

INTRODUCTION

Tremor is defined as rhythmic involuntary oscillatory movement of the body part that is brought about by alternating or synchronous contractions of reciprocally innervated antagonist muscles¹. It is classified under the hyperkinetic movement disorders that are rhythmic and predictable. Tremor is also the most common movement disorder that affects mankind. In clinical practice, the diagnosis of tremor is obvious and cannot be missed. Identification of the type of tremor is the next important

step in further differentiating the tremors for treatment and prognostication. This review will classify the tremors, enumerate the characteristics and differentiating points for individual tremor syndromes, provides an algorithmic approach to the tremors and finally various treatment options.

TREMOR CHARACTERISTICS AND CLASSIFICATION

Description of the tremor is done using a number of characteristics. In clinical practice a complete description

Table 1: Classification of tremors

Nature	Location	Frequency
<ol style="list-style-type: none"> 1. Simple- involves single muscle group 2. Compound – several muscle groups 	<ol style="list-style-type: none"> 1. Head – entire head, chin, face, tongue, palate 2. Upper extremity- proximal, distal 3. Trunk 4. Lower extremity- proximal, distal 	<ol style="list-style-type: none"> 1. Low (<4 Hz) 2. Medium (4-7 Hz) 3. High (>7 Hz)
Amplitude	Rhythmicity	Relation to rest and movement
<ol style="list-style-type: none"> 1. Fine 2. Coarse 	<ol style="list-style-type: none"> 1. Regular 2. Irregular 	<ol style="list-style-type: none"> 1. Rest tremors 2. Action tremors <ol style="list-style-type: none"> i. Postural ii. Kinetic <ol style="list-style-type: none"> A. Non visual guided B. Visually guided <ol style="list-style-type: none"> a. Simple(non-target directed) b. Intentional(target directed) iii. Task specific iv. Isometric
Pathology:	Etiology:	Mode of onset
<ol style="list-style-type: none"> 1. Physiological 2. Enhanced physiological 3. Pathological 	<ol style="list-style-type: none"> 1. Cortical tremor 2. Parkinson tremor 3. Mesencephalic or holmes tremor 4. Cerebellar tremor 5. Essential tremor 6. Dystonic tremor 7. Wilson tremor 8. Tremors in peripheral neuropathy 9. Drug induced tremor 10. Psychogenic 	<ol style="list-style-type: none"> 1. Sudden 2. Insidious

