Parkinson’s Disease

Update for the Primary Care Provider

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No disclosures

History of Parkinson’s
Parkinson's Disease
Background

• Parkinson's disease is the second most common neurological disorder after Alzheimer's disease.
• About 1 million people in the US and 5 million worldwide are affected by Parkinson's disease.
• Normal age range is 45-75; the symptoms start (average age is 60).
• 5-10% of all cases diagnosed began before the age of 40.
• Risk of developing PD increases with age.
• Prevalence increases with age.
• Men and women are equally affected.
• All races are affected by Parkinson's disease.
• Parkinson's follows a chronic, slowly progressive course with severe disability in advanced stages.

Epidemiology

• Environmental risk factors
  • Rural living, well water
  • Pesticides, herbicides other toxins
  • Head trauma
  • Possibly Protective: Smoking, caffeine drinking
• Does it start in the gut?
• Genetic causes (5-10%)
  • Increasing number of Parkinson's genes identified
• Presumably, risk of getting Parkinson's involves genetic–environment interactions

DOPAMINE!

• Parkinson's is caused by a loss of dopamine-secreting neurons in the substantia nigra, which is in the basal ganglia.
What is happening in the brain?

- **What**: Reduced brain dopamine
  - Dopamine is a neurotransmitter found throughout the brain and nerves in the body
  - Dopamine supports normal movement
  - Dopamine producing brain cells likely become damaged by accumulation of an abnormal protein (Lewy bodies)

- **Where**: The area that is specifically abnormal in the brain is the substantia nigra. Over time, many other areas of the brain and body also become affected.

- **How**: Lewy bodies spread throughout the nervous system, progressively causing more nerve dysfunction.

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General vs Specialist Care

- Up to 70% of PD patients rely solely on a PCP for management of their disease
- One study reported that more PCPs (30%) than specialists (16%) didn’t offer patients as much information as they wanted
- Patients wanted to be more involved in decisions about managing their Parkinson’s disease

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How is Parkinson’s disease diagnosed?

- There is no single diagnostic test
- Most diagnoses are made exclusively via physical exam in the provider’s office by:
  - Identifying main motor symptoms
  - Asking about non-motor symptoms
  - Ruling out medical problems and medications that cause Parkinson’s like symptoms
  - Brain CT and MRI scans should look normal
  - Blood tests should be normal
- A T2 scan can differentiate PD from essential tremor although it is often not needed
Does my patient have Parkinson’s? Let’s start at the beginning.

Phenomenology/Appearance

- Observe and try to describe your patient’s movements:
  - Which body parts and movements are affected?
  - Hypo- or hyperkinetic movement?
  - Intermittent or persistent? Distractible?
  - Frequency and amplitude of movements?
  - Supersensible or not?
  - Variable or stereotyped?

Parkinsonism as defined by the Movement Disorder Society

*bradykinesia* in combination with rest tremor or rigidity, or both

These features must be clearly demonstrable and not attributable to confounding factors.

Parkinson’s is a HYPOKINETIC movement disorder

Motor features of Parkinson’s

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
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<tbody>
<tr>
<td>Resting Tremor</td>
<td>- 77% of patients</td>
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<td>- Almost always starts on one side of the body</td>
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<td>- “Pill-rolling” tremor in hands</td>
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<td>- Can involve lips, chin, upper or lower extremities</td>
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<tr>
<td>Bradykinesia</td>
<td>- 80-90% of patients</td>
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<td>- Most disabling symptom of PD</td>
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<td>Rigidity</td>
<td>- &gt;50% of patients</td>
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<td>- &quot;Cogwheeling&quot; or &quot;lead pipe&quot;</td>
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<tr>
<td>Postural Instability</td>
<td>- Indicative of advanced-stage Parkinson’s or a Parkinson’s variant</td>
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<td>- Frequent cause of falls</td>
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Rest Tremor

4- to 6-Hz (cycles per second) tremor in the fully resting limb, which is suppressed during the initiation of movement.

Bradykinesia

Slowness of movement AND decrement in amplitude or speed (or progressive hesitations/haits) as movements are continued.
Rigidity

* slow passive movement of major joints with the patient in a relaxed position and the examiner manipulating the limbs and neck.

* Rigidity refers to “leadpipe” resistance; that is, velocity-independent resistance to passive movement not solely reflecting failure to relax (this is different than spasticity).

Parkinsonism vs. Parkinson’s Disease

Does your patient have Parkinsonism?
If yes, we need to decide if he meets criteria for Parkinson’s Disease as the cause of this Parkinsonism.

