% have anxiety disorder.

ADHD Stimulant Treatment and Tics

According to the *Physician's Desk Reference*, methylphenidate is contraindicated "in patients with motor tics or with a family history or diagnosis of Tourette syndrome." This statement apparently is based on a number of case reports and retrospective series that probably have not considered that ADHD is present in approximately 50% of all patients who have TS and that the natural history in these patients is for ADHD symptoms to tend to precede the onset of tics. The basis for the *PDR* listing is a good example of the shortfalls of anecdotal and retrospective analysis. Several recent studies have indicated that stimulant medications typically do not exacerbate tics, and if they do, the exacerbation usually is transient. However, most prescribing physicians, by stating the warning in the *PDR* in the discussion of risks and benefits of treating with stimulants, prime parents to anticipate tics. When tics emerge or worsen (tic disorders likely wax and wane independent of medication) in the presence of stimulants, the medication is considered the culprit.

A recent study by the Tourette Syndrome Study Group addressed this issue in a randomized, placebo-controlled, double-blind study to assess the efficacy of methylphenidate and clonidine individually or in combination for treatment of ADHD among children who had chronic tics or TS. The study provided solid evidence that methylphenidate, if anything, lessens tic severity. The study concluded, "Prior recommendations to avoid methylphenidate in these children because of concerns of worsening tics are unsupported by this trial." Whether these results can be generalized to other stimulants (such as pemoline and dextroamphetamines) is not known.

Chorea

Definitions

Chorea is characterized by frequent, brief, unpredictable, purposeless movements that tend to flow from body part to body part chaotically and unpredictably. The movements of chorea are more chaotic and less brief and "shocklike" than myoclonus. They are briefer than the sustained contractions of dystonia. When of low ampli-

tude, chorea may cause the appearance of fidgeting, but when they are of large amplitude, chorea can involve dramatic, flinging limb movements. When the amplitude is very large, the term ballismus often is used. Choreic movements can be sudden and jerky or continuous and flowing. In the latter case, the term choreoathetosis is used. In current parlance, the term "choreiform" frequently is used to describe the minimal twitching or "piano playing" movements seen in many normal young children when arms are extended during the neurologic examination. We do not find the term "choreiform" to be useful because historically its usage has meant "chorea." Instead, we prefer the descriptive term "minimal chorea."

Causes

Chorea can be classified by cause into primary and secondary disorders. Primary chorea, which is uncommon in childhood, can be caused by benign familial (hereditary) chorea and Huntington disease. Huntington disease

In a randomized, placebo-controlled trial, methylphenidate and clonidine (for treatment of ADHD) did not worsen tics.

rarely presents in childhood with chorea; juvenile-onset Huntington disease usually is characterized by parkinsonism and dystonia. Most chorea in childhood is secondary. More than 100 causes of secondary chorea have been identified, but usually chorea is not the only sign or symptom. The most common cause of chorea in childhood is ARF. Other important causes include systemic lupus erythematosus (SLE), pregnancy (chorea gravidarum), vascular disorders, drug ingestion, hyperthyroidism, infection, inflammation, cardiac surgery ("post-pump chorea"), degenerative disorders, disorders of intermediary metabolism, and perinatal hypoxia-ischemia (Table 4). A diagnostic strategy based on the more likely causes, with an emphasis on treatable causes, is shown in Table 5.

Sydenham (Rheumatic) Chorea

Chorea is one of the major Jones criteria for diagnosing ARF. In fact, the presence of chorea without any other criteria is sufficient to make the diagnosis. Although it is widely accepted that chorea can follow GABHS infec-

Table 4. Causes of Secondary Chorea

Metabolic

- Hypo/hyponatremia
- Hypo/hyperglycemia
- Hypocalcemia
- Hyperthyroidism

Perinatal Hypoxia–Ischemia

Infectious

- Epstein–Barr virus
- Human immunodeficiency virus
- Rheumatic fever
- Viral encephalitis

Psychogenic

Vascular

- Antiphospholipid antibody syndrome
- Stroke
- Global hypoxia
- Moyamoya syndrome

