



Diagnosis and Treatment of Parkinson's Disease

MARA SEIER, MD

ASSISTANT PROFESSOR UNMC NEUROLOGICAL SCIENCES

MOVEMENT DISORDER DIVISION



UNIVERSITY OF
Nebraska
Medical Center

How is Parkinson's Disease Diagnosed?

How is PD diagnosed?



- ▶ A **clinical diagnosis** by a Neurologist or a Movement Disorder Neurologist
- ▶ There is not one specific test to diagnose PD
- ▶ Your doctor should ask you about your symptoms
- ▶ Your doctor should do a thorough neurological exam
 - ▶ Including watching movements of face, upper and lower extremities, strength, reflexes, sensation and walking

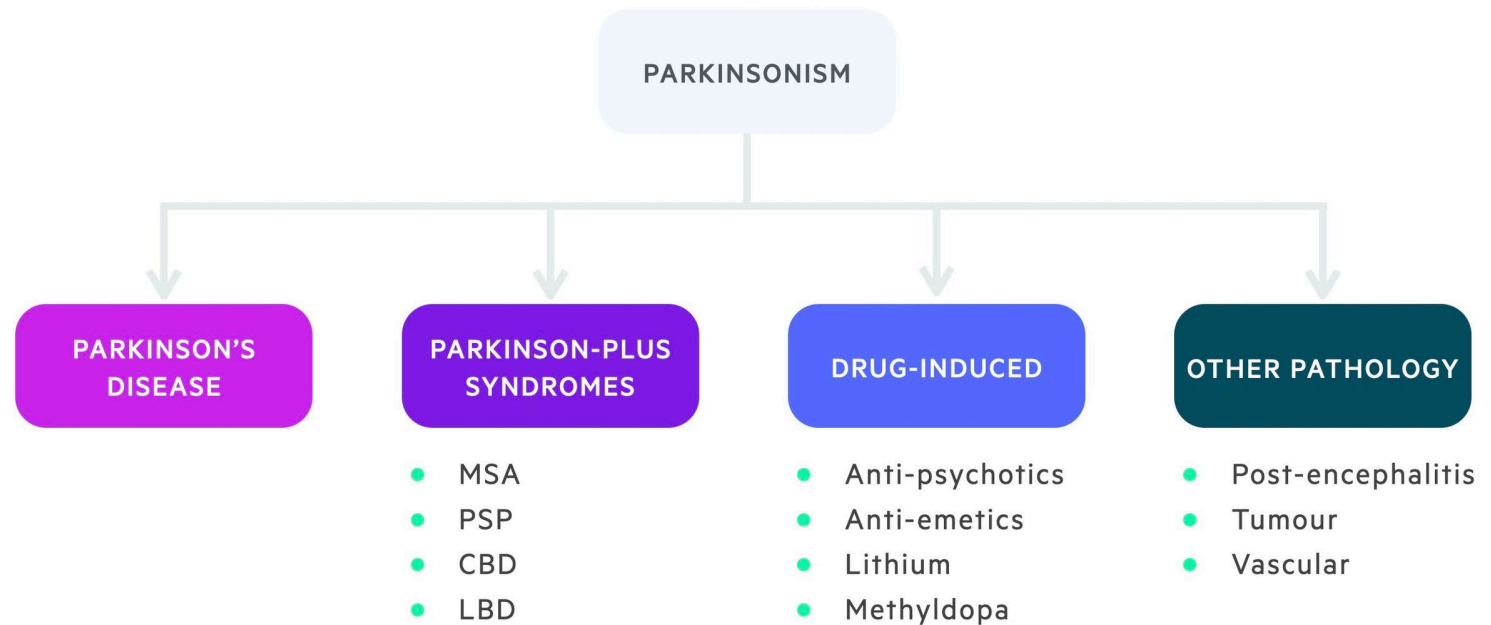
Parkinsonism

- ▶ **Bradykinesia** – slowness of movement, decreased amplitude, hesitation and halted movement
- ▶ Rigidity – stiffness felt when major joints are moved passively
- ▶ Rest Tremor – a tremor seen when hand/leg are fully at rest



▶ An “umbrella” term describing certain signs on exam

▶ Can have many causes



Ways that Parkinson's motor symptoms can manifest

- ▶ Smaller handwriting
- ▶ Reduced volume of voice
- ▶ Less facial expression
- ▶ Slowing down of everyday activities
- ▶ Issues with dexterity
- ▶ More difficulty rolling over in bed; getting up from a chair
- ▶ Reduced arm swing with walking
- ▶ Shuffling gait and stooped posture
- ▶ Tremors – both resting and during action
- ▶ Drooling
- ▶ Stiffness in the joints
- ▶ Cramping/curling of feet/toes

Not everyone will have the same type of symptoms; for example, 30% of PD patients do not have tremor!

Symptoms that may also occur in PD

- ▶ Loss of sense of smell
- ▶ Autonomic symptoms: Constipation, Drop in blood pressure upon standing (dizziness), Urinary urgency or frequency, Sexual dysfunction
- ▶ Sleep issues: Insomnia, Daytime sleepiness, Rapid Eye Movement (REM) sleep behavior disorder
- ▶ Psychiatric issues: Depression, Anxiety, Hallucinations or Paranoid thoughts
- ▶ Cognitive changes: Slowness in thinking, Memory changes, Difficulty with multi-tasking
- ▶ Drooling
- ▶ Fatigue
- ▶ Pain

Non-Motor Symptoms
of PD

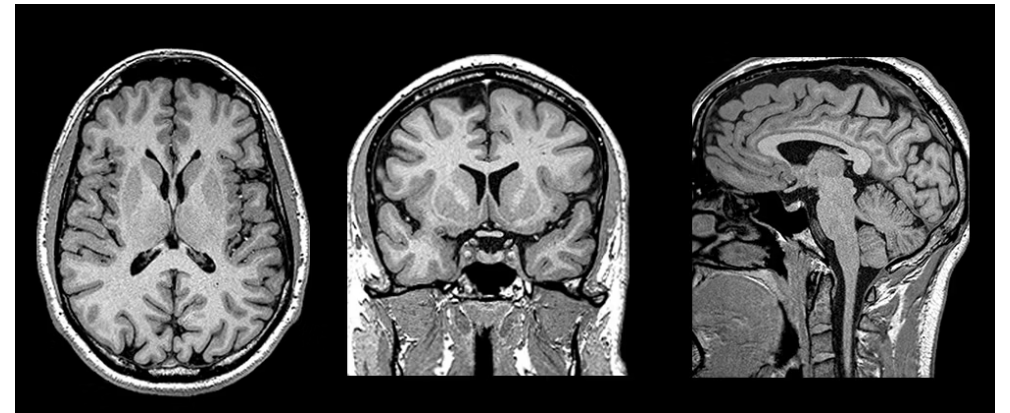
Tests your doctor may order



- ▶ Routine blood tests
 - ▶ Complete blood count
 - ▶ Metabolic panel
 - ▶ Thyroid function tests
 - ▶ Vitamins levels: B1 (thiamine), B9 (folate), B12, Vit D
 - ▶ Inflammatory/Rheumatologic markers
 - ▶ Infectious causes: Syphilis
 - ▶ Copper and copper storage markers

