

WELCOME TO EXPERT BRIEFINGS

Medications 101

James Beck, PhD

Chief Scientific Officer, Parkinson's Foundation

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The Parkinson's Foundation makes life better for people with Parkinson's disease by improving care and advancing research toward a cure. In everything we do, we build on the energy, experience and passion of our global Parkinson's community.

**We have everything you need to
live better with Parkinson's.**



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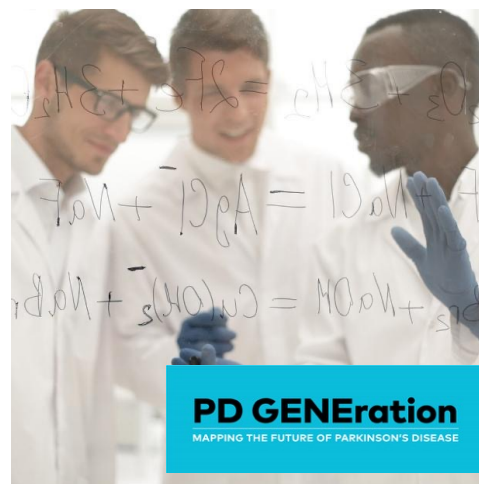
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Today's Expert Briefing is presented by



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Parkinson's Medications 101

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Disclosures

- Speaker's Bureau: Teva Pharmaceuticals, Neurocrine Biosciences, Supernus Pharmaceuticals, Amneal, Abbvie Pharmaceuticals
- Consultant: GLG, Teva Pharmaceuticals, Abbvie Pharmaceuticals, SOM Biotech, Clearview Consulting, Ultragenyx
- Grants: Huntington Disease Society of America, Parkinson Foundation

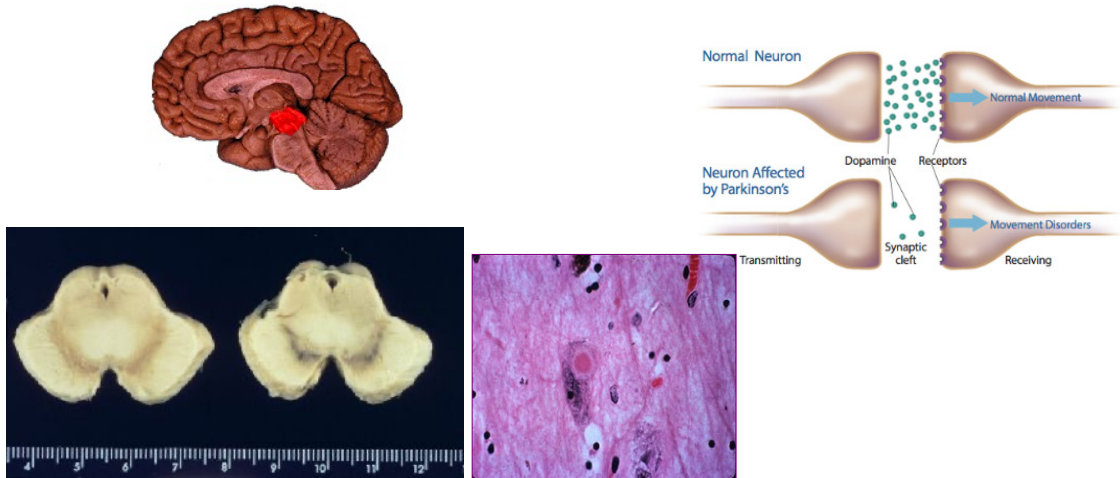
Learning Objectives

- Gain insight into how medications fit within a comprehensive care plan for Parkinson's disease (*a care plan is more than medications*)
- Learn how different Parkinson's medications work, their intended benefits, and their role in symptom management.
- Recognize potential side effects of Parkinson's medications and strategies for managing them.
- Learn how medication regimens may need to evolve over time (*due to the progression of the disease*).
- Develop realistic expectations around medication outcomes.
- Learn how to have more informed discussions with health care providers about their medication options.

