Hyperkinetic Movement Disorders

Refresher Course 2562

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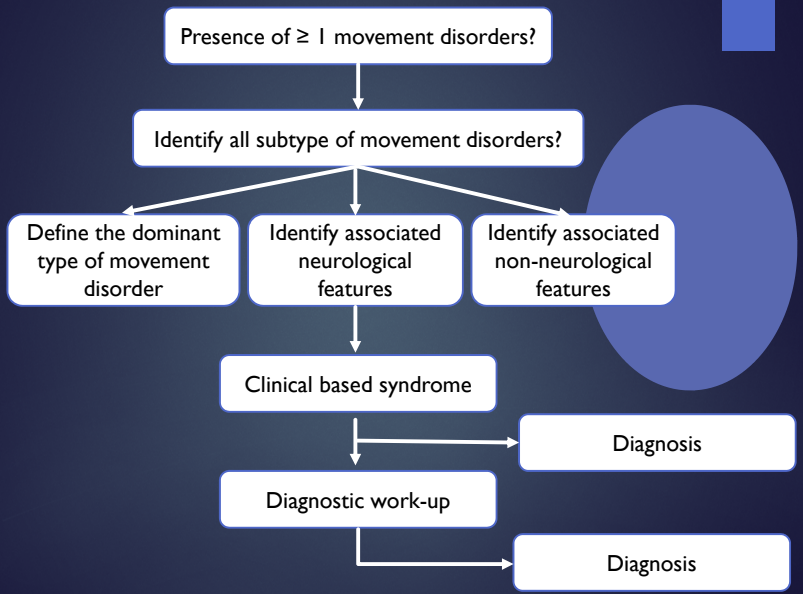
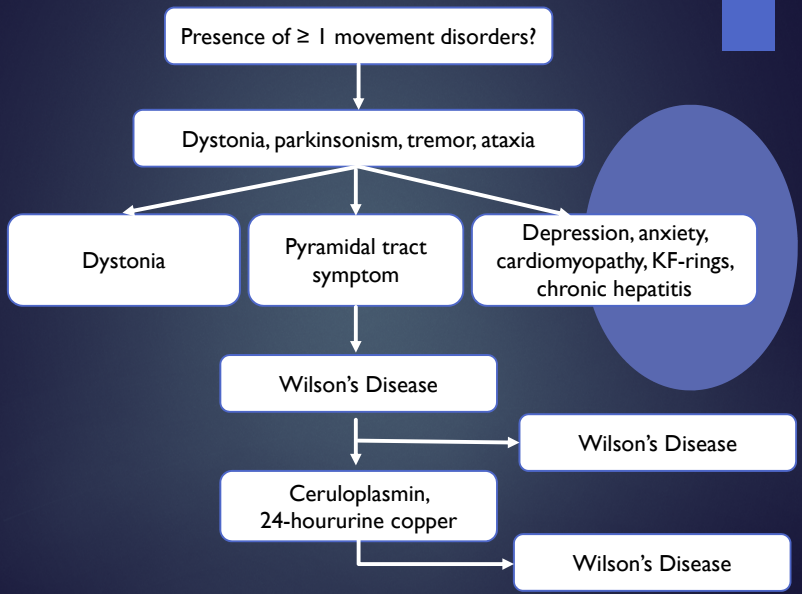
Approach to Movement Disorders

- Voluntary or Involuntary
  - Suppressible
  - Psychogenic movement disorders
- Hyperkinetic or Hypokinetic or Mixed
- Characteristics & Natural History
  - Phenomenology
  - Onset, duration, aggravating/ relieving factors
  - Distribution
  - Progression
- Associated Features, Medications





Tremor

- A **rhythmic** mechanical **oscillation** of at least one functional body region that is produced by alternating or synchronous contractions of opposing muscles.
- The most common movement disorders in adults.

Defining tremors

Rest Tremor

- Parkinson's Disease
- Drug-Induced
- Wilson's Disease
- Severe Essential Tremor