Tests your doctor may order

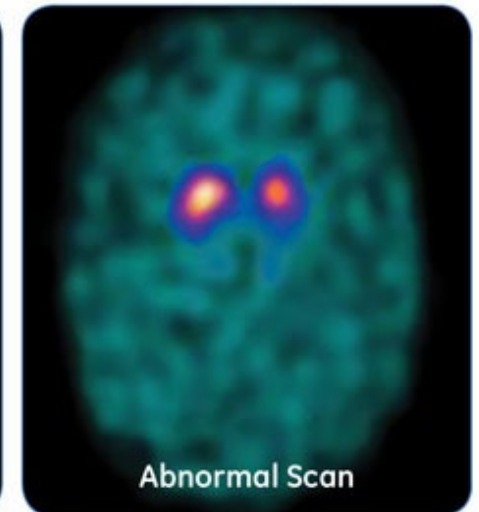
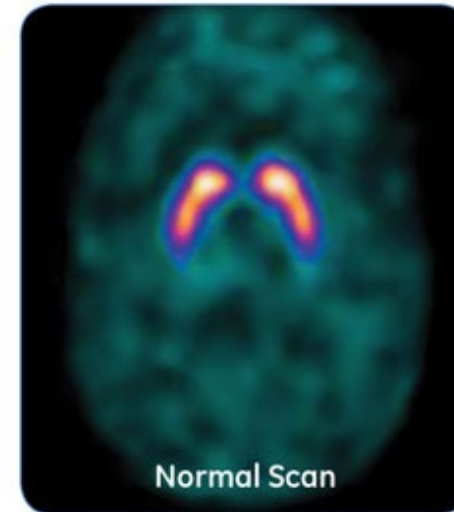
- ▶ MRI of the brain
- ▶ These tests are not necessarily done to “detect” Parkinson’s Disease but to rule out other mimics or conditions that could be contributing to symptoms



Tests your doctor may order

▶ DaTscan

- ▶ A radioactive tracer is given that labels dopamine transporters which are found in a part of the brain called the “striatum”
- ▶ A healthy dopamine system has normal uptake of signal; whereas the signal in a brain with neurodegenerative parkinsonism is abnormal

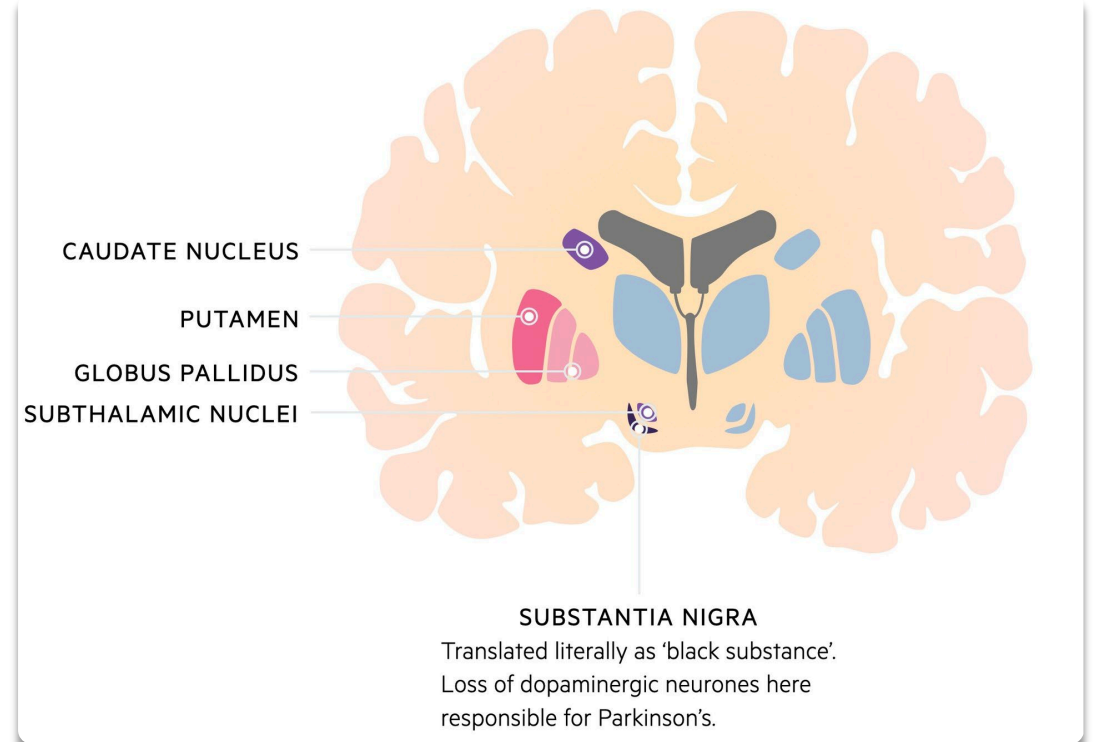


NOT essential for making the diagnosis of Parkinson's disease
False positives and false negatives can occur!