PD: Motor & Non-Motor



PD: A Neurodegenerative Disorder



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Goal of Treatment



What is the goal of all current PD treatments?

- Improve symptoms
- Improve QoL

When there is no significant motor disability consider:

- No treatment?
- Neuro-protection oriented trials?
- Exercise / optimizing lifestyle
- Rehab-oriented services
- Education

Pharmacologic therapy

Levodopa
MAO-B inhibitors
COMT inhibitors
Dopamine agonists
Anticholinergics
Amantadine
A2A Receptor Antagonists
Medications for Non-Motor Symptoms

Nonpharmacologic therapy

Education
Exercise
Nutrition
Support services
Speech therapy
PT/OT

Advanced therapy

Deep brain stimulation
Focused Ultrasound
Levodopa intestinal gel
SubCutaneous Infusions

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Categories of PD Severity (*variable)



Very early: mild symptoms not impacting daily activities -> may not need pharmacological treatment for motor symptoms (*year -5 to +5)

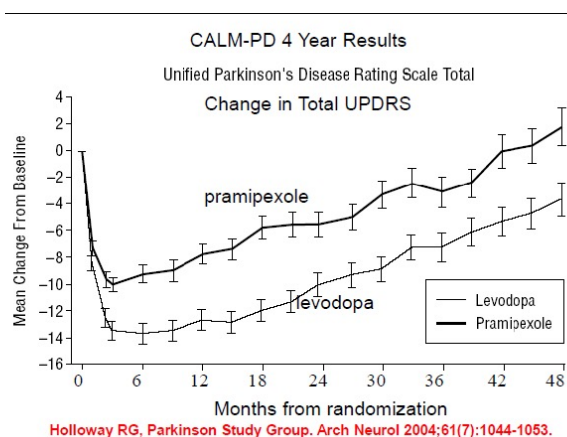
Mild: symptoms begin to interfere with activities, typically smooth response to meds (*year 1-10)

Moderate: inadequate or complicated response to simple regimen or low doses, narrowing therapeutic windows, some disability, gait may be more impacted (*year 5-20)

Advanced: significant complications and fluctuations, freezing/falling, often increase in non-motor issues like dementia (*year 10-20+)

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Basics of Managing Motor Symptoms: Dopamine Replacement



Dopamine Agonists (Pramipexole, Ropinirole, Rotigotine)

- Can treat all motor symptoms of PD
- Side effects can include: sleepy, dizzy, nausea, confused, impulse control disorders
- Less risk of movement side effect (dyskinesia)
- 28% stop due to side effect
- 40% need to add another medication by 2 years

Levodopa:

- Most effective for all motor symptoms of PD
- Side effects can include: nausea, dyskinesia
- 2% stop due to side effects
- 15% need to add another medication by 2 years

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Other Options: Anticholinergics, MAO-B Inhibitors, Amantadine



Anticholinergic (Trihexyphenidyl, Benztropine): Treats Tremor, Dystonia

Anticholinergic drugs and risk of dementia: case-control study

Kathryn Richardson,¹ Chris Fox,² Ian Maidment,³ Nicholas Steel,² Yoon K Loke,² Antony Arthur,¹ Phyo K Myint,⁴ Carlota M Grossi,¹ Katharina Mattishent,² Kathleen Bennett,⁵ Noll L Campbell,⁶ Malaz Boustani,⁷ Louise Robinson,⁸ Carol Brayne,⁹ Fiona E Matthews,¹⁰ George M Savva¹

MAO-B Inhibitors (Rasagiline, Selegiline, Safinamide):

ORIGINAL ARTICLE

A Double-Blind, Delayed-Start Trial of Rasagiline in Parkinson's Disease

C. Warren Olanow, M.D., Olivier Rascol, M.D., Ph.D., Robert Hauser, M.D., Paul D. Feigin, Ph.D., Joseph Jankovic, M.D., Anthony Lang, M.D., William Langston, M.D., Eldad Melamed, M.D., Werner Poewe, M.D., Fabrizio Stocchi, M.D., and Eduardo Tolosa, M.D., for the ADAGIO Study Investigators*

