

Parkinson's Disease and Movement Disorders Center

Parkinson's Update

Northwestern University Feinberg School of Medicine

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Promising New Research for Parkinson's Prevention

By Yasaman Kianirad, MD, and Tanya Simuni, MD

Neurodegenerative disorders like Parkinson's disease (PD) and Alzheimer's disease are characterized by the progressive accumulation of misfolded proteins that aggregate and collect in the brain. In PD, the protein alpha-synuclein accumulates in brain cells. While the normal function of synuclein is not well understood, the protein normally exists in a soluble form. In PD, however, the protein can misfold and form soluble aggregates and insoluble fibrils. Scientists believe that those clumps (called Lewy bodies) are toxic and contribute to the disease's pathology.

Exploring how to prevent, break up, or clear out Lewy bodies is one of the most promising targets for new drugs that will stop or slow PD. A number of companies are working to develop new therapeutics in this area, including vaccination.

Developed by AFFiRiS, PD01A is an immunotherapy vaccine against alpha-synuclein. The Phase 1 clinical study of 22 subjects with PD showed that the vaccine is safe and well tolerated and caused an expected immune response in 86 percent of vaccinated subjects. The company has completed recruiting subjects for a Phase 1B study, which is focused on long-term safety and clinical activity after one boost vaccination. Although the safety results have been reassuring, longer observation periods and larger studies are required to determine whether the vaccine is able to slow progression of PD.

BIB054 is a monoclonal antibody designed to bind to alpha-synuclein. The Biogen company is conducting an early Phase 1 study, recruiting healthy subjects and patients with early PD

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in order to evaluate the safety and tolerability of a range of single doses administered by IV infusion.

Additionally, Prothena has developed PRX002, another monoclonal antibody targeting alpha-synuclein. The Phase 1 clinical trial in healthy subjects and patients with PD showed that the drug is safe and well tolerated. A Phase 2 clinical study is expected to begin this year.

This exciting new avenue of PD research is very promising, though much more work is required before researchers can establish the efficacy of these therapies. Most of these studies target patients with newly diagnosed PD, and we encourage potentially qualifying patients to find out more about participating.

For more information, visit clinicaltrials.gov and foxtrialfinder.michaeljfox.org.

ClinicalTrials.gov Identifiers:

PD01A Phase 1B study: NCT02216188

BIB054 Phase 1 study: NCT02459886

Parkinson's Disease and Palliative Care

By Carolyn Taylor

You may have heard the term “palliative care” but assumed it’s for people with terminal illnesses or cancer, or that it’s similar to hospice care. Widespread misunderstanding of what palliative care is, both by patients and healthcare providers, has resulted in underutilization of this important treatment option.



/// Palliative care providers focus not only on symptom management but also on improving quality of life more broadly. ///

The National Hospice and Palliative Care Organization defines palliative care as “patient- and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering.” Palliative care providers focus not only on symptom management but also on improving quality of life more broadly, offering spiritual care and caregiver support as well as providing medical support along with your regular doctors.

As many patients and caregivers know, Parkinson’s disease comes with a uniquely high symptom burden. PD patients suffer physical symptoms as well as a host of nonmotor symptoms, including depression, anxiety, fatigue, light-headedness, drooling, and constipation—not to mention the financial and psychosocial burdens the disease can place on patients and families. What’s more, no two patients’ symptoms are alike, making it all the more important to consider individual needs.

By taking a holistic perspective, palliative care providers address motor, nonmotor, and psychosocial symptoms of Parkinson’s. Patients often have multiple medical issues and see a number of specialists, and the palliative care team can assist in managing multiple illnesses by assessing symptoms and communicating with appropriate physicians. They can also treat the stiffness and pain that often accompany Parkinson’s.

For people with more advanced disease, the team can provide guidance to navigate such legal matters as designating power of attorney and creating a living will.

Palliative care providers are able to provide care to patients in the comfort of their own homes once every two weeks, easing the burden of traveling to see a doctor. In this way, a palliative care provider can be a valuable addition to a movement disorders specialist.

Northwestern Medicine offers outpatient palliative care consultations at the request of your neurologist. Your physician can also recommend several home-based programs depending on your location and needs. Talk to your movement disorders specialist to learn more about palliative care and whether it’s right for you and your family.



Carolyn Taylor, RN, MSN, AGPCNP-BC, is a board-certified adult geriatric nurse practitioner. She received her bachelor’s degree in medicine, health, and society at Vanderbilt University and went on to complete Vanderbilt’s accelerated master of science in nursing program, specializing in adult and geriatric health. She spent two years in private practice before joining Northwestern’s Movement Disorders team in February 2016. Her professional interests include advanced Parkinson’s therapeutics, palliative care, exercise, and caring for women with PD.

