Tremor is defined as a rhythmical, involuntary oscillatory movement of a body part. The formulation of a clinical diagnosis for an individual’s tremor involves two discrete steps:

- The observed tremor is classified on phenomenological grounds.
- An attempt is made to find the cause of the tremor by looking for aetiological clues in the patient’s history and physical examination and also, in some cases, by investigation.

**PHENOMENOLOGICAL CLASSIFICATION OF TREMOR**

The phenomenological classification of tremor is determined by finding out:

- which parts of the patient’s body are affected by tremor?
- what types (or components) of tremor, classified by state of activity, are present at those anatomical sites?

The following definitions are used to describe the various tremor components evident on examination:

- **Rest tremor** is a tremor present in a body part that is not voluntarily activated and is completely supported against gravity (ideally resting on a couch).
- **Action tremor** is any tremor that is produced by voluntary contraction of a muscle. It includes postural, kinetic, intention, task specific, and isometric tremor:
  - **Postural tremor** is present while voluntarily maintaining a position against gravity.
  - **Kinetic tremor** is tremor occurring during any voluntary movement. Simple kinetic tremor occurs during voluntary movements that are not target directed.
  - **Intention tremor** or tremor during target directed movement is present when tremor amplitude increases during visually guided movements towards a target at the termination of that movement, when the possibility of position specific tremor or postural tremor produced at the beginning and end of a movement has been excluded.
  - **Task specific kinetic tremor**—kinetic tremor may appear or become exacerbated during specific activities. Occupational tremors and primary writing tremor are examples of this.
  - **Isometric tremor**—tremor occurring as a result of muscle contraction against a rigid stationary object.

**CLASSIFICATION OF TREMOR BY AETIOLOGY**

Many of the main causes of tremor are shown in table 1.

A full clinical history and examination should always be undertaken and are invaluable for elucidating the cause of a tremor. The main points to establish from the patient’s history are shown in table 2.

Neurological examination should aim to discover the anatomical location of tremor, the tremor types/components present at those sites, and their severities (on a 0–10 rating scale) (fig 1). In addition it is useful to record specimens of the patient’s handwriting and a drawing of a spiral, as estimates of tremor severity (on a 0–10 rating scale) correlate with tremor related disability and provide useful permanent records for comparison with future assessments (fig 2). Furthermore, other neurological signs should be sought, particularly those related to the conditions listed in table 3.

The extent to which a tremulous patient is investigated depends on the complexity of the case and whether a diagnosis can be established on clinical grounds. However, thyroid function should be routinely tested in patients with an action tremor. The issue of excluding Wilson’s disease should be considered in patients in whom tremor began before their 50th birthday; initially check serum copper and caeruloplasmin.

A cerebral magnetic resonance scan may identify a focal lesion (for example, in Holmes’ tremor) and can be useful if symptoms and signs are entirely confined to one side of a patient—a hemi-tremulous state. Nerve conduction studies/electromyelogram (EMG) confirm the presence of tremor.
frequency bands frequently overlap. Characteristic of specific aetiologies than others, though their precise roles require further definition. Only primary orthostatic tremor has a unique frequency band (14–18 Hz) (table 5), although intermittently its frequency can halve to between 7–9 Hz.8

Bursts of EMG activity separated by relative silence occur in all types of pathological and enhanced physiological tremor, but not in normal, low amplitude, physiological tremor. The relation of the EMG bursts in agonist/antagonist muscle pairs—for example, the forearm flexor and extensor muscles—has been studied in various types of pathological tremor. Unfortunately, the recorded patterns—namely, cocontraction, alternating, switching from alternating to cocontraction and agonist (anti-gravity activation alone) as well as other more diffuse patterns—are not confined to any one tremor type and can vary over short periods of time within the same muscles of an individual patient.

