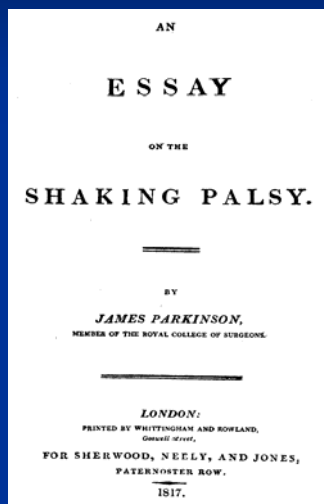


# Medications for Parkinson's Disease

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## History of Parkinson's Disease

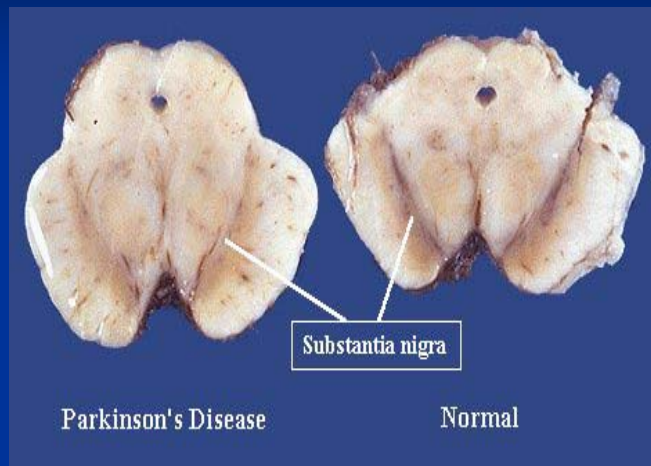


- First described in 1817 by James Parkinson, English physician
- Disease named in his honor 50 years later

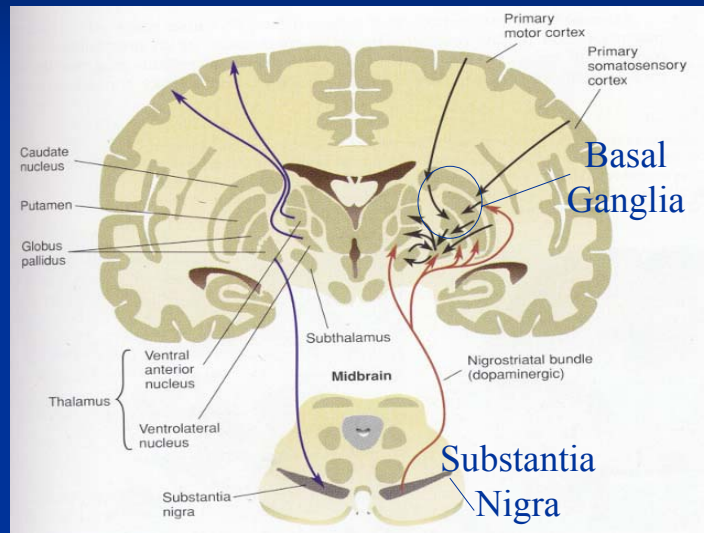
## Parkinson's Disease

- Average age of onset: 60 years
- Approximately 1 million individuals in United States
- Second most common neurodegenerative disease
- Slightly higher rate of PD in men
- Rural living, agricultural work and exposure to well water associated with higher incidence
- Minority of cases have strong family history

## What happens to the brain in Parkinson's Disease?



## Abnormal Communication of Motor Pathway in PD



## Primary Clinical Features of Parkinson's Disease

*A neurological disorder characterized by:*

- Slowness of movement
- Tremor
- Rigidity
- Postural instability

## What types of treatment are there for Parkinson's Disease?

- Symptomatic
  - Pharmacological
    - Motor
    - Non-motor
  - Surgical
- Neuroprotective
- Restorative