Toxins

- Manganese
- Methanol
- Carbon monoxide

Hereditary Degenerative Disease

- Ataxia telangiectasia
- Niemann–Pick type C
- Gangliosidosis
- Lesch–Nyhan disease

tion, it can be difficult to demonstrate the antecedent infection. Depending on the series, 10% to 40% of children who have ARF have chorea. Sydenham chorea (SC) is most common in children ages 5 to 15 years. There is a 2:1 female predominance after 10 years of age. SC begins several weeks to several months after a GABHS infection. The onset of symptoms usually is insidious, with gradually progressive clumsiness and behavior change, usually accompanied by emotional lability. After a week or more, choreic movements become more obvious and typically become generalized. There frequently is asymmetry, and in some cases, the chorea can be unilateral. Hypotonia and dysarthria commonly accompany the chorea. Behavioral changes may be striking and include impulsivity, aggression, and obsessive-compulsive behaviors. The typical natural history of SC is weeks to months of a waxing and waning course, with

Table 5. Diagnostic Testing in Chorea

- Throat culture
- Antistreptolysin O titer
- AntiDNase B titer
- Electrocardiogram
- Echocardiogram
- Thyroid function tests
- Complete blood count
- Antinuclear antibody
- Erythrocyte sedimentation rate
- Magnetic resonance imaging of brain
- Serum ceruloplasmin
- Antiphospholipid/anticardiolipin antibodies
- Urine drug screen

Other testing for rare diseases is based on presence of other symptoms and clinical suspicion. If results of the above tests are normal, referral to a neurologist is recommended.

ultimate resolution of the chorea. Some individuals have behavioral changes that persist for months. Relapse(s) can occur with or without subsequent GABHS infection, and an increased risk of relapse is associated with pregnancy (chorea gravidarum) or oral contraceptives.

The diagnosis of SC is based on clinical history and can be supported by laboratory data. However, laboratory data should not be viewed as confirmatory. Most affected children have positive serology (antistreptolysin O and antiDNase B antibodies) for GABHS, but more than 25% are serologically negative. Most children who have SC have negative throat cultures for GABHS. Magnetic resonance imaging may show signal abnormalities in the basal ganglia, but diagnostically this technique is neither sensitive nor specific for SC. The presence of carditis or other manifestations of ARF supports the diagnosis of SC. Every child believed to have SC should be evaluated for rheumatic heart disease. Depending on the series, 40% to 75% of children who have SC have carditis. Arthritis is less common.

Treatment of SC depends on the impairment or disability associated with the chorea. In many cases, the chorea causes only mild disability, and symptomatic treatment is not required because SC is usually self-limited. When symptomatic treatment is desired, antiepileptic medications such as carbamazepine or valproate can be effective and usually associated with fewer adverse effects than phenothiazines or butyrophenones. Benzodiazepines also may be beneficial. Symptomatic treatment for 2 to 4 months generally is sufficient. Some authors have advocated the use of corticosteroids, IVIG,

Table 6. Classification of Dystonia

Age of Onset

- Childhood onset
- Adult onset

Cause

- Primary (idiopathic)
- Secondary

Somatic Distribution

- Focal
- Segmental
- Multifocal
- Hemi
- Generalized

or plasma exchange based on the presumed autoimmune cause, but there has been no study of long-term outcome of these treatments compared with placebo.

Penicillin prophylaxis to prevent repeated bouts of GABHS is recommended and described in detail by Dajani et al (see Suggested Reading).

Chorea in SLE

Chorea is an uncommon manifestation of SLE, but it can be the presenting symptom. When chorea is the sole manifestation of SLE, it can remain so for years. Although fewer than 10% of children who have SLE have chorea, about 50% of individuals who have chorea due to SLE are younger than 16 years of age. The presence of neurologic manifestations such as chorea in SLE conveys a less favorable prognosis. The diagnosis and treatment of SLE are beyond the scope of this review. When chorea is due to SLE, treatment of the underlying SLE is indicated. Additional symptomatic treatment of the chorea may be indicated if the condition is bothersome. Haloperidol has been reported to be effective for SLE chorea, but the other treatments described previously for SC also may be effective.