### Physiological and enhanced physiological tremor

A fine action tremor is normally present in everyone's limbs. This normal physiological tremor becomes more pronounced (enhanced physiological tremor) during periods of muscular fatigue, fear or excitement, and in certain medical conditions—for example, hyperthyroidism. It is the result of

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**Table 1** Aetiological classification of tremor

<table>
<thead>
<tr>
<th>Normal tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (physiological) tremor</td>
</tr>
<tr>
<td>Enhanced physiological tremor (e.g. anxiety)</td>
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</tbody>
</table>

Pathological tremors

- Enhanced physiological tremor (e.g. hyperthyroidism)
- Essential tremor—hereditary or sporadic
- Parkinson's disease and other causes of parkinsonism
- The dystonic tremor syndromes
- Drug induced tremors or drug withdrawal states
- Multiple sclerosis associated tremor
- Neuropathic tremor, including porphyrias
- Holmes’ tremor (midbrain or rubral)
- Primary writing tremor and other task specific tremors
- Primary orthostatic tremor
- Cerebellar tremors
- Post-traumatic tremor
- Cerebrovascular disease
- Psychogenic

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**Table 2** Clues to pathogenesis obtained from the patient's history

- Patient's age at onset of tremor
- Mode of onset of tremor (sudden or gradual)
- Anatomical site first affected by tremor
- Other sites subsequently affected by tremor
- Sequence of spread of tremor
- Rate of progression to other sites and rate of increase in severity
- Familial or sporadic tremor
- Family history of other movement disorder or neurological condition
- Previous drug intake
- Drug/alcohol responsiveness of the tremor

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**Figure 1** A validated (0–10) rating scale for scoring tremor severity.
numerous factors including the heart beat, low pass filtering properties of striated muscle, motor neurone firing, and synchronisation by spindle feedback. Physiological tremor amplitude can be modulated by temperature and supraspinal influences, such as vision, and also by drugs that interact with β receptors.

Parkinson’s disease
A “pill rolling” rest tremor is said to be characteristic of the disease, but postural tremor is present in most cases and is symptomatic in about 60% of patients with Parkinson’s disease. In 10–20% of cases a rest component never appears.

Typically the tremor of Parkinson’s disease is asymmetrical, at least initially, and affects an upper limb involving the ipsilateral leg after a latency of approximately two years. This hemi-tremulous state may remain for several years before the contralateral limbs become involved, although this is by no means always the case and occasionally this sequence is delayed or tremor appears first in the legs. The disease may also produce tremor of the lips, tongue or jaw but it rarely causes significant head or vocal tremor. Cogwheeling is tremor that is palpable on passive manipulation of a limb. Other signs of parkinsonism are usually apparent or develop, making the diagnosis obvious in time. However, tremor is the presenting complaint in about 60–70% of cases and may remain the main manifestation of the condition for several years (benign tremulous Parkinson’s disease).

Indeterminate tremor syndrome
Some patients, particularly elderly, have symptoms and signs that satisfy the criteria for essential tremor, except that one or two mild extrapyramidal features are present—for example, hypomimia or reduced arm swing. These may not be sufficient

Table 3 Clues to pathogenesis obtained from examination of the patient

<table>
<thead>
<tr>
<th>Signs of:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinsonism—bradykinesia, rigidity, postural instability</td>
</tr>
<tr>
<td>Cerebellar disease—eye movements, speech</td>
</tr>
<tr>
<td>Dystonia—spasmodic torticollis, vocal dystonia, writer’s cramp</td>
</tr>
<tr>
<td>Neuropathy—pes cavus, LMN signs, sensory signs</td>
</tr>
<tr>
<td>Drug induced dystonia—oro-facial dystonia</td>
</tr>
<tr>
<td>Multiple sclerosis—other signs of MS usually evident</td>
</tr>
<tr>
<td>Orthostatic tremor—unsteadiness and palpable leg tremor on standing</td>
</tr>
<tr>
<td>Alcoholism—signs of liver disease</td>
</tr>
<tr>
<td>Wilson’s disease—KF rings, splenomegaly, hepatosplenomegaly</td>
</tr>
</tbody>
</table>

Examination of a tremulous patient’s relatives or their photographs may be useful.

KF, Kayser-Fleischer; LMN, lower motor neuron; MS, multiple sclerosis.

