If you are viewing this course as a recorded course after the live webinar, you can use the scroll bar at the bottom of the player window to pause and navigate the course.

This handout is for reference only. It may not include content identical to the powerpoint. Any links included in the handout are current at the time of the live webinar, but are subject to change and may not be current at a later date.
Objectives

At the end of the presentation the participant will be able to:

1. Identify at least three key clinical signs and symptoms that differentiate idiopathic Parkinson's disease (PD) from vascular parkinsonism and Parkinson plus syndromes.

2. List at least three signs and symptoms of idiopathic PD versus vascular parkinsonism and Parkinson plus syndromes.

3. Describe at least two best evidence findings related to the physical therapy management of individuals with PD and Parkinson plus syndromes.
Classification of Parkinsonism

- Primary Parkinsonism, Idiopathic PD
- Secondary Parkinsonism
  - Vascular Parkinsonism (brain injury from strokes)
  - Toxins, trauma (boxing), infections (encephalitis, HIV), metabolic abnormalities (thyroid, end-stage renal, liver disease), drug-induced
- Parkinson-plus syndromes
  - Progressive supranuclear palsy
  - Multiple system atrophy
  - Cortical basal ganglionic degeneration
  - Dementia with Lewy bodies

Idiopathic Parkinson’s Disease

- Onset = 50-60 years
- Demographics
  - Men > Women
  - Hispanics & Caucasians slightly more affected

  - Parkinsonism is defined as bradykinesia plus a resting tremor or rigidity, or both.

Cardinal Parkinsonism Symptoms

- **Tremor**: 4-6-Hz tremor in the fully resting limb, which is suppressed during movement initiation.
- **Rigidity** (tested with slow passive movement of limbs and neck with person relaxed):
  - “Lead pipe”: velocity-independent resistance.
  - “Cogwheel”: may reflect tremor felt while assessing tone.
- **Akinesia/bradykinesia**: slowness of movement and decrement in amplitude or speed as movements are continued.
- **Postural instability** occurs later in the disease; early presence suggests alternative diagnosis.

---

Idiopathic Parkinson’s Disease

- **Motor Symptoms**
  - Asymmetrical, stooped posture
  - Balance & gait disorders
  - Hypomimia
  - Dysphagia
  - Dysarthria
  - Decreased hand dexterity & finger coordination

---
Non-Motor Signs and Symptoms

<table>
<thead>
<tr>
<th>Sensory</th>
<th>Cognitive/Sleep</th>
<th>Autonomic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Anosmia</td>
<td>• Depression</td>
<td>• Drooling</td>
</tr>
<tr>
<td>• Proprioceptive deficits</td>
<td>• Anxiety</td>
<td>• Sweating</td>
</tr>
<tr>
<td>• Visuospatial deficits</td>
<td>• Apathy</td>
<td>• Orthostatic hypotension</td>
</tr>
<tr>
<td>• Sensory integration deficits</td>
<td>• Fatigue</td>
<td>• Urinary frequency/urgency</td>
</tr>
<tr>
<td>• Muscle aches or cramps</td>
<td>• Memory problems</td>
<td>• Constipation</td>
</tr>
<tr>
<td>• Restlessness</td>
<td>• Confusion/Dementia</td>
<td>• Sexual dysfunction</td>
</tr>
<tr>
<td>• Pain</td>
<td>• Sleeping disorders</td>
<td></td>
</tr>
</tbody>
</table>

Pathology of PD

- Disease affects melanin-containing dopamine (DA) neurons in the substantia nigra pars compacta (SNpc) of the brainstem.

- A pathologic hallmark of PD are round intracytoplasmic inclusions called "Lewy bodies" consisting mainly of misfolded alpha-synuclein protein.

- Results in decreased DA levels in other parts of the basal ganglia with important motor functions.


Pathology of Parkinson’s Disease

- Disease progression results in hallmark pathological inclusions called “Lewy Bodies”

Basal Ganglia Motor Pathways

- Loss of dopaminergic input from the SNpc to the striatum results in relatively increased activity in the indirect motor pathway and decreased activity in the direct motor pathway due to different actions of DA on these pathways.
- Net effect: increased activity of the BG output nuclei (Gpi and SNpr) that produces increased inhibition of the thalamocortical neurons and the pedunculopontine nucleus (PPN) of the midbrain that leads to:
  - Lack of volitional and automatic movements
  - Bradykinesia, hypokinesia, and tremors

Kloos & Kegelmeyer, 2016, pg. 286.
Supportive Criteria for PD

- Clear and dramatic beneficial response to dopaminergic medications.
- Presence of levodopa-induced dyskinesia.
- Rest tremor of a limb, documented on clinical examination.
- Positive results from at least one ancillary diagnostic test:
  - Olfactory loss: anosmic or hyposmic
  - Metaiodobenzylguanidine (MIBG) scan showing cardiac sympathetic denervation.