Dystonia

Definitions

Dystonia is a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal postures. There are several classification schemes for dystonia, based on age of onset, cause, or body part affected (Table 6). Primary dystonias are those disorders in which dystonia is the only feature or the primary feature, are accompanied only by other movement disorders, and have a specific causative genetic

mutation or unknown cause. Secondary dystonias are those disorders in which the dystonia is due to another identifiable cause. Focal dystonia occurs when a single body part is affected. Almost any part of the body can be affected. Examples of focal dystonia include torticollis and writer's cramp. Segmental dystonia refers to involvement of more than one adjacent body part; multifocal dystonia is involvement of multiple nonadjacent body parts. Hemidystonia affects only one side of the body, and generalized dystonia involves the entire body. Note that these classification schemes are overlapping. For example, childhood-onset primary dystonia frequently starts in the lower extremities, trunk, or arms and most commonly progresses to generalized involvement, with involuntary twisting of nearly all parts of the body. Adult-onset primary dystonias more typically are focal or segmental.

Clinical Features

There are several characteristic clinical features of dystonia. Stress exacerbates most forms of dystonia. Dystonia commonly is triggered or exacerbated by attempted voluntary movement and may fluctuate in presence and severity over time. Dystonic contractions resolve during sleep. The dystonic posturing may occur only with selected movements and paradoxically not with others that may use the same muscles. For example, walking forward may elicit severe lower extremity and truncal twisting, yet walking backward, running, or swimming may be completely normal. Individuals who have dystonia often find that touching one part of the body relieves the dystonic spasms; this phenomenon is called a sensory trick or *geste antagoniste*. For example, rubbing the back of the hand may diminish writer's cramp.

Causes

Historically, dystonia has been divided into primary (idiopathic) and secondary causes. A full discussion of the many causes of dystonia is beyond the scope of this review. The two most important types of primary dystonia in children are dopa-responsive dystonia and idiopathic torsion dystonia associated with the *DYT1* mutation. The most important causes of secondary dystonia in children are listed in Table 7.

Dopa-responsive Dystonia

Dopa-responsive dystonia (DRD) is the most common cause of primary dystonia with onset in childhood. This syndrome is characterized by childhood-onset, progressive dystonia that has a sustained, dramatic response to low doses of levodopa. DRD is also known as hereditary

Table 7. Causes of Secondary Dystonia in Children

Hereditary/Genetic Disorders

- Ataxia telangiectasia
- Gangliosidoses
- Glutaric aciduria
- Huntington disease
- Lesch–Nyham disease
- Metachromatic leukodystrophy
- Methylmalonic acidemia
- Mitochondrial disorders
- Niemann–Pick type C
- Pantothenate kinase–associated neurodegeneration (PKAN)*
- Wilson disease

Drugs/Toxins (see Table 8)

Psychogenic

Structural Brain Lesions

- Acute disseminated encephalomyelitis
- Infection
- Perinatal hypoxia–ischemia
- Stroke
- Tumor

*Also known as Hallervorden-Spatz syndrome

progressive dystonia with diurnal fluctuations or Segawa syndrome. DRD typically presents with a gait disturbance due to foot dystonia starting between 1 and 12 years of age. In untreated older children, diurnal fluctuation may develop, with worsening of symptoms toward the end of the day and marked improvement in the morning. The diurnal fluctuation need not be a presenting feature. In late adolescence or early adulthood, features of parkinsonism can develop. There are two major forms of DRD: a more common autosomal dominant form due to deficiency of GTP cyclohydrolase and a relatively uncommon autosomal recessive form caused by a deficiency in tyrosine hydroxylase. Both forms produce dopamine deficiency without loss of nigrostriatal dopamine neurons. A few clinical differences may help distinguish the two deficiencies, but these are neither sensitive nor specific. DRD due to tyrosine hydroxylase deficiency can be distinguished from GTP cyclohydrolase deficiency by measuring cerebrospinal fluid (CSF) catecholamines, their metabolites, and pterins. In practice, the exquisite response to levodopa generally is sufficient for the diagnosis of DRD. In some cases, a specific diagnosis for the purpose of genetic counseling or in atypical cases may

warrant CSF investigations. Although the locus for GTP cyclohydrolase is known, the variability in the genetic defect is sufficiently great for genetic testing not to be routinely available.