## Medications to Treat Motor Symptoms

- *Dopaminergic Medications*
  - Sinemet
  - Dopamine agonists (pramipexole, ropinirole, apomorphine, rotigotine)
- *MAO-B Inhibitors*
  - selegiline, rasagiline
- *COMT Inhibitors*
  - entacapone, tolcapone

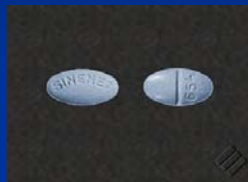
## Sinemet (Carbidopa/Levodopa)

- Levodopa was discovered in early 1960's
- Remains most effective pharmacological treatment for Parkinson's Disease
- Metabolizes to dopamine in the brain as well as in the rest of the body

### Sinemet has two components: carbidopa and levodopa



Sinemet 25/100



Sinemet 25/250



Sinemet SA 50/200

## **Carbidopa helps in minimizing side effects of Levodopa**

- Carbidopa helps minimize stomach upset and lightheadedness
- Need at least 75 mg carbidopa for every 300 mg levodopa
- Additional supplementation is available

## **Timing of when Sinemet is taken**

- Protein can interfere with the absorption of levodopa to the brain
  - take Sinemet 45 minutes before or after meals
  - If have stomach upset, can take with non-protein containing food
  - Directions for administration from pharmacy may be incorrect

## **What symptoms typically improve with Sinemet?**

- Slowness of movement
- Tremor
- Rigidity
- +/- Balance and Freezing

## **What symptoms do not typically improve with Sinemet?**

- Memory problems
- Depression
- Urinary problems
- Low blood pressure

## Potential Side Effects of Sinemet

- Nausea/vomiting
- Lightheadedness/decrease in blood pressure
- Fatigue
- Confusion/Hallucinations
- Dyskinesias

## Methods to Counteract Potential Side Effects of Sinemet

- Nausea/Vomiting
  - Carbidopa
  - Non-protein containing food
  - Anti-nausea medications
- Fatigue
  - Minimize naps during day
  - Exercise
  - Provigil
  - Selegiline



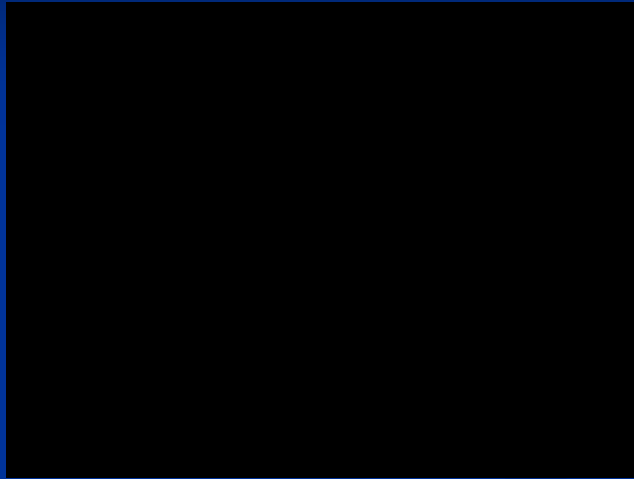
## Methods to Counteract Decrease in Blood Pressure

- Decrease/discontinue medications which may be contributing (blood pressure medications, diuretics, selegiline, dopamine agonist)
- Increase salt/fluids in diet
- Eat small meals
- Raise head of bed
- Support hose to prevent pooling of blood in legs

## Methods to Treat Psychosis

- Reduce or eliminate any non-essential medications which may be contributing to confusion
- Reduce Parkinson's disease medications if possible from motoric standpoint
  - 1<sup>st</sup> discontinue selegiline, Artane, amantadine
  - 2<sup>nd</sup> lower dopaminergic medications
- **Anti-psychotic medications**
  - Quetiapine (Seroquel)
  - Clozapine (Clozaril): need for weekly blood draw; 1% patients develop drop in white blood cell count

