

## Syndromic Classification of Tremors

In addition to classic ET, the MDS consensus criteria describe several additional syndromes based upon clinical observations of specific tremor elements. Important in the differential diagnosis of ET, these syndromic classifications include the following:

*Physiologic tremor.* A normal phenomenon, physiologic tremor occurs in all contracting muscle groups. Ranging in frequency from 8 to 12 Hz, it is subtly detectable on electromyography (EMG). Although seldom visible to the naked eye, physiologic tremor may often be detected when the fingers are firmly outstretched with a piece of paper placed over the hands.

*Enhanced physiologic tremor* or an intensification of physiologic tremor to detectable levels. Physiologic tremor may be enhanced under conditions of stress, anxiety, fatigue, exercise, cold, hunger, stimulant use, alcohol withdrawal, or metabolic disturbances, such as hypoglycemia or hyperthyroidism. Although the tremor is typically low in amplitude and high in frequency (8 to 12 Hz), it may be clinically indistinguishable from ET. In fact, some authors suggest that certain kinetic and postural tremors, including ET, may represent enhanced physiologic tremor. More specifically, some believe that physiologic tremor may be a *forme fruste* of ET, with both originating from the same neuronal oscillators. These investigators indicate that ET may begin as enhanced physiologic tremor that progresses in severity to a pathologic tremor. However, evidence has been presented suggesting that physiologic tremor and ET are different. Thus, the issue remains unresolved.

*Indeterminate tremor syndrome.* Patients with indeterminate tremor syndrome fulfill the criteria for classic ET yet have additional neurologic signs that are insufficient for diagnosis of another neurologic disorder. Previously categorized as "possible ET type Ib" by the TRIG criteria, the designation "indeterminate tremor syndrome" has been proposed by the MDS consensus authors in an effort to avoid difficulties stemming from incorrect or conflicting diagnoses.

*Primary orthostatic tremor,* a postural tremor of lower limb, trunk, and, possibly, upper limb muscles during stance yet absent when sitting or reclining. In most patients, orthostatic tremor is suppressed upon walking. As seen on EMG, orthostatic tremor is characterized by high frequency, 13 to 18 Hz entrainment of synchronous motor unit activity of contralateral and ipsilateral muscles, primarily of the lower limbs.

*Dystonic tremor.* Although consensus has not been reached concerning the definition of dystonic tremor syndrome, authors of the MDS consensus criteria have proposed a number of definitions within this general category. For example, "dystonic tremor" refers to primarily postural and kinetic tremor occurring in a body part affected by dystonia. Dystonia is a neurologic movement disorder characterized by sustained muscle contractions that frequently cause repetitive, twisting, or writhing movements accompanied by distorted, sometimes painful, postures or positions. Dystonic tremor may affect any voluntary muscle in the body. Postural hand tremor commonly affects dystonia patients and is frequently indistinguishable from ET. As with dystonia, *gestes antagoniste*, such as tapping or stroking of affected or adjacent muscles, may alleviate dystonic tremor by reducing tremor amplitude. In addition, the designation of "tremor associated with dystonia" applies to dystonia patients who have tremor in a body part that is not affected by dystonia.

*Task- and position-specific tremors.* These tremors occur upon performance of specific, highly specialized motor activities. They include primary writing tremor, defined as tremor occurring solely or primarily while writing yet not with other hand activities; occupational tremors, such as specific tremors affecting athletes or musicians; or isolated voice tremors. Voice tremor may be characterized by tremulousness of the voice in the absence of other tremor manifestations -- or by focal dystonia of the vocal cords, such as tremor that subsides with changes in pitch or *gestes antagoniste*.