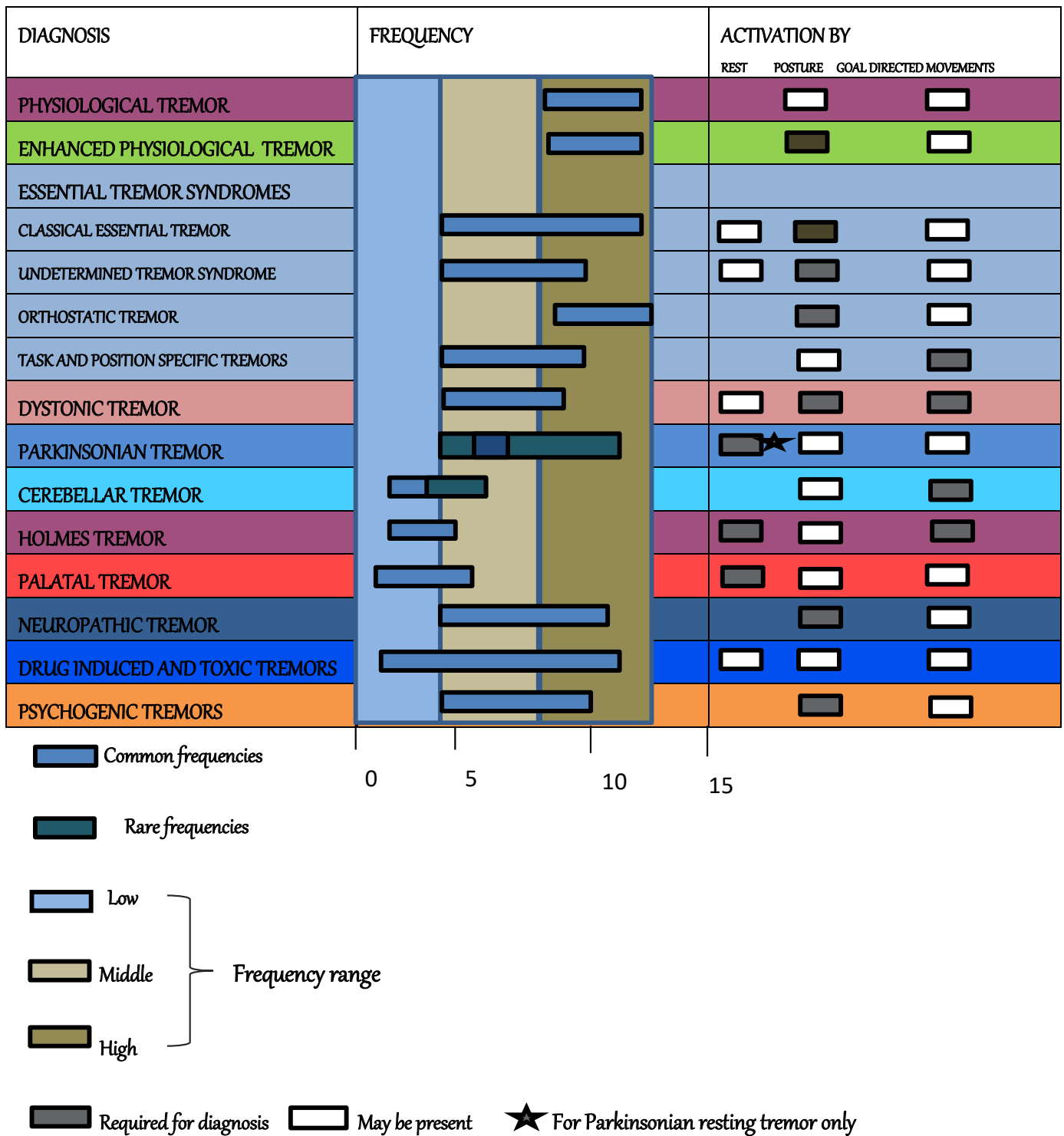


Fig. 1: Syndrome classification of tremors

of the tremor using these characteristics is useful to narrow down the differentials.

1. Nature
2. Location
3. Frequency
4. Amplitude
5. Rhythmicity
6. Relation to rest and movement
7. Pathology
8. Etiology
9. Age of onset

Based on the above parameters tremors are classified (Table 1). Classification based on the relation to rest and movement is used widely, because of its ease to administer and high yield in clinical practice.

Most of the tremors have more than one component.

Table 2: Causes of Rest tremors

Idiopathic Parkinson Disease	
Parkinsonian syndromes	Multiple Systems Atrophy Corticobasal Syndrome Progressive Supranuclear Palsy Diffuse Lewy Body disease Parkinsonism-Dementia-ALS complex of Guam Progressive Pallidal Atrophy
Heredodegenerative disorders	Huntington's disease Neurodegeneration with Brain Iron Accumulation Chorea-acanthocytosis Gerstmann-Strausler-Scheinker disease Neuronal CeroidLipofuscinosis.
Secondary parkinsonism	Toxins (CO,MPTP, Manganese, methanol, cyanide) Drugs (Table 5) (neuroleptics, dopamine depleting medications, antiemetics) Infections (CJD, SSPE, fungal)/ post encephalitic (von economos disease) Metabolic (hypothyroidism, chronic acquired hepatocellular degeneration, mitochondrial cytopathies) Miscellaneous (stroke, head trauma, neoplastic/ paraneoplastic conditions)
Severe essential tremor	
Mesencephalic tremor	
Psychogenic tremor	

Predominant component and associated signs are used to diagnose the etiology of the tremor.

REST TREMORS

Rest tremor is defined by tremor that occurs in a body part that is not voluntarily activated and is completely supported against gravity¹.

MANEUVER

Patient is examined in a relaxed posture. Forearms are rested on the arms of the chair or patients own lap in repose position. Patient can be asked to count backward

from 100 with eyes closed or arithmetic stress test can be performed to distract and bring the tremor

ACTION TREMORS

Action tremor encompasses postural, kinetic tremor, task specific and isometric. Both these tremors can be present in the same individual.¹ Each of this group has a prototype example that is explained below.

Postural tremor

Postural tremor is present while voluntarily maintaining a position against gravity. It most commonly involves the hand and forearm. Other areas that may be involved are head, voice, chin, legs and trunk.

Maneuver

Patient is asked to outstretch the arms in front. Patient can be asked to count backward from 100 with eyes closed or arithmetic stress test can be performed to distract and bring the tremor.