Diagnosis of clinically established Parkinson’s disease requires:
1. Absence of absolute exclusion criteria
2. At least two supportive criteria
3. No red flags
Parkinsonism vs. Parkinson’s Disease

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Example of a RED FLAG:
A common cause of Parkinsonism

Treatment with a dopamine receptor blocker or a dopamine-depleting agent in a dose and timeframe consistent with drug-induced parkinsonism
Examples:
Risperidone
chlorpromazine (Thorazine)
olanzapine

Examples of Supportive Criteria

• Clear and dramatic beneficial response to dopaminergic therapy

• Presence of levodopa-induced dyskinesia
Other common Features

- constipation
- poor sense of smell
- Changes in walking/gait (shuffling, freezing, decreased arm swing)
- Micrographia (small handwriting)
- Soft and/or slurred speech (hypophonic dysarthria)
- Loss of facial expression - decreased blink
- sialorrhoea

Gait Videos

Putting it Together

The classic syndrome:
- Tremors-asymmetric at onset
- Rigidity (Stiffness)
- Akinesia/Bradykinesia
- Postural Instability (usually not an early sign)

= TRAP
Parkinson’s Differential Diagnosis

- Essential Tremor
- Secondary Parkinsonism secondary to stroke, tumor, carbon monoxide, neuroleptic medications
- Degenerative Parkinsonism (Parkinson’s Plus Syndromes):
  - Progressive supranuclear palsy (PSP): impairment in vertical eye movement, hyperextension of the neck, early falls (within first year), significant rigidity, poor levodopa response
  - Multiple system atrophy (MSA): prominent and early autonomic dysfunction, cerebellar signs, stridor
  - Corticobasal degeneration (CBD): dystonia, myoclonus, apraxia, alien limb phenomenon
  - Dementia with Lewy bodies: psychiatric symptoms early in disease course -- usually within the first two years

Something worth mentioning...
The Spectrum of Parkinson’s/Lewy body dementias

Motor symptoms for >3 years, hallucinations and cognitive problems

- Parkinson’s disease Dementia (PDD)
- Dementia with Lewy bodies (DLB)

Cognitive problems -- visual hallucinations with mild motor symptoms
Medications and Treatments for Motor Symptoms

- carbidopa-levodopa (Sinemet, Ryter)
- dopamine agonists (pramipexole, ropinirole, rotigotline)
- MAO B inhibitors (rasagiline/Azilect, selegiline)
- other (Amantadine, Extended Release Amantadine (Gocovri))
- Deep Brain Stimulation
- Duodonal levodopa infusion therapy (Duopa®)
- Exercise - 150 minutes per week!

Neuroprotection

- No medications or agents approved for neuroprotection
- Parkinson's Outcomes Study (The Parkinson's Foundation) tracked 2,940 people with Parkinson's over 2 years and found that those who exercised at least 2.5 hours per week are associated with better health-related quality of life and slower decline.

Treatment: Where do I begin?

Levodopa

- carbidopa/levodopa (Sinemet)
- "the most effective drug" for managing motor symptoms of Parkinson's
- Levodopa:
  - absorbed by the small intestine
  - travels through the blood to the brain
  - converted to dopamine
  - available in PR (immediate release and controlled-release) liquid, orally disintegrating tablets, Ryter, duodenal gel (these are not 1:1 dose interchangeable)
Levodopa is the GOLD STANDARD

Carbidopa/Levodopa, Rytary (extended release), Duopa (Intestinal levodopa)

- Preferred for patients over 65

- Adverse Effects
  - Nausea
  - Vomiting
  - Loss of appetite
  - Confusion
  - Hallucinations/Blurred vision
  - Decreased blood pressure
  - Lightheadedness
  - Dyskinesia

How to initiate therapy with carbidopa-levodopa

- CDLD 25 100 IMMEDIATE release - NOT CR or ER

- ½ tablet three times daily for a week at 8am 2pm 8pm [sample schedule]

- Then

- 1 tablet three times daily for a week – evaluate response

- Then if needed

- 1.5 tabs three times daily for a week

- Then if needed

- 2 tablets three times daily for a week

- Re-evaluate response to medications and refer to neurology for additional evaluation and treatment

Carbidopa-levodopa

- When levodopa is taken 30-60 minutes before a meal or 1-2 hours after a meal, many people notice an improvement in motor symptoms beginning after about 30 minutes.

- For most people with Parkinson’s the benefit of levodopa lasts about 3-5 hours

- The plasma half-life of levodopa is about 50 minutes, without carbidopa. When carbidopa and levodopa are administered together, the half-life of levodopa is increased to about 2.5 hours.

- Carbidopa allows people to use lower doses of levodopa and prevents nausea from levodopa

- Carbidopa inhibits peripheral metabolism of levodopa which allows a greater proportion of peripheral levodopa to cross the blood-brain barrier and improves central nervous system effect.
Dopamine Agonists:

- can be difficult to titrate
- **Adverse Effects**
  - sedation
  - sleep attacks
  - peripheral edema
  - impulse control disorders (shopping, gambling, hypersexuality)
  - confusion
  - hallucinations

⇒ Often initial treatment for younger patients with milder symptoms
HOWEVER they are not the same as carbidopa-levodopa

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**How to initiate therapy with a dopamine agonist**