Amantadine:

-Blocks a chemical that causes extra movement (NMDA), so may help tremor or dyskinesia or both

-Risk of confusion/hallucinations is 20-30% in older age group (>70), leg swelling, skin change

MAO-B Inhibitors:

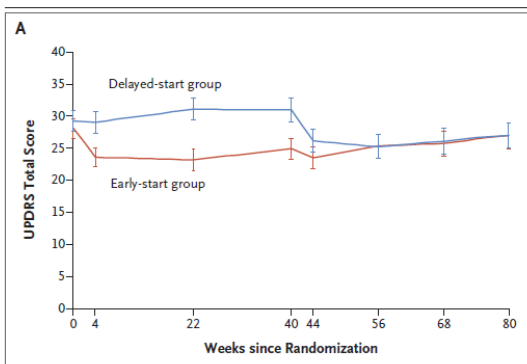
-Slow the breakdown of levodopa, so overall impact on motor symptoms alone is small

-Well-tolerated

-70% need to add another medication by 2 years

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Is it too soon for levodopa?



Risk of Motor Complications is Associated with:

- Disease severity / duration, 50% at 5-years, 90% at 10-years (severity varies widely)
- Dose required
- Individual factors: body size, genetics, gender, absorption

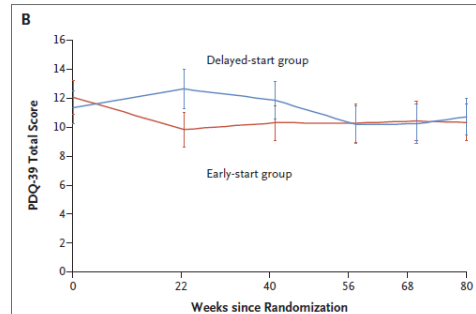


Figure 2. Unified Parkinson's Disease Rating Scale and Parkinson's Disease Questionnaire-39 Scores during the Trial.

Majority of people are more bothered by OFF time than Dyskinesia time

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Why Isn't Levodopa Working for Me?



Dose is too low

Symptom you are focused on is not a levodopa-responsive symptom for you

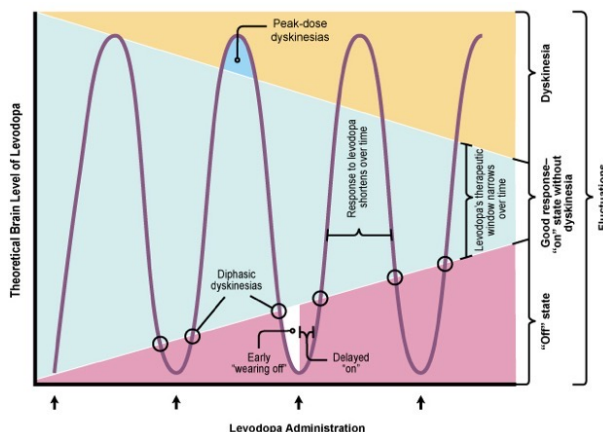
Not absorbing it well

Not classic PD

Duration of effect is too short, or threshold for side effects is too low (your brain doesn't handle it smoothly)

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Motor Complications / Fluctuations



Half-life of sinemet = 90 minutes

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Options in Dealing with Fluctuations: Simple



Improve OFF time, Dyskinesia Neutral

- Fractionate: taking levodopa more frequently, sometimes with reducing the amount taken for each dose (example: 2 pills four times a day may become 1.5 pills 5 times per day)
- Use longer-acting formulations of levodopa (CR / ER types)
- Avoid food interactions

Improve OFF time, Potential to Increase Dyskinesia

- Add in medications that boost the duration/effect of levodopa: Dopamine agonists, MAO-B inhibitors, COMT-inhibitors (entacapone, opicapone), A2A antagonists (istradefylline)
- On-demand therapy (as needed): Inhaled levodopa, injected apomorphine

