

# Tremor

Tremor is a common condition that can occur in isolation or be part of an evolving neurological condition. It is amenable to treatment in most cases, but if first line therapies fail then often the management is complex and consideration for deep brain stimulation is considered. In this short review we outline a pragmatic approach to the patient with tremor.

## Definition and Classification

Tremor is defined as a rhythmic sinusoidal movement of a body part, due to regular rhythmic muscle contractions. The most useful classification of tremors is clinical and based on the circumstances in which they are seen (see Table 1). Static tremor occurs when a relaxed limb is fully supported at rest. Postural tremor appears when a part of the body is maintained in a fixed position and may also persist during movement. Kinetic or action tremor occurs specifically during active voluntary movement of a body part. If the amplitude of such an action tremor increases as goal-directed move-

ment approaches its target, it is termed an intention tremor. This latter tremor suggests damage in the cerebellum and its efferent connections to the brainstem and is of a frequency of 2-3Hz. Psychogenic tremors are generally rare and typically are of sudden onset with a variable but rarely remitting clinical course and typically affect the trunk or limb with standing and/or using the limb respectively.

Physiologic tremor has a frequency in the 7-11 Hz band and is typically symptomatic in states of increased sympathetic nervous activity whilst symptomatic postural tremors occur in association with a wide range of neurologic



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Table 1: Classification of tremor

Type	Definition	Causes
STATIC or REST	Present with hands or head held relaxed at rest	<ul style="list-style-type: none"> <li>• Parkinson's disease</li> <li>• Parkinsonism (inc. drug-induced, postencephalitic)</li> <li>• Other extrapyramidal diseases</li> <li>• Multiple sclerosis</li> </ul>
POSTURAL	When limb or body is held in certain position	<ul style="list-style-type: none"> <li>• Physiological tremor</li> <li>• Exaggerated physiological tremor, as in: Thyrotoxicosis anxiety states and stress alcohol drugs (e.g. sympathomimetics, anti depressants, sodium valproate, lithium) heavy metal poisoning (i.e. mercury—the 'hatter's shakes')</li> <li>• Structural neurological disease, as in: severe cerebellar lesions ('red nucleus or midbrain tremor')<sup>1</sup> Wilson's disease Neurosyphilis peripheral neuropathies</li> <li>• Essential (familial) tremor</li> <li>• Task specific tremors (e.g. primary writing tremor)<sup>2</sup></li> </ul>
KINETIC or ACTION (inc intention)	When performing an action of some sort, such as picking up cup of tea	<ul style="list-style-type: none"> <li>• Brain-stem or cerebellar disease, as in: Multiple sclerosis Spinocerebellar degenerations Vascular disease Tumour</li> </ul>
PSYCHOGENIC		

<sup>1</sup> Midbrain tremors results from damage in the region of the red nucleus, typically in the context of either MS, head trauma or a vascular insult. It is characterised by a combination of rest, postural and action tremor which is often severely disabling and very hard to treat, and this includes using stereotactic surgical thalamic lesions.  
<sup>2</sup> Dystonic tremors can be kinetic, postural or task specific and are irregular asynchronous and usually affect the arm and neck. Primary writing tremor is such an example.

disorders. These tremors can be distinguished neurophysiologically as they have a different frequency, although there is significant overlap in tremor frequency in several common conditions associated with tremor (for example, essential tremor and Parkinson's disease).

## Clinical approach to the patient with tremor

The most useful approach to a patient with tremor is a clinical one.

### History and examination:

#### • When did it first appear?

Long standing implies essential tremor (ET)

#### • Where is the exaggerated physiological tremor?

Hands: Unilateral versus bilateral with bilateral tremor implying exaggerated physiological or ET. Unilateral tremor is more suggestive of either Parkinson's disease or dystonic tremor

Voice involvement implies dystonic or ET

Head involvement with head titubation suggests either cerebellar/brainstem pathology, dystonic head tremor or ET

Legs/body involvement especially when at rest with a feeling that standing still produces an intense sense of imbalance that passes off with walking is highly suggestive of orthostatic tremor

#### • What, if anything, makes it better?

Alcohol helping the tremor suggests ET

#### • What brings out the tremor?

Certain actions or movements implying it is either an action tremor, postural tremor, intention tremor or dystonic (e.g. with writing) (see Table 1).

