Intro to Parkinson's Disease

Justin P Martello, MD
Christiana Care Neurology Specialists
Newark, DE
Objectives

- Current epidemiology of PD
- Brief pathophysiology
- Criteria for the diagnosis of PD
- Medical management updates
- Future Directions of Therapy
What is PD?

- Neurodegenerative disease
- Attacks dopamine producing cells in substantia nigra in the brain
- Causes slowness, stiffness, tremors, balance impairment
  - And much more...
PD Epidemiology

- PD affects ~ 1-2/1000
  - 1% over 60
- annual incidence of 4–20 per 100,000
- rising prevalence with age
  - ~Average life expectancy
- 2011 University of Delaware Study:
  ~2000 in DE
PD Epidemiology

- ~1 million in USA: > multiple sclerosis, muscular dystrophy and ALS combined
- ~60,000 Americans dx’d with PD each year
- >10 million worldwide
- Men: Women 1.5: 1

NPF Data 2016
Parkinsonism

- Bradykinesia
- Cogwheel rigidity
- Resting tremor (“pill rolling”)
  - (absent in ~20-30% with PD)
- Postural instability
  - (not at presentation in PD)

Most people with parkinsonism have PD.
Cognitive Impairment
Nightmares/vivid dreams
Insomnia
REM sleep behavioral disorder
Apathy
Depression, anxiety
Hallucinations/delusions

Blurred vision
Anosmia
Hypophonia/dysarthria
Drooling, nasal drip
Dysphagia
Orthostatic hypotension
Constipation
Gastroparesis
Erectile dysfunction
Urinary incontinence

Bradykinesia
Rigidity
Tremors
Fatigue
Dystonia
Gait and balance impairment

The PD Body
Cognitive Impairment
Nightmares/vivid dreams
Insomnia
REM sleep behavioral disorder
Apathy
Depression, anxiety
Hallucinations/delusions

Fatigue
Dystonia

Blurred vision

Anosmia

Hypophonia/dysarthria
Drooling, nasal drip
Dysphagia

Orthostatic hypotension

Constipation
Gastroparesis

Erectile dysfunction
Urinary incontinence

Bradykinesia
Rigidity
Tremors
Fatigue
Dystonia
Gait and balance impairment

The PD Body
### Additional Motor Features of Parkinsonism

- Decreased arm swing while walking
- Micrographia (small handwriting)
- Decreased blink rate and facial expression (hypomimia)
- Shuffling gait
- Difficulty arising from a chair, car, or turning in bed
- Soft, monotone voice (Hypophonia)
- Freezing
- *En bloc* turning
- Flexed posture
- Festination
- Drooling
How accurate is the clinical diagnosis of PD?

- 35% incorrect at initial diagnosis
  - Rajput AH. Can J Neurol Sci 1991
- 24% incorrect at final diagnosis

How well do movement disorders specialists do?
MDS Clinical Diagnostic Criteria

- **Bradykinesia** (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive actions)
- And at least one of the following:
  - Muscular rigidity
  - 4-6 Hz rest tremor
Ancillary Testing

- CT or MRI is not necessary in “typical” (most) cases of PD
- DA transporter imaging (DaT scan) is not necessary!
  - Only FDA indication to distinguish PD tremor from ET
  - Cannot be used for disease severity or prognosis
  - Can help with drug-induced parkinsonism, vascular parkinsonism, NPH, psychogenic
  - DaT scan cannot distinguish PD from a parkinsonian syndrome due to nigrostriatal degeneration (PSP, MSA, CBD, LBD)
- Insurance issues…
Marked asymmetry of dopamine loss is a hallmark of early Parkinson’s Disease.
Early, Typical PD
Atremulous PD
“Pseudo-hemiplegic PD”
Progression and Prognosis

- **Early disease**
  - Smooth, extended response
  - Absent or infrequent dyskinesia

- **Moderate disease**
  - Plasma Levodopa Concentrations
    - Diminished duration
    - Increased incidence of dyskinesia

- **Advanced disease**
  - Short, unpredictable response
  - OFF times
  - “On” time is associated with dyskinesias
1. MAO-B Inhibitors
   - Rasagiline (Azilect)
   - Selegeline
   - Safinamide (Xadago)

2. Dopamine Agonists
   - Ropinirole (ReQuip)
   - Pramipexole (Mirapex)
   - Rotigotine (Neupro)

3. COMT Inhibitors
   - Entacapone (Comtan)
   - Tolcapone

4. Levodopa (Carbidopa/Levodopa)- Sinemet IR/CR, Rytary, Duopa, Inbrija

5. Others: Amantadine (Gocovri), trihexiphenidyl (Artane), apomorphine (Apokyn)
Medical Marijuana and PD

- FDA approved in PD with painful spasms
- Not an exact science…
- No long term risk data… dementia?
- Not a miracle cure, no thanks to FB
- Insurance does not cover; ≈ $60-80/wk
Therapy Updates since 2015

- Duopa (pimavanserin) 04/’15
- Nuplazid (pimavanserin) 08/’16
- Focused Ultrasound for Essential Tremor and PD tremor 08/’16
- Xadago (safinamide) 04/’17
- Gocovri (Amantadine ER) 08/’17
- Inbrija (inh levodopa) 01/’19
- Abbott St. Jude DBS 11/’16
- Boston Scientific DBS 12/’17
- Nourianz (istradefylline) 12/’17
Advanced Therapy Management
St. Jude Abbott Directional Lead System
Levodopa Intestinal Gel Infusion (DUOPA)
Physical Therapy

- Balance training
- Teaches adaptive strategies
- Trains in the use of assistive devices
- Methods/cues to break freezing
- PD experience is important!
Speech Therapy

• LOUD technique proven to be the one helpful method to improve hypophonia in PD
• Need to keep up with exercises
• Audio cues and more recently singing to oneself can help break freezing of gait
Nutrition and Supplements

• No proven supplements are helpful except melatonin for sleep and RBD

• Mediterranean diet
  – helpful for brain health
  – ward off dementia
  – No diet specific for PD

• The protein issue…
Wearable Technologies

• Analyzing gait, fall risk, exercise relationships
• Feasibility?
• Costs?
• Adherence?
The Future for PD

• New levodopa delivery systems (e.g. inhalers, subcutaneous pumps, patch systems)
• True disease modifying therapy (e.g. Nilotinib, GLP-1 agonists, stem cells)
• Blood markers for PD and other parkinsonian plus syndromes
• FUS (MRI-guided focused ultrasound)