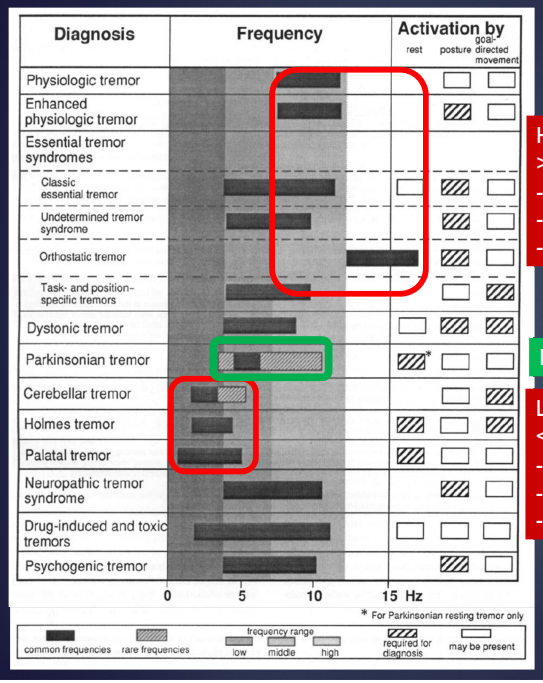
Action Tremor

Postural Tremor

- Enhanced physiologic
- Drug Induced
- Essential Tremor
- Neuropathy

Kinetic Tremor

- Simple kinetic
- Intention Tremor (target-direct)
- Task-specific
- Isometric



High frequency tremor
> 7 Hz
- Physiologic tremor
- ET
- OT

PD 4-7 Hz of tremor

Low frequency tremor
< 4 Hz
- Cerebellar tremor
- Holmes tremor
- Palatal tremor

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Physiologic tremor

- Present in every normal subject during postural/action
- **Low amplitude, high frequency** (6-12 Hz)
- Enhanced physiologic tremor (EPT):
  - Easy visibility, predominant postural, high-frequency, <2 years, reversible
- **Endogenous/ exogenous intoxication**
  - Stress, anxiety
  - Hyperthyroidism
  - Caffeine
  - Drugs-induced tremor: valproate, AMT, lithium

New Criteria of ET

Fulfils consensus criteria for definite (classic) ET

- Hereditary ET
  - **Family history** of at least 1 first-degree affected relative
  - Onset of both must be **before 65 years**
- Sporadic ET
  - Does not have immediate family member with ET
  - Onset is **before 65 years**
- Senile ET
  - Onset is **after 65 years**
  - Family history may or may not be present

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Tremor	Parkinson's Disease	Essential Tremor
Distribution	Hands, legs, chin, lip, jaws (usually asymmetric)	Hands (usually symmetric) head, voice
Behavioral setting	Resting tremor	Postural +/- kinetic tremor
Frequency	4-6 Hz	8-12 Hz
Amplitude	May lessen/ disappear with treatment, advanced PD	Worsens ET progresses
Age	Typically onset in 60-70	Any age, common with advancing age
Family history	May have positive, usually negative	Often positive (50%)
Associated features	Bradykinesia, rigidity, shuffling gait	Absent as a rule
Responsive	Levodopa	Alcohol, beta-blockers, antiepileptic

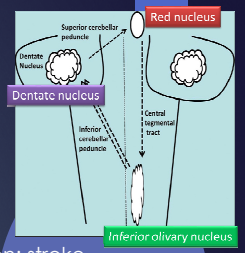
Task/Position specific tremor

- The most common: primary writing tremor (PWT)
- A variant of ET or writer's cramp
- A non-progressive condition
- Sporadic or dominantly inherited
- Treatment:
  - Medication: response rate 50%
  - Anticholinergics, beta-blockers, primidone
  - Levodopa, topiramate, benzodiazepines
  - Botulinum toxin injections
  - Thalamotoy , DBS (Vim)

Holmes (midbrain) tremor / Rubral tremor

- Rest and action (intension, postural) tremor
- Slow frequency (<4.5 Hz) and not regular
- More proximal tremor, sometime lower limb
- Other brain stem signs: CN, nystagmus, dysarthria
- Involvement of contralateral red nucleus and cerebellar outflow tract (cerebellothalamic)
- Ischemic, hemorrhagic, mass, post traumatic
- Rx: Levodopa (30%)

Palatal tremor (PT)
Palatal myoclonus (1-3Hz)



- Essential PT (25%)
  - Rhythmic contractions of tensor veli palatini (CN v3)
  - Ear clicking (opening/closing Eustachian tube)
  - Disappears with sleep
  - Frequency <2 Hz
- Symptomatic PT (75%)
  - Focal brainstem lesion: stroke, encephalitis, demyelinating disease, mass, degenerative disease
  - Guillain–Mollaret triangle (dentate nucleus-red nucleus - inferior olivary)
  - Contractions of levator veli palatini (CN9,10,7)
  - Elevation of corneas/ soft palate, nystagmus, face, tongue, neck, diaphragm
  - Persist in sleep
  - Unilateral or bilateral involvements