It is important to recognize the entity of DRD because it responds dramatically to low doses of levodopa. DRD frequently is misdiagnosed as cerebral palsy, particularly spastic diplegia, so it is important to develop an index of suspicion for DRD in children who have motor impairment, prominent dystonia, and a slowly progressive rather than static course. With appropriate diagnosis and treatment, affected children can lead normal lives.

Idiopathic Generalized Torsion Dystonia

Childhood-onset idiopathic torsion dystonia, formerly known as dystonia musculorum deformans, is an autosomal dominant condition that has incomplete (30%) penetrance. Genetic studies have found that a GAG deletion at the *DYT1* locus on chromosome 9 causes most autosomal dominant, early-onset primary generalized dystonia affecting Ashkenazi Jewish families (90%) and nonJews (50% to 60%). In childhood-onset idiopathic torsion dystonia, symptoms usually begin in a limb at a mean onset age of 12.5 years. Onset usually is before 28 years of age, but seldom before age 6 years. The legs generally are affected before the arms, and symptoms typically become generalized within 5 years. Diagnosis is based on identifying a GAG deletion in the *DYT1* gene; genetic testing is available commercially.

Treatment

Most types of dystonia are difficult to treat, and often the response is incomplete. The clear exception is DRD, which responds dramatically to low doses of levodopa. For this reason, a trial of levodopa is recommended for all children who have primary dystonia. Because some secondary dystonias also may respond to levodopa, a trial of the drug is recommended for any child in whom dystonia is a prominent component of the neurologic syndrome. The anticholinergic medication trihexyphenidyl has been used with good success in some patients who have dystonia. Some patients who were believed to have idiopathic torsion dystonia and experienced a dramatic response to anticholinergic medication have been shown to have DRD due to a GTPCH mutation. Thus, a dramatic response to trihexyphenidyl suggests the possibility of DRD.

If there is inadequate benefit from levodopa or trihexyphenidyl, baclofen alone or in combination with

trihexyphenidyl may be beneficial. Intrathecal baclofen has been found to be effective in dystonia due to cerebral palsy, but adverse effects are frequent and can be serious. For that reason, we recommend an adequate trial of oral baclofen before considering intrathecal baclofen.

Benzodiazepines also may be beneficial, but often the benefit is limited by adverse effects or tolerance. If oral medications are ineffective, botulinum toxin injections may be highly effective, especially if the impairment or disability can be attributed to a few muscle groups. Stereotaxic neurosurgery has been used with increasing success for a select group of patients who have dystonia and may be the most effective treatment for dystonia due to the *DYT1* mutation.

Myoclonus

Myoclonus has been called the most protean of abnormal movements because of its presence in normal (associated with sleep, exercise, anxiety) and numerous pathologic situations, both epileptic and nonepileptic. Thus, an appropriately detailed description is beyond the scope of this text. Myoclonic movements are very brief, abrupt, involuntary, nonsuppressible, jerky contractions (or interruption of contraction) involving a single muscle or muscle group. The rapidity of these movements warrants the descriptor “shocklike,” as if an electrical shock had been applied to the peripheral nerve innervating the muscle. Myoclonus can be rhythmic, in which case it often appears tremorlike. However, the movement in true tremor oscillates with near equal amplitude around a midpoint; in myoclonus, the movement has a more “saw-tooth” character. In some cases, myoclonus can be elicited by a sensory stimulus (reflex myoclonus, the most famous example of which is the acoustic startle response in infancy) or volitional movement (action myoclonus). Myoclonus can be focal, multifocal, segmental, or generalized.