Absolute Exclusion Criteria

- Cerebellar abnormalities
- Downward vertical supranuclear gaze palsy
- Diagnosis of frontotemporal dementia or primary progressive aphasia within the first 5 yrs. of disease.
- Parkinsonian features restricted to the legs for > 3 yrs.
- Treatment with a DA receptor blocker or DA-depleting agent in a dose and time-course consistent with drug-induced parkinsonism.

**Absolute Exclusion Criteria**

- Absence of observable response to high-dose levodopa despite at least moderate severity of disease.
- Cortical sensory loss (ie, graphesthesia, stereognosis with intact primary sensory modalities), limb ideomotor apraxia, or progressive aphasia.
- Normal functional neuroimaging of the presynaptic dopaminergic system.
- Documentation of an alternative condition known to produce parkinsonism and plausibly connected to the patient’s symptoms.


**Red Flags**

- Rapid progression of gait impairment requiring regular use of wheelchair within 5 yrs. of onset.
- Absence of progression of motor symptoms or signs over 5 or more years unless stability is related to treatment.
- Early bulbar dysfunction (severe dysphonia, dysarthria, or dysphagia) within the first yr. of disease.
- Inspiratory respiratory dysfunction.
- Severe autonomic failure in the first 5 yrs. of disease.
  - Orthostatic hypotension (decrease of BP within 3 min of standing by at least 30 mmHg or 15 mmHg diastolic).
  - Severe urinary incontinence or urinary retention in the first 5 yrs. of disease.

Red Flags

- Recurrent (> 1/year) falls because of impaired balance within 3 yrs. of onset.
- Presence of disproportionate anterocollis (dystonic in nature) or contracture of hands or feet within first 10 yrs.
- Absence of any of the common nonmotor features of the disease despite 5 yrs. disease duration:
  - Sleep dysfunction
  - Autonomic dysfunction: constipation, daytime urinary urgency, symptomatic orthostasis.
  - Hyposmia
  - Psychiatric dysfunction: depression, anxiety, or hallucinations.


Red Flags

- Otherwise unexplained pyramidal tract signs, defined as pyramidal weakness or clear pathologic hyperreflexia.
- Bilateral symmetric parkinsonism throughout the disease course.

Diagnostic Categories

- **Clinically Established PD** requires:
  1. Absence of absolute exclusion criteria
  2. At least 2 supportive criteria, and
  3. No red flags.

- **Clinically Probable PD** requires:
  1. Absence of absolute exclusion criteria
  2. Presence of red flags counterbalanced by supportive criteria:
     - If 1 red flag is present there must be at least 1 supportive criterion.
     - If 2 red flags, at least 2 supportive criteria needed.
     No more than 2 red flags are allowed.

---

Clinical Course Idiopathic PD

- Begins slowly, usually on one side of the body and then involves the other side.
- Slow variable rate of progression, lasting between 20 to 30 years after onset.
- Progression of disability assessed using:
  - **Hoehn and Yahr Classification of Disability**
    - Five stages with Stage I indicating minimal disease involvement to stage V indicating severe involvement.
  - **Unified Parkinson Disease Rating Scale (UPDRS)**
    - Contains 1) Mentation, Behavior, and Mood, 2) ADL and 3) Motor scales.
- Copies of these scales can be found at:
  http://www.movementdisorders.org/MDS/Education/Rating-Scales.htm
Different clinical and evolitional patterns in late idiopathic and vascular parkinsonism

<table>
<thead>
<tr>
<th></th>
<th>Idiopathic PD</th>
<th>Vascular Parkinsonism (VP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>Significantly younger</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>Longer</td>
<td>Shorter</td>
</tr>
<tr>
<td>Levodopa response</td>
<td>Good (100%)</td>
<td>Poor (only 38% respond)</td>
</tr>
<tr>
<td>MRI</td>
<td>75% normal findings</td>
<td>All had cerebral vascular lesions</td>
</tr>
<tr>
<td>Disease severity measures</td>
<td></td>
<td>UPDRS scores higher at baseline More rapid decline in scores</td>
</tr>
<tr>
<td>Postural tremor, gait disorders, and LE pyramidal signs</td>
<td>More frequent</td>
<td></td>
</tr>
</tbody>
</table>


Drug-Induced Parkinsonism

<table>
<thead>
<tr>
<th>Action</th>
<th>Drug Type</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-synaptic Dopamine Receptor Blockers</td>
<td>Neuroleptics</td>
<td>Haloperidol (Haldol)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chlorpromazine (Thorazine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risperidone (Risperdal)</td>
</tr>
<tr>
<td></td>
<td>Antiemetics</td>
<td>Prochlorperazine (Compazine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Promethazine (Pherergan)</td>
</tr>
<tr>
<td></td>
<td>Gastroprokinetics</td>
<td>Metoclopramide (Reglan)</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Antihypertensives</td>
<td>Flunarizine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nifedipine (Procardia)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Verapamil (Calan)</td>
</tr>
<tr>
<td>Pre-synaptic dopamine blockers</td>
<td></td>
<td>Reserpine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tetrabenazine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylodopa (Aldomet)</td>
</tr>
<tr>
<td>Sodium channel blockers</td>
<td>Anticonvulsants</td>
<td>Phenytoin (Dilantin)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sodium Valproate (Depakote)</td>
</tr>
<tr>
<td>Noradrenergic uptake inhibitors</td>
<td>Antidepressants</td>
<td>Fluvoxamine (Luvox)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amitriptyline (Triavil)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trazodone (Desyrel)</td>
</tr>
<tr>
<td>Norepinephrine blocker/Serotonin facilitator</td>
<td>Mood stabilizers</td>
<td>Lithium</td>
</tr>
</tbody>
</table>