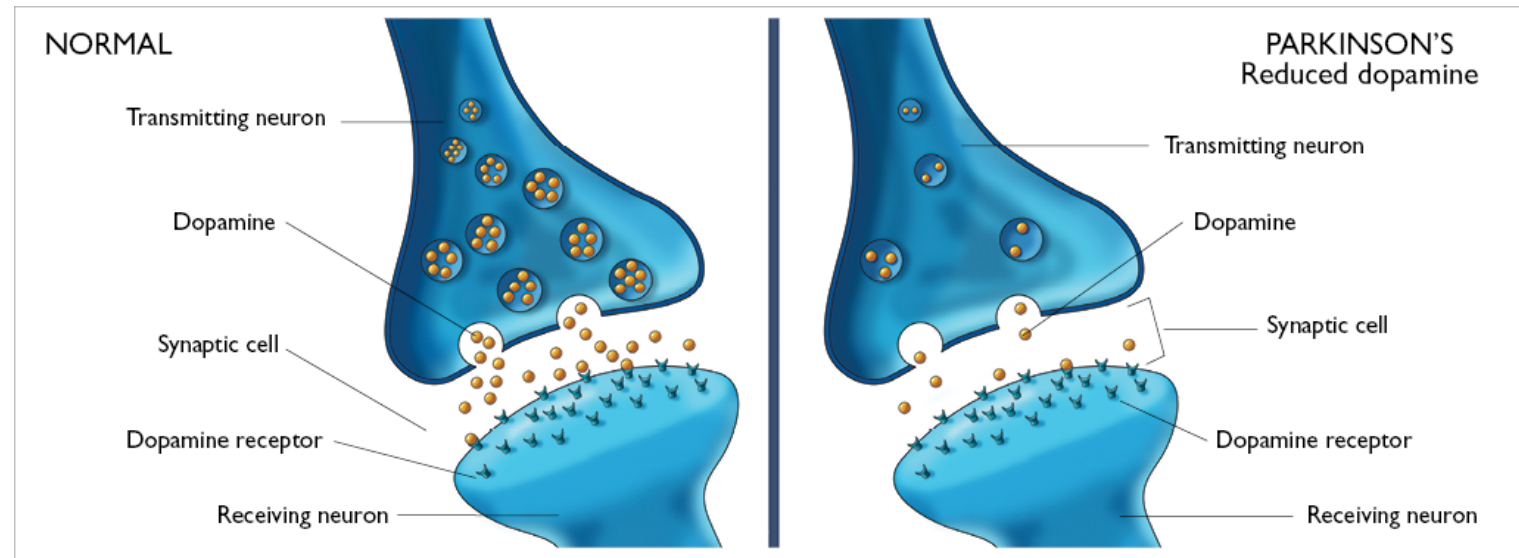
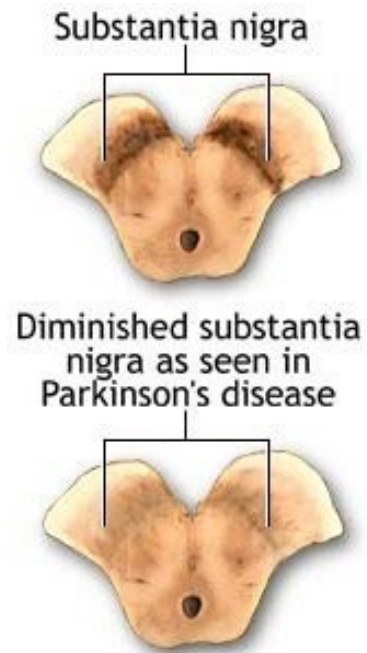
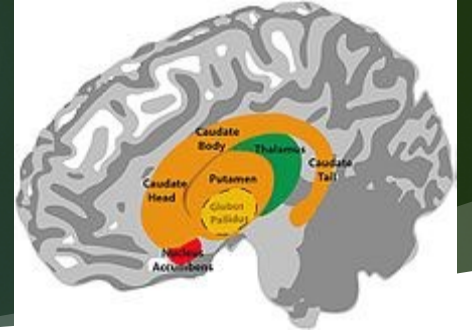
What causes Parkinson's
Disease?

What causes Parkinson's Disease?

- ▶ Chronic, progressive condition that occurs secondary to loss of brain cells (neurons) that produce **dopamine**
 - ▶ These neurons are found within the substantia nigra
- ▶ **Dopamine** is a chemical (neurotransmitter) that the brain uses to regulate movement



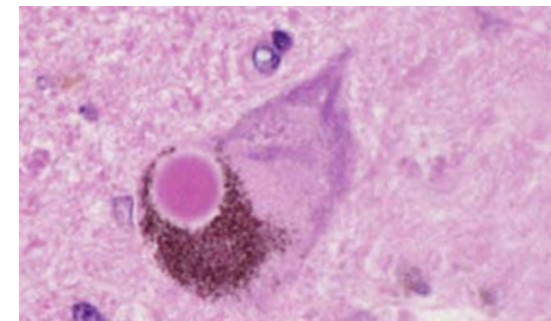
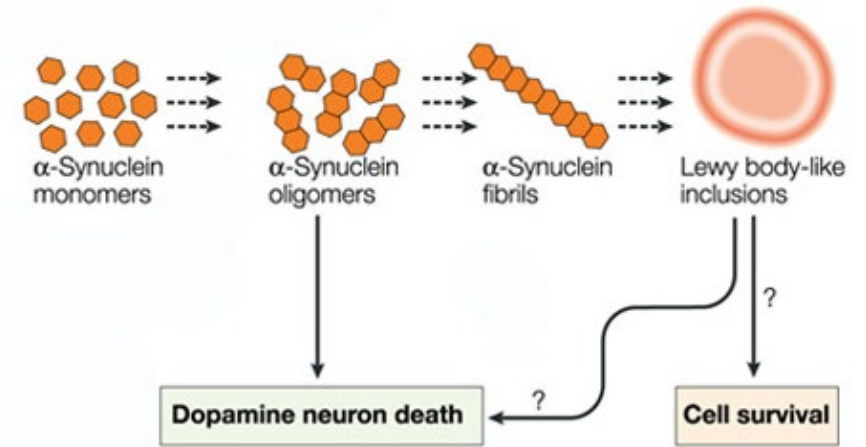
Loss of dopamine...



Results in loss of movement

What causes PD?

- ▶ **Alpha-synuclein** is a protein normally found in neurons (brain cells)
- ▶ For reasons we do not yet understand, in brains of people with PD it accumulates and forms clumps in neurons
- ▶ These abnormal clumps within neurons are called **Lewy Bodies**
- ▶ **Abnormal α -syn is also found in other parts of the body**



Lewy Body

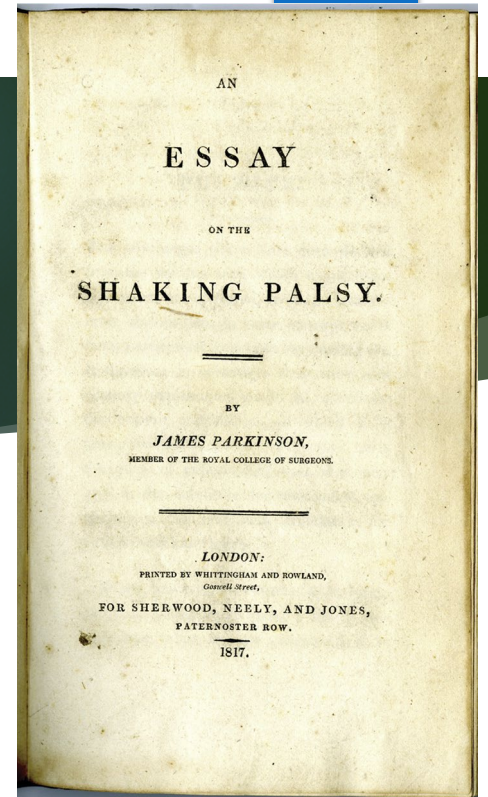
Blood test for PD?