*Parkinsonian tremor syndromes,* i.e., the presence of pathologic tremor in patients with PD or parkinsonism. PD is a slowly progressive, degenerative disorder of the central nervous system (CNS) that may be characterized by tremor (primarily resting tremor), rigidity, and bradykinesia (slowness and poverty

of movement). Additional findings may include postural instability, shuffling gait, start hesitancy and freezing, "mask-like" facies, hypophonia, micrographia, depression, or dementia. Whereas rest tremor is the most common, other forms of tremor may also be present. For example, some parkinsonian patients may have rest tremor and kinetic/postural tremor with similar or higher, non-harmonically related frequencies. Less commonly, isolated postural/kinetic tremors may be present.

*Cerebellar tremor syndromes*, described as pure or primary intention tremors with a frequency predominantly less than 5 Hz, possibly in association with postural (but not resting) tremor. The terms "cerebellar" and "intention" tremor are often used interchangeably. Other forms of tremor, such as postural tremor, are deemed of cerebellar origin only when coexistent with other cerebellar signs.

*Holmes tremor*. Traditionally known as rubral or midbrain tremor, so-called Holmes tremor is defined as a symptomatic rest, intention, and possibly postural tremor due to lesions affecting the cerebellothalamic and dopaminergic systems -- such as involving the brainstem, cerebellum, and thalamus and, possibly, their pathways.

*Palatal tremors*. These rhythmic movements of the soft palate may or may not occur subsequent to lesions of the brainstem and cerebellum and associated olivary pseudohypertrophy.

*Neuropathic tremor syndrome*. Certain peripheral neuropathies, particularly dysgammaglobulinemic neuropathies, are commonly associated with tremor, primarily kinetic and postural tremor of the affected extremities.

*Drug-induced and toxic tremor syndromes*. Pharmacologic agents used to treat other medical conditions may induce tremor. Such medications may include theophylline, valproate, lithium, tricyclic antidepressants, neuroleptics, sympathomimetics, amphetamines, steroids, certain agents used to treat endocrine and metabolic disorders, or other miscellaneous agents. Toxin-induced tremor, such as seen in manganese, arsenic, or mercury intoxication or poisoning, occurs in association with other neurologic symptoms, such as gait disturbances, rigidity, dystonia, ataxia, dysarthria, confusion, etc.

*Psychogenic tremor*. This form of tremor may be suggested by a history of somatization, the presence of unrelated neurologic signs, and sudden tremor onset or remissions. Additional signs may include a decrease of amplitude or variation of frequency upon distraction, unusual combinations of postural/intention and rest tremors, and co-activation resembling voluntary co-contraction during passive movements of a trembling limb about a joint.

*Myorhythmia*. A slow tremor of 2 to 4 Hz as seen in patients with lesions of the brainstem (similar to Holmes tremor).

## **Tremor Classification Based on Relative Frequency**

Tremors may also be classified based on the number of repetitions of complete waveforms per second. Physiologic and enhanced physiologic tremor have a relatively high frequency, often ranging from approximately 7 to 12 cycles per second. In contrast, the rate of many pathologic tremors is about 2 to 7 Hz. Primary orthostatic tremor is a notable exception, with a 13 to 18 Hz entrainment of motor unit activity. In addition, cortical tremor, recognized as a form of rhythmic myoclonus, is characterized by irregular, postural and kinetic tremor-like jerks with a range between 7 to 18 Hz.

Cerebellar and rubral or Holmes tremors tend to be of relatively low frequency, primarily occurring below 4.5 or 5 Hz. The pure rest tremor seen in some with PD is characteristically greater than 4 Hz, although the upper frequency limit of these tremors has not been firmly established. For those parkinsonian patients with a combination of rest and postural/kinetic tremors, relative frequencies may be similar -- or postural/kinetic tremors may have a frequency that is more than 1.5 Hz higher as related to rest tremor rate.

In classic ET, the rate of tremor may vary between 4 to 12 Hz, with older patients typically demonstrating tremor frequencies toward the lower range. In contrast, younger patients with mild ET tend to have tremor frequencies that extend into the 7 to 12 Hz range of physiologic tremor.

Essential Tremor: A Clinical Review

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