**Parkinson-Plus Syndromes**

- Neurodegenerative conditions other than idiopathic PD that have Parkinsonism
- Clinical features suggestive of Parkinson-Plus syndromes:
  - Lack of or diminished response to levodopa
  - Early onset of dementia or postural instability
  - Symmetry of signs in early stages of the disease
  - Truncal symptoms more prominent than limb symptoms
  - Prominent motor apraxia
  - Ocular signs, such as impaired vertical gaze, nystagmus
  - Cerebellar signs
  - Frequent falls and autonomic symptoms such as postural hypotension and incontinence early in the course of the disease

21 Kloos & Kegelmeyer, 2016, pg. 284.

---

**Progressive Supranuclear Palsy**

- Most common PPS (5%)
- Onset: 60-65 yrs. old
- Demographics
  - Men = Women
- Prognosis: mean survival time is 6-7 years (range 1-13 yrs.)
- Clinical Diagnosis
  - Frequent, sudden posterior falls/postural instability*
  - Ineffective response to medications
  - Gaze palsy (downward)*
  - Speech and swallowing changes

*Required for diagnosis

22 Colosimo et al., 2011.
Progressive Supranuclear Palsy

- **Motor Symptoms**
  - Postural instability & falls
    - Wide-based, slow & unsteady gait
  - Supranuclear vertical gaze palsy followed by horizontal gaze abnormalities
  - Bradykinesia
  - Minimal to no tremor
  - Symmetrical limb signs
  - Axial > limb rigidity
    - neck (retrocollis) > trunk involvement
  - Contracted facial muscles (“Sustained surprise”)
  - Dysarthria/dysphagia

---

Progressive Supranuclear Palsy

- **Cognitive Symptoms**
  - Florid frontal lobe symptoms
  - Executive dysfunction
  - Emotional & personality changes

- **Autonomic symptoms**
  - Lack of sweating
  - Constipation
  - Urinary/fecal incontinence
  - Sexual dysfunction

- **Sleep abnormalities**
  - REM sleep behavior disorders (RBD)
  - Scream/talk while asleep
  - Insomnia
  - Daytime sleepiness

---


Progressive Supranuclear Palsy

- Pathology
  - Areas affected
    - Basal Ganglia (SN, GP, STN)
    - Brainstem (especially midbrain tectum)
    - Thalamus (VA, VL nuclei)
    - Frontal Cortex
    - Cerebellar dentate nucleus and superior cerebellar peduncles
  - Dopaminergic, cholinergic, & adrenergic neurotransmitter systems affected
- Neuronal Tau Pathology
  - Pathological hallmark = neurofibrillary tangle (NFT) globose in shape


Progressive Supranuclear Palsy

- Disease Severity Rating Scales
  - Unified Parkinson’s Disease Rating Scale
    - Motor section of scale valid and reliable for PSP
  - Progressive Supranuclear Palsy Rating Scale (PSPRS)
    - Assesses health history, mentation, bulbar function, eye and lid movement, limb movement, and gait/trunk movement.
    - Total possible score is 100, reflecting higher level of impairment.

Zampieri C, Di Fabio RD. *Phys Ther.* 2006; 86:870-880.
Corticobasal Ganglionic Degeneration (CGBD)

- Onset = 60-80 yrs (mean 63)
- Demographics
  - Women > men
- Prognosis: severe disability and death in 6-8 yrs.

Motor Symptoms

- Parkinsonism
  - Asymmetric limb rigidity, bradykinesia, myoclonic tremor (no resting tremor)
  - Asymmetric limb dystonia or myoclonus (usually UEs)
  - Orofacial or limb apraxia (ideomotor apraxia)
  - Apraxia of speech and/or nonfluent aphasia
  - Delayed initiation of horizontal /vertical saccadic eye movements.
  - Gait abnormalities with postural instability and falls


Corticobasal Ganglionic Degeneration (CGBD)

- Sensory Symptoms
  - Cortical sensory deficits (visual/tactile spatial neglect, impaired graphesthesia and stereognosis)
  - Alien limb phenomena (50%)

Cognitive/Behavioral Symptoms

- Impaired executive function, memory, word fluency, verbal comprehension, perceptual organization, and cognitive flexibility.
- Progressive frontotemporal dementia in later stages characterized by apathy, bizarre or antisocial behavior, personality changes, irritability, disinhibition, and hypersexuality.

