Parkinson’s Disease: a geriatrics syndrome

Primary Care

Gerald Jogerst, M.D.

April 3, 2014
What do I know about Parkinson’s Disease?

How much do you *REALLY* know about Parkinson’s Disease?

Click here for an informative slideshow that will give you the straight facts about Parkinson’s Disease and what options are available for those suffering from this debilitating disease.
Objectives

• Describe a new approach to Parkinson’s disease.
• Discuss the diagnostic criteria for Parkinson’s disease.
• Compare conditions misdiagnosed as Parkinson’s disease.
• List drug and non-drug therapies.
• Provide recommendations for practice.
Faces of Parkinsonism
Parkinson’s Disease

- Described by James Parkinson in 1817
- Kampavata (tremor and akinesia) described in literature in India 4500-1000 B.C.
- Prevalence of 1 to 2 million people in North America
- Mortality is 2 to 5 times higher versus age-matched controls
- Age is the single most consistent risk factor
Epidemiology

• Occurs throughout the world, in all ethnic groups
• Slight male predominance
• Incidence
  – Lowest among Asians and African blacks
  – Highest among whites
  – African blacks much lower than Afro-Americans
  – Exponential increase between ages 65 and 90
  – Only 5-10% of patients have symptoms before age 40 (risk reduction with smoking)
Genetics

• Early studies of twins excluded genetic contribution
• 1997 study found high concordance among monozygotic twins (one twin had young-onset disease)
• Linkage to chromosome 2p13 in six families
Pathological Findings

• Progressive death of selected but heterogeneous populations of neurons

• Sites
  – Pars compacta of substantia nigra (dopaminergic)
  – Selected aminergic brain stem nuclei (Catecholaminergic and serotoninergic)
  – Nucleus basalis of Meynert (cholinergic)
  – Hypothalamus
  – Small cortical neurons
  – Olfactory bulb, sympathetic ganglia, and parasympathetic neurons in the gut
Parkinson’s Disease: A New Multidisciplinary Approach for this Old Actor

Premotor Phase

Aspecific non-motor symptoms:
- Hyposmia
- Constipation
- Depression
- Articular pain
- Fatigue
- Orthostatic Hypotension

Clinically Evident (PD)

Specific motor symptoms:
- Bradykinesia (plus at least)
- Rigidity
- Tremor
- Postural Instability

Diagnosis
2 yr

Frail “in situ”: mean 10 years

With Complications (PD-D)

Aspecific non-motor symptoms, specific in the geriatric setting
- Memory Impairment
- Sleep Disorder
- Acute Delirium
- Nocturia
- Dysphagia with pneumonia

> 1 yr

Frail: mean 10 years

ADL-Disability: mean 7 years

F. Lauretani et al. / Archives of Gerontology and Geriatrics 54 (2012) 242-246
# Parkinson’s Disease: A New Multidisciplinary Approach for this Old Actor

## Braak’s Stage 1-2
- **✓ locus coeruleus**
- **✓ dorsal IX/X nucleus**

### Clinical Symptoms
**Premotor Phase:**
- Hyposmia
- Constipation
- Depression
- Articular pain
- Fatigue
- Orthostatic hypotension

## Braak’s Stage 3-4
- **✓ mesocortex**
- **✓ substantia nigra**
- **✓ locus coeruleus**
- **✓ dorsal IX/X nucleus**

### Clinical Symptoms
**Clinically Evident (PD):**
- Bradykinesia (plus at least)
  - Rigidity
  - Tremor
  - Postural Instability

## Braak’s Stage 5-6
- **✓ neocortex (sec. & prim.)**
- **✓ neocortex association**
- **✓ mesocortex**
- **✓ substantia nigra**
- **✓ locus coeruleus**
- **✓ dorsal IX/X nucleus**

### Clinical Symptoms
**With Complications (PD-D):**
- Memory Impairment
- Sleep Disorder
- Acute Delirium
- Nocturia
- Dysphagia with pneumonia

---

F. Lauretani et al. / Archives of Gerontology and Geriatrics 54 (2012) 242-246
Diagnosis

• No biologic marker to confirm the diagnosis
• Underdiagnosis and incorrect diagnosis are common
• Classic signs and symptoms - tremor, rigidity, bradykinesia and postural instability
• Best differentiate from other parkinsonisms by:
  – Asymmetry
  – Resting tremor
  – Good response to levodopa
UK Parkinson’s Disease Society clinical criteria