Improve OFF time, Potential to Decrease Dyskinesia

- Add amantadine / amantadine ER



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Options in Dealing with Fluctuations: Advanced



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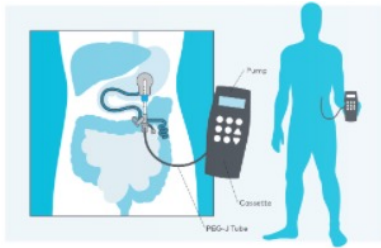
Options in Dealing with Fluctuations: Advanced



Intestinal continuous infusion of levodopa

Subcutaneous continuous infusion of levodopa

Subcutaneous continuous infusion of apomorphine



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Foscarbidopa/foslevodopa subQ Infusion



Data:

- Avg 2.75 hrs improved OFF time per day vs oral levodopa
- Avg 3.8 hrs improved good ON time per day vs oral levodopa
- Improvement in early morning OFF time symptoms

Who:

- Advanced Parkinson's disease with bothersome OFF periods
- Currently private insurance, awaiting medicare approval

What to be aware of:

- Lifestyle change – requires training (home nurse visit) and commitment
- Skin care / risk of skin irritation and infections (reduced by good skin care)
- Pump needs to be carried and filled with medication
- 2-hour initiation session in the clinic



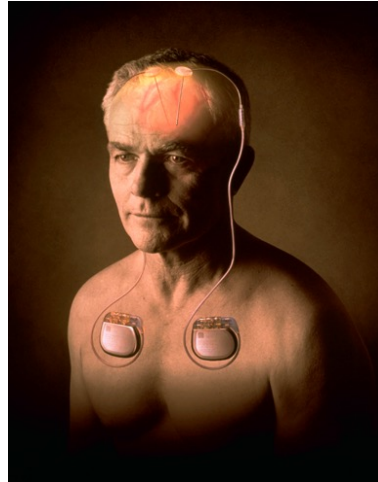
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Options in Dealing with Fluctuations: Advanced



Deep Brain Stimulation

Focused Ultrasound



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Surgical Therapies: DBS



Who:

- Parkinson's disease (not atypical parkinsonism)
- Responds to levodopa – symptoms that don't respond to levodopa generally won't respond to surgical therapy (tremor can be exception)
- Has complications from levodopa – dyskinesias, frequent wearing off
- No dementia, generally healthy in terms of surgical risks

Goal:

- Reduce medications while maintaining benefits
- Get smoother and more consistent benefits without fluctuations
- Reduce side effects from medications like dyskinesias

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Surgical Therapies: Focused Ultrasound



Who:

- Tremor on one-side that is very bothersome – due to Parkinson's disease or benign essential tremor
- Skull thickness needs to be measured for eligibility

Goal:

- Reduce tremor on one side of the body

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Surgical Therapies: A Comparison



DBS

Surgery
Device
Adjustable
Reversible
Long-term benefits clear
Can be done on one or both sides
Can target areas associated with tremor or areas associated with stiffness/slowness

Focused Ultrasound

No surgery / no cutting / easier
No device
Not adjustable
Not reversible
Long-term benefits less known
Currently approved for one side
Currently approved for tremor target area

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Symptoms Where We Need to Think Beyond Dopamine (Motor)

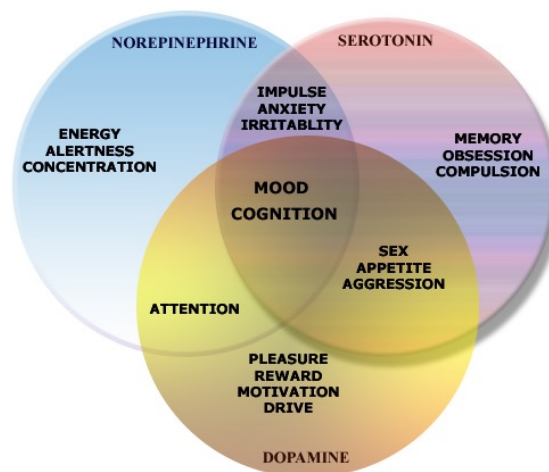


Tremor – sometimes (although surgery works well)
Postural instability and Freezing of Gait



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Dopamine is only part of the story ...