Corticobasal Ganglionic Degeneration (CGBD)

- Probable CGBD Clinical Diagnosis:
  - Asymmetric presentation of 2 of:
    - Limb rigidity or akinesia
    - Limb dystonia
    - Limb myoclonus
  - Plus 2 of:
    - Orobulical or limb apraxia
    - Cortical sensory deficit
    - Alien limb phenomena (more than simple levitation)


Corticobasal Ganglionic Degeneration (CGBD)

- Pathology
  - Areas affected
    - Frontal, parietal, and temporal cortex
    - Basal Ganglia
  - Neuronal Tau Pathology
    - Pathological hallmark = wispy, fine filamentous inclusions within neuronal cell bodies and glia composed of hyperphosphorylated tau

Multiple System Atrophy (MSA)

- Onset: 33-76 yrs. (mean = 55)
- Demographics
  - Men = women
- Prognosis: median survival 6-9 yrs.
- Unification of previously split syndromes:
  - MSA-C = Olivopontocerebellar atrophy (OPCA): prominent cerebellar symptoms
  - MSA-P = Striatonigral degeneration: predominant parkinsonian symptoms
  - Shy-Drager syndrome (SDS): predominant autonomic presentation.


Multiple System Atrophy

- Motor Symptoms
  - Parkinsonism (asymmetrical tremor, rigidity, bradykinesia, postural instability)
  - Cerebellar dysfunction (gait and limb ataxia, ataxic dysarthria, sustained gaze-evoked nystagmus)
  - Orofacial and hand dystonia
  - Anteflexion of neck
  - Dysphagia
- Autonomic
  - Orthostatic hypotension
  - Urinary incontinence or erectile dysfunction
- Other Symptoms
  - Pyramidal signs (Babinski & Hyperreflexia)
  - Cognitive (mild executive functioning deficits, REM behavioral disorder)

**Multiple System Atrophy**

- Probable MSA Clinical Diagnosis:
  - Autonomic failure or urinary dysfunction
    - Orthostatic fall in blood pressure (by ≥ 30 mmHg systolic or ≥15 mmHg diastolic after 3 minute standing) or
    - Urinary incontinence (inability to control the release of urine from the bladder, with erectile dysfunction in men)
  - Poorly levodopa-responsive parkinsonism or
  - Cerebellar dysfunction


**Multiple System Atrophy**

- Pathology (areas affected)
  - Basal Ganglia
    - Substantia nigra, putamen, caudate
  - Cerebellum
    - Inferior olives, cerebellar Purkinje cells
  - Brainstem
    - Locus Ceruleus, pontine nuclei (middle cerebellar peduncle)
  - Spinal Cord
    - Intermediolateral cell columns and Onuf’s nucleus

- Pathologic hallmark = Glial Cytoplasmic Inclusions (GCI)
  - GCIs containing Alpha-synuclein in oligodendrocytes

Dementia with Lewy Bodies

- Onset = 60-85 yrs
- Demographics: Men > women
- Prognosis: Median survival 8 years after diagnosis.
- Probable DLB Clinical Diagnosis
  - Progressive cognitive decline that interferes with normal social or occupational functioning.
  - 2 out of the 3 core features:
    - Parkinsonism
    - Fluctuations in cognitive performance with pronounced variations in attention and alertness
    - Recurrent visual hallucinations that are typically well formed and detailed


Dementia with Lewy Bodies

- Motor Symptoms
  - Parkinsonism
    - Rigidity > resting tremors (uncommon)
- Cognitive Symptoms
  - Progressive deterioration of cognitive performance
    - Memory, attention, language, executive functions, & visuospatial and visuoconstructional abilities
  - Unprovoked visual hallucinations
    - Neuroleptic Sensitivity
  - REM Sleep Behavioral Disorder (RBD)
- Autonomic Symptoms
  - Syncope, Orthostatic hypotension

## Dementia with Lewy Bodies

- **Pathology**
  - **Areas affected**
    - Basal Ganglia (SN)
    - Cortex (Frontal, parietal, and temporal)
    - Limbic areas (amygdala, cingulate gyrus)
  - **Pathological hallmark** = cortical Lewy bodies containing alpha-synuclein