- ▶ We are getting closer to having a blood test that may be capable of identifying alpha-synuclein
 - ▶ Seed amplification assay
- ▶ This testing has also been studied on cerebral spinal fluid, but does require getting a spinal tap (lumbar puncture)
- ▶ **Not currently available** – still needs more studies until is it available
 - ▶ Still not good enough to detect in EVERYONE that has PD (false negative)
 - ▶ Still not reliable enough to be the only way to diagnose PD (false positives)

What causes PD?



- ▶ The cause of Parkinson's disease is **unknown**
- ▶ **James Parkinson** described the disease in 1817; 200 years later we are still not sure
- ▶ Likely a combination of factors involved

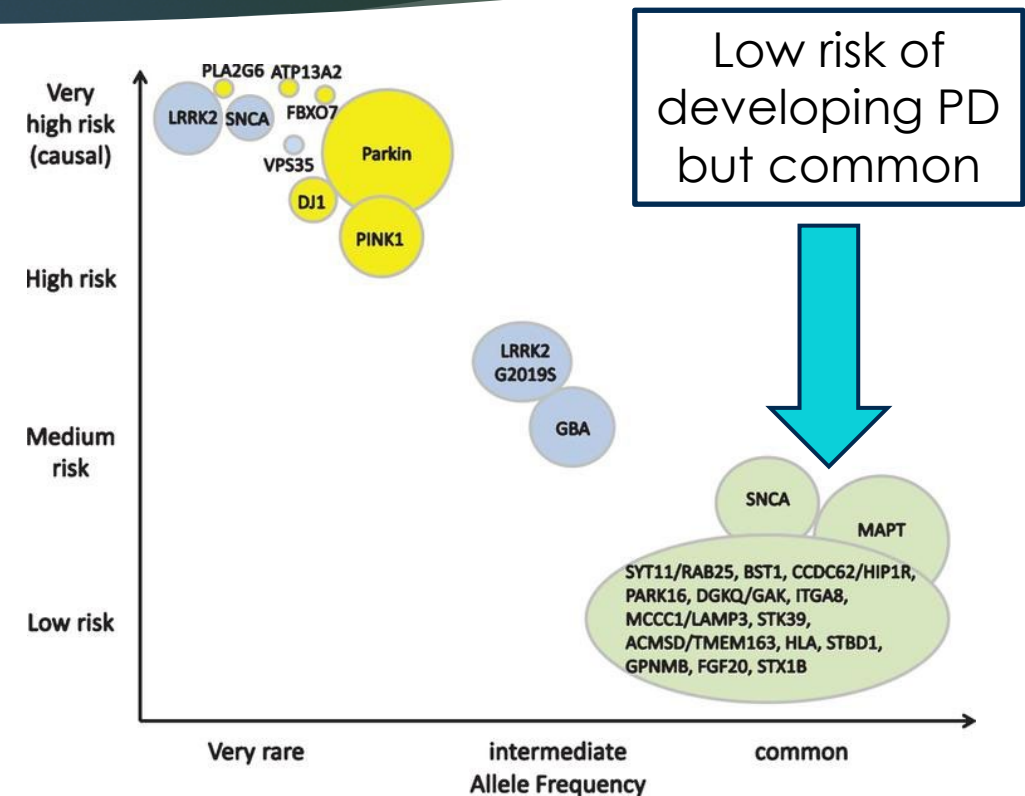


What causes PD?

High risk of developing PD but rare

Genetics

- ▶ Still in the “early stages” of our understanding
 - ▶ Genetic causes of PD only discovered within the past 20 years
- ▶ 90% of patients do not have gene mutation known to cause PD
 - ▶ In the 10% of patients with a gene mutation; their children and other family members have an increased risk of developing Parkinson’s Disease



The graphic features a dark green background with a light blue rectangular area in the center. The text 'PD GENERation: Mapping the Future of Parkinson's Disease' is written in white and light blue. The Parkinson's Foundation logo is at the bottom left of the light blue area. A vertical light blue bar with a white dot pattern is on the right side of the light blue area. A solid blue vertical bar is on the far right of the dark green background.

PD GENERation:
Mapping the Future
of Parkinson's Disease



- ▶ **PD GENERation** – a national initiative that offers genetic testing for clinically relevant Parkinson's related genes and genetic counseling at NO cost for people with PD
 - ▶ Can be done at home through a telemedicine appointment and at-home cheek swab collection kit
 - ▶ Tests for 7 most common causes of genetic-PD

PD GENERation: **Mapping the Future** **of Parkinson's Disease**



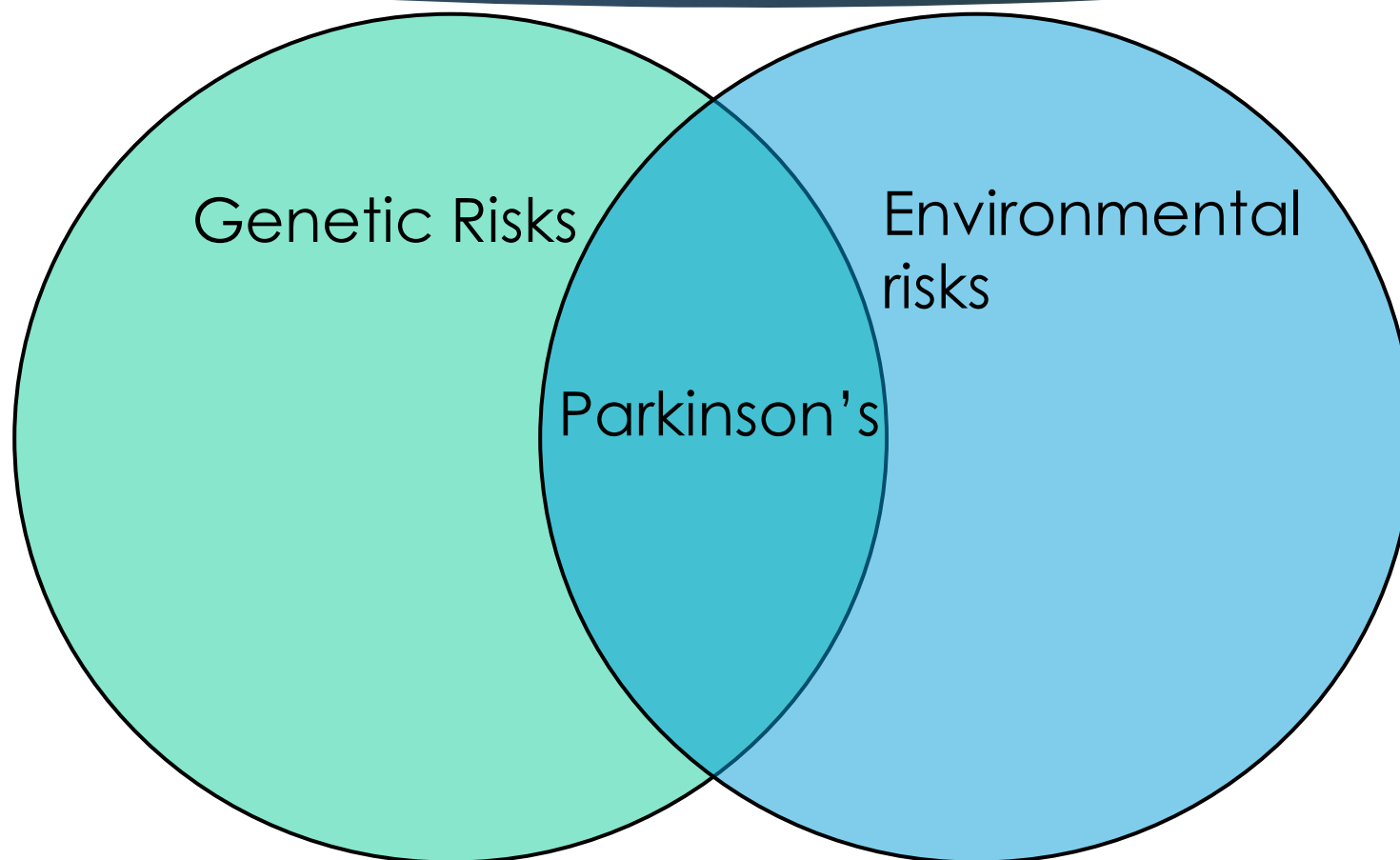
- ▶ As of this summer >10,000 people have been enrolled for genetic testing
- ▶ The study has identified that 12.7% of people have a genetic form of PD
- ▶ Goals of this study:
 - ▶ **Accelerate clinical trials for PD**
 - ▶ **Improve PD care and research**
 - ▶ **Empower people with PD (and their families)**