Staff Profiles

Steven J. Lubbe, PhD

ASSISTANT PROFESSOR OF NEUROLOGY AND GENETIC MEDICINE, DEPARTMENT OF NEUROLOGY, FEINBERG SCHOOL OF MEDICINE

After completing his master of science in medicine (specializing in human genetics) at the University of the Witwatersrand in Johannesburg, Steven Lubbe undertook a PhD program in cancer genetics at the Institute of Cancer Research, London. During his time there, he focused on the identification and characterization of the familial and population risks of both known and novel genetic variants in the etiology of colorectal cancer. Lubbe then worked as a postdoctoral research associate at the Institute of Neurology at University College London, where he analyzed whole-exome sequencing data in early-onset Parkinson's disease to identify novel disease-causing mutations.

Lubbe joined the faculty of the Ken and Ruth Davee Department of Neurology at the Feinberg School of Medicine in April 2016. His laboratory's primary focus is identifying changes in DNA that can cause or influence disease through the bioinformatic analysis of next-generation sequencing data from patients with PD and other movement disorders. Lubbe is also interested in studying the role of oligogenic inheritance and potential genetic modifiers in Parkinson's disease, as well as investigating the epidemiological link between PD and malignant melanoma.

By working with the clinical team at the Parkinson's Disease and Movement Disorders Center Biorepository, he hopes to drive neurogenetics research and facilitate better genetic diagnoses. Lubbe believes that by looking at this type of data, researchers will gain a better understanding of the underlying causes of Parkinson's disease, which could pave the way to finding better treatments.



Niccolò E. Mencacci, MD, PhD

RESEARCH ASSISTANT PROFESSOR, DEPARTMENT OF NEUROLOGY, FEINBERG SCHOOL OF MEDICINE

Niccolò Mencacci is a neurologist and geneticist with extensive clinical and research expertise in movement disorders, including Parkinson's disease, dystonia, and choreic syndromes.

Mencacci received his medical degree in 2006 and completed his residency in neurology in 2012 at the University of Milan. He then joined the department of molecular neuroscience at University College London, where he conducted research under



the supervision of professors John Hardy and Nick Wood.

During that time he became proficient in the application of a variety of genetic techniques, including genome-wide genotyping, homozygosity mapping, linkage, and exome sequencing analysis.

Through applying these techniques and building a close collaboration between the Queen Square movement disorders clinical team and the lab, Mencacci successfully identified several new genetic causes of movement disorders. He was awarded his PhD in July 2016.

Combining genetics and a range of in vivo and in vitro models of basal ganglia dysfunction, Mencacci investigates as a clinician scientist the molecular pathophysiological mechanisms that underlie movement disorders.

Lake Forest Resources

As the population of people with Parkinson's disease and other movement disorders continues to grow, we've seen more and more patients seeking therapy services at Lake Forest Hospital. Our Parkinson's Disease and Movement Disorders team, made up of occupational and physical therapists and speech-language pathologists, works closely with a group of patients and their families to provide therapy and support throughout the rehabilitation process. Begun last year at the hospital's Lake Forest Health and Fitness Center, the group provides an opportunity for people with PD, family members, and caregivers to share ideas, trials, and successes to improve their everyday experience and quality of life.

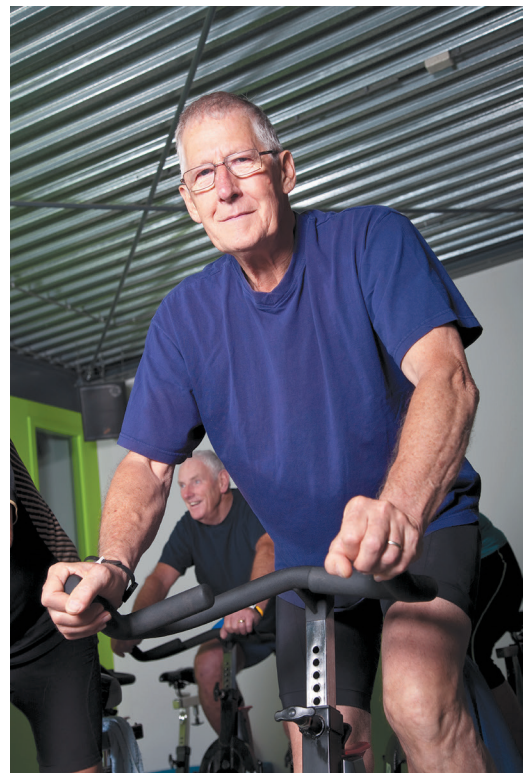
The group's two-hour meetings include components of exercise, a "caring and sharing" discussion, and an educational presentation. Featured topics have included PD 101, PD and nutrition, National Parkinson Foundation resources, Rock Steady Boxing, and voice and swallowing concerns.

