TREMOR
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Tremor definition
- Rhythmic, involuntary, oscillatory movement of a body part
- Multiple etiologies; multiple clinical syndromes
- Oscillatory nature - to distinguish tremor from other involuntary movements
- Amplitude - not critical

• Common
  - Essential tremor
  - Parkinsonian tremor
  - Physiological
  - Dystonic tremor
  - Cerebellar tremor
  - Drug induced

• Uncommon
  - Psychogenic
  - Post-traumatic or post-stroke tremor

Rare
  - Neuropathic tremor
  - Primary orthostatic tremor
  - Holmes’ tremor

Classification of tremors

(A) Axis 1: clinical features
- Historical features
- Tremor characteristics
- Associated signs
- Additional laboratory tests

(B) Axis 2: etiology
- Acquired
- Genetically defined
- Idiopathic

International Congress of Parkinson's Disease and Movement Disorders
5-9 Oct 2018 – Hong Kong
www movimiento disorders.org

Membership
- Regular
- Junior
- Health Professional
- Student
- Waived dues

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FIG. 1. The current narrow definition of ET may still be too restrictive. The two main activation classifications are rest-tremor and action/ intention tremor (when tremor is increased by activity). Tremor in the upper arms affects the upper and lower body. Tremor in the hands or lower limbs or trunk during standing is called orthostatic tremor. Tremor in the head is called thalamic tremor. Tremor does not affect the face. Tremor in or below the knee is called leg tremor. Tremor in the arms may be differentiated from tremor in the legs by asking the patient to extend their arms straight out in front of them. (A) Axis 1 classification of tremor is based on clinical features from the patient’s medical history and physical examination. Additional tests that can be performed include blood testing, imaging studies, and neurological testing to detect abnormalities. (B) Axis 2 classification is etiology. A syndrome in Axis 1 may have multiple etiologies, and a particular etiology may produce multiple clinical syndromes. The identification of causative factors is important in guiding diagnostic and therapeutic approaches. 

The epidemiology of ET was almost unknown in the past. The first systematic studies that revealed normal striatal dopamine reuptake in ET were performed by Marsden et al.13 The epidemiology of ET was later studied. Case ascertainment and other aspects of these studies have not been consistent, and if at all, a uniform worldwide prevalence has not been established. Studies have shown rates of 0.4%–6.1% in the general population. The prevalence of ET among older people is very important, as it may increase with age. Younger-onset ET may affect any age group. However, age of onset should always be documented as accurately as possible. Age of onset is important in guiding diagnostic and therapeutic approaches. 

A recent meta-analysis of almost 30 studies found the overall prevalence to be 0.4%–6.1%. Rates vary according to age; ET is most common in people over 60 years of age. The highest rates are close to 90% in monozygotic twins and around 4.6% in the general population. However, age of onset should always be documented as accurately as possible. 

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part approaches its visual target. Other forms of action tremor increase in tremor occurs as the affected body region is also activated. It should be assessed when the patient is attempting to relax and is given adequate time to perform the task.

- **Kinetic tremor** occurs during a specific task or during any voluntary movement.
- **Postural tremor** occurs when making a fist or squeezing an examiner's fingers.
- **Orthostatic tremor** occurs in the lower limbs or trunk during standing.
- **Hemitremor** occurs in which a crested body part is not voluntarily activated. It should be assessed when the patient is attempting to relax and is given adequate time to perform the task.

### Tremor Syndromes

<table>
<thead>
<tr>
<th>Tremor Syndromes</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinsonian tremor</td>
<td>Essential tremor, PD, dystonic, cerebellar, psychogenic, rubral, writing</td>
</tr>
<tr>
<td>Physiological tremor</td>
<td>Essential tremor, PD, orthostatic, psychogenic</td>
</tr>
<tr>
<td>Essential tremor</td>
<td>Cerebellar, psychogenic, orthostatic</td>
</tr>
<tr>
<td>Dystonic tremor</td>
<td>Dystonic, essential tremor, cerebellar</td>
</tr>
<tr>
<td>Orthostatic tremor</td>
<td>PD, dystonic, tardive</td>
</tr>
<tr>
<td>Cerebellar tremor</td>
<td>Essential tremor, tardive</td>
</tr>
<tr>
<td>Holmes’ tremor</td>
<td>Drug induced, PD</td>
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</tbody>
</table>

