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

Presence of ≥ 1 movement disorders?

Identify all subtype of movement disorders!

Define the dominant type of movement disorder

Identify associated neurological features

Identify associated non-neurological features

Clinical based syndrome

Diagnostic work-up

Diagnosis

Dystonia, parkinsonism, tremor, ataxia

Dystonia

Pyramidal tract symptom

Depression, anxiety, cardiomyopathy, KF-rings, chronic hepatitis

Wilson's Disease

Ceruloplasmin, 24-hour urine copper

Wilson's Disease

Wilson's Disease
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
- Action Tremor
- Postural Tremor
- Kinetic Tremor
  - Simple kinetic
  - Intention Tremor (target-direct)
  - Task-specific
  - Isometric

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Activation by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiologic tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enhanced physiologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Essential tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Essential tremor syndromes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postural tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinetic tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple kinetic tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intention tremor (target-direct)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Task-specific tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isometric tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson's Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug-Induced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilson's Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe Essential Tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palatal tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug-induced tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychogenic tremor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

PD 4-7 Hz of tremor

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

Mov Disord 2009;24:2033-2041

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

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
- Thalamotomy, 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

<table>
<thead>
<tr>
<th></th>
<th>ET</th>
<th>OT</th>
<th>Task</th>
<th>Dystonic</th>
<th>PD</th>
<th>Cerebellar</th>
<th>Holmes</th>
<th>Neuro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Primidone*</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBZ</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Alprazolam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levodopa</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Botulinum</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetrabenazine*</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dystonia

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

<table>
<thead>
<tr>
<th>Distribution</th>
<th>Myoclonus</th>
<th>Seizure (EPC)</th>
<th>Tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized or multifocal area &gt; focal Distal</td>
<td>Focal, Jacksonian spread or 2nd generalized</td>
<td>Unilateral or bilateral limbs, head, chin</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rhythmicity</th>
<th>Myoclonus</th>
<th>Seizure (EPC)</th>
<th>Tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmic &gt; rhythmic</td>
<td>Rhythmic</td>
<td>Rhythmic</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Speed</th>
<th>Myoclonus</th>
<th>Seizure (EPC)</th>
<th>Tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast, usually 10-50ms up to 100ms</td>
<td>0.1-6Hz</td>
<td>Slow, usually 4-8 Hz</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enhancing factors</th>
<th>Myoclonus</th>
<th>Seizure (EPC)</th>
<th>Tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postural, stimulus, action</td>
<td>Spontaneous, action, stimulus</td>
<td>Rest, postural, action</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Myoclonus</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical myoclonus</td>
<td>Sodium valproate</td>
</tr>
<tr>
<td></td>
<td>Clonazepam</td>
</tr>
<tr>
<td></td>
<td>Piracetam</td>
</tr>
<tr>
<td></td>
<td>Levetiracetam</td>
</tr>
<tr>
<td></td>
<td>Zonisamide</td>
</tr>
<tr>
<td>Brainstem myoclonus</td>
<td>Clonazepam</td>
</tr>
<tr>
<td>Spinal myoclonus</td>
<td>Clonazepam</td>
</tr>
<tr>
<td>Peripheral myoclonus</td>
<td>Botulinum toxin (for hemifacial spasm)</td>
</tr>
</tbody>
</table>

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
  - Dentatorubral-pallidoluysian 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 Orofaciolingual
- Risks: Old female
- >3 months 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)

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

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

Secondary PK

<table>
<thead>
<tr>
<th>Suspected cause</th>
<th>Diagnosis</th>
<th>Duration</th>
<th>Frequency</th>
<th>Predominant movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>PNKD, PHT</td>
<td>1-2 hr</td>
<td>5/day</td>
<td>Dystonia and stereotypy</td>
</tr>
<tr>
<td>Peripheral trauma</td>
<td>PKD</td>
<td>1 min</td>
<td>1/2 day</td>
<td>Dystonia</td>
</tr>
<tr>
<td>Central trauma</td>
<td>Mixed</td>
<td>1-45 min</td>
<td>1-5 day</td>
<td>Dystonia</td>
</tr>
<tr>
<td>Kernicterus</td>
<td>PNKD</td>
<td>10 sec-2 min</td>
<td>0-20/day</td>
<td>Dystonia</td>
</tr>
<tr>
<td>Meningovascular syphilis</td>
<td>Mixed</td>
<td>10-15 min</td>
<td>3/day</td>
<td>Chorea</td>
</tr>
<tr>
<td>CMV, encephalitis</td>
<td>PNKD</td>
<td>20-30 min</td>
<td>2 week → 2 day</td>
<td>Dystonia and ataxosis</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>PNKD</td>
<td>10-5 sec</td>
<td>0-20 day</td>
<td>Dystonia</td>
</tr>
<tr>
<td>Migraine</td>
<td>PNKD</td>
<td>5 min</td>
<td>2-3 week</td>
<td>Dystonia</td>
</tr>
</tbody>
</table>

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