All tremors worsen with stress and anxiety, so this is non-discriminatory

#### • Is there any family history of a tremor?

Helpful for ET and other inherited conditions where tremor is a feature (beware of the patient diagnosed as "tremor dominant Parkinson's disease" where ET was actually more likely). Are there any other neurological symptoms – bradykinesia, myoclonus and so on suggestive of Parkinson's disease or other neurodegenerative condition

#### • Are there any medical problems and what drugs is the patient taking?

Especially important to look for thyrotoxicosis or paraproteinaemic neuropathies. For example, consider cimetidine, valproate, amiodarone,  $\beta$ -agonist inhalers.

Investigation (see Table 2)

Treatment (see Table 3)

## Certain specific tremor conditions

### ESSENTIAL (FAMILIAL) TREMOR

An illness characterised by a 5-8Hz postural tremor of the arms and head. ET can present at any age, is slowly progressive and generally causes mild disability although severe cases may be functionally incapacitating (hence the potentially inappropriate use of the term "benign", sometimes used to prefix this disorder). It can cause handwriting to be

tremulous or "corrugated". The cause of ET is unknown but a positive family history is obtained in over half of such patients and the pattern of inheritance in such families indicates an autosomal dominant trait. No pathological or biochemical abnormality has been identified in essential tremor, but recent functional imaging studies have pointed towards abnormal activation of the cerebellum, red nucleus and thalamus, and in some patients alcohol relieves the tremor. In a small number of families, genetic loci, but not the causative gene(s), have been isolated.

The typical clinical presentation is tremor in one or both hands on maintaining a posture, as when holding a cup or glass, but is not present at rest. On movement, as in finger-nose testing, the tremor continues but does not get strikingly worse, as is the case with cerebellar intention tremor. Tremor of the head (titubation) and jaw is present in about 50 per cent of cases, and tremor of the legs occurs in about a third. Despite the tremor, tests of co-ordination usually are performed normally, walking is unaffected, and there are no other neurological abnormalities.

Some other variants of the syndrome are encountered occasionally. Thus isolated, inherited, head tremor may occur, with either 'yes-yes' or 'no-no' movements, and tremulous 'writer's cramp' (primary writing tremor) is recognised. This is classified by some as a dystonic tremor. Tremor of the legs on standing, at around 5 to 8 Hz may occur in some patients with essential tremor and is thought to be different from primary orthostatic tremor (see below).

The treatment of this condition involves beta-blockers which work in about 30-40% of cases (up to a dose of 240mg/day). Primidone, in standard anticonvulsant dosages, also helps some patients but is very sedating. These two classes of drug have a reasonably solid evidence base for efficacy in ET. Other therapies, with little or no evidence to support their use, include clonazepam, gabapentin and topiramate, (see Table 3). Stereotaxic thalamotomy may be required in the very small number of patients whose tremor is so severe although more recently this has been superseded by the use of deep brain stimulation in the ventral intermediate nucleus of the thalamus.

### ORTHOSTATIC TREMOR

This is a very rare condition in which there is tremor of the legs and body especially when the patient stands still, which gives the patient the feeling of being very unsteady when standing still. As soon as they start moving the condition improves.

The tremor can be seen in some patients although in others it is best diagnosed by listening over the thighs where the tremor can be heard as the sound of distant helicopters. It responds well to clonazepam.

Table 2: Investigation of tremor

Routine haematology and biochemistry to exclude major metabolic problem including renal failure, liver disease +/- alcoholism  
Thyroid function tests  
Immunoglobulins and electrophoretic strip  
Copper/Caeruloplasmin in young patients  
Consider genetic tests such as SCA screening

Consider imaging, EMG-NCS, and CSF but only if tremor is late onset or evolving with other neurological signs and symptoms

Table 3: Treatment of tremor\*

Stop any drug that may be causing tremor  
Inc. Lithium, SSRIs, neuroleptics, sodium valproate, beta agonists, thyroxine, aminophylline etc

#### Drugs which are worth trying:

Beta blockers  
Primidone  
Benzodiazepines  
Gabapentin  
Topiramate

Botulinum toxin injections for some dystonic tremors

Deep brain stimulation/Thalamotomy of VIM thalamic nucleus

#### Other drugs and manipulations which have been tried in the treatment of tremor (ET unless otherwise indicated) with possible benefit in some cases:

Phenobarbitone  
Carbonic anhydrase inhibitor (Methazolamide)  
Clonidine  
Amantadine  
Clonidine (probably not effective in ET)  
Isoniazid (probably not effective for intention tremor)  
Clozapine/Olazepine/Quetiapine  
Mirtazapine  
Vagal nerve stimulation

\* the treatment of the tremor in PD lies outside the scope of this article but clearly revolves around the use of L-dopa and dopamine agonists. It is controversial whether anti-cholinergic agents and the newer dopaminergic agonists have more anti-PD tremor effects than L-dopa based therapies.

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