### Tremor Frequency

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rest</th>
<th>Postural</th>
<th>Kinet</th>
<th>Frequency</th>
</tr>
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<tr>
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<tr>
<td>Palatal tremor</td>
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</tbody>
</table>

### Diagnostic Clues

- **History**
  - Age at onset
  - Mode at onset and course
  - Affected body region
  - Spread during course
  - Other signs
  - Concomitant diseases
  - Medications
  - Family history
  - Toxic exposure

- **Examination**
  - Observe: rest, postural, kinetic
  - Positional dependence
  - Abnormal postures
  - Mental or motor distractibility of tremor
  - Writing and spiral drawing
  - Specific tasks

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**Consensus Statement** - Bhatia K et al. Mov Disord 33; 2018

**Ranking** - J. Deuschl G. Curr Opin Neurol. 2009
**Associated clinical signs**

- **Neurological**
  - Dystonia or dystonic posturing
  - Parkinsonism
  - Cerebellar
  - Pyramidal
  - Neuropathy

- **Systemic**
  - Kaiser-Fleischer ring
  - Hepatosplenomegaly
  - Hyperthyroidism

- **Psychiatric**

**Additional tests**

<table>
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<tr>
<th>Regular</th>
<th>By indications</th>
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<tbody>
<tr>
<td>Thyroid function tests</td>
<td>EMG, nerve conduction studies</td>
</tr>
<tr>
<td>Copper metabolism</td>
<td>DaTSCAN imaging</td>
</tr>
<tr>
<td>Brain structural imaging (if unilateral or persistent tremor)</td>
<td>Toxicology studies: if on relevant drugs</td>
</tr>
<tr>
<td>Metabolic blood tests (porphyria screen, etc)</td>
<td>Tests for infections</td>
</tr>
<tr>
<td>Genetic testing</td>
<td>Genetic testing</td>
</tr>
</tbody>
</table>

**Etiology**

- Neurodegenerative diseases
  - PD, MSA, PSP, Wilson, SMA, neuroferritinopathy, ..
- Mitochondrial genetic diseases
- Endocrine and metabolic diseases
- Neuropathies
- Infectious and other inflammatory diseases
  - SM, SSPE, HIV, tuberculosis, syphilis, neuroborreliosis, ..
- Toxins
  - Metals (Hg, Pb, Mn, As), cyanide, toluene, ..
- Drugs
  - Anticonvulsants, antidepressants, neuroleptics, metoclopramide, anticancer, ..
- Others
  - Brain tumors, trauma, vascular
  - Anxiety and stress, fatigue, ..

**ESSENTIAL TREMOR (ET)**

- **Clinical picture:**
  - Persistent, bilateral, largely symmetric
  - Action or postural tremor involving hands and forearms
  - May spread to other body parts (head, voice, legs)
  - Isolated tremor of the head in the absence of abnormal posturing.
- **No other neurological signs or disease**
- At least 3 years history

**Essential tremor: diagnostic challenges**

- **Exclusion**
  - isolated focal tremors
  - orthostatic tremor
  - task-specific tremor
  - sudden onset
- **Differential diagnosis**
  - Dystonic; Neuropathic; Functional tremor
- **ET-plus: additional neurological signs**
  - impaired tandem gait, postural disorder
  - mild memory impairment

**Essential tremor**

- **Common movement disorder**
  - 1% of the general population; 5% over 65 years
- Positive family history
- Molecular mechanisms uncovered
- Treatment: effect in half cases but rarely completely
- **Medications**
  - Primidone, propranolol
  - Topiramate, gabapentin
  - Alprazolam
  - Atenolol
- **Botulinum toxin**
  - VIM-DBS
  - Thalamic lesions

