Stop That Essential Tremor!

By W.R. Wayne Martin, MD, FRCPC
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Julie’s tremor

Julie, 35, presents with complaints of a tremor in the right upper limb. The school teacher’s tremor is present primarily with voluntary movements, such as handwriting, taking soup with a spoon, and holding a coffee cup. Although she has been aware of a minor tremor for many years, it seems to be worsening and has become embarrassing in the classroom. When she is under stress, such as when dealing with students’ parents, the tremor can be so severe that she must hold a cup with two hands to keep from spilling its contents. She reports that a single glass of wine has a dramatic effect on reducing the tremor. She is uncertain about family history, but thinks her father may have a similar tremor. She is otherwise healthy, but does have a history of asthma, for which she uses a bronchodilator.

Virtually everyone has been aware of a tremor at some time in his or her life. Tremor can occur as a symptom in a variety of common and rare disorders, but also occurs as a normal physiologic process, and need not indicate a significant underlying disease process. Essential tremor is a common entity, unassociated with known structural pathology.

Tremor can be defined as an involuntary movement characterized by rhythmic oscillation of a body part. The movement results from regular contractions of reciprocally innervated muscles, in either an alternating or synchronous pattern. Tremor can be readily classified according to its relation to activity. A rest tremor is present

In this article:

1. What is the differential diagnosis?
2. What are the different types of tremor?
3. How is the essential tremor managed?
4. What can be done to help?
when a limb is completely relaxed and there is no voluntary muscle contraction. Two types of tremor can be observed with action:

- **Postural tremor**: Present while voluntarily maintaining a position against gravity; and
- **Kinetic tremor**: Present during volitional limb movement, such as with finger-nose testing.

How is a physiologic tremor managed?

Patients with an exaggerated physiologic tremor are best managed with reassurance that such tremors are not pathologic. They should be educated on avoiding potential exacerbating factors.

What is a physiologic tremor?

A low amplitude, 10 to 12 hertz postural tremor is present in all individuals, and is typically symptomatic only during activities that require extreme precision. This physiologic tremor may be exacerbated by a variety of clinical situations, and the apparent worsening may cause a patient to seek medical attention. Emotional stress, such as anger, anxiety, fatigue, excitement, or metabolic stress (e.g., fever, thyrotoxicosis, or hypoglycemia), may accentuate a physiologic tremor. Dietary factors, such as methylxanthines (contained in coffee, tea, and colas), monosodium glutamate, drugs (Table 1), or toxic states (e.g., alcohol or drug withdrawal) are also frequent aggravating factors. Sustained muscle contraction may produce muscle fatigue associated with tremor.

### Table 1

**Drugs that accentuate physiological tremor**

<table>
<thead>
<tr>
<th>Category</th>
<th>Drugs</th>
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<tbody>
<tr>
<td><strong>Beta-adrenergic agonists</strong></td>
<td>• Theophylline</td>
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<td></td>
<td>• Metaproterenol</td>
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<td>• Terbutaline</td>
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<td><strong>Dopaminergic drugs</strong></td>
<td>• Levodopa</td>
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<td>• Amphetamine</td>
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<td><strong>Psychiatric drugs</strong></td>
<td>• Tricyclic antidepressants</td>
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<td></td>
<td>• Selective serotonin reuptake inhibitors</td>
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<td></td>
<td>• Neuroleptics</td>
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<td></td>
<td>• Lithium</td>
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<tr>
<td><strong>Other drugs</strong></td>
<td>• Valproic acid</td>
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<td></td>
<td>• Amiodarone</td>
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<td></td>
<td>• Cyclosporin</td>
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<td>• Corticosteroids</td>
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What is essential tremor?

Essential tremor is probably the most common movement disorder, although the true prevalence is unknown (since mildly affected individuals often do not seek medical attention). Some investigators suggest essential tremor may be up to 20 times more common than Parkinson’s disease, implying a prevalence of as many as four to six per 100. Essential tremor occurs in all age groups and all ethnic populations. Several studies have reported, however, that prevalence increases with age.

Essential tremor is characterized by the presence of a postural and kinetic tremor, most often affecting both upper limbs. Tremor frequency is in the four to 12 hertz range with a tendency to slow as it worsens. The onset is often unilateral, with gradual progression to both sides over several years. There is a bimodal distribution of age of onset with peaks in the second and sixth decades. The disorder typically advances very slowly over several decades. The severity varies widely amongst affected individuals. In many, it is a harmless feature unassociated with significant disability. In others, it may be a source of considerable embarrassment, or it may

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**Dr. Martin**

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interfere dramatically with nearly all voluntary activities. Although widely considered benign, essential tremor can impose disabling psychosocial and physical constraints. Tremor amplitude in a given individual will vary from time to time, and all the factors described previously that enhance physiologic tremor have similar effects on essential tremor.

What parts of the body are directly affected by tremor?

Upper limbs are involved most frequently, and handwriting is probably the activity that is most commonly affected. Other body parts can be involved. Head tremor may occur in isolation, or in association with limb tremor. Voice tremor is rarely seen alone, but frequently accompanies tremor elsewhere. This is best elicited by having the patient vocalize a sustained vowel sound. Lower limb tremor is less commonly seen.