Kinetic tremor

Kinetic Tremors are present during any voluntary movement. Kinetic tremors can be non visual guided or visually guided. Among the visually guided category the tremors are sub classified into simple tremor (non goal directed) and intentional tremor (goal directed).

Simple kinetic tremor

Simple kinetic tremor occurs during voluntary movements that are not target-directed. They may persist during voluntary,goal-directed movement without an increase in amplitude during the terminal phase of movement.

Maneuver

Patient is asked to perform simple pronation/supination movement or flexion/extension of wrist joints.

Intentional tremor

Classic intention tremor is present when amplitude increases during visually guided movements toward atarget at the termination of the movement and the possibility of a position-specific tremor or a postural tremorproduced at the beginning or end of a movement is excluded.

Maneuver:

Patient is asked to do a finger nose test. Tremor worsening at the end point suggests intentional tremor.

TREMOR SYNDROMES

The above given tremor phenomenology are combined into specific syndromes (Figure 1).

SYNDROMES WITH PREDOMINANT REST TREMORS

Parkinson tremor

Tremor associated with Parkinson disease (PD) is the prototype tremor under this category. It is present in almost 60% of PD cases. It is typically asymmetrical, unilateral to start and slowly progresses to the uninvolved side. Most PD tremors are upper extremity tremors to start with, but tremors that begin with leg, jaw and larynx have also been reported. Average frequency of Parkinson

Table 3: Causes of enhanced physiological tremor

Stress, anxiety and fatigue (rock climber's tremor/elvis leg)-commonest cause	Endocrine disturbances 1. Hypoglycemia 2. Thyrotoxicosis 3. Pheochromocytoma 4. Adrenocorticosteroids	Drugs and toxin induced (Table 5) Drug withdrawal (eg. alcohol)
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Table 4: Characteristics of essential tremor

Inclusion criteria	Characteristic features	Red flags
1. Bilateral, largely symmetric postural or kinetic tremor involving hands and forearms that is visible and persistent.	postural tremor + kinetic tremor (amplitude more than postural tremor)	Amplitude of postural tremor > than kinetic tremor
2. Additional or isolated tremor of the head may occur but in the absence of abnormal posturing.	Somatotropic spread-head tremor after hand tremor	Hand tremor after head tremor
Exclusion criteria	Severity markers	
1. Other abnormal neurologic signs, especially dystonia.	Tremor at rest	
2. The presence of known causes of enhanced physiologic tremor, including current or recent exposure to tremorogenic drugs or the presence of a drug withdrawal state.	Intentional tremor of the head	
3. Historic or clinical evidence of psychogenic tremor.	Jaw tremor	
4. Convincing evidence of sudden onset or evidence of stepwise deterioration.		
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		

tremor is 4-6 Hz². The classical pill rolling movement of the PD is a resting tremor due to the alternate contraction of agonist and antagonist, involving the flexors, extensors, abductors and adductors of the finger and thumbs. Other upper extremity tremors in PD include wrist Flexion/extension and forearm supination/pronation. Some PD patients also have a postural tremor. This postural tremor appears only a few seconds after the new posture is made from the resting position (re-emergence phenomenon). Head tremor is a uncommon feature of PD.

PD is not the only cause of rest tremor. There are other causes that should be considered along with PD when encountered with a rest tremor³ (Table 2).

Syndromes with predominant postural tremors

Postural tremor, commonly seen physiologically in all human beings due to mechanical and neural factors, is of high frequency (10-12 Hz), low amplitude, and symmetrical character and can be just seen with naked eyes in extended fingers. This physiological tremor can be enhanced under certain situations (Table 3), such that it becomes coarse enough to make it clearly visible and is termed as enhanced physiological tremor.

Essential tremor

Essential tremor is the most common cause for pathological postural tremors. Age of onset has a bimodal peak in the second and sixth decade and the prevalence increases with advanced age (>20% in people aged >95 years). Definition, characteristic features, red flags signs to the diagnosis of essential tremor and the severity markers are listed in Table 4. Tremor frequency ranges between 4-12 Hz. Tremors may also involve the head (no-no>yes-yes), jaw, tongue and voice along with hand tremors⁴. More than 50% have intentional arm tremor and ataxia suggesting an underlying abnormality in cerebellum or cerebellar systems. Leg tremor, isolated head and voice tremors are uncommon features of essential tremor.

