



Tremor Disorders in Children

a guide for healthcare professionals

Tremor

Tremors are rhythmic, involuntary oscillations. While there are no data on the prevalence of tremor in children, essential tremor (ET) has an overall prevalence of 300 to 400 per 100,000 per year among all age groups. The incidence of tremor increases with age. Tremor often raises concern about a structural central nervous system lesion, such as a tumor, or other serious disease. In children, however, tremor is most commonly idiopathic, related to medication side effects, or the result of self-limited conditions.

Tremor Classification

Tremor is classified by its frequency, distribution or location, diurnal variation, and whether it is present at rest or induced by motion. (See Table 1.) It is highly stereotyped, repetitive, and rhythmic with frequency ranging from six to 10 cycles per second.

Important clues to the nature of tremor are absence during sleep, distribution (unilateral or bilateral), precipitating factors (action, intention, or assuming certain postures), and associated neurologic abnormalities.

- Is it present at rest or during movement (action, intention, or sustentation)?
- Are there associated cerebellar or brainstem signs such as nystagmus, past-pointing on finger-to-nose testing, or ataxia?
- Is there a family history of tremor or abnormal movements?
- Has the patient been under stress, abusing alcohol/drugs, or consuming excessive amounts of caffeine?
- What other medications is the patient taking?

Table 1:
Classification of tremor

Cause	Appearance
Cerebellar	Intention
Essential	Action, sustentation
Palatal	Quivering palate
Parkinsonian	Resting
Physiological	Action, sustentation
Rubral	Acting, resting

Determining classification of tremor

- Sustentation tremor occurs when the child holds their arms outstretched in front of the body.
- Action tremors are elicited by tasks such as writing, drinking from or pouring from a cup or drawing an Archimedes' spiral (a spiral spinning outward from a central point).
- Intention tremor appears during finger-to-nose testing.
- Flexing and abducting the arms to allow index fingers to touch elicits rubral (wing-beating) tremor.

Differential diagnosis

The differential diagnosis of tremor includes asterixis (negative myoclonus), rhythmic movements in dystonia, clonus, and certain forms of myoclonus. In children, tremor-like repetitive head movements may have specific meanings. Head bobbing with third ventricular cysts gives the appearance of the bobble-headed doll syndrome. Head tremor in spasmus nutans is compensatory for the associated nystagmus and disappears when the child is supine. Infants may exhibit hereditary chin quivering. The jittery newborn exhibits generalized symmetric movements resembling a coarse tremor. In children with oculomotor apraxia, head-thrusting movements compensate for the child's visual disturbance.



Parents and siblings should also be examined for tremor.

Etiologies of tremor

Physiologic tremor

Enhanced physiologic tremor has a frequency of six to 10 Hz, similar to essential tremor, and is also an action/intention tremor. The conditions are additive, occurring with hyperadrenergic states, consumption of caffeine containing beverages and withdrawal from alcohol, sedatives, or opiates. (See Table 2.) Tremor may also be provoked by anxiety, stage fright, fatigue, or hypoglycemia—all conditions resulting in increased endogenous catecholamines. Other drugs such as corticosteroids, lithium, valproate, and tricyclic anti-depressants may cause tremor. Experimental evidence has shown this type of tremor to be mediated by peripheral, rather than central mechanisms.

Table 2:
Drug-induced tremor

Class	Examples
β -adrenergic agonists	Metaproterenol, Terbutaline, Epinephrine
Dopamine agonists	Levodopa, Amphetamine
Psychiatric drugs	Tricyclic antidepressants, Neuroleptics, Lithium
Anticonvulsants	Sodium valproate, Carbamazepine
Endocrine drugs	Thyroxine, Hypoglycemics, Adrenocorticosteroids
Drugs used in neuroimaging	Metrizamide
Methylxanthines	Coffee, Tea, Cola drinks
Other drugs	Cimetidine, Monosodium Glutamate

Essential tremor

Essential or primary tremor (ET), also known as familial tremor, is an action tremor that occurs in otherwise normal individuals. The tremor becomes more prominent at the end of movements as the patient attempts to control movements more precisely – drinking from a glass, for example. ET is not present at rest. Familial ET may be inherited as an autosomal dominant trait with variable penetrants. There is a positive family history in approximately 50 percent of ET patients. ET is seen in families with essential myoclonus or in combination with familial chorea, dystonia, or migraine headaches. One gene for essential tremor maps to chromosome 2p 2-25.

ET presents at any age, but in childhood the frequency usually peaks around puberty. Tremor may be trivial or disabling. It is usually present in the distal upper extremities, but head, neck, and lower extremities may be affected as well. ET may affect the voice, giving it a quavering quality. With presentation in childhood, shuddering attacks have been reported.

Over time, the movements become more pronounced. ET is slowly progressive, increasing in amplitude and decreasing in frequency with time. It is usually eight to 10 Hz frequency. While the mechanism of essential tremor is not known, it appears to be generated within the central nervous system. Enhanced olivocerebellar oscillation has been implicated in the pathophysiology of essential tremor, giving the cerebellum an important role. In childhood, essential tremor is most likely to be confused with the tremor of cerebellar dysfunction because both are made worse with action or intention. Cerebellar tremors, however, tend to affect proximal muscle more than distal ones and occur with ataxia or other cerebellar signs.



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Symptomatic or secondary tremor

Tremor may herald or accompany systemic disorders. Acute abnormality of serum glucose, calcium, or magnesium as well as thyrotoxicosis can all produce tremor. Additionally, tremor can result from intoxication with lead, mercury, or other heavy metals. Central nervous system disorders giving rise to tremor include encephalitis, vasculitis, metabolic disorders and head trauma. In these cases, tremor is usually not the only abnormality.