Table 4 Investigation of tremulous patients

<table>
<thead>
<tr>
<th>Routine:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid function tests</td>
</tr>
<tr>
<td>Copper and caeruloplasmin (if aged &lt;50 years)</td>
</tr>
<tr>
<td>Others:</td>
</tr>
<tr>
<td>Cerebral magnetic resonance scan</td>
</tr>
<tr>
<td>Genetic studies</td>
</tr>
<tr>
<td>DAT or PET scan</td>
</tr>
<tr>
<td>Nerve conduction studies/EMG</td>
</tr>
<tr>
<td>Investigation for causes of neuropathy</td>
</tr>
<tr>
<td>Paroxysmal screen</td>
</tr>
<tr>
<td>Toxicology studies</td>
</tr>
</tbody>
</table>

DAT, dopamine transporter; EMG, electromyelogram; PET, positron emission tomography

Figure 2 Specimens of handwriting and a spiral drawing obtained from a patient with essential tremor.

Figure 3 [123I]-FP-CIT (DaTSCAN) images demonstrating: (top left) normal tracer uptake in the putamen and caudate nuclei; then progressively decreasing uptake in scans from patients with mild (top right), moderate (bottom left), and severe (bottom right) parkinsonism.
to allow a diagnosis of parkinsonism to be made with confidence, at least initially. Consequently, it may be preferable to label these patients as having the indeterminate tremor syndrome rather than pushing the diagnoses of either essential tremor or parkinsonism, until time provides more definitive evidence one way or another. It is possible that in future functional imaging with PET or SPECT may provide useful information in these circumstances, but further studies with these techniques are required.

**Essential tremor**

The following clinical criteria are used to make the diagnosis of classical essential tremor:

- **Inclusion criteria:**
  - (1) The presence of bilateral, largely symmetrical postural or kinetic tremor involving hands and forearms that is visible and persistent
  - (2) Additional or isolated tremor of the head may occur but in the absence of abnormal posturing. (The inclusion of isolated head tremor in these criteria is controversial as many experts, including the author, consider this to represent a “forme fruste” of cervical dystonia.)

- **Exclusion criteria:**
  - (1) Other abnormal signs, especially dystonia
  - (2) The presence of known causes of enhanced physiologic tremor, including current or recent exposure to tremorgenic drugs or a drug withdrawal state
  - (3) Historic or clinical evidence for a psychogenic origin of tremor
  - (4) Convincing evidence of sudden onset or evidence of stepwise deterioration of tremor
  - (5) Primary orthostatic tremor
  - (6) Isolated voice tremor
  - (7) Isolated position specific or task specific tremors, including occupational tremors and primary writing tremor
  - (8) Isolated tongue or chin tremor
  - (9) Isolated leg tremor.

Essential tremor is classified as hereditary or sporadic and estimates of its overall population prevalence vary widely between 0.08 and 220 cases per 1000 people depending on the methodologies used. The hereditary form is thought to be inherited via an autosomal dominant gene that has not yet been identified, although linkage to two different loci (3q13 and 2p22-25) have been reported with LOD scores of 3.71 and 5.92, respectively. The age of onset is bimodally distributed with a median age of about 15 years. About 50% of affected individuals respond to alcohol, although the tremor rebounds about 3–4 hours later, in an exacerbated form.

**Dystonic tremor syndromes**

The dystonic tremor syndromes are defined as follows:

- **Dystonic tremor**: tremor in a body part affected by dystonia
- **Tremor associated with dystonia**: tremor occurs in a body part not affected by dystonia, but the patient has dystonia elsewhere
- **Dystonia gene associated tremor**: tremor as an isolated finding in patients with a dystonic pedigree.

These types of tremor occur on action and can be broadly divided into three categories:

1. A postural tremor which is apparent in the outstretched arms and is clinically indistinguishable from enhanced physiological or essential tremor. This type of tremor is often associated with spasmodic torticollis but may occur as the sole manifestation of hereditary torsion dystonia

2. A jerky irregular action tremor intermingled with sustained muscular spasms that can last several seconds. This type of tremor is often very disabling and can affect the muscles of the neck, face, trunk or limbs

3. A task specific movement disorder in which tremulousness and jerky spasms develop concurrently during the performance of highly skilled acts. The most common examples are tremulous writer’s and typist’s cramps.