What’s the difference between physiologic tremor and essential tremor?

Essential tremor is unassociated with significant central or peripheral nervous system structural pathology. Physiologic tremor is related to the interaction between afferent impulses from muscle stretch receptors and efferent impulses producing muscle contraction. Physiologic tremor has a characteristic frequency and amplitude related to inertia and stiffness of the limb. Essential tremor, however, does not share these physiologic characteristics, suggesting that it is not merely an enhanced physiologic tremor. Current thinking is that a central oscillator is involved, and that synchronized firing of cerebellar olivary neurons may be responsible.

How important is family history?

Family history, like the effect of ethanol, is an important clinical point. Many patients will volunteer the observation that ethanol has a dramatic effect with a marked reduction in tremor amplitude following a single drink. Although some have suggested ethanol as a diagnostic test for essential tremor, it should be noted that the absence of a beneficial response does not preclude the diagnosis. Ethanol has been reported to suppress tremor in two-thirds of patients. More patients with early onset tremor respond to ethanol than do patients with late onset tremor. Many patients report a family history that is consistent with an autosomal dominant pattern of inheritance, but a negative family history does not rule out a diagnosis of essential tremor. Figures in the literature vary widely, but it seems that about 60% of patients with essential tremor have a positive family history.

About 60% of patients with essential tremor have a positive family history.
How do I reassure my patient?

If the tremor is mild, many patients are satisfied with the assurance that this is a “benign” condition that may not require active treatment. Lifestyle changes, such as reducing caffeine and nicotine intake, may be helpful. The intermittent use of ethanol or a short-acting benzodiazepine to lessen the tremor in specific situations, such as during meal times or in social settings, may be appropriate. Alcohol has a rebound effect, however, and patients should be cautioned regarding the risk of alcoholism. Alprazolam is the only benzodiazepine shown to be effective in controlled trials.\textsuperscript{5}

<table>
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<th>Table 2</th>
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<tr>
<td>Potential side-effects of propranolol</td>
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- Depression
- Impotence
- Insomnia
- Fatigue

A comment on Julie’s tremor

Julie’s postural/kinetic tremor is typical of essential tremor. The improvement with alcohol and the positive family history are common, but not universal, features.

Although propranolol is often a viable therapeutic option for essential tremor, it was contraindicated in this patient because of the coincident history of asthma.

As is often the case, a low dose of primidone was associated initially with side effects, but with persistence, these symptoms faded and a sustained tremor reduction ensued.

Which patients should receive medication?

Pharmacologic treatment should be considered in patients experiencing a more severe degree of disability. Beta blockers are generally used as the initial treatment, with propranolol being the most studied compound. About 50\% of patients benefit from treatment with beta blockers. Older patients are more susceptible to side-effects from beta blockers. Propranolol is started at a low dose and gradually increased, depending upon the individual patient’s response to about 80 mg to 160 mg a day. Higher doses can be tried if there are no adverse reactions (Table 2). Sustained release preparations provide a similar symptomatic benefit and compliance is often better.\textsuperscript{6}

Most patients continue to respond to beta blockers even after prolonged administration, although the dose may need to be increased to maintain efficacy.\textsuperscript{7} Occasionally, an individual will respond to a different beta antagonist, such as metoprolol or nadolol, if propranolol is ineffective or poorly tolerated. Pindolol, because of its partial agonist activity, may actually increase tremor. The mechanism of beta blockers in essential tremor is poorly understood, but may be mediated through a blockade of peripheral beta-2 adrenoreceptors. All beta blockers are contraindicated in patients with coexisting asthma.

The anticonvulsant primidone is another appropriate first-line agent for the treatment of essential tremor. A similar proportion benefit from primidone, as is the case with propranolol.\textsuperscript{8} Primidone may be helpful in those who fail to respond to propranolol. The initial dose is typically 62.5 mg a day, and can be gradually increased up to 750 mg a day. Tolerability is a common problem with primidone. Even with this very low starting dose, an
acute toxic reaction consisting of nausea, vomiting, or ataxia can occur, requiring discontinuation of primidone in up to 20% of patients.9 There is some evidence that long-term tolerability of primidone is superior to that of propranolol.10

Other lines of pharmacologic treatment are occasionally effective. Gabapentin is well-tolerated, and has been shown to be effective in open-label trials. Topirimate may also be beneficial, although tolerance may be limited.

Stereotactic surgery is an important option in patients with disabling tremor which is resistant to medication. A surgical lesion of the ventral intermediate nucleus of the thalamus, or continuous deep-brain stimulation through an electrode placed in the same structure can be dramatically effective at reducing contralateral tremor. Thalamic stimulation is the preferred procedure because there are fewer adverse effects, particularly when bilateral surgery is being contemplated.11

References

Take-home message

What is tremor?
Essential tremor is a common condition unassociated with known pathologic changes. Although often considered benign, it does gradually progress, and can become disabling.

What is the treatment?
Pharmacologic treatment with propranolol or primidone can be considered, if the symptoms affect a patient’s day-to-day functioning. Stereotactic surgery can be considered in patients with a disabling tremor that is resistant to medication.