Wilson disease causes progressive accumulation of copper within the brain, liver, and cornea (Kayser Fleischer ring). Tremor at rest, which becomes worse with intention, is often present. Gradually the tremor becomes of higher amplitude, affecting proximal muscles to a greater extent, and has a wing-flapping quality. Therapy with the chelating agent D-penicillamine can halt progression but may not reverse symptoms. This diagnosis must, therefore, be considered in patients with acquired tremor. Elevation of serum copper and absence or depression of serum ceruloplasmin levels are diagnostic. Essential tremor is sometimes misdiagnosed as Wilson disease.

Palatal tremor (formerly called palatal myoclonus) is an extremely rapid tremor associated with lesions of the brainstem. The idiopathic form is more common in children. Fluttering of the soft palate gives rise to clicking in the ears, which can be quite bothersome and persist during sleep. Sometimes a dentist observes the palatal movement and refers the child. The evaluation for a structural lesion should be thorough. Certain patients harbor serum antibodies to glutamic acid decarboxylase (GAD).

Resting tremor is most commonly the result of parkinsonism, an uncommon syndrome in pediatrics associated with bradykinesia and rigidity. Childhood parkinsonism is usually secondary to encephalitis, head trauma, hydrocephalus, or drugs. Parkinsonism as a component of a dystonic syndrome with diurnal fluctuation of symptoms is important to recognize because it is levodopa-responsive. Primary parkinsonism (Parkinson's disease or paralysis agitans) is extremely rare in children. Drugs that block the action of dopamine within the central nervous system may induce parkinsonism. Neuroleptic medications such as phenothiazines and haloperidol are frequent offenders. Therapy involves drug discontinuation and sometimes the addition of anticholinergic medications like diphenhydramine.

Management

Correcting the underlying cause

Management, which includes diagnostic studies and treatment, centers around a thorough history and physical examination. Laboratory tests should exclude reversible etiologies. (See Table 3.)

Based on history and degree of suspicion, a heavy metal screen or catecholamine determination may be indicated. Neuroimaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI) scanning are indicated in cases of unilateral tremor of any type, other nonessential type tremors (e.g., resting, rubral, and intention tremors), abnormalities on neurologic examination, or history of a central nervous system insult.

Most tremors are not disabling and require no treatment. However, thyrotoxicosis, Wilson disease, and metabolic disturbances require therapy directed toward the underlying cause. Enhanced physiologic tremor is usually responsive to lifestyle modification or to the removal of precipitating factors.

Symptomatic treatment

The pharmacologic or symptomatic treatment of tremor depends on the type of tremor, its severity, and the age of the child. (See Table 4.)

Not until school-aged or in the teens will a child typically request or require treatment for ET. Monotherapy is a goal, but dual therapy can be necessary in moderate to severe cases.

Table 3:

Some diagnostic tests for tremor

Drug or toxicology screen
T4, TSH
ANA, ESR
Head MRI
Glucose and electrolytes
Copper and ceruloplasmin

Table 4:

Treatment of essential tremor

Drug options
Topiramate (Topamax®)
Gabapentin (Neurontin®)
Primidone (Mysoline®)
Propranolol (Inderal®)
Nadolol (Corzide®)
Metoprolol

Topiramate is an anti-epileptic drug of the sodium-channel blocking class. In a recent double-blinded placebo-controlled trial, it was efficacious in ET at doses lower than those required in epilepsy. Side effects are usually minimal and reversible, but can include cognitive slowing, lack of sweating (anhidrosis), acute glaucoma, and kidney stones.

Primidone, a barbiturate anticonvulsant, can be effective in treating ET. It is metabolized to phenobarbital and phenylethyl-malonamide, but phenylethyl-malonamide has little, if any, action against tremor. Phenobarbital has been used for tremor, but levels in excess of those obtained with primidone therapy are required for a beneficial effect. Thus, primidone itself appears to be responsible. Because very small doses are required, side effects tend to be minimal. Side effects include sedation, rash and nausea. Owing to frequent intolerance to propranolol, primidone is being increasingly used for essential tremor. In a placebo-controlled trial, gabapentin and propranolol showed comparable effectiveness in ET. Gabapentin is a good option for younger children because the risk of side effects is low. In the past, other anticonvulsants such as clonazepam have also been used.

β -adrenergic blocking drugs, such as propranolol, tend to be tolerated better by teenagers than younger children. These agents are also effective against enhanced physiologic tremor. Therapy in children is begun at a low dosage and slowly increased. The goal is not necessarily abolition of tremor but rather sufficient control to allow the patient to participate normally in daily activities. Once the lowest effective dose has been determined, some patients may be switched to extended-release formulations to facilitate compliance. Side effects, such as nightmares, lethargy, and hypotension, may limit clinical usefulness.

The β -blockers nadolol and metoprolol have anti-tremor effects. Avoid β -blockers with intrinsic sympathomimetic properties as they may increase tremor.

ET often responds dramatically to alcohol ingestion. Of course, this is not a recommended treatment.

For palatal tremor, many drug treatments have been tried, but sumatriptan seems to hold promise. In refractory cases, Botulinum toxin injections have been helpful.

Parkinsonian tremor in childhood, because it is most often secondary not primary, is best treated by reversing the underlying cause. When pharmacologic treatment is required, low doses of levodopa (Sinemet® 25-100), trihexyphenidyl or benzotropine may be useful. Caution is indicated. Secondary parkinsonism in children is usually a reversible disorder and long-term pharmacologic treatment is not required.



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Your Voice for Essential Tremor

The mission of the International Essential Tremor Foundation (IETF) is to provide hope to the ET community worldwide through awareness, education, support and research.