• Step 1
  Bradykinesia
  At least one of the following:
  - Rigidity
  - 4-6 Hz rest tremor
  - Postural instability not caused by primary visual, vestibular, cerebellar or proprioceptive dysfunction
UK criteria

- Step 2
  Exclude other causes of parkinsonism
- Step 3: at least 3 of the following criteria:
  Unilateral onset, rest tremor, progressive disorder, asymmetry primarily affecting side of onset, 70-100% response to levodopa, severe levodopa induced dyskinesia, levodopa response for 5 years or more, clinical course of 10 years or more.
Features suggestive of alternative diagnoses

- Dementia preceding motor symptoms
- In first 3 years: postural instability, freezing, hallucinations (not related to medication)
- Supranuclear gaze palsy (downward gaze)
- Severe symptomatic dysautonomia
- Documentation of plausible cause of parkinsonism (focal brain lesion, neuroleptic)
Conditions Misdiagnosed as Parkinson’s Disease

• Essential tremor
• Vascular parkinsonism
• Drug-induced parkinsonism
• Dementia with Lewy bodies
• Atypical parkinsonism (progressive supranuclear palsy, multisystem atrophy)
Tremor

- Resting tremor
- 4-6 Hz
- Prominent in hands
- Absent in 25%
# Tremor

## Parkinson’s disease
- Age at onset  55-75 yrs
- Family Hx +/-
- Frequency (Hz) 4-6
- Characteristics: Sup-pronation- asymmetric
- Rest -> increase
- Writing dec. (micrographia)
- Face, jaw, lips, chin

## Essential tremor
- 10-80 years
- Family Hx ++
- Hz 5-10
- Flexion-extension- symmetric
- Rest -> decrease
- Increases (tremulous)
- Head, voice
Rigidity

- Increased tone throughout range of motion
- Increases when limbs are moving
- By itself, not disabling
- Spasticity versus rigidity
Bradykinesia

• One of the more disabling symptoms
• Delay in starting all movements
• Slowness and poverty of movement
• Arrest of ongoing movements
Postural Instability

- Inability to maintain equilibrium
- Inability to react to abrupt changes in position
Modified Hoehn & Yahr Staging

- Stage 0 = No signs of disease
- Stage 1 = Unilateral disease
- Stage 1.5 = Unilateral plus axial involvement
- Stage 2 = Bilateral disease, no imbalance
- Stage 2.5 = Mild bilateral, recovery on pull test
- Stage 3 = Postural instability but independent
- Stage 4 = Severe disability; still able to walk
- Stage 5 = Wheelchair or bed bound.
Treatment of Parkinson’s Disease
Decision to Start Medical Therapy
(consider)

• Effect of disease on dominant hand
• Significant bradykinesia or gait disturbance
• Personal philosophy regarding drug use
• DEGREE TO WHICH DISEASE EFFECTS
  FUNCTION
Protective Therapy

• No proven treatment to slow progression
• Selegiline-ameliorated symptoms/question of increased mortality
• High dose Vitamin E ineffective
Symptomatic Therapy

- Levodopa remains the most effective treatment (Sinemet 25/100 TID)
  - Most patients benefit over the entire course of the illness
  - No evidence that it accelerates the neuro-degenerative process
  - Increases life expectancy
  - Survival reduced if drug is delayed until greater disability
Symptomatic Therapy

- Anticholinergics (Artane 0.5-1 mg BID)
- Amantadine (100 mg BID)
- Selegiline (5 mg BID - last dose mid-day) (rasagiline 1 mg daily)
  - All have mild to moderate benefit, but levodopa or dopamine agonists are required as disability progresses
- Tolcapone (COMT inhibitor) 100 mg TID monitor LFT’s
Symptomatic Therapy

Dopamine agonists

- May provide inadequate benefit (1/3 of patients have good responses)
- Always require supplementary levodopa but may be adequate alone for two to five years
- Infrequent fluctuations and dyskinesias

“I take three blues at half past eight to slow my exhalation rate.
On alternate nights at nine p.m.
I swallow pinkies. Four of them.”
Figure Legend:
Cumulative probability of reaching the first dopaminergic complication (A) and the individual complications wearing off (B), dyskinesias (C), and freezing (D) by treatment assignment. First dopaminergic complication is defined as the first occurrence of wearing off, dyskinesias, or on-off fluctuations.
Dopamine Agonists