What causes PD?



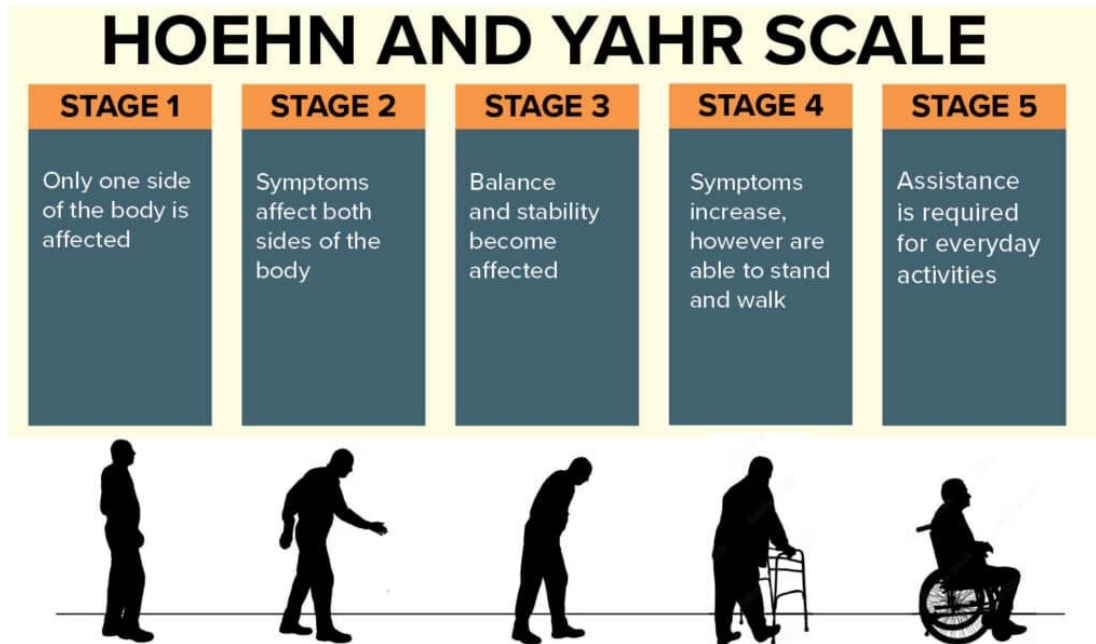
- ▶ **Older age:** 1 out of 100 people over the age of 60, average age of onset is 60
- ▶ **Male Gender:** Male to Female ratio is 1.5-2x higher
- ▶ **Environmental/Chemical exposures**
 - ▶ Pesticides/Herbicides (including permethrin, beta-hexachlorocyclohexane, rotenone, paraquat, “Agent Orange”)
 - ▶ Solvents/Cleaning chemicals (tetrachloroethylene)
- ▶ **Head injuries**
- ▶ **Smoking and Coffee consumption = protective**

What causes PD?