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Symptoms Where We Need to Think Beyond Dopamine (Non-Motor)



- **Affective disorders**
 - Anhedonia (32%)
 - Anxiety (30%)
 - Apathy (31%)
 - Depression (43%)
- **Autonomic dysfunction**
 - Orthostatic hypotension (20-30%)
- **Cognitive dysfunction**
 - Bradyphrenia
 - Inattention (28%)
 - Memory impairment (32%)
 - Hallucinations (30-50%)
- **Fatigue** (36%)
- **GI dysfunction / constipation** (39%)
- **Sexual dysfunction**
 - Erectile dysfunction (28%)
 - Reduced libido (42%)
- **Sleep disturbances**
 - Sleep fragmentation
 - Vivid dreams (24%)
 - REM behavior disorder (28%)
 - Excessive daytime sleepiness (28%)
 - Insomnia (36%)
- **Urinary dysfunction** (30%)

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Balancing Motor / Non-Motor Symptoms to Improve Quality of Life



Tremor	Stiffness	Hallucinations	Low blood pressure
Dexterity	Mobility	Confusion	
<u>Treat by raising dopamine</u>		<u>Treat by lowering dopamine</u>	

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Treating Non-Motor Issues



Mood (anxiety, depression)

- SSRIs, SNRIs, Mirtazapine (avoiding benzos and antipsychotics if possible)
- Counseling / therapy
- Exercise and Mind-body activities
- PD medications (i.e. dopamine) might help in some cases

Autonomics

- May be worsened by PD medications and cardiac/BP medications – may need to lower
- Salt/hydration, compression
- Midodrine, fludrocortisone, droxidopa; can be complicated if also have high blood pressure
- Other: Drooling (botulinum toxin); Runny nose (ipratropium nasal spray), Sweating, erectile dysfunction, Constipation

Sleep / Fatigue

- Need to identify type of sleep problem (motor, restlessness, fragmented, urinary, breathing, RBD, etc)
- Sometimes PD medication can help (on rare occasions can be a side effect)
- Melatonin, Doxepin, Mirtazapine, Trazodone, Quetiapine, Gabapentin (generally avoiding traditional sleep aids)
- Sleep hygiene, CBT-I

Cognition / Hallucinations

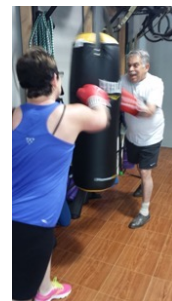
- May be worsened by PD medications and other medications – may need to lower
- Review all medical issues / meds as potential triggers
- Cholinesterase inhibitors (donepezil, rivastigmine), Memantine
- Pimavanserin, Quetiapine, Clozapine
- Mental and physical activity

Dopa-Dysregulation

- Worsened by PD medications – may need to lower DA

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Balancing Motor / Non-Motor Symptoms: Incorporating a Holistic Approach to Care to Connect Mind & Body



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Non-Pharmacological Therapies



Exercise & Physical Therapy

OT and speech therapy

Expressive Therapies: art, music, improv/theater, humor

Cognitive Exercises: arts/crafts, puzzles, math games

Mind-Body Physical Exercises: Tai Chi / yoga, Dance

Healthy lifestyle: brain-healthy diet, good sleep, scheduled activity, social interactions

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R_x Exercise Prescription

1. Keep active: find a physical activity that you enjoy!
2. Aerobic activity: 30 minutes of moderate intensity (get the heart rate up) activity 5 days per week (brisk walk, cycling, boxing, swimming, etc).
3. Strength building: Use weights or resistance bands for 30 minutes 2x per week (may need a trainer or therapist to show you technique such as squats, lunges, rowing, etc).
4. Balance training: Consider tai chi, yoga, or dance therapy for 30 minutes 2x per week. Interventions with mind-body benefits are preferable

