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Conflict of Interest & Disclosure Statements

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No commercial funding has been accepted for this activity.

Featured Speaker

Miran Salgado, MD
- Chairman, Department of Neurosciences, New York Methodist Hospital
- Medical Director, American Parkinson Disease Association’s Information and Referral Center at New York Methodist Hospital

Evaluations & CE

Nursing Contact Hours, CME, CHES and Social Work credits are available.

Please visit www.phlive.org to fill out your evaluation and complete the post-test.
Objectives

At webcast conclusion, viewers will be able to

- List the early clinical signs of Parkinson's disease that are often missed;
- Identify at least two of the treatments offered to manage disease symptoms; and
- Recall at least three examples of local support, resources and services for the Parkinson's patient and their care partners.

First Account of Parkinson’s

- First described by James Parkinson in 1817
- Involuntary unilateral tremor
- Lessened muscular power
- Tendency to bend forward & pass from walking to running pace
- Sleep problems, constipation, Hypophonia (soft speech) & Sialorrhea (excessive drooling)

Common Age-Related Disorder

- 2nd most common neurodegenerative disorder, after Alzheimer's
- Afflicts approximately 1 million people in North America
- Onset between 40 and 70 years; peak age of onset in 60s
- Prevalence: 160 per 100,000 people
- Incidence: 20 per 100,000 people
- At age 70, prevalence approximately 55 per 100,000 and incidence approximately 120 per 100,000
- Slight male predominance (3:2)

Epidemiology of Parkinson’s

Progression is highly variable

- About 60% of untreated patients become severely disabled or dead 5-9 years after onset
- 80% of untreated patients become severely disabled or dead within 10-14 years

Incidences Increases With Age

Predicted to almost double between 2005-2030 among those over aged 50

Cause of Parkinson’s

Experts believe Parkinson’s Disease is the result of interaction between genetic and environmental causes
Genetics
- Several genes and specific mutations associated with PD have been identified
- Approximately 20% of patients have a family history
- Only 5% of PD patients have a monogenic form
- Majority of PD cases are sporadic (also known as idiopathic) in nature

Environment
- Rural living and exposure to environmental toxins, such as pesticides
- No single environmental cause of Parkinson’s
- Personal habits (including smoking cigarettes and drinking coffee) associated with a lower risk of PD

Cause of Parkinson’s
- Primarily a sporadic or idiopathic disorder
- Most have no genetic component
- Primary genes associated with familial and sporadic PD: LRRK2, PRKN, SNCA
- Genetic testing is available for certain genes
- Clinical recommendations for management remain unchanged, regardless of genetic mutation status

Pathogenesis
- Nigrostriatal degeneration and α-synuclein aggregates
- Symptoms manifest with approximately 60% loss of nigral cells
- NOT exclusively a dopaminergic deficiency

Intra-neuronal cytoplasmic inclusions, or “Lewy Bodies”
Lewy bodies: abnormal aggregations of protein that develop inside nerve cells in Parkinson’s Disease

Braak Hypothesis of Disease Progression
- Lewy bodies (abnormal aggregations of α-synuclein) a prerequisite for postmortem PD diagnosis
- Not known if they are causative or protective mechanism
- Braak et al. hypothesize that Lewy bodies spread through the brain in a predictable pattern as PD progresses
- Pathological studies found Lewy pathology in brain, cardiac and enteric autonomic nervous systems
The Parkinson’s Complex

- Predate motor symptoms
- Olfactory abnormalities in 80%
- Constipation
- Depression & anxiety
- Mild cognitive deficits
- Cardiac autonomic markers
- REM Behavior Disorder and visual abnormalities
- Rheumatological complaints

Early Non-Motor Features

- Non-specific and usually seen in elderly
- Patients use cognitive resources to reduce impact of dopamine deficits
- Assessment of gait variability, acceleration of static sway, flexion extension of wrist
- Alternate Tap Test, Perdue Peg Board Test, Timed Up and Go, slowing of hand movements, subjective complaints of slowness and stiffness