---

### Differential Diagnosis of Parkinson-Plus Syndromes

<table>
<thead>
<tr>
<th>PD</th>
<th>Age of Onset</th>
<th>Demographics</th>
<th>Clinical Diagnosis</th>
<th>Motor Symptoms</th>
<th>Sensory Symptoms</th>
<th>Cognitive Symptoms</th>
<th>Autonomic Symptoms</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPD</td>
<td>50-60</td>
<td>Men = women</td>
<td>&quot;TRAP&quot; Tremor (resting), Rigidity, Akinesia, Postural instability, Freezing</td>
<td>Asymmetrical rest tremor, bradykinesia, freezing episodes, hypokinesia, lability, postural instability, freezing to initiate, dystonia</td>
<td>Anomia, prosopagnosia, dysautonomia, sensory integration, visual extinction, memory loss, pain</td>
<td>Depression, anxiety, apathy, fatigue, impaired memory, confusion, dementia, sleeping disorders</td>
<td>Drooling, sweating, orthostatic hypotension, urinary incontinence, constipation, sexual dysfunction</td>
<td>~15 years</td>
</tr>
<tr>
<td>PSP</td>
<td>60</td>
<td>Men = women</td>
<td>&quot;FGS&quot; Frequent sudden falls, inefficient response to levodopa, Gait instability (crouch, broad-based, shuffling), Speech/nasal stammering</td>
<td>Postural instability, wide-based gait, vertical gaze palsy, asymmetric gait signs, axial + limb rigidity, sustained supine suspension, dysphagia</td>
<td>Flaccid frontotemporal changes, impaired executive function, emotional &amp; personality changes</td>
<td>Depression, anxiety, apathy, fatigue, impaired memory, confusion, dementia, sleeping disorders</td>
<td>Drooling, sweating, orthostatic hypotension, urinary incontinence, constipation, sexual dysfunction</td>
<td>&lt;10 yrs</td>
</tr>
<tr>
<td>CBGD</td>
<td>60-80</td>
<td>Women &gt; Men</td>
<td>Parkinsonism (myoclonic tremor), poor response to levodopa, unilateral limb signs, unilateral sensory signs, unilateral visual neglect</td>
<td>Parkinsonism (hypokinesia, tremor, rigidity), dysphagia, apraxia, ataxia, supranuclear gaze palsy</td>
<td>Visual &amp; tactile neglect, anosognosia, alien limb phenomena</td>
<td>Depression, anxiety, apathy, fatigue, impaired memory, confusion, dementia, sleeping disorders</td>
<td>Drooling, sweating, orthostatic hypotension, urinary incontinence, constipation, sexual dysfunction</td>
<td>&lt;3 yrs</td>
</tr>
<tr>
<td>MSA</td>
<td>55</td>
<td>Men = women</td>
<td>Parkinsonism or cerebellar dysfunction, Oligohydramnios, incontinence, Supranuclear gaze palsy, Postural instability, Autonomic insufficiency, Speech/arthroglossus apraxia, Postural instability</td>
<td>Parkinsonism, gait &amp; balance deficit, Extrapyramidal signs, Autonomic dysfunction</td>
<td>Bulbar, hypohyphasia, RBD, MCI, Executive dysfunction, Deficient WAIS</td>
<td>Orthostatic hypotension, urinary incontinence, ED</td>
<td>Drooling, sweating, orthostatic hypotension, urinary incontinence, constipation, sexual dysfunction</td>
<td>6-7 yrs</td>
</tr>
<tr>
<td>DLB</td>
<td>60-85</td>
<td>Men = Women</td>
<td>Parkinsonism, fluctuation &amp; cognitive performance, visual hallucinations</td>
<td>Parkinsonism (rigidity &gt; tremor), Autonomic dysfunction</td>
<td>Progressive fluctuation of cognitive performance, unprovoked visual hallucinations, RBD</td>
<td>Syncope, orthostatic hypotension</td>
<td>Drooling, sweating, orthostatic hypotension, urinary incontinence, constipation, sexual dysfunction</td>
<td>Survival 8 yrs after dx</td>
</tr>
</tbody>
</table>

### Differential Diagnoses of Gait Disturbance

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Lesion</th>
<th>Gait</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>SN</td>
<td>Narrow and shuffling gait; reduced arm swing; FoG and falls late in disease</td>
<td>Lateralization; tremor; bradykinesia; drug responsive</td>
</tr>
<tr>
<td>DLB</td>
<td>BG; cortex</td>
<td>Less lateralization; narrow gait; early falls</td>
<td>Early dementia; fluctuating alertness; visual hallucinations</td>
</tr>
<tr>
<td>MSA</td>
<td>BG; cerebellum; brainstem</td>
<td>MSA-C: wide-based ataxic gait; impaired postural stability; early falls; MSA-P: parkinsonian gait</td>
<td>Oculomotor signs; orthostatic dysregulation; neurogenic bladder dysfunction</td>
</tr>
<tr>
<td>PSP</td>
<td>Brainstem</td>
<td>Axial rigidity; early falls with injuries; early FoG; reckless falls</td>
<td>Supranuclear gaze palsy; disinhibition; eyelid opening apraxia</td>
</tr>
<tr>
<td>CBGD</td>
<td>BG; cortex</td>
<td>FoG and falls usually not at disease onset</td>
<td>Cortical deficits; alien limb; limb apraxia</td>
</tr>
<tr>
<td>VP</td>
<td>Thalamus; BG; brainstem</td>
<td>May mimic PD; sometimes disequilibrium</td>
<td>May respond to dopamine replacement medication</td>
</tr>
</tbody>
</table>