**Task specific tremor**

Tremor may occur only during the performance of specific tasks (task induced tremor) or postures (positionally sensitive tremor). The most common example is primary writing tremor (PWT), which has been defined as “being present when tremor occurs only or predominantly during writing but not during other tasks in the active hand”. Similar task specific tremors can affect typists, musicians, and sportsmen.

PWT was first described by Rothwell et al in 1979 and a number of patients with similar symptoms have subsequently been documented. Bain et al studied the clinical and neurophysiological features of 21 patients (20 males and 1 female) with PWT and found a degree of non-specific action tremor of the upper limbs in most cases, which was of smaller magnitude than the writing tremor. In 20% of cases a preceding history of trauma to the dominant arm was obtained, although there was a delay between trauma and the appearance of tremor that varied from 18 months to 12 years. A family history of PWT can be obtained from about one third of the patients. The mean age at PWT onset is 50.1 years, which is between 15–20 years later than that reported for writer’s cramp, and significantly older than that reported for hereditary idiopathic torsion dystonia and hereditary essential tremor. Patients with PWT have been subclassified into type A (task induced tremor) or type B (positionally sensitive tremor). However, no significant differences were found between these two PWT subgroups in regard to age, at tremor onset or duration of tremor, and the condition is usually non-progressive.

The aetiology of PWT is controversial and opinion is divided into the following views: (1) that PWT is a variant of essential tremor; (2) that it is a type of focal dystonia, a variant of writer’s cramp; (3) that it is a different entity to both focal dystonia and essential tremor; (4) that some cases of PWT are related to essential tremor and others to torsion dystonia.

Tremor frequencies of 5–7 Hz have consistently been found in patients with PWT but it is noteworthy that rhythmic EMG activity (at about 4–7.7 Hz) is seen in healthy individuals during normal handwriting. The time course of reciprocal inhibition of the forearm median nerve H reflex was found to be normal in patients with PWT but is known to be abnormal in
patients with writer’s cramp. PET and magnetic resonance studies have demonstrated abnormal bilateral cerebellar activation in patients with PWT but also activation of other cerebral regions that integrate those found in essential tremor and writers cramp, supporting the view that PWT is distinct from both of these entities. There have been no postmortem studies involving patients with PWT.

**Primary orthostatic tremor**
Primary orthostatic tremor typically presents with unsteadiness on standing still, which improves on walking. The patient may or may not be aware of tremulous legs. The tremor and postural instability tend to worsen with prolonged stance. A fine tremor of the legs is usually palpable or visible while standing and a broad based gait or poor tandem walk may be detected. The tremor may affect other parts of the body if certain postures are maintained—for example, the arms may become tremulous if the patient leans on them. Primary orthostatic tremor has been divided into type 1 (pure) and type 2 (symptomatic, associated with cerebellar degeneration). This tremor has a diagnostic frequency band of 14–18 Hz, although epochs of doubling may occur, and has a high degree of coherence between muscles in each leg.

**Neuropathic tremor**
Tremor is one of the manifestations of peripheral neuropathy, having been described more frequently in demyelinating than axonal neuropathies. It is observed in patients with acute and chronic inflammatory demyelinating polyneuropathies, hereditary motor, sensory, and IgM paraproteinaemic neuropathies, and less often in other forms of peripheral nerve disease. Characteristically an action tremor is produced, which resembles essential tremor, although rest tremor has also been reported. Tremor can be the presenting symptom, although more frequently patients present with sensory disturbances. Signs of a peripheral neuropathy are usually present on examination and nerve conduction studies/EMG are performed to confirm the diagnosis and help guide management. Porphyria should be considered, particularly if the tremor is paroxysmal.

The mechanisms underlying neuropathic tremor are poorly understood. However, for tremor associated with benign IgM paraproteinaemic neuropathy a correlation between the frequencies of thumb tremor and ulnar nerve motor conduction velocities has been reported. Complex physiological studies suggest that distorted and mistimed peripheral sensory inputs reach a central nervous system processor that is intact but misled into producing tremor. Activation studies using PET have indicated that cerebellar hemispheres appear to be overactive in IgM paraproteinaemic neuropathic tremor in a way similar to that detected in essential tremor.