MD: _____

Signature: _____



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A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

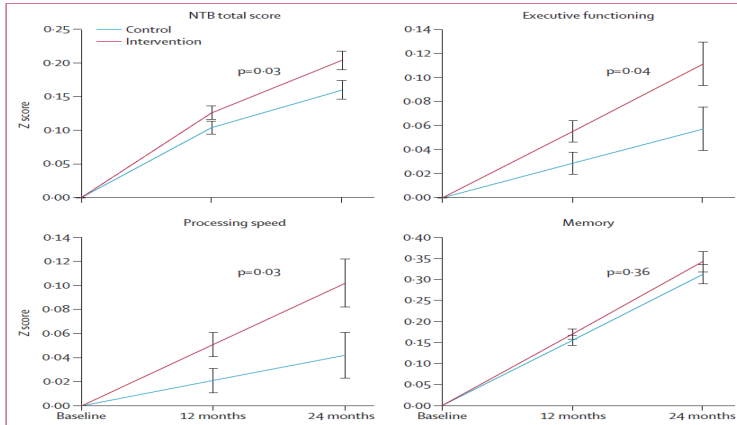


Figure 2: Change in cognitive performance during the 2 year intervention

Ngandu, Lancet, 2015

- Diet
- Exercise
- Cognitive training
- Vascular risk monitoring

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Important Elements of Exercise for Parkinson's



Involve goal-based practice for acquisition of a skill.

A supervised environment to help with learning through reinforcement.

Something enjoyable.

Something social.

Well-trained instructors who understand PD.

Appropriate level classes.

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Lifestyle Interventions



Counseling, Support Groups
Social activities, reducing isolation
Group exercise programs
Healthy eating
Good sleep hygiene
Good mental health
Appropriate environment for level of support needs
General medical wellbeing and check-ups

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Other Non-Motor Symptom Tips



Orthostatic hypotension

- Review BP meds
- Hydration + salt
- Compression
- BP raising meds

Constipation

- Hydration
- Diet / fiber
- Miralax

Sleep

- Sleep hygiene strategies, CBT-I
- Certain antidepressant/anti-anxiety meds (not traditional sleep aids)

Excessive Sleepiness

- Check for sleep apnea
- Schedule/routine physical and cognitive activities

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Plan for Non-Motor Symptoms



Constipation

Parkinson's Disease & Movement Disorders Center

Constipation has many causes; many can be controlled by diet, fluid intake and activity. Other causes are due to medications or medication side-effects. One issue that comes with Parkinson's disease is decreased gastric motility (the stomach and intestines do not move normally). This is due to the autonomic nervous system slowing down. This system is responsible for regulating smooth muscles. If the system is not working properly, then all other systems it works with will not work properly.

There are options available for Parkinson's disease patients. The options require change on the part of the patient and family members. As the body adapts, the changes will make a difference. But, remember, the changes will take some time, up to 3 to 4 weeks.

Be patient, and avoid trying to solve the problem with the use of laxatives and enemas. Such products can cause worse constipation and can damage the lining of the intestines. Laxatives and enemas should be used as a last resort, and should be discussed with your physician.

Here is what you can do to help prevent constipation:

- Drink 6 to 8 8oz glasses of water every day.
- Avoid caffeine and alcohol, as they can act as a diuretic.
- Increase daily fiber by eating more fruits and vegetables: 5 to 9 servings a day.
- Use bulking agents like Fibercon or Metamucil.
- Become more active. Increased activity also stimulates the intestines.
- Exercise regularly. Exercise helps your body and mind feel better.
- Move your bowels when you feel the urge.

If you are already dealing with constipation, here are some suggestions:

- Drink an additional 2 to 4 8oz glasses of water.
- Try warm liquids, especially first thing in the morning.
- Add additional servings of fruits and vegetables to your diet.
- Eat prunes or bran cereal.
- Add a bulking agent like Fibercon or Metamucil.
- Exercise regularly.

