An Overview of Parkinson’s Disease

Rebecca Thompson, MD
Assistant Professor of Neurology
Epidemiology of PD

• 2\textsuperscript{nd} most common neurodegenerative disorder after Alzheimer’s
• 1-2% of the population over 60 years (increasing over time)
• Combination of genetic and environmental components
• Lower risk of PD associated with coffee/tea consumption, smoking and alcohol
• Higher risk of PD with well-water, herbicide/pesticide exposure, welding and agent orange exposure
Research from WashU epidemiological study of PD in the US. Reviewed 36 million Medicare records representing 98% of the US population over age 65.
PD basic reminders

• Decreased dopaminergic cells in the Substantia nigra in midbrain

• Less dopamine leads to less movements

• PD is a hypokinetic movement disorder

• Symptom treatment is commonly aimed at replacing dopamine
4 Cardinal Features of PD

• Tremor
• Bradykinesia
• Rigidity
• Postural instability
Tremor in PD

• Present at rest
• Goes away or improves with action
• Usually worse on one side
• Usually thumb involvement
• sitting with eyes closed and perform mental exercises may bring out a very mild tremor
• Worse when nervous, tired or excited
Bradykinesia

- Not just slowness
- Also irregularity and decreasing amplitude
- Many maneuvers to elicit symptoms
- Usually worse on one side
- Includes hypomimia, dry eyes and drooling
Rigidity

• Classically described as “cogwheel”
• Check multiple joints at once with rotational movement
• Usually worse on one side
• May need to activate contralateral side to feel
Postural instability

• Lose ability to reflexively catch self
• Assessed with pull test
• Major cause of falls and loss of mobility
Other common gait problems

• Freezing of gait
• Tripping over low objects
• Slowing of gait
• Asymmetric arm swing
Different flavors of idiopathic PD

“idiopathic” = regular/run of the mill

• Akinetic rigid (may not have any tremor at all)
• Tremor predominant
• Some genetic cases have particular characteristics
• Gait may be the primary issue in some cases
Red flags that this is not idiopathic PD

- Early falls
- Very symmetric symptoms
- Early dementia (within 1-3 years)
- Autonomic dysfunction
- Eye movement problems
- Unresponsive to typical PD meds
- Abnormal brain imaging findings
- Abnormal lab findings
- Use of antipsychotics
Hoehn and Yahr Staging

1. Symptoms on one side of the body only
2. Bilateral symptoms; no balance impairment
3. Impaired postural reflexes; physically independent
4. Severe disability, yet still able to walk or stand unassisted
5. Wheelchair bound or bedridden

Increasing Disability; Decreasing Independence
Non motor symptoms in PD

Braak stages 1 and 2
Autonomic and olfactory disturbances

Braak stages 3 and 4
Sleep and motor disturbances

Braak stages 5 and 6
Emotional and cognitive disturbances

Via olfactory bulb
Via vagus nerve
Premotor symptoms
Motor symptoms

Brainstem Lewy body
Cortical Lewy body
Sleep disturbances

• Unable to fall or stay asleep
• Day time sleepiness
• Sundowning
• REM behavior sleep disorder
Sleep disturbances

• PD patients may not respond well to typical sleep aids
• Avoid benadryl or “PM” versions of OTC meds
• Avoid zolpidem etc.
• First line should be melatonin (taken 2-3 hrs before desired bedtime)
• Second line clonazepam (especially useful for RBD)
Constipation

• A “regular” complaint in PD patients
• Often precedes PD motor symptoms
• Theories that PD starts in the gut
• Standard recommendations apply:
  • Increase H2O
  • High fiber
  • Miralax and stool softeners before stimulants
  • Severe cases may require referral to GI
Dementia

- About 30% of PD patients develop dementia
- Dementia within first year of motor symptoms is a red flag
- Common complaints of word finding or multitasking difficulty
- Neuropsych testing may be useful for pattern of deficits
- At least annually should have in office screening
- Family is usually the most helpful in identifying problems
- Consider driving safety and any use of heavy equipment
Treating dementia in PD

• Consider exacerbation from current meds
• Acetylcholinesterase inhibitors first line
  • Donepezil, rivastigme, galantamine
• Memantine (often added in AD when symptoms become moderate) has not been shown to be efficacious in PD
• Participation in brain teaser type activities “active mind” and maintaining social connections is also important
Hallucinations

- Presence hallucinations and well formed visual hallucinations
- Having hallucinations = PD psychosis
- Always consider medication effects first
- Taper off dopamine agonists, amantadine, artane first
- Sinemet and MAO-B inhibitors less common culprits
- Pimavanserin (Nuplazid) was approved May 2015, FIRST LINE
- Second line: seroquel
Hallucinations

• Absolutely no Haldol EVER in PD patients!!!

• Haldol and other typical antipsychotics block dopamine and can severely worsen PD symptoms causing neuro malignant syndrome
Autonomic dysfunction

• Dizziness on standing, urinary symptoms and sexual dysfunction
• Bring these issues up with you physician!
• Formal autonomic reflex screen may determine severity
• Severe autonomic dysfunction may be suggestive of multiple systems atrophy
• Treat symptomatically
Autonomic dysfunction

• Symptomatic treatment
• Compression stockings and increased fluids for orthostatic hypotension (OH)
• Droxidopa (Northera), midodrine, florinef for persistent OH
• Urinary exercises may be useful (available by online search)
• Typical medical treatment for ED but with reminder that these meds may worsen dizziness
• Referral to specialist may be needed
Common Medications for PD

• Current medication options are for symptom treatment only
• We do not have any medication to slow disease progression
Levodopa

- Carbidopa/levodopa IR and Carbidopa/levodopa CR
- Rytary
- Levodopa intestinal gel
- Inhaled levodopa
- Future subcutaneous levodopa pump

- Nausea, dizziness, orthostatic hypotension, dyskinesias
- May improve or worsen gait, dystonia, cognition
Dopamine agonists

• Pramipexole
• Ropinirole
• Rotigotine

• Impulse control disorders, hallucinations, swelling
MAO-B Inhibitors

- Rasagiline
- Selegiline
- Salfinamide (new)

- Many physicians believe this class of medication may slow the progression of Parkinson’s disease but the evidence is weak
Exercise and Physical Therapy

• Exercise MAY slow the progression of PD!!!
• Physical activity is extremely important in PD
• Delay the disease, LSVT Big&Loud programs, Rock steady
Advanced PD

- more motor complications and fluctuations
- Roller coaster ride of motor symptoms
- Failed medication doses
- Worsening mobility

- Basically routine care is not providing acceptable quality of life
Goals for advanced PD patients

• Maintain independence
• Maintain mobility
• More ON time without troublesome dyskinesias
• Less OFF
• Smooth out motor symptoms

• Rytary, Deep Brain stimulation, Levodopa Intestinal gel
Deep Brain Stimulation

Note: Wire and electrodes are under the scalp.
Carbidopa/Levodopa intestinal gel

**Positives**
- Less invasive than DBS
- Quick recovery
- May be better for in case of dementia
- Continuous drug delivery
- Improves motor fluctuations

**Negatives**
- Large
- Complications from insertion
- Must keep supply refrigerated
- Vitamin deficiencies?
- Peripheral neuropathy?
- Levodopa side effects
Ongoing research for stopping disease progression

- Uric acid levels (SUREPD study)
- DBS and disease progression, DBS for early onset PD
- Immunotherapy
- Isradipine