**Holmes’ tremor syndrome**
Holmes’ tremor syndrome has in the past been variously termed rubral tremor, midbrain tremor, thalamic tremor, myorhythmia, and Benedikt’s syndrome (figs 4, 5, and 6). This may arise from various underlying structural disorders including stroke, vascular malformations or tumours. It is not usually present in multiple sclerosis. If the onset of a lesion can be identified (for example, a stroke), a variable delay (typically two weeks to two years) between that lesion and the first appearance of tremor is characteristic of the condition. Holmes’ tremor syndrome is characterized by a low frequency rest and intention tremor, with the first appearance of tremor in those cases where the onset of a lesion is identified. Holmes’ tremor syndrome arises from lesions that interrupt the dentate–thalamic and the nigrostriatal tracts thus causing both an action and a rest tremor.

**Cerebellar tremor**
The intention component of kinetic tremor is considered to be characteristic of cerebellar pathology, although it is probable that lesions of the superior cerebellar peduncle, rather than the cerebellum itself, are responsible for this. Various types of

**Abbreviations**
- **DoTSCAN**: [123I]-FP-CIT
- **EMG**: electromyelogram
- **PET**: positron emission tomography
- **PWT**: primary writing tremor
- **SCA-12**: spinocerebellar ataxia-12
- **SPECT**: single photon emission computed tomography

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**Figure 4** Gordon Holmes.

**Figure 5** Magnetic resonance scan showing atrophy of the right cerebral peduncle in a patient who developed Holmes’ tremor following haemorrhage from an angioma located at the tip of the basilar artery.
postural tremor have been described including slow oscillations of the arms about the shoulders, or legs about the hips. This type of tremor is referred to as titubation when it affects the head and trunk, and it can be particularly striking when a patient is standing. It is often accompanied by other signs of cerebellar disease and is most commonly seen in patients with multiple sclerosis, although mass lesions, vascular disease, and hereditary or acquired cerebellar degenerations, particularly spinocerebellar ataxia-12 (SCA-12), may all result in this form of movement. The characteristics of tremor associated with multiple sclerosis are shown in table 7.

Drug induced tremor
Numerous drugs are known to produce tremor in man. The most common miscreant is probably alcohol (withdrawal or prolonged heavy ingestion) which can cause an action tremor. Similarly insulin, by inducing hypoglycaemia, can precipitate enhanced physiological tremor in diabetic patients. An action tremor resembling enhanced physiological tremor can also be produced by a variety of substances including salbutamol, theophylline, adrenaline, amphetamine, lithium, caffeine, and steroids.

In neurological and psychiatric practice iatrogenic tremor is frequently seen and both drug induced parkinsonism and tremulous dyskinesias are common, as are action tremors resulting from the use of tricyclic antidepressants. The antiparkinsonian drugs used in the treatment of vertigo, nausea, vomiting, and psychosis can all incite a rest tremor similar to that seen in Parkinson’s disease, but more typically these drugs cause a symmetrical action tremor.

The anticonvulsants phenytoin and sodium valproate can produce action tremors when administered in sufficiently high doses for prolonged periods.

Psychogenic tremor
Psychogenic tremor is used to describe tremor that is produced or exacerbated voluntarily or “subconsciously” by a patient. The following phenomena suggest a psychogenic aetiology: (1) sudden onset of tremor, which may present as an emergency or go into remission or both; (2) unusual clinical combinations of rest and postural/intention tremors; (3) decrease in tremor amplitude on distraction or changes in tremor frequency during voluntary movements of the contralateral hand; (4) the presence of the co-activation sign of psychogenic tremor, in which resistance to passive movement about a joint causes the appearance and disappearance of tremor to mirror changes in tone; (5) a clear past medical history of a somatisation disorder and the appearance of additional and unrelated neurological signs with tremor. Furthermore, loading may increase the amplitude of psychogenic tremor, unlike essential or parkinsonism tremors that decrease with external loading. However, organic tremors often present at times of great stress and may be paroxysmal—for example, in porphyria or in the early phase of development of either essential or parkinsonian tremors.