Therapeutic options for tremor

	ET	OT	Task	Dystonic	PD	Cerebellar	Holmes	Neuro
Propranolol	X	X	X	X	X	X	X	X
Primidone*	X	X	X	X		X		
Gabapentin	X	X						
Topiramate	X							
CBZ				X		X		
Clonazepam		X		X		X	X	X
Alprazolam	X							
Levodopa		X		X	X		X	
DA		X			X		X	
Anticholinergic			X	X	X		X	
Botulinum	X		X	X				
Tetrabenazine*				X				
Clozapine	X				X		X	
Neurosurgery	X			X	X	X	X	X

Dystonia

- **Sustained** muscle contractions, frequently causing **twisting** and repetitive movements or **abnormal postures**
- +/- dystonic tremor & dystonic jerk
- **Sensory tricks** in localized dystonia (Alleviating maneuvers)

TABLE 3. Proposed classification of dystonia

Axis I. Clinical characteristics
- Clinical characteristics of dystonia
  - Age at onset
    - Infancy (birth to 2 years)
    - Childhood (3–12 years)
    - Adolescence (13–20 years)
    - Early adulthood (21–40 years)
    - Late adulthood (>40 years)
  - Body distribution
    - Focal
    - Segmental
    - Multifocal
    - Generalized (with or without leg involvement)
    - Hemidystonia
  - Temporal pattern
    - Disease course
      - ○ Static
      - ○ Progressive
    - Variability
      - ○ Persistent
      - ○ Action-specific
      - ○ Diurnal
      - ○ Paroxysmal
- Associated features
  - Isolated dystonia or combined with another movement disorder
    - Isolated dystonia
    - Combined dystonia
  - Occurrence of other neurological or systemic manifestations
    - List of co-occurring neurological manifestations

Axis II. Etiology
- Nervous system pathology
  - Evidence of degeneration
  - Evidence of structural (often static) lesions
  - No evidence of degeneration or structural lesion
- Inherited or acquired
  - Inherited
    - Autosomal dominant
    - Autosomal recessive
    - X-linked recessive
    - Mitochondrial
  - Acquired
    - Perinatal brain injury
    - Infection
    - Drug
    - Toxic
    - Vascular
    - Neoplastic
    - Brain injury
    - Psychogenic
  - Idiopathic
    - Sporadic
    - Familial

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Treatment

- **Focal dystonia**
  - Botulinum toxin
  - Anticholinergic
  - Baclofen
  - Benzodiazepines
  - Surgery
- **Generalized dystonia**
  - Levodopa
  - Anticholinergic
  - Baclofen
  - Benzodiazepines/
  - Surgery

Myoclonus

- Sudden, **brief, jerky involuntary movements**, involving face, trunk, and extremities
- Positive (muscular contraction)
- Negative (muscular inhibitions)
  - e.g. asterixis, postural lapses

Myoclonus

- **Physiologic myoclonus**
  - Sleep jerks, hiccup
- **Essential myoclonus**
- **Epileptic myoclonus**
- **Symptomatic myoclonus**
  - Infection, postinfectious syndromes
  - Electrolyte disorders, renal/ hepatic failure
  - Drug induced syndromes
  - Post hypoxia (Lance-Adams syndrome)
  - Paraneoplastic
  - Opsoclonus-myoclonus syndrome

Drug-induced Myoclonus

- Psychiatric medications
  - SSRIs, MAOI, lithium, tricyclic
- Drug withdrawal
- Calcium channel blockers
- Narcotics
- Anticonvulsants
- Contrast media

Myoclonus vs. seizure vs. tremor

	Myoclonus	Seizure (EPC)	Tremor
Distribution	Generalized or multifocal area > focal Distal	Focal , Jacksonian spread or 2nd generalized	Unilateral or bilateral limbs, head, chin
Rhythmicity	Arrhythmic > rhythmic	Rhythmic	Rhythmic
Speed	Fast, usually 10-50ms up to 100ms	0.1-6Hz	Slow, usually 4-8 Hz
Enhancing factors	Postural, stimulus, action	Spontaneous, action, stimulus	Rest, postural, action

EPC: epilepsia partilalis continua

Treatment

- Treat the underlying disorder
  - Correction of metabolic abnormalities
  - Removal of an offending drug
- Symptomatic treatment
  - Consider antimyoclonic agents

Antimyoclonic Agents

Myoclonus	Treatment
Cortical myoclonus	Sodium valproate Clonazepam Piracetam Levetiracetam Zonisamide
Brainstem myoclonus	Clonazepam
Spinal myoclonus	Clonazepam
Peripheral myoclonus	Botulinum toxin (for hemifacial spasm)