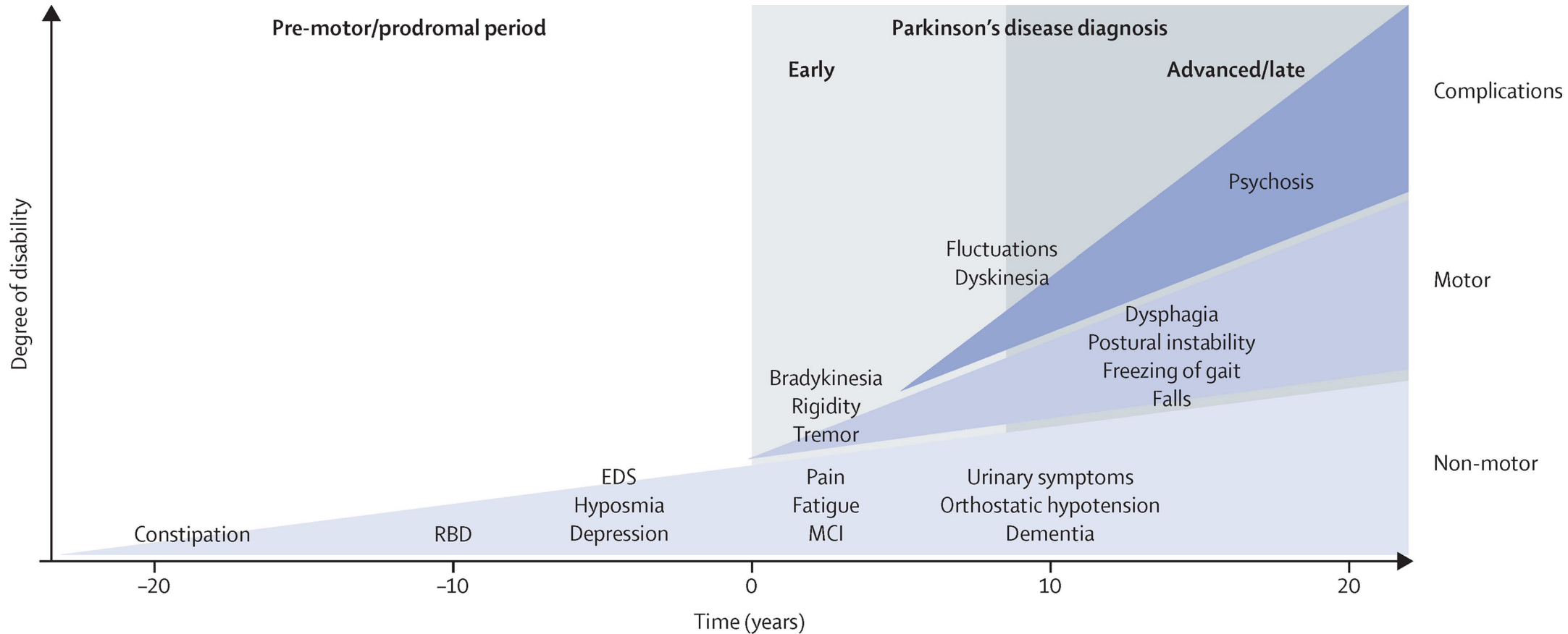


Progression of PD

- ▶ Progression of PD is difficult to predict
- ▶ The experience of living with Parkinson's over the course of a lifetime is unique to each person
 - ▶ As symptoms and progression vary from person to person, neither you nor your doctor can predict which symptoms you will get, when you will get them or how severe they will be



Progression of PD



How is Parkinson's Disease Treated?

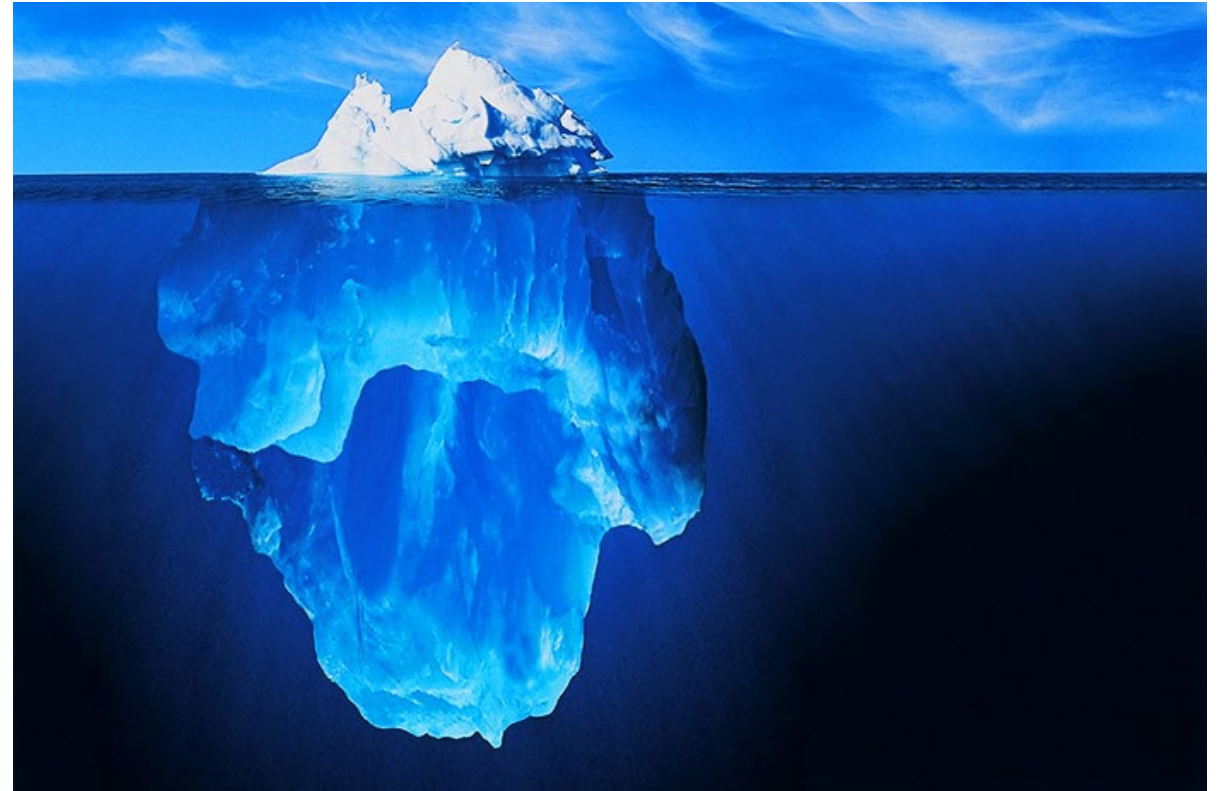
Treatment of PD

▶ Motor symptoms

- ▶ Bradykinesia/akinesia
- ▶ Tremor
- ▶ Rigidity/stiffness
- ▶ Gait/balance changes

▶ Non-motor symptoms

- ▶ Depression/anxiety
- ▶ Sleep disturbance
- ▶ Cognitive changes
- ▶ Urinary dysfunction
- ▶ Constipation
- ▶ Dizziness and hypotension
- ▶ Hyperhidrosis
- ▶ Sexual dysfunction
- ▶ Fatigue
- ▶ Pain

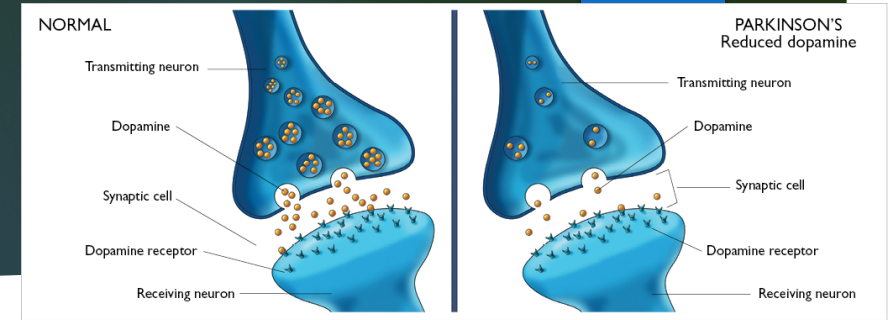


Treatment of PD



- ▶ Treatment is individualized
- ▶ Education is critical
 - ▶ Expectations, potential side effects, need for dose increase in the future, additional medications in the future
- ▶ “Team” decision
 - ▶ Patient and physician making choices together
- ▶ Combination of medication and exercise
- ▶ Guiding principal about treatment decision
→ Quality of life