Diagnosis

- Evidence of two of the cardinal features:
  - Tremor
  - Rigidity
  - Bradykinesia
  - Postural instability
- At least two of the following:
  - Marked sustained response to L-Dopa
  - Asymmetric signs
  - Asymmetric onset
  - Absence of clinical features of alternative Dx
  - Absence of etiology known to cause similar features
**Genetic and Neurochemical Biomarkers of Preclinical PD**

<table>
<thead>
<tr>
<th>Method</th>
<th>Biomarker</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF</td>
<td>α-Synuclein, LRRK2, DJ-1, NURR1</td>
<td>No change with disease progression</td>
</tr>
<tr>
<td>Blood</td>
<td>α-Synuclein, ST13 urate</td>
<td>Not helpful for all patients</td>
</tr>
<tr>
<td>System biology techniques</td>
<td>Genomic, transcriptomic, proteomic, metabolomic</td>
<td>Needs more study</td>
</tr>
</tbody>
</table>

**Neuroimaging Biomarkers of Preclinical PD**

<table>
<thead>
<tr>
<th>Method</th>
<th>Biomarker</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT</td>
<td>DAT SPECT</td>
<td>Not clear if changes with disease progression</td>
</tr>
<tr>
<td>PET</td>
<td>F-flurodopa and DAT PET</td>
<td>Sensitive to preclinical PD but expensive and may be affected by levodopa</td>
</tr>
<tr>
<td>Sonography</td>
<td>SN hyperechogenicity</td>
<td>Not clear if changes with disease progression</td>
</tr>
<tr>
<td>fMRI</td>
<td>Iron in SN; fractional anisotropy in DTI</td>
<td>Helpful if combined with clinical biomarkers, needs more study</td>
</tr>
<tr>
<td>Scintigraphy</td>
<td>MIBG</td>
<td>Insensitive</td>
</tr>
</tbody>
</table>

**DaTscan™ SPECT Images**

- Differentiates between patients with/without a dopaminergic deficit
- Potential adjunct in diagnosis of Parkinsonian syndromes

SPECT = single photon emission tomography

**Parkinson’s Disease Dementia**

- Cognitive dysfunction - up to 90%
- In 30% - impaired visual-spatial functions, mildly impaired memory, normal retention, mildly impaired verbal fluency
- Severely affected executive and verbal fluency
- Lewy Body Dementia (LBD)
- Parkinson’s Disease + Alzheimer’s Disease
- Parkinson’s Disease Dementia

**Lewy Body Dementia**

- Progressive cognitive decline & prominent memory loss
- Frontal lobe and visual-spatial dysfunction
- Parkinsonism
- Fluctuating cognition/consciousness
- Repeated falls
- Syncope, neuroleptic sensitivity
- Recurrent visual hallucinations

**Treatment Approaches**

- Medical, surgical and non-pharmacological treatments
- Neuroprotective vs. symptomatic
- For early PD - “watch and wait”
- Non-pharmacologic: exercise and counseling
- Pharmacologic:
  - Initiate pharmacotherapy for depression
  - Add PD monotherapy when motor/non-motor symptoms worsen
**Goals of Medical Treatment**
- Retard progression (if possible)
- Short term treatment to alleviate symptoms and reverse functional disability
- Improve quality of life (QOL)
- Long term treatment to maintain effectiveness and limit the complications of therapy

**Treatment Management**
- Patient-related:
  - Age
  - Lifestyle
  - Employment status
  - Co-morbidities
  - Cognitive/psychiatric profile
  - Caregiver status
- Treatment-related:
  - Efficacy
  - Tolerability and side-effect profile
  - Timing of treatment initiation