Ergot-derived (lung and cardiac valve fibrosis)

- Bromocriptine 20-40 mg/day

Non-Ergot-derived (as first-line and adjunctive therapy)

- Ropinirole up to 24 mg/day, divided TID or SR
- Pramipexole up to 4.5 mg/day, divided TID or SR
- Rotigotine up to 6 mg/24 hr patch
Late Stage Problems (Disease)

- Motor-dysarthria, freezing of gait, postural instability with falls
- Nonmotor-dysautonomia, weight loss, pain, changes in mood or behavior, sleep disturbance, cognitive dysfunction, dementia
Late Stage Problems (Treatment and Disease)

Motor fluctuations: (in 70% treated for 15 years)
  • Wearing off of drug effect
  • On-off phenomenon

Dyskinesia: (may respond to amantadine)
  • Peak-dose dyskinesia
  • Diphasic dyskinesia
  • Off-period dystonia

Psychiatric disturbances - vivid dreams, visual hallucinations, mania, hypersexuality, paranoid psychosis
Surgical Candidate
Surgical Therapy

• Reserved for disabling, medically refractory symptoms
• Ventrointermediate thalamic nucleus lesions reduce contralateral arm tremor by 80%
• Pallidotomy - 80% improvement in contralateral drug-induced dyskinesia (akinesia, rigidity and tremor reduced)
• Stimulation of subthalamic nuclei-benefits all aspects of parkinsonism
Deep Brain Stimulation

• For intolerable dyskinesias or motor fluctuation while on levodopa
• Appropriate candidates have cognition relatively intact and are less than 70 yrs old.
• Benefit: reduction in levodopa dose, improvement in off-medication function and reduced dyskinesias when taking medication.
• Risks: depression, decreased verbal fluency, increased falls and impulsivity.
Fetal Cell transplantation

- 2 patients
- Intrastriatal grafts of human fetal ventral mesencephalic tissue (dopaminergic neuroblasts)
- Assessed 15 & 18 years post graft.
  * motor gains over first yr. sustained 18yrs.
  * patient remained off dopaminergic drugs.
Kefalopoulou Z et al, JAMA Neurol. 2013.4749
Non-Medical Functional Assistance
Support Services

• Usual Elder Services

• Specific Disease Oriented Organization  

• Physical therapy – disability improves

• Occupational therapy- in home interventions

• Speech therapy- intensive therapy for 2 week can improve voice problems and gain may last up to 3 months.
Assisted Devices
Recommendations for Practice

• Carbidopa/levodopa, nonergot dopamine agonists, or MAOB-I for initial treatment.
• Nonergot dopamine agonists, COMT-I or MAOB-I added to levodopa to treat motor complications.

• Consistent, good-quality patient-oriented evidence.
Recommendations for Practice

• Amantadine for dyskinesias in advanced disease.
• Deep brain stimulation for functional impairment despite optimal medical tx.
• PT to improve gait and speech therapy to improve speech volume.
• Inconsistent patient-oriented evidence.
Recommendations for Practice

• Physicians with limited experience should refer patients to confirm diagnosis.
• OT may help patients maintain family, social and work roles, continue ADLs and improve safety.
• Consensus, usual practice, expert opinion, case series.
Dementia and Depression

Caregiver burden  Isolation and Loneliness
Diagnosis

2 yr > 1 yr

Premotor Phase Clinically Evident (PD) With Complications (PD-D)

Aspecific non-motor symptoms:
• Hyposmia
• Constipation
• Depression
• Articular pain
• Fatigue
• Orthostatic Hypotension

Specific motor symptoms:
• Bradykinesia (plus at least)
• Rigidity
• Tremor
• Postural Instability

Aspecific non-motor symptoms, specific in the geriatric setting
• Memory Impairment
• Sleep Disorder
• Acute Delirium
• Nocturia
• Dysphagia with pneumonia

Frail “in situ”: mean 10 years
Frail: mean 10 years
ADL-Disability: mean 7 years

F. Lauretani et al. / Archives of Gerontology and Geriatrics 54 (2012) 242-246
References


Screening Tests

- University on Penn Smell Identification Test (UPSIT)- (questionable accuracy)
- SPECT
- PET – (expensive)
- Genetic tests – parkin gene (small fraction of PD)
- Dopamine transporter scan (DaT scan) essential tremor vs PD
- Voice change.