SLEEP HYGIENE INSTRUCTIONS

Homeostatic Drive for Sleep

- Avoid naps, except for a brief 10 to 15 minutes nap eight hours after arising, but check with your physician first, because in some sleep disorders naps can be beneficial.
- Restrict sleep period to average number of hours you have actually slept per night in the preceding week. Quality of sleep is important. Too much time in bed can decrease quality on subsequent nights.
- Get regular exercise each day, preferable 40 minutes each day of an activity that causes sweating. It is best to finish exercise at least six hours before bedtime.

Circadian Factors

- Keep a regular time out of bed 7 days a week.
- Do not expose yourself to bright light if you have to get up at night.

Arousal in Sleep Setting

- Keep clock face turned away, and do not find out what time it is when you wake up a night.
- Avoid strenuous exercise after 6:00 P.M.
- Do not eat or drink heavily for three hours before bedtime. A light bedtime snack may help.
- Keep your room dark, quiet, well ventilated, and at a comfortable temperature throughout the night. Earplugs and eyeshades are OK.
- Use a bedtime ritual. Reading before lights-out may be helpful if it is not occupationally related.
- List problems and one-sentence next steps for the following day. Set aside a worry time. Forgive yourself and others.
- Learn simple self-hypnosis to use if you wake at night. Do not try too hard to sleep; instead, concentrate on the pleasant feeling of relaxation.
- Use stress management in the daytime.
- Avoid unfamiliar sleep environments.
- Be sure mattress is not too soft or too firm, pillow is right height and firmness.
- An occasional sleeping pill is probably all right.
- Use bedroom only for sleep; do not work or do other activities that lead to prolonged arousal.

Managing Orthostatic Hypotension

- ✓ Drink lots of water – at least one cup (8 ounces) with meals and several more throughout the day. Check with your doctor for the right amount for you.
- ✓ Practice regular, gentle exercise and avoid long periods of inactivity.
- ✓ Work with a physical or occupational therapist to learn exercises that increase blood flow to the heart.
- ✓ Eat small, frequent meals. Reduce alcohol and avoid hot drinks and hot foods.
- ✓ After consulting your doctor, increase your salt intake by eating prepared soups or pretzels. Note: People with heart disease should avoid this.
- ✓ If you expect to be standing for a long period of time, drinking two 8-ounce glasses of cold water quickly will increase blood volume and blood pressure will go up.
- ✓ Try wearing thigh or waist-high compression stockings or an abdominal binder.
- ✓ Move slowly from lying to sitting and then standing.
- ✓ Avoid overheating by limiting your exposure to midday sun during warmer months, very hot showers, hot tubs, saunas, etc.

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Summary



Parkinson's disease is different for everyone, and includes motor and non-motor symptoms

Levodopa is the gold-standard for managing motor symptoms

There are many strategies for addressing motor fluctuations

Advanced therapies including surgical options and infusions

All medical/surgical options have pros and cons – need to weigh these individually

Many symptoms require thinking beyond dopamine – in some cases there can be a trade-off between managing motor and non-motor symptoms

Non-pharmacological and lifestyle focused interventions are valuable in PD as well

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2025 Expert Briefings



Wednesday, March 12

Nourishing Wellness: Nutrition in Parkinson's

Wednesday, April 9

The Latest Advances in Parkinson's Research & Treatment

Wednesday, May 14

Managing Nighttime Interruptions in Parkinson's Disease

Wednesday, September 17

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Wednesday, October 15

Steady Steps: Improving Gait and Balance in Parkinson's

Wednesday, November 12

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Before You Go...



Your feedback is important to us!
Please complete the evaluation after the close of this webinar.

EXPERT BRIEFING EVALUATION

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1. What best describes your connection to Parkinson's disease (PD)?

- ☐ Person with Parkinson's
- ☐ Spouse / Partner
- ☐ Parent has / had Parkinson's
- ☐ Other family of person with Parkinson's
- ☐ Friend of person with Parkinson's
- ☐ Healthcare Professional
- ☐ Other

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