**Medical Treatment Options**
- Neuroprotective?
  - Selegiline HCl
  - Rasagiline
  - Antioxidants
  - Amantadine
  - Neurotrophic factors
  - Antioxidants
  - Mitochondrial bioenergetics
- Symptomatic
  - Selegiline HCl
  - Anti-cholinergics
  - Amantadine
  - Dopamine agonists
  - Catechol-O-methyl-transferase (COMT) inhibitors
  - Anti-convulsant Drug (AED's)
  - L-Dopa
  - Apo-morphine

**Most Effective Treatment**
- Levo-Dopa Remains the Most Effective Treatment
  - Provides rapid symptomatic relief, thereby improving QOL
  - Prolongs survival
  - Long-term use is often associated with motor complications
  - “Wearing-off,” “on-off” phenomena & Dyskinesias

**Levo-Dopa Considerations**
- Older individuals
- Those with cognitive impairment or severe disease with gait instability
- “Start low, go slow” - use lowest dose that brings adequate symptom reversal
- Patients who fail to respond to high doses (>1000mg) of Levo-dopa probably do not have Parkinson's Disease and unlikely to respond to other dopaminergic agents

**Therapy & Disease Progression**
- As the disease progresses, the therapeutic window narrows
- Symptom and side effects occur as the levodopa therapeutic window diminishes
Surgical Treatment Options

Restorative
- Fetal mesencephalic cell transplantation
- Porcine fetal cell transplantation
- Adrenal medullary transplantation
- Stem cell
- Neurotrophic factor infusions

Palliative
- Pallidotomy
- Thalamotomy
- Deep Brain Stimulation (DBS)
  - Thalamic
  - Pallidal
  - Subthalamic nucleus (STN)
- Gene therapy

Non-Pharmacological Interventions

- Education
- Support
- Emotional, peer and group counselling, legal/financial and occupational counselling
- Exercise
- Speech and swallowing
- Nutrition
- Cognitive training

Evidence Based Exercise Regimens

- Increase muscle strength with moderate volume (3 sets each), high-load, eccentric resistance training
- High/moderate intensity cardiovascular exercise (treadmill/cycling) 30 minutes per session/three times a week
- Tai Chi optimal balance training:
  - Improves postural control and walking ability - recommend twice-weekly for 24 weeks
  - Patient can complete at home without clinical equipment
- Lee Silverman Voice Treatment (LSVT®) BIG program to improve movement amplitude

Voice Therapy

- Voice symptoms caused by significant respiratory difficulties, bowed vocal folds
- Most effective approach: exaggerate one component of speech to improve all other components (e.g. loudness, voice, quality, pitch, rate)
- Observations have been formalized into the Lee Silverman Voice Treatment (LSVT®) Program

American Academy of Neurology (AAN)

Guidelines for Care of Parkinson’s Disease
1. Annual Parkinson Disease diagnosis review
2. Psychiatric disorders or disturbances assessment
3. Cognitive impairment or dysfunction assessment
4. Querying about symptoms of autonomic dysfunction
5. Querying about sleep disturbances

AAN Guidelines

6. Querying about falls
7. Parkinson Disease rehabilitative therapy options
8. Parkinson Disease-related safety issues counseling
9. Querying about Parkinson Disease medication-related motor complications
10. Parkinson Disease medical and surgical treatment options reviewed
American Parkinson Disease Association

- Established in 1961 to *Ease the Burden - Find the Cure*
- Largest national grassroots network in the U.S.
- APDA Information & Referral Center at New York Methodist Hospital in Brooklyn

Find the Cure

- Funding partner in most of the major Parkinson’s disease scientific breakthroughs in the last 50 years
- 8 Centers for Advanced Research across the country
- Research Grants and Fellowships supporting promising research
- Focus on launching careers of young scientists

Ease the Burden

APDA National Network
- Information & Referral Centers
- Chapters
- Support Groups
- Educational literature
- Professional Education

www.apdaparkinson.org
800-223-2732

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