- **Ropinirole Immediate release**
  - 0.25mg three times daily (every 8 hours) for a week
  - 0.5mg three times daily for a week
  - 0.75mg three times daily for a week
  - 1mg three times daily for a week
  - Then
    - 1.5mg three times daily for a week
    - 2mg three times daily for a week
    - 2.5mg three times daily for a week
    - 3mg three times daily for a week

DO NOT stop abruptly

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**How to initiate therapy with a dopamine agonist**

- **Pramipexole immediate release**
  - 0.125 mg three times daily for a week
  - 0.25 mg three times daily for a week
  - 0.5mg three times daily for a week
  - 1mg three times daily for a week
  - Max dose 1.5-4.5 mg per DAY

DO NOT stop abruptly
Response to dopaminergic therapy

- Bradykinesia and rigidity show the best response to levodopa
- Response of tremor to levodopa is variable
- Non-motor symptoms are usually resistant to levodopa therapy

Parkinson’s: It is not only motor features

<table>
<thead>
<tr>
<th>Non-motor features of Parkinson’s</th>
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<tbody>
<tr>
<td>Psychiatric disorders</td>
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<td>Cognitive disorders</td>
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<td>Sleep abnormalities</td>
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<td>Autonomic dysfunction</td>
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<td>Sensory dysfunction</td>
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<td>Miscellaneous</td>
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Managing Psychosis and Neurocognitive Changes in Parkinson’s

- Psychosis (such as visual hallucinations, delusions)
- Depression
- Anxiety
- Apathy
- Cognitive Impairment (from Mild Cognitive Impairment to Dementia)
Depression, Anxiety, Apathy

- Sometimes people get extremely anxious when cd/id is wearing off
- Don’t be shy about getting help from mental health providers
- Consider SSRIs which can also help with anxiety
  - citalopram
  - escitalopram
  - sertraline

Anxiety can be debilitating!
Consider:
- Buspirone for anxiety — need to weigh against potential adverse effects
- Clonazepam — need to consider and weigh against risk for falls
- Mental Health Counseling

Drugs to Avoid in Parkinson’s
eka drugs that block dopamine at the receptor

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<th>Alternate</th>
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<tr>
<td>pimozide (Periakor)</td>
<td>haloperidol (Haldol)</td>
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Avoid valproate acid (Depakene) if possible

Parkinson’s Disease Psychosis

- Hallucinations — need to consider if they are they bothersome to the patient or causing distress or safety concerns
- Delusions — same as above

Medications
- Pimavanserin (Nuplazid) – only medication approved for Parkinson’s psychosis
- Quetiapine (Seroquel) – usually at lower doses in Parkinson’s than in disease process like schizophrenia
  - all antipsychotics carry a black box warning for elderly patients who have DEMENTIA
  - Antipsychotics can cause QT prolongation
Cognitive Impairment

- Screening Tools
  - MOCA
  - MMSE
- Formal Neurocognitive Assessment ➔ Psychology
  - Helps tease out and better identify cause of impaired cognition/dementia such as Alzheimer’s, Frontotemporal Dementia, PD Dementia
  - Can also help identify depression and apathy and how they are impacting cognition

Managing Sleep Disturbances

- Video sleep study can be helpful to identify the source of the disturbance
  - REM Sleep Disorder
  - Comorbid Restless leg syndrome
  - Insomnia
  - Up to void?
- Consider melatonin ➔ research grade is most reliable (need to order it)
  - Start at 3-5mg 1-2 hours before bedtime ➔ use this routinely

Thoughts about medications and Parkinson’s Treatment

- Be deliberate and thoughtful and understand potential adverse reactions especially since this is primarily an older population AND since many medications can worsen Parkinson’s symptoms
- Stay in your wheelhouse ➔ if you need help, call.
- It’s OK to tell a patient you need to consult with experts before prescribing a medication
Parkinson’s Disease

What do the specialists have to offer?

- Individualized pharmacologic and non-pharmacologic management for motor and non-motor symptoms
- Access to and Knowledge of Resources
  - PPS/POST who specialize in Parkinson’s, support groups, education
- Advanced Treatments
- Guidance and co-management of complex issues

Parkinson’s – Surgical treatment

Deep Brain Stimulation (DBS)

High frequency electrical stimulation of brain structures via electrodes implanted deep in the brain

FDA approved for:
- tremor in 1997
- Parkinson’s disease in 2002
- dystonia in 2003

Intestinal Levodopa (Duopa)

Important Things to Remember

- Parkinson’s disease has common themes BUT the disease isn’t the same for everyone
- Different people are impacted differently—of you have seen one patient with Parkinson’s, you have seen one patient with Parkinson’s
- We (all of us in this room) are a team whose goal is to provide excellent care
Game Time...

Parkinson’s
or
Something Else???
Our Movement Disorder Clinical Team

- Kathryn LaFaver, MD
- Victoria Holiday, MD
- Laura Dixon, DNP, APRN
- Shelly Gates, RN
- Kelly Bickett, RN
- Albertine Fabi, MA
- Sandra Simmons, Receptionist

http://www.ucip.org