Chorea & Ballism

- **Chorea :**
  - Involuntary hyperkinetic movement disorder consisting of sudden, **irregular**, **flowing**, purposeless movements that are **distally** prominent
- **Athetosis :**
  - A continuous stream of slow, **sinuous** movements, typically of the **hands and feet**
- **Ballism :**
  - **Proximal**, high amplitude, high velocity movements

Chorea: Classification

- **Primary (genetic)**
  - Huntington's disease
  - Neuroacanthocytosis
  - McLeod syndrome
  - Benign hereditary chorea
  - Wilson's disease
  - Dentatorubralpallidoluysian atrophy (DRPLA)
- **Secondary**
  - Vascular chorea
  - Autoimmune chorea: Sydenham's chorea
  - Metabolic chorea: hyperglycemia
  - Drug-induced chorea
  - Infectious chorea

Chorea: treatment

- **Depend on etiology**
  - Hyperglycemia : control blood sugar
  - Sydenham's chorea : observe, self limited
  - Drug induced : stop medication
- **Medication**
  - Neuroleptic : Haloperidol
  - Atypical neuroleptics eg. Olanzapine, Risperidone

Tics & Tourette

- Spontaneous, purposeless, simple and complex movements or vocalizations that abruptly interrupt normal motor activities
- Temporarily suppressible
- Urge
- Multiple body regions eg. Face, neck, shoulder, eye

Dyskinesia

- Complex involuntary movement: Chorea(most), tremor, ballism, dystonia, tics, myoclonus
- Commonly used for drug induced abnormal movements
  - Drugs: Levodopa

Tardive dyskinesia

- Usually Chorea
- Commonly Orobuccolingual
- Risks: Old female
- >3months dopaminergic blocking
- Neuroleptic, antiemetic drugs

Paroxysmal dyskinesias

- Abnormal involuntary movements that are intermittent or episodic in nature, with sudden onset and with no change in consciousness
- Dystonia, chorea, ballismus, complex combination of movements
- idiopathic (primary) or secondary (symptomatic)

Paroxysmal dyskinesias

	PKD	PNKD	PED	PHD
Duration	Very brief	30 min – 1 hr (4hr)	2min- 2hrs	30-60sec
Triggering factor	Sudden movement: speed, force, strength	Alcohol, coffee, tobacco, emotional, hunger, fatiuge	Prolonged or sustained exercise	NREM sleep
Age at onset	7-15 years (6mo-33yr)	2-79 years	2-30 years	Adolescence
Sex	M > F	F > M		
Treatment	CBZ, PHT, acetazolamide Topiramate, PB	Benzodiazepine, anticonvulsant, acetazolamide, L-dopa	Gabapentin, L-dopa (20%)	CBA, PHT, acetazolamide
Gene	Chr. 16p11 (60-70%)	Chr.2q33-35 (AD)	Chr.16p11	15q24, 20q13.2-13.3

KD: kinesigenic dyskinesia, NKD: nonkinesigenic dyskinesia, ED: exercise-induced dyskinesia, HD: hypnogenic (noctunal) dyskinesia

Secondary PK

Suspected cause	Diagnosis	Duration	Frequency	Predominant movement
Stroke	PNKD	1–2 hr	5/day	Dystonia and stereotypy
	PNKD	15–45 sec	1/every 2 min	Dystonia
	PHD	<5 min	1/night	Dystonia
	Mixed	<5 min	1/mo → 1/week	Dystonia
Peripheral trauma	PKD	1 min	1–3/day	Dystonia
	PKD	<30 sec	5/week → 5/day	Dystonia
	Mixed	15–20 min	1/3 days → 5/day	Dystonia
Central trauma	Mixed	1–45 min	1–5/day	Dystonia
	PNKD	30 sec–2 min	3–6/day	Dystonia
	PNKD	10–15 days	1–4/yr	Dystonia
	Mixed	5–10 min	1/30 min	Dystonia
Kernicterus	PNKD	10 sec–2 min	0–20/day	Dystonia
	PNKD	1–2 hr	Multiple/day	Dystonia and chorea
Meningovascular syphilis	Mixed	10–15 min	3/day	Chorea
CMV encephalitis	PNKD	20–30 min	2/week → 2/day	Dystonia and athetosis
Multiple sclerosis	PNKD	10–5 sec	0–20/day	Dystonia
Migraine	PNKD	5 min	2–3/week	Dystonia

PNKD, paroxysmal nonkinesigenic dyskinesia; PKD, paroxysmal kinesigenic dyskinesia; PHD, paroxysmal hypnogenic dyskinesia; (→), symptoms increased in frequency.

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Thank you!