Peter Daniel, an active participant, finds tremendous value in sharing his experiences at meetings. "I feel like I fit into this group because we have something in common," he says. "I'm making new friends and like to attend because I never know what I'm going to learn."

In addition to the support group, the Health and Fitness Center offers dance and stationary bicycle classes at no charge for people with PD and their caregivers.

For more information, contact the Rehabilitative Services Department of Lake Forest Hospital at 847-535-8060.

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Why Do I Feel Light-Headed?

By Kenny Tan and Danny Bega

Parkinson's disease involves both motor and nonmotor symptoms. The motor symptoms, such as tremor, slow movements, and stiffness, result from the loss of dopamine-producing cells in the midbrain. Over time, we have come to learn that PD is not localized to these cells only. PD's nonmotor symptoms, such as depression, cognitive impairment, and sleep disturbances, are likely due to the disease's affecting other areas of the brain and nervous system.

One troublesome nonmotor symptom, which may occur in 20 percent of PD patients, is orthostatic hypotension (OH), a positional drop in blood pressure that leads to light-headedness, dizziness, falling, and sometimes fainting. This is due to disease involving the autonomic nervous system, which controls nonconscious organ functions such as blood flow, breathing, and digestion. It is important to recognize and treat OH, as it may pose significant consequences for quality of life, balance, and ability to tolerate PD treatments.

What is orthostatic hypotension?

Many PD patients develop low blood pressure (or hypotension) at some point. Patients typically experience symptoms of OH during positional change (e.g., moving from lying down to sitting or standing, or from kneeling to standing). OH is diagnosed when there is a sustained reduction of systolic blood pressure (the top number when your blood pressure is taken) of at least 20 mmHg or diastolic blood pressure (the bottom number) of 10 mmHg within three minutes of standing.

How does it occur?

Essentially, our nervous system is supposed to automatically increase blood flow to our brain to counter gravity when we stand up or stand still for a prolonged period. Failure of this automatic signaling in PD can lead to a problematic drop in blood pressure. Parkinson's medications (dopaminergic drugs) can also lower blood pressure and further worsen the symptoms of OH.

DROPS IN BLOOD PRESSURE IN PARKINSON'S PATIENTS CAN CAUSE LIGHT-HEADEDNESS, DIZZINESS, FATIGUE, CLOUDED THINKING, AND FAINTING.

OH can occur at any stage but is usually more problematic in moderate-to-advanced patients. If it occurs early, an alternative diagnosis such as multiple system atrophy is sometimes considered.

It's important to note that these drops in blood pressure can occur even in people who have had high blood pressure most of their lives. It's also possible, and further complicating, for someone to have high blood pressure when sitting or lying down but low blood pressure when standing up. Therefore, a diagnosis of high blood pressure (hypertension) does not exclude a diagnosis of OH.

What are the symptoms of OH and how is it diagnosed?

Light-headedness or dizziness after standing is a common OH symptom, along with fatigue, clouded thinking, and fainting. Some patients with OH may appear to be asymptomatic.

Clinical history, measurement of orthostatic blood pressure after standing for three minutes, and home monitoring of orthostatic blood pressure will help in making a diagnosis.

What are the treatment options for OH in PD?

There are nonpharmacological and pharmacological treatments for PD. Your doctor will usually start with a nonpharmacological approach.

Nonpharmacological

Apply helpful behavioral strategies. Some of the following strategies can be practiced to prevent OH symptoms:

Slow position change: When rising from lying down, try sitting on the edge of the bed or sofa for a few minutes before standing up.

Bed position: Keep your head elevated at night so there is less of a drop in blood pressure when you stand up in the morning.

Perform exercises: Try exercises like squeezing a rubber ball or tapping your feet for a few minutes before standing. These exercises will raise your blood pressure and prevent a drop when you stand up.

Consider other drugs that may contribute to low blood pressure: Many non-PD medications may cause reduced blood pressure. Diuretics and drugs for hypertension may further worsen hypotension and cause more OH symptoms. You may need to discuss with your physician whether using these drugs is still necessary or whether dosage can be reduced to minimize side effects. Other drugs that may lower blood pressure include prostate