The location and quality of myoclonic movements can be helpful in determining the cause. For example, segmental myoclonus of the thoracic muscles suggests spinal cord pathology, and segmental myoclonus of palatal muscles suggests a brainstem lesion or Whipple disease. Negative myoclonus, as in asterixis, suggests metabolic encephalopathy. Myoclonus in the setting of opsoclonus or ataxia suggests paraneoplastic syndrome (eg, neuroblastoma) or a peri-infectious autoimmune process. Myoclonus can be the manifestation of epileptic neurode-

generative diseases, such as progressive myoclonic epilepsy, Lafora body disease, neuronal ceroid lipofuscinosis, and mitochondrial diseases such as MERRF. It can be a manifestation of other neurodegenerative processes, including lysosomal storage diseases, Wilson disease, and Huntington disease. Diffuse central nervous system injury from virtually any cause (toxic, infectious, metabolic, hypoxic) can result in myoclonus. Essential myoclonus typically is a diagnosis of exclusion. Myoclonus, even nonepileptic forms, tends to respond to anticonvulsant medications such as valproate, carbamazepine, and clon-

Dopa-responsive dystonia,
the most common cause of primary dystonia
with onset in childhood, responds
dramatically to low doses of levodopa.

azepam. Given the complex differential diagnosis associated with myoclonus, we recommend that any pediatric patient noted to have myoclonus be evaluated by a neurologist.

Stereotypies

Stereotypies are intermittent, involuntary, repetitive, purposeless, patterned movements that are usually rhythmic. Examples of stereotypies occurring in children are arm flapping, rocking, licking, mouth opening, and hand waving. Stereotypies commonly are associated with mental retardation, autism, Rett syndrome, and blindness, but they also occur in otherwise normal children. Stereotypies occurring in the absence of other neurologic or behavioral features are likely to be benign. Many other terms have been used to describe stereotypies, including “rhythmic habit patterns,” “gratification phenomena,” and “motor rhythmias.”

Stereotypies usually begin in infancy and, unlike tics, tend not to change in type over time. The course is variable, with resolution over a short period of time in some children and persistence for years in others. The movements tend to occur in bouts and usually are associated with excitement, stress, or fatigue. Stereotypies cease when the child is distracted. Many children appear not to be aware that they are making the movements.

Stereotypies must be distinguished from complex tics, which are more likely to change over time, have an associated premonitory urge, and occur in the setting of

Table 8. Common Drug-induced Movement Disorders

Medications*	Reaction
Dopamine antagonists (antipsychotics)	Acute dystonic reaction
• Haloperidol	Tardive dyskinesia
• Pimozide	Withdrawal dyskinesia
• Chlorpromazine	Parkinsonism
• Metoclopramide	Neuroleptic malignant syndrome
• Prochlorperazine	
• Risperidone	
Antiepileptics	Chorea
• Phenytoin	Dystonia
• Carbamazepine	Tremor
• Sodium valproate	
Beta-adrenergic agonists	Tremor
• Metaproterenol	
Amphetamines	Chorea
	Tremor
Cocaine	Chorea
Lithium	Chorea
	Tremor

*Common examples are listed, but the list is not intended to be comprehensive.

other tics. Stereotypies typically do not bother the patient, but can be distressing to the parents. Stereotypies respond inconsistently to medications such as clonazepam, SSRIs, and haloperidol. Medical therapy usually is not indicated.

Tremor

Tremor is a rhythmic oscillation about a central point or position that involves one or more body parts. Tremor in childhood is not rare, but few epidemiologic data are available to indicate the incidence or prevalence. Tremor is classified by when it occurs: with rest, intention, or action. Rest tremor is defined as tremor involving a body part that is inactive and supported against gravity. It is associated most commonly with other signs of parkinsonism, but it may occur in isolation. The most common cause of rest tremor in children is antipsychotic (neuroleptic) medications. Intention tremor occurs as a moving body part approaches a target and usually is associated with other signs of cerebellar dysfunction. Action tremor occurs during maintained posture, voluntary movement, or both. When evaluating the child who has tremor, attention should be paid to possible other neurologic signs or symptoms. When present, these features usually direct the diagnostic evaluation. When tremor is the only abnormality, it is important to identify potential tremor-enhancing medications. The primary laboratory tests to be considered are thyroid function tests.