Dystonic tremor⁵

Dystonia, a movement disorder that causes abnormality of posture of any part of the body, is commonly associated with tremor that is predominantly postural. The classical example is the head tremor in patients with cervical dystonia. But sometimes these tremors occur in parts that are not affected by dystonia and so are named as tremor associated with dystonia. Example for the above is postural hand tremors in patients with cervical dystonia.

Cerebellar tremors

Tremors occurring in cerebellar dysfunction assume a kinetic property with predominant intentional component. These tremors may also persist for posture but never in rest. The kinetic component usually is 3-5 Hz and the postural component 5-10 Hz⁶. Cerebellar tremor occurs due to wide range of diseases. Acute onset with asymmetry is noted in conditions like stroke, multiple sclerosis and tumor with sudden hemorrhage. Gradual and symmetrical tremors are seen in degenerative neurological conditions like spinocerebellar ataxia.

Holmes tremor¹

Holmes tremor is characterized by combination of intentional tremor and rest tremor. The rest tremor

worsens with the posture with still more worsening on action. Tremor frequency is usually less than 4.5 Hz. Tremor is usually unilateral and occurs after a latency of 4 weeks – 2 years following a midbrain lesion. It is postulated to occur due to the involvement of the substantia nigra and the cerebellar outflow tracts in the midbrain. Common causes are stroke and tumors.

Task specific and position specific tremors

Some forms of tremors appear only in relation to a particular position or task.

1. Primary writing tremor¹: tremors occur only during writing(task specific or type A) or when the hand adopts a writing position(position specific or type B). No observable dystonia present.
2. Orthostatic tremor⁷ (shaky legs syndrome): tremors appear only on standing and disappear on movement and sitting. These are the tremors with highest frequency (13-16 Hz). Because of the high frequency tremors are not visible to clinical examination and most often present as difficulty in balance and falls.

OTHER TREMOR SYNDROMES**Drug and toxin induced tremors**

Drugs and toxins induce tremors in all the positions. Table 5 lists the drugs responsible for tremors.

Wilson's tremor

Patients with Wilson's disease have both postural and kinetic tremor. The characteristic wing beating tremor is a large amplitude tremor demonstrated in patients shoulders abducted to 90 degrees and elbows flexed. This is one example of a proximal tremor. Other signs like dystonic limb posturing, rigidity and choreiform movements aid the diagnosis.

Table 5: Drugs causing tremor

Postural	Intentional	Rest
Alcohol (withdrawal)	Alcohol	Metaclopramide
Amiadarone	Lithium	Neuroleptics
Amphetamines		Reserpine
Beat adrenergic agonists.		
Caffeine		
Cyclosporine		
Dopamine		
Steroids		
Theopylline		
Thyroid hormones		
Tricyclic antidepressants		
Valproic acid		

Table 6: History and examination for a tremor case

History	Examination (7step approach)
Age at onset	1. Examination with arms at rest
Body part or parts affected	2. Examination with arms stretched in front(posture)
Nature of onset(sudden, insidious)	3. Examination with arms stretched in front with arms abducted, elbows flexed and extended, supination and pronation of forearms to look for position specificity of dystonic tremor
Course of tremor(static, progressive)	4. Examination during movement like finger nose test and look for both simple kinetic and intentional tremor
Exacerbating and relieving factors	5. Ask the patient to write and draw a Archimedes spiral to bring about the task specific tremor, quantify the severity of tremor and distinguish various tremors.
Associated neurological symptoms	6. Examination of neurological system to look for pathological cerebellar signs, extrapyramidal signs of Parkinson and dystonia, long tact signs for holmes tremor, other movement disorders like myoclonus, chorea to rule out infective and degenerative conditions of nervous system and neuropathic signs.
Associated systemic symptoms- h/o for thyroid illness, diabetes, etc,	7. Consider systemic signs like thyroid swelling, eye signs of hyperthyroidism, postural hypotension in pheochromocytoma, cushingoid habitus in corticosteroid intake, malar and palatal rash with photosensitivity for SLE, cutaneous and hair signs for toxin exposure if relevant.
Drug exposure	
Family history	
Level of day to day functional impairment	