**Video**

Fasano C et al. Mov Disord 33; 2018
Hopfner E, Deuschl G. Mov Disord 32: 2017
Espay AJ et al. Mov Disord 22: 2018
**PARKINSONIAN TREMOR**
- Classic Parkinsonian rest tremor is a "pill rolling" tremor of 4-7 Hz
- Hallmark of a parkinsonian syndrome
- In ~80% of PD patients
- Up to 10% of patients with atypical parkinsonism (MSA, PSP, CBD, VP)
- Predominantly in hands; can also occur in legs, jaw or tongue
- PD patients may also have postural or kinetic tremor of faster frequency

**DYSTONIC TREMOR**
- Tremor can be a element of dystonia
- Postural/kinetic tremor, occurring in the region affected by dystonia
- Worsens with voluntary movements against dystonia (e.g. torticollis)
- Geste antagoniste (sensory trick)
- TAD – tremor associated with dystonia – in a different region
- Dystonic vs essential tremor?
  - Hand tremor - subtle dystonic posturing of fingers or wrist
  - Head tremor - subtle dystonic posturing of neck

**ORTHOSTATIC TREMOR**
- Isolated tremor syndrome in legs when standing
- 13-18 Hz
- Palpation – if not visible
- Auscultation: "helicopter sign"
- EMG confirmation
- Treatments:
  - Clonazepam, levetiracetam
  - DBS
- Primary orthostatic tremor plus: in combination of other neurological conditions
  - Dementia, parkinsonism, ataxia

**CEREBELLAR TREMOR**
- Dominant intention component, but also can be postural
- Usually slow (<5 Hz) but can be faster
- Often disabling
- Etiology: stroke, multiple sclerosis, trauma
- Treatment of limited effect: isoniazid, carbamazepine, propranolol, gluthemiside

**Differentiating PD and essential tremor**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Tremor in PD</th>
<th>Essential tremor</th>
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<tr>
<td>Type</td>
<td>Rest tremor 4-7 Hz</td>
<td>Kinetic and postural 8-12 Hz</td>
</tr>
<tr>
<td>Body parts</td>
<td>Hands, upper and lower limbs</td>
<td>Hands, head, voice</td>
</tr>
<tr>
<td>Bradykinesia</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Age at onset</td>
<td>Middle and older</td>
<td>Any age</td>
</tr>
<tr>
<td>Course</td>
<td>Progressive</td>
<td>Slowly progressive</td>
</tr>
<tr>
<td>Family history</td>
<td>Mostly negative</td>
<td>50% positive</td>
</tr>
<tr>
<td>Alcohol</td>
<td>No effect</td>
<td>Reduces tremor</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Effective</td>
<td>No effect</td>
</tr>
<tr>
<td>β-blockers</td>
<td>No effect</td>
<td>Effective</td>
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**Treatment of dystonic tremor**

- BoNT: effective in dystonic tremor of head/jaw/vocal cord
- DBS: effective in dystonic tremor of limbs
- Unilateral DBS: not effective in dystonic tremor
- Sparing DBS: effective in dystonic tremor of limbs
- Sparing BoNT: not effective in dystonic tremor

**Video**
HOLMES TREMOR

- Or: rubral tremor, midbrain tremor
- Syndrome of rest, postural and intention tremor
- Slow: <5 Hz
- May worsen in certain position
- Other neurological signs

PSYCHOGENIC TREMOR

- Any combination of rest, postural or kinetic tremor
- Sudden onset and remissions
- Variability
- Antagonistic muscle coactivation
- Distractibility with mental or motor tasks
- Other signs of psychogenic illness
  - Somatisation in history
  - Other non-organic signs

MEDICATION INDUCED TREMOR

- Antiarhythmic
- Antidepressant
- β-adrenergic agents
- H2 antagonist
- Anticonvulsants
- Neuroleptics
- Antipsychotics
- β-adrenergic inhibitors
- Antiobstructive agent
- Triazole antifungal agent

OTHER TREMOR SYNDROMES

- Isolated focal tremors
  - Head
  - Voice
  - Tongue
  - Face
  - Jaw
  - Palatal
- Task specific tremors
  - Writing
  - Musicians

Conclusions

Tremor is the most common movement disorder
- Multiple etiologies
- Multiple clinical syndromes

Challenging diagnosis
Challenging treatment