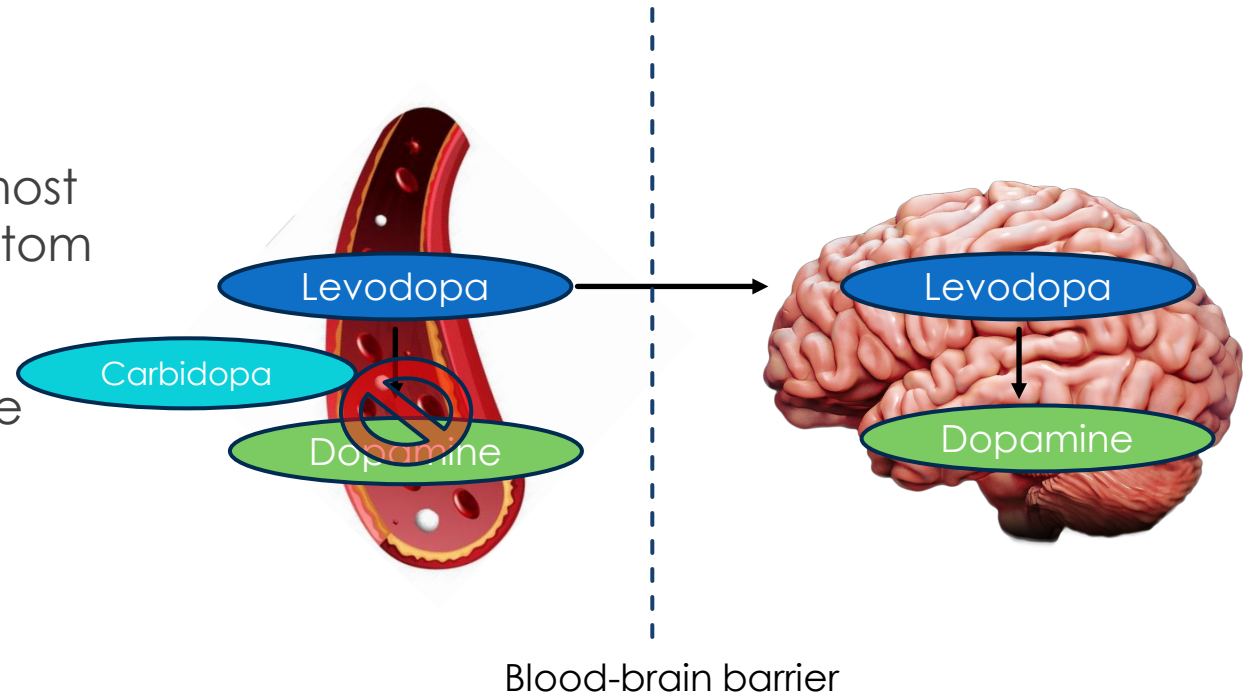
Medication Options in PD



- ▶ PD is from lack of dopamine in the brain → our goal is to increase dopamine signaling in the brain
- ▶ Many different ways to approach this:
 - ▶ Raise dopamine levels (carbidopa/levodopa)
 - ▶ Block enzymes in the brain that breakdown dopamine (rasagiline, entacapone)
 - ▶ Stimulate dopamine receptors
 - ▶ Dopamine agonists (ropinirole, pramipexole, rotigotine)
 - ▶ Other (amantadine)

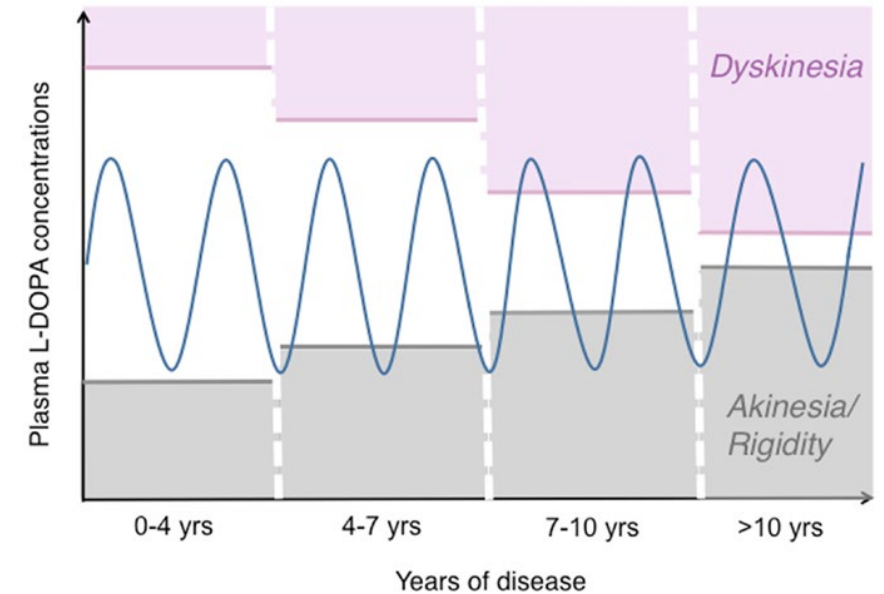
Carbidopa/Levodopa (Sinemet)

- ▶ Levodopa is converted into dopamine in the brain
 - ▶ Fits like a “key in a lock”
- ▶ Since it is a “replacement” therapy it is the most effective and potent at treating motor symptom
 - ▶ **Gold standard** in treating PD
- ▶ Given with carbidopa to decrease risk of side effects and improve its effectiveness
- ▶ Typically, people with PD should notice an improvement in symptoms within 1-2 weeks



Carbidopa/Levodopa (Sinemet)

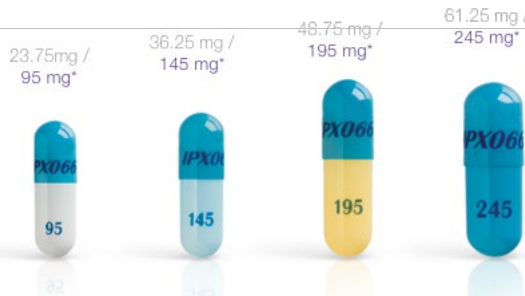
- ▶ Possible common side effects: nausea/upset stomach, lowered blood pressure, sedation, abnormal dreams, hallucinations
- ▶ Effects that can occur later in disease:
 - ▶ Motor Fluctuations – early wearing off before next dose is due causing reemergence of parkinsonian symptoms
 - ▶ Nearly half of all patients will experience this by 2-5 years after disease onset
 - ▶ Levodopa Induced Dyskinesia – involuntary movements that can affect head, trunk or extremities
 - ▶ Typically occurring at peak levodopa levels, but can also occur when medication levels rising/falling