Table 6 Characteristic features of Holmes’ tremor
- Holmes first to describe this tremor in detail
- Slow (<4.5 Hz) irregular tremor
- Present at rest and intention, often also on posture
- Typically involves proximal and distal muscles
- Variable delay from lesion to tremor onset
- Typically from 2 weeks to 2 years
- May respond to levodopa or direct acting dopamine agonist
- Lesion site varies from thalamus to midbrain
- PET: may show decreased F18-dopa uptake in:
  - Ipsilateral putamen and caudate

Table 7 Features of multiple sclerosis (MS) tremor
- 57% of definite clinic based MS cases have tremor
- Parts of body affected by tremor in MS
  - 55% arms
  - 8% legs
  - 7% head
  - 5% trunk
- Invariably an action tremor, with several distinct subtypes
- Mean duration from MS to tremor onset of 13.5 years
- Tremulous patients more likely to have progressive MS
- 27% of MS patients report tremor related disability
- 10% of MS patients have incapacitating tremor
- Tremor severity correlated with:
  - Dysarthria
  - Dysesthesia
  - Walking time (inverse correlation)
MANAGEMENT OF TREMOR

The management of tremor depends on its severity and underlying etiology. Propranolol (up to 320 mg/day) and primidone (up to 250 mg three times daily) are the main treatments for essential tremor, but are also useful for patients with dystonic tremor syndromes. The combination of propranolol and primidone is more effective at suppressing essential tremor than either drug alone, while clonazepam can be useful for patients with kinetic predominant essential tremor. About 50% of patients with essential tremor respond to 2–4 units of alcohol, which if used in moderation can facilitate feeding, drinking, and social engagement. However, alcohol responsiveness is not diagnostic of essential tremor as patients with dystonic tremor syndromes, PWT, myoclonic dystonia, and rarely parkinsonian tremors can respond to it.

The treatment of choice for severe isolated head tremor or head tremors associated with essential or dystonic tremors is intramuscular botulinum toxin. Propranolol, primidone, anticholinergics, and botulinum toxin may all have a role in treating task specific tremors but their efficacy has not been systematically studied in these conditions.

Propranolol has been demonstrated in randomised controlled studies to reduce parkinsonian rest and postural tremors and is thus useful for Parkinson's disease patients who present with tremor, or as adjunctive treatment for those with tremor predominant Parkinson's disease. Anticholinergic medications, direct acting dopamine agonist drugs, and levodopa preparations can all variably decrease Parkinson's disease tremor. The issue of whether primipexole has a greater anti-tremor effect than other direct acting dopamine agonist class medications is currently under investigation.

Neuropathic tremors, tremor associated with multiple sclerosis, and other cerebellar tremors are difficult to treat effectively using medication, but propranolol and clonazepam are worth trying. Primary orthostatic tremor is usually treated with clonazepam. Some patients benefit from using a “tripod” portable stool, which allows them to sit rather than stand for long periods. Although phenobarbital or levodopa may also have a role in the treatment of some cases of primary orthostatic tremor, the results are usually unimpressive. Holmes’ tremor may respond to levodopa, but disabling dyskinesias may develop. Consequently, direct acting dopamine agonist or anticholinergic drugs may be preferable, at least initially.

Stereotactic surgery can alleviate contralateral limb tremor in patients with Parkinson’s disease, essential tremor, dystonic tremor syndromes, writing tremor, Holmes’ tremor, post-traumatic tremor, and tremulous multiple sclerosis. (For a fuller discussion see Gregory, p ii2.) The preferred intracerebral target for parkinsonian tremor is the subthalamic nucleus rather than the nucleus ventralis intermedius of the thalamus, as the former also ameliorates rigidity and bradykinesia. The thalamus has been the target of choice for Holmes’ tremor as well as essential and dystonic tremor syndromes, although ventralis oralis posterior or zona incerta may be as effective as ventralis intermedius; in multiple sclerosis the zona incerta may be the preferred target, particularly when there is a proximal tremor component. Presently deep brain stimulation is considered to be safer than lesional surgery, particularly for bilateral procedures, although the former requires considerably more postoperative servicing.

REFERENCES