---

### Summary of Key Differential Diagnosis Features of the Parkinsonisms

<table>
<thead>
<tr>
<th>Signs/ Symptoms</th>
<th>Suspect:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradykinesia, resting tremor, rigidity good response to dopamine medications</td>
<td>Idiopathic Parkinson’s Disease</td>
</tr>
<tr>
<td>Acute or shorter onset of symptoms; predominant involvement of the LEs</td>
<td>Vascular Parkinsonism</td>
</tr>
<tr>
<td>Falls as early first symptom; vertical gaze palsy (downward)</td>
<td>Progressive supranuclear palsy</td>
</tr>
<tr>
<td>Prominent orthostatic hypotension</td>
<td>Multiple system atrophy-p (MSA-P)</td>
</tr>
<tr>
<td>Early dystarhia; wide-based ataxic gait</td>
<td>Multiple system atrophy-c (MSA-C)</td>
</tr>
<tr>
<td>Unilateral limb dystonia and/or apraxia, alien limb phenomenon</td>
<td>Corticobasal ganglionic degeneration</td>
</tr>
<tr>
<td>Early visual hallucinations, fluctuations in attention and consciousness, and dementia</td>
<td>Dementia with Lewey Body</td>
</tr>
</tbody>
</table>
Neuroimaging Biomarkers

- Modern imaging techniques may be able to assist in the pre-clinical diagnosis of PD or in differentiating different Parkinsonian syndromes.
- Diffusion tensor imaging (DTI)
  - Functional anisotropy (FA) alterations detected in all parkinsonian syndromes, with distribution varying differentially with disease type.
    - PD: substantia nigra and frontal lobe
    - Progressive supranuclear palsy: corpus callosum and frontal lobe
    - Multiple system atrophy: cerebellum, middle cerebellar peduncle, pons, and internal capsule


Neuroimaging Biomarkers

- Functional imaging using positron emission tomography (PET), single-photon emission computed tomography (SPECT), or functional MRI (fMRI) with radiotracers that evaluate pre- or postsynaptic DA receptors, glucose metabolism, or regional cerebral blood flow (rCBF) have been used to study DA system in parkinsonian disorders.
- Using 18F-FDG PET images, Zhao et al. (2012) demonstrated the following reductions in glucose metabolism in PD and PD-plus syndromes:
  - bilateral parietal areas in PD;
  - bilateral putamen in MSA-P;
  - bilateral cerebellum in MSA-C;
  - bilateral occipital and parieto-occipital areas in DLB;
  - midbrain and the middle frontal cortex in PSP;
  - unilateral cortex and basal ganglia in CBGD.

Biomarkers: Biological fluids

- Cerebrospinal fluid biomarkers may aid in differential diagnosis of parkinsonian conditions.
  - **A beta 42**: has a role in predicting cognitive decline in PD.
  - **Total alpha-synuclein**: most promising marker; differentiates synucleinopathies from other neurodegenerative diseases and control but is not specific.
  - **Neurofilament light chain protein (NF-L)**: useful in differentiating PD from atypical parkinsonian conditions.


Pharmacological Management

- **Levodopa**
  - Still "gold standard" for PD medications.
  - Combination of levodopa and carbidopa (Parcopa, Sinemet) crosses the blood-brain barrier.
  - Alleviates bradykinesia and rigidity with less effect on tremor.
  - May increase postural sway in later stages due to dyskinesias.
  - Improves gait disturbances in early stages, but not as effective in later stages.

Deep Brain Stimulation (DBS)

- Electrodes placed in the brain are connected by wires to an impulse generator (IPG) implanted under the skin of the chest, below the collarbone. Unclear whether stimulation suppresses or activates cells.
- Indicated when person has symptoms not adequately controlled with medications.
- Person still has to have a good response to levodopa.
- Stimulators may last 3-5 years.

Deep Brain Stimulation (DBS)

- Many patients experience reduction of their PD symptoms (tremors, rigidity, bradykinesia, dyskinesias) and can greatly reduce their medications.
- Some improvement in gait disturbances and FoG if person is dopa-responsive before surgery, bilateral stim better than unilateral.
- No improvement or worsening of reactive postural adjustments.

Medical Management of Parkinson-Plus Syndromes

- No cures or interventions to delay the progression of diseases.
- Symptomatic Medications:
  - Parkinsonism symptoms: dopaminergic meds
  - Dystonia and myoclonus: muscle relaxants (Botox) or anti-seizure medications (clonazepam).
  - Memory/behavior problems: hallucinations- acetylcholinesterase inhibitors (donepezil and rivastigmine)
  - Depression & anxiety: antidepressants, such as sertraline, citalopram or escitalopram.
  - Orthostatic hypotension: sympathomimetic amines, droxidopa
- Other Interventions
  - Referrals to PT, OT, Speech
  - Glasses with prisms for visual disturbances
  - Percutaneous endoscopic gastrostomy (PEG)

PT Intervention Guidelines for PD

- European Physiotherapy Guideline for Parkinson’s Disease (www.parkinsonnet.info/euguideline)
- Strong recommendations for these interventions:
  - Conventional PT to improve walking speed, muscle strength, and movement functions (UPDRS III)
  - Treadmill to improve walking speed, stride length
  - Cueing for gait (visual, auditory, tactile) to improve walking speed
  - Strategies for complex motor sequences to improve functional mobility (TUG, 5TSTS)
  - Tai chi to improve movement functions (UPDRS III)


Keus et al., 2014
Evidence-Based PT Treatment-PSP

- 3 Case studies
  - Individualized programs: Limb-coordination exercises, balance training, gait and transfer training, strengthening exercise, strategies to compensate for impaired visual scanning (scanning, prism glasses).
  - Outcomes: improved standing balance, gait, and ability to scan the environment.
  - BWSTT (1.5 hours, 3 days/week, 8 weeks): different directions of walking with 15% body weight support and postural reactions to perturbations with 0% BWS practiced. Outcomes: improved Berg, Functional reach, spatiotemporal gait measures, and falls.