Carbidopa/Levodopa Formulations



Carbidopa/Levodopa IR tablets



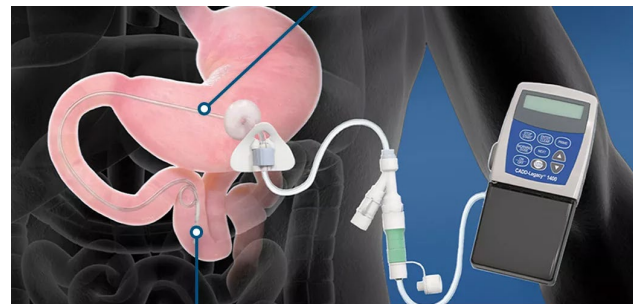
Carbidopa/Levodopa ER capsules (Rytary)



Carbidopa/Levodopa Inhaled (Inbrija)



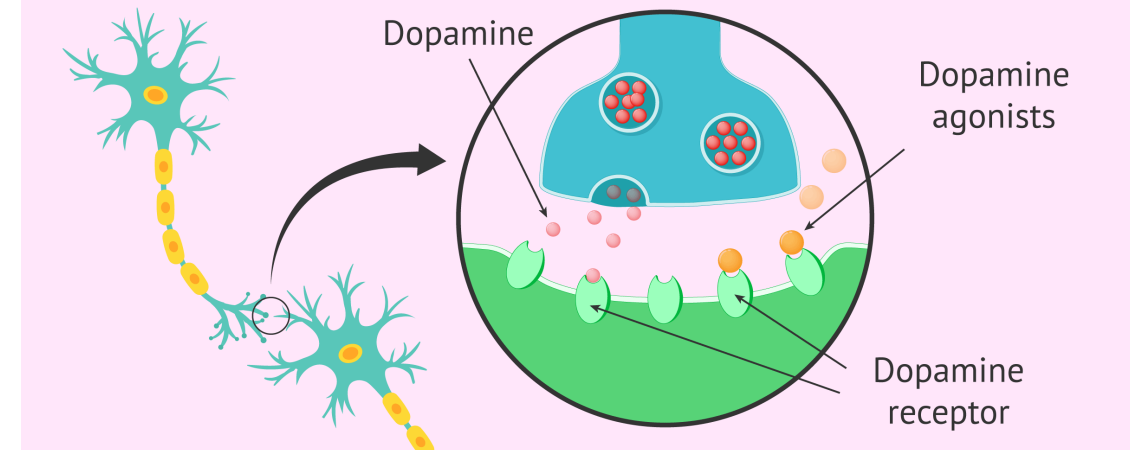
Carbidopa/Levodopa CR tablets



Carbidopa/Levodopa intestinal infusion (Duopa)

Dopamine Agonists

- ▶ Act on dopamine receptor but not as efficiently as dopamine
- ▶ Not as potent as levodopa; but lower rates of dyskinesia
- ▶ Oral formulations
 - ▶ Ropinirole (Requip) – IR and ER forms
 - ▶ Pramipexole (Mirapex) – IR and ER forms
- ▶ Transdermal patch
 - ▶ Rotigotine (Neupro) – long-acting form
- ▶ Subcutaneous (injection)
 - ▶ Apomorphine – used as a “rescue”



Dopamine Agonists

Advantages

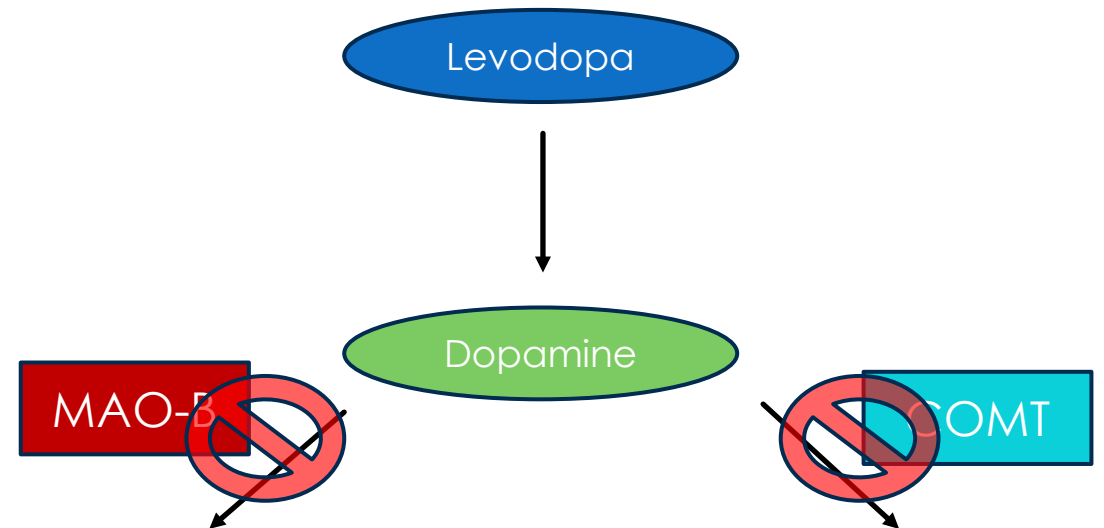
- No dietary concerns with protein for absorption into the gut and brain
- Have a longer half life than IR levodopa

Disadvantages

- Similar side effects to Levodopa: nausea, vomiting, hypotension
- Hallucinations** (especially in older patients)
- Excessive daytime sleepiness (“sleep attacks”)
- Lower leg edema
- Impulse Control Disorders(ICD): pathologic gambling, hypersexuality, and compulsive eating and shopping

Blocking enzymes that breakdown dopamine

- ▶ **Monoamine oxidase-B inhibitors** (MAO-B inhibitors)
 - ▶ Rasagiline
 - ▶ Selegiline
 - ▶ Safinamide
- ▶ **Catechol-O-methyl Transferase inhibitors** (COMT inhibitors):
 - ▶ Entacapone
 - ▶ Opicapone
 - ▶ Tolcapone



These medications have **modest** benefit in reducing symptoms; can increase "On" time

Amantadine

- ▶ Antiviral agent that also has antiparkinsonian effects
 - ▶ Increases dopamine release and inhibits dopamine reuptake
 - ▶ Reduces glutamate hyperactivity which may contribute to both **improved Off time and reduction of Dyskinesia**
- ▶ Used as a treatment for parkinsonian symptoms, **decrease dyskinesia**, also can be helpful for dystonia and gait/freezing
- ▶ Side effects: **Hallucinations**, confusion, nightmares, blurred vision, “lacy” appearing rash, edema

Treatment of PD

- ▶ Various therapies, treatments, medications for the Non-Motor symptoms of PD that I did not cover today
 - ▶ **Non-motor symptoms:** Depression/anxiety, Sleep disturbance, Cognitive changes, Urinary dysfunction, Constipation, Dizziness and hypotension, Hyperhidrosis, Sexual dysfunction, Fatigue, Pain
- ▶ EXERCISE!!!
 - ▶ We do not have any medication that can slow the progression of PD but studies have shown that exercise is the closest thing we have!





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Thank
you!