The most important childhood tremors are action tremors and include physiologic tremor and essential (familial) tremor. Physiologic tremor is a normal phenomenon, consisting of a 6- to 12-Hz oscillation that usually is noticed by the individual or other observers only under certain conditions. A few individuals have visible physiologic tremor that is termed “enhanced physiologic tremor.” These individuals are otherwise indistinguishable from those who have no enhanced physiologic tremor. Physiologic tremor may increase with anxiety, excitement, fear, or certain medications, including sodium valproate, theophylline, beta-agonists, corticosteroids, and stimulants. The tremor of hyperthyroidism is an enhanced physiologic tremor.

Essential tremor frequently is considered a disorder of adults, but it can begin in infancy or childhood. Essential tremor is present with posture and with action, but it usually is greatest with maintained posture. It typically involves the upper extremities, but may involve the head and neck, voice, and legs. By definition, essential tremor is unaccompanied by other neurologic abnormalities, although individuals may have slight clumsiness. Essential tremor is “familial” (autosomal dominant) in about 60% of cases. There have been no treatment studies of essential tremor in children, but experience has shown that children respond to the same medications that are effective in adults. The most effective medications are propranolol (or other beta-blockers) and primidone. Clonazepam may be effective in some cases.

Drug-induced Movement Disorders

The phenomenologic classification of drug-induced movement disorders is the same as for nondrug-induced disorders. However, because medications are a relatively common cause of movement disorders in children, they deserve special consideration. Perhaps the best known drug-induced movement disorders are those associated with antipsychotic (neuroleptic) treatment. These medications are dopamine receptor antagonists and cause both acute and tardive (ie, “late”) syndromes. The acute adverse effects of dopamine antagonists include parkinsonism and acute dystonic reactions. Acute dystonic re-

actions can occur after a single dose of a dopamine antagonist. The typical acute dystonic reaction involves involuntary gaze deviation (oculogyric crisis), torticollis, and appendicular twisting postures involving axial more than appendicular muscles. It can last for hours, but is treated readily with anticholinergic medications such as diphenhydramine (1 mg/kg per dose every 6 h) and benztropine (0.5 to 2 mg per day bid). The most severe reaction to dopamine antagonists is the neuroleptic malignant syndrome, which is characterized by hyperthermia, hypertonia, dystonia posturing, tremor, and autonomic instability, and can be fatal. Treatment primarily is supportive and includes fever control and correction of metabolic abnormalities. Dantrolene should be given to diminish excessive muscle contraction. Dopamine agonists such as bromocriptine may be effective. Neuroleptic medications should be discontinued.

Tardive dyskinesia (TD) is uncommon in childhood. The dyskinesia can manifest as any of the hyperkinetic movement disorders. TD typically manifests as an orobuccal-lingual stereotypy, but it can involve other body parts. The risk of TD increases with total dose and treatment duration of antipsychotic medication and with the age of the patient. There is some evidence that children who have had brain injuries are more likely to develop TD.

Extrapyramidal adverse effects such as acute dystonic reaction, parkinsonism, and TD are substantially more likely to occur with the older, so-called “typical” neuroleptics such as haloperidol and pimozide and other dopamine-blocking agents such as metoclopramide and prochlorperazine. Atypical neuroleptics, such as risperi-

done, quetiapine, olanzapine, and ziprasidone, have a demonstrably lower incidence of such extrapyramidal adverse effects. Treatment of TD can be difficult and requires referral to a neurologist or psychiatrist experienced in its treatment. Prevention of TD requires care to avoid indiscriminate use of antipsychotic medications and attempts to limit the duration of treatment and minimize the total daily dose.

Many other medications have been associated with movement disorders. The more common ones are summarized in Table 8. The treatment of drug-induced movement disorders is to eliminate the offending agent whenever possible. In most cases, it does not make sense to use another medication to treat adverse effects from an offending medication.