Evidence-Based PT Treatment-PSP + CBGD

- Long-Term Group Exercise Training (1 hr, 2x/wk)
  - 72 yo dentist with mixed PSP and CBD features participated in an exercise group for people with PD consisting of:
    - 20 min trunk & LE stretching/strengthening, 10 min upright balance & strengthening exercises, and at least 20 min of treadmill walking (forward and backwards).
  - Outcomes
    - After 2.5 year, reduced fall frequency, maintained balance & endurance, & retained community ambulation using a walker.
    - After 10 years, falls decreased from 1.9 falls per month in year 1 to 0.3 falls per month. Balance, walking endurance, and general mobility declined slightly. Gait speed (both comfortable and fast) declined; the client was unable to vary gait speed. Quantitative brain measurements indicated a slow rate of whole brain volume loss and ventricular expansion compared with clients with autopsy-proven CBD or PSP.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gait/balance</th>
<th>Other sx</th>
<th>Eval and Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular PD</td>
<td>More rapid decline</td>
<td>UPDRS scores higher at baseline</td>
<td>Motor and sensory exam</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Based on impairments</td>
</tr>
<tr>
<td>PSP</td>
<td>Early postural instability</td>
<td>Vertical gaze paresis especially downward</td>
<td>Evaluate eye movement (UPDRS)</td>
</tr>
<tr>
<td></td>
<td>with falls in first year</td>
<td></td>
<td>Check for ability to visually scan</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>environment and avoid obstacles</td>
</tr>
<tr>
<td>MSA</td>
<td>Cerebellar dysfunction</td>
<td>Orthostatic hypotension</td>
<td>Examine for orthostatic hypotension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Teach to deal with hypotension</td>
</tr>
<tr>
<td>CBGD</td>
<td>Bradykinesia-focal rigidity</td>
<td>Limb apraxia, dystonia</td>
<td>Eval coordination</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Look for apraxia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Train coordination</td>
</tr>
<tr>
<td>LBD</td>
<td>parkinsonian motor symptoms</td>
<td>progressive cognitive decline, &quot;fluctuations&quot;</td>
<td>Check cognition - MOCA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>in alertness and attention</td>
<td>Train safety as performance is highly variable</td>
</tr>
</tbody>
</table>

- More in-depth look at strength and sensory as would be done for stroke
- May need to train for a hemiplegic type gait that is slow and rigid
- Progress will be slower than with either PD or CVA alone but can be made
### Syndrome

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Prognosis</th>
<th>Gait/balance</th>
<th>Other sx</th>
<th>Eval and Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSP</td>
<td>Varies, choking leads to aspiration</td>
<td>Early postural instability with falls in first year</td>
<td>Vertical gaze paresis especially downward</td>
<td>Evaluate eye movement (UPDRS) Check for ability to visually scan environment and avoid obstacles</td>
</tr>
</tbody>
</table>

- Early on work on eye movement
- Train to scan environment – especially the floor
- Work on maneuvering obstacles and safe gait.
- Consider adaptive device to assist with object location and balance if they do bump an object
- Early training with rollator
- Lots of work with balance

---

### Checking and rating eye movement

**Ocular Pursuit** (ability of the eyes to follow an object up and down (vertical) and side to side (horizontal))

<table>
<thead>
<tr>
<th>Vertical</th>
<th>Horizontal</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Doesn’t move to follow</td>
<td>□ Doesn’t move to follow</td>
</tr>
<tr>
<td>□ Partial movement</td>
<td>□ Partial movement</td>
</tr>
<tr>
<td>□ Completes movement</td>
<td>□ Completes movement</td>
</tr>
</tbody>
</table>
- Teach to do ankle pumps and other calf exercises before standing up
- Teach to make movements from supine to sit and sit to stand slowly
- If coordination is impacted do ataxia exercises

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Prognosis</th>
<th>Gait/balance</th>
<th>Other sx</th>
<th>Eval and Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSA</td>
<td>9-10 years</td>
<td>Cerebellar dysfunction</td>
<td>Orthostatic hypotension</td>
<td>Examine for orthostatic hypotension, Examine coordination, Teach to deal with hypotension</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Prognosis</th>
<th>Gait/balance</th>
<th>Other sx</th>
<th>Eval and Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBGD</td>
<td>6-8 years</td>
<td>Bradykinesia, focal rigidity</td>
<td>Limb apraxia, dystonia</td>
<td>Eval coordination, Look for apraxia, Train coordination</td>
</tr>
</tbody>
</table>

- Treat for coordination (ataxia exercises)
- Work on compensatory strategies for ataxia
- Train within function
- Be flexible and creative!
## Extremity Exercises for Ataxia and Coordination

### Upper Extremities:
- Alternate Flexion/Extension of elbows, wrists, shoulders
- Supination and Pronation of forearms
- Finger Dexterity: touch each digit to thumb.
- Rock, Paper Scissors: fist to palm of opposite hand, palm to palm, and ulnar side of hand to opposite palm.