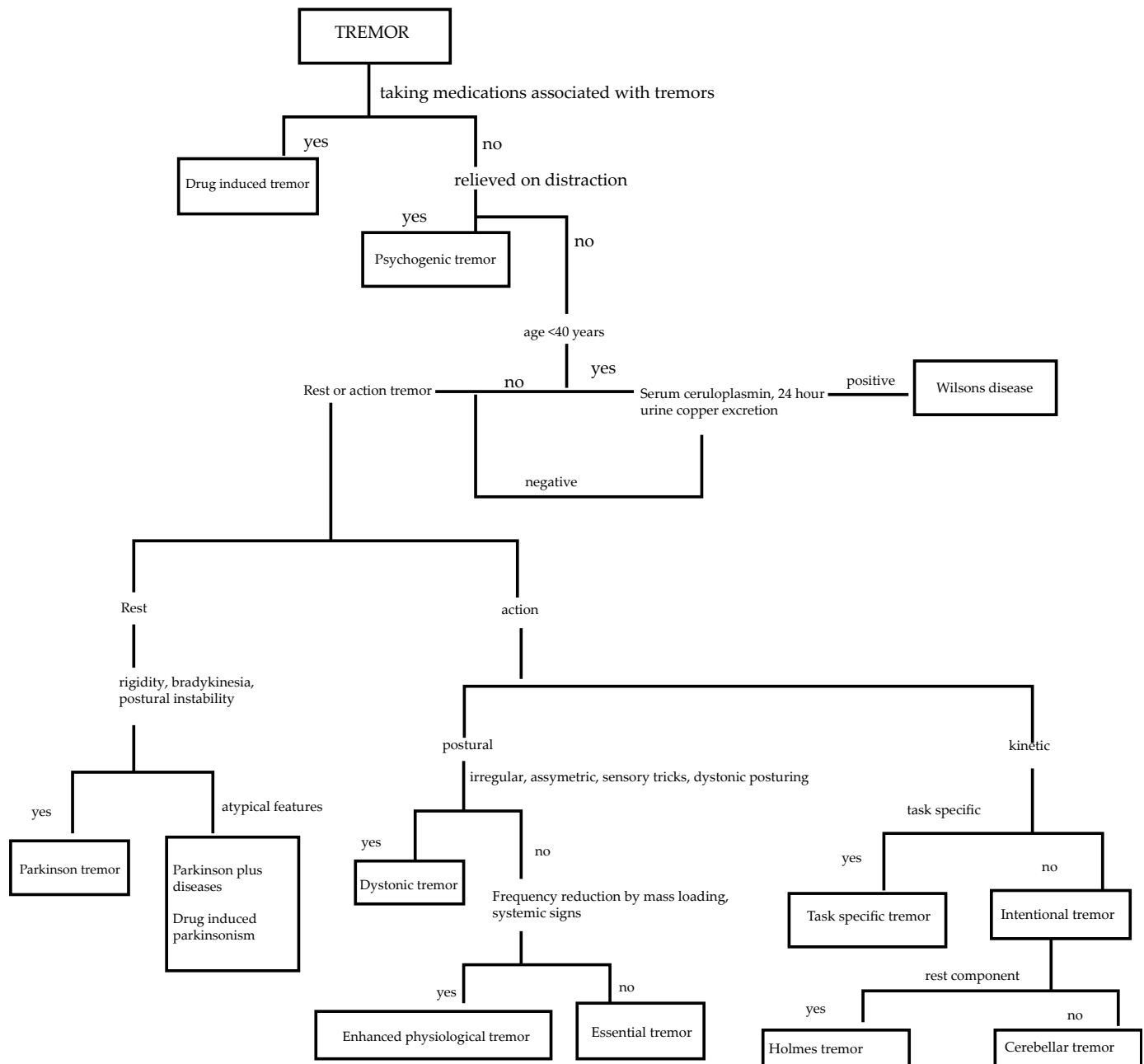


Chart 1: Algorithmic approach to tremor

Tremors in peripheral neuropathy

Tremors occur in hands of patients with peripheral neuropathy especially demyelinating, connective tissue disorder associated and dysgammaglobulinemic neuropathy.

Psychogenic tremors

Sometimes tremors can be a part of psychogenic disorder. A careful history is the only available to diagnose this entity. The following points are characteristic of psychogenic tremors¹

1. Sudden onset of the condition, remissions, or both.
2. Unusual clinical combinations of rest and postural/intentional tremors.
3. Decrease of tremor amplitude during distraction.