## Dyskinesia Video



## Dyskinesias and Sinemet

- Dyskinesias typically begin three to five years after treatment initiation
- More common in patients with younger onset of disease
- Non-pulsatile delivery may decrease or delay risk of dyskinesias

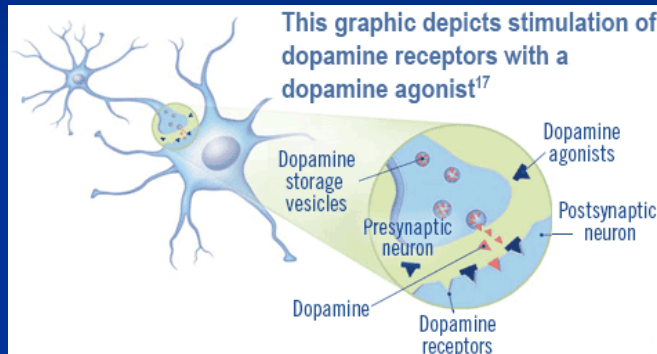
## Treatment of Dyskinesias

- Decrease Sinemet dosage amount
- Consider addition of dopamine agonist
- Consider addition of amantadine
- If severe dyskinesias, consider deep brain stimulation surgery

## Dopamine Agonists

- Examples:
  - Pramipexole (Mirapex)
  - Ropinirole (Requip)
  - Apomorphine infusion (Apokyn)
  - Rotigotine patch

## How is a dopamine agonist different from Sinemet?



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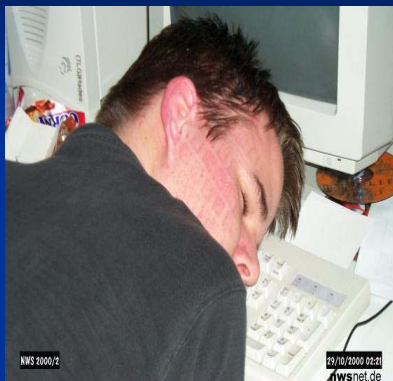
### Advantages of Dopamine Agonists

- Can be effective at treating all of motor symptoms of Parkinson's disease, especially tremor
- Can delay need for Sinemet
- Can decrease "off time" when used in combination with Sinemet
- Delay in development of dyskinesias when used as monotherapy early in disease
- Provides possible neuroprotection
- Good choice for initial treatment in many patients, especially young-onset

## Potential Side Effects of Dopamine Agonists

- Nausea/vomiting
- Lightheadedness/Decrease in Blood Pressure
- Confusion/Hallucinations
- Fatigue
- Sleep Attacks
- Impulse Control Behaviors

## Sleep Attacks



# Impulse Control Behaviors



## Apomorphine (Apokyn)

- Fast-acting “rescue” treatment
- Self-injected under the skin
- Premedication with anti-nausea medication



## Rotigotine Patch (Neupro)

### ■ Advantages:

- only requires once a day administration
- absorption not influenced by food
- continuous drug delivery



### ■ Disadvantages:

- skin area irritation
- less effective than oral dopamine agonists
- dosages used in some studies were higher than FDA approved dose

## MAO-B Inhibitors: Rasagiline

- 5x more potent than selegiline
- No methamphetamine metabolite
- Mild benefit in motor symptoms
  - In patients not taking any other PD medications (TEMPO study, 2002)
  - Decreases “off” time by almost two hours in patients already taking Sinemet (PRESTO study)

## **MAO-B Inhibitors: Rasagiline**

- May provide some degree of neuroprotection
  - metabolite may aid in cell death prevention
  - patients on rasagiline for one year had less severe motor problems in comparison to individuals on rasagiline for only six months (Delayed-Start TEMPO study, 2004)
- Well-tolerated; most common side effects include weight loss, nausea/vomiting

## **Final Tips for Management of PD Medications**

- Pill timer
- Symptoms in relation to timing of medications
- Recognize each patient's medication regimen is tailored for him/her
- Ongoing communication with health care provider regarding benefits/side effects