### Lower Extremities:
- Flexion and Extension of the hips and knees.
- Ankle dorsi and plantar flexion.
- Bilateral ankle dorsi and plantar flexion
- Alternate ankle dorsi and plantar flexion.
- Tracing: draw a circle on the floor using toes or heel of foot.
- Using a box diagram, point toes in different boxes.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Prognosis</th>
<th>Gait/balance</th>
<th>Other sx</th>
<th>Eval and Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBD</td>
<td>8 years</td>
<td>parkinsonian motor symptoms</td>
<td>progressive cognitive decline, “fluctuations” in alertness and attention</td>
<td>Check cognition Train safety as performance is highly variable</td>
</tr>
</tbody>
</table>

- Change treatment to accommodate for cognitive changes, focus on problem solving
- Motor learning more severely impacted so more blocked practice and less random
- More of a focus on safety and training it early – before cognitive decline too severe
- Allow more time to meet goals as issues with attention will negatively impact some therapy sessions
Case #1
A retired electrician experienced problems with driving at age 65. At age 66, his limbs stiffened and his movements slowed. He also began to ignore his right arm; even though it was not weak, it hung at his side as if he no longer knew how to use it. In addition, his right hand grabbed onto anything that happened to be in front of him. He also lost the ability to manage his finances. Over several months, he became unable to make meals, brew coffee, or dress himself. He became increasingly apathetic, and displayed obsessive-compulsive and rigid behavior. For example, he asked for things repeatedly and demanded that they be done immediately (e.g., requesting that candlesticks be moved back and forth).

59

Case #1
- **Mental status**: MMSE score 20/30; The patient exhibited perseveration, deficits in attention (could not repeat more than 5 digits) and working memory (anterograde and retrograde).
- **Communication**: Unable to write a sentence; severe visual-spatial impairments when copying pictures.
- **Cranial Nerves**: intact.
- **Sensation**: Intact to light touch and proprioception; unable to recognize by feel alone including a key or coin placed on his palm and numbers or letters written on his palms.
- **Motor Control**: Severe right arm apraxia. Evidence of right hemi-neglect; he used his left arm almost exclusively for spontaneous actions even when instructed to perform the actions with the right arm. He also had difficulty flexing and extending his right knee on command. Fine motor coordination and dexterity was impaired as tested with the 9-hole peg test.
- **Gait**: Slow with shortened step lengths, right greater than left. Steps were discontinuous with the right leg appearing to “lag” slightly behind the left. During walking, the patient’s right arm frequently flexed briefly at the elbow, wrist, and fingers, and his right toe extended intermittently and remained briefly in the extended position (right arm and right big toe dystonia). With turns, the patient exhibited slight festination of steps.
Case #2

A 64-year-old man diagnosed with neuropathy and gait disorder was referred to physical therapy. The patient’s wife reported that 6 years before his referral to PT, she noticed some behavioral changes. He had difficulty making financial decisions, and had difficulty writing a check. He was also easily irritated and depressed when something went wrong at work. Five years previously, the patient started losing his balance and developed very slow movements. Three years before his referral, he lost his teaching job because of micrographia and slurred, quiet speech. He went to a neurologist and underwent a battery of diagnostic tests which were reported to be normal. Most recently the patient demonstrated reduced facial expression and kyphotic posture when he was walking, and he was falling more frequently. He was taking levodopa/carbidopa (Sinemet), amantadine, and Vitamin E.

Mental Status: MMSE score of 27/30; He could comprehend and respond to any command, but he rarely started a conversation.

Cranial Nerves: eyes movements were normal except for an inability to gaze downward; his speech was slurred and hypophonic and his wife reported that choked occasionally when eating. Generally his facial expression and emotions appeared normal.

Sensation: no deficits in light touch, proprioception.

Motor Control: No tremors were noted; Getting up from a chair was difficult due to an inability to weight shift anteriorly and inappropriate placement of the lower extremities. When going standing to sitting, he would abruptly fall into a chair.

Gait: The patient ambulated with a stooped posture of the head, neck, and shoulders with a slow and unsteady gait pattern. He could walk without an assistive device but sometimes carried a cane for better balance. His wife reported frequent, backward falls at home but no episodes of freezing.
References


References

- Parnetti L, Castrioto A, Chiasserini D, Persichetti E, Tambasco N, El-Agnaf O, Calabresi P.
References