Suggested Reading

- Budman C, Bruun R, Park K, Lesser M, Olson M. Explosive outbursts in children with Tourette’s disorder. *J Am Acad Child Adolesc Psychiatry*. 2000;39:1270–1276
- Dajani A, Taubert K, Ferrieri P, Peter G, Shulman S. Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals. *Pediatrics*. 1995;96:758–764
- Fernandez-Alvarez E, Aicardi J. *Movement Disorders in Children*. London, England: MacKeith Press; 2001
- Robertson MM. Tourette syndrome, associated conditions and the complexities of treatment. *Brain*. 2000;123:425–462
- Tourette Syndrome Study Group. Treatment of ADHD in children with tics: a randomized controlled trial. *Neurology*. 2002;58:527–536
- Watts RL, Koller WC. *Movement Disorders: Neurologic Principles and Practice*. New York, NY: McGraw-Hill; 1997
- Zinner SH. Tourette disorder. *Pediatr Rev*. 2000;21:372–383

PIR Quiz

Quiz also available online at www.pedsinreview.org.

- The recommended initial intervention for treatment of tics (with sufficient morbidity) associated with Tourette syndrome is a (an):
 - Alpha-2-adrenergic agonist.
 - Biofeedback program to assist with voluntary suppression.
 - Neuroleptic.
 - Stimulant.
 - Selective serotonin reuptake inhibitor (SSRI).

2. You have diagnosed attention-deficit/hyperactivity disorder in an 11-year-old boy whose attention difficulties are causing significant learning impairments. The boy also has a 1-year history of brief, mild, intermittent facial twitching and throat-clearing when he is anxious or tired. A psychological assessment reveals no additional learning disability. The *Physician's Desk Reference* states that methylphenidate is contraindicated in children who have tics. Of the following, which is the best plan of action?
 - A. Begin a trial of methylphenidate after discussing with the parents that initiation of this therapy may correlate with a transient increase in tics, but that tics are unlikely to worsen and may improve overall.
 - B. Implement a behavior plan for ADHD and forego medical intervention.
 - C. Initiate a medication trial using a second-line drug for ADHD, such as a tricyclic antidepressant.
 - D. Initiate a medication trial with an SSRI to treat the anxiety because it seems to be causing the tics.
 - E. Initiate treatment with an alpha-2-adrenergic agonist because it has been demonstrated as superior to methylphenidate in treating both ADHD and tics.
3. Of the following medications, the one that is most likely to cause a clinically significant movement disorder is:
 - A. Albuterol.
 - B. Cocaine.
 - C. Lithium.
 - D. Methylphenidate.
 - E. Neuroleptics.
4. The best intervention for acute drug-induced dystonia is:
 - A. Baclofen.
 - B. Clonidine.
 - C. Dantrolene.
 - D. Diphenhydramine.
 - E. Propranolol.
5. Of the following, a true statement regarding the diagnosis of Sydenham chorea (SC) is that:
 - A. An antecedent group A beta-hemolytic streptococcal (GABHS) infection (ie, a positive throat culture) must be identified before SC can be diagnosed.
 - B. Asymmetry of involuntary movements is incompatible with the diagnosis of SC and indicates a focal neurologic lesion.
 - C. Coexisting carditis or arthritis must be present for the diagnosis of SC.
 - D. Positive serology tests (ie, antistreptolysin O and antiDNase B antibodies) for GABHS are required to diagnose SC definitively.
 - E. The appearance of significant behavior problems in conjunction with chorea is consistent with the diagnosis of SC.
6. Of the following, the most common cause of chorea in childhood is:
 - A. Acute rheumatic fever.
 - B. Haller-Verden-Spatz disease.
 - C. Hyperthyroidism.
 - D. Juvenile Huntington disease.
 - E. Systemic lupus erythematosus.
7. The factor that best differentiates Tourette syndrome from other chronic tic disorders is the presence of:
 - A. A familial inheritance pattern.
 - B. Both motor and vocal tics.
 - C. Complex motor tics.
 - D. Coprolalia.
 - E. Male gender.