4. Variation of tremor frequency during distraction orduring voluntary movements of the contralateral hand.
5. Coactivation sign of psychogenic tremor (resistance to passive movements in the tremulous limb with disappearance of tremor during these movements)
6. Somatization in the past history.
7. Appearance of additional and unrelated neurologic signs.

Practice points for differentiating the tremors

Most of the patients who present with tremors have a combination of tremor syndromes that might pose a challenge to diagnosis. A patient with severe Parkinson tremor (rest and action) can be differentiated from a severe form of Essential tremor by the re-emergence phenomenon

Table 7: Laboratory investigations in a tremor case

Cerebellar tremor	CT/ MRI
Enhanced physiological tremor	Serum glucose level, thyroid-stimulating hormone level, liver function testing, patient history to evaluate for anxiety and caffeine use.
Essential tremor	No specific test; complete blood count, thyroid-stimulating hormone level, serum chemistry profile may rule out other disease
Parkinson tremor	No specific test; positron emission tomography or single-photon emission computed tomography for atypical presentation
Psychogenic	Careful history
Young age <40 years	Slit lamp for KF ring, Serum ceruloplasmin, urine copper excretion, screening for heavy metal poisoning.
Orthostatic tremor	EMG

Table 8: Medications for tremor treatment

Essential tremor	Beta blockers(propranolol/nipradilol Primidone Clonazepam(for kinetic component) Botox injection(for head, voice tremors)
Dystonic tremor	Clonazepam Botox injection
Parkinson tremor	Levodopa Dopaminergic agonist Anticholinergic drugs
Cerebellar tremors	Less amenable to drugs Carbamazepine, topiramate, isoniazid, buspirone tried with varying efficacy.

in posture, and from the Holmes tremor by the severity of tremor in relation to position. Positional preference (amplitude increase when hand positioned near nose) and frequency reduction with mass loading to the hands can help in differentiating a physiological tremor from essential tremor. Less regular, asymmetric, myoclonic component, sensory tricks (geste antagoniste), aggravation for specific posture or null point, muscle hypertrophy and pain are the points which help distinguish a dystonic tremor from postural tremor. Presence of a jerky tremor,

Table 9: Interventional treatment for tremors

Essential tremor	1. deep brain stimulation of the thalamic nucleus ventralisintermedius (Vim) and posterior subthalamic area 2. ventralisintermedius (Vim) thalamotomy
Dystonic tremor	1. Deep brain stimulation
Parkinson tremor	1. deep brain stimulation of sub thalamic nuclei 2. Gamma knife thalamotomy
Cerebellar tremors	1. thalamic DBS surgery 2. thalamotomy

head tremor, dystonic voice (characterised by change in voice tremor during emotional speech and singing), rapid emergence of a postural tremor, normal olfaction, lack of response to dopaminergic medication, relatively stable natural history help to differentiate a dystonic tremor from Parkinson tremor. Absent tremor at rest, fading of tremor on posture and lower frequency of tremor help distinguish a cerebellar tremor from essential and Parkinson tremor. Cortical tremors or rhythmic myoclonus are intermittent brief muscle jerks that are rhythmic or irregular with a lower frequency and hyperkinesia limited to segmental levels and should be differentiated from a tremor. Flapping tremor which is actually a negative myoclonus, can be differentiated from tremors by less regular, long duration (>200ms) of lapses of the outstretched hand.

DIAGNOSTIC APPROACH

History and examination

History and examination in a tremor patient is targeted to identify the type of tremor, the cause for the tremor and the complications. Table 6 enumerates the historical and examination details in a tremor patient⁸. Chart 1 provides an algorithmic approach to a case of tremor.

LABORATORY INVESTIGATIONS (TABLE 7)

Treatment

Treatment of tremor is based mainly on

1. treatment of underlying condition/ removal of the offending agent.
2. pharmacological treatment for reduction of tremors (Table 8).
3. deep brain stimulation.
4. surgical treatment.

Treatment of systemic conditions like hyperthyroidism, pheochromocytoma and removal of the offending drug that causes tremor is the first step in the treatment of enhanced physiological tremors.

PHARMACOLOGICAL MEASURES (TABLE 8)

Deep brain stimulation and surgical management

When the tremors are refractory to medical management

deep brain stimulation and surgical management are considered (Table 9).

CONCLUSIONS

Tremor is a frequent neurological entity faced by physician in day to day practice. A comprehensive knowledge into the tremor characteristics, etiological agents and an algorithmic approach will help the physician from ordering unwanted investigations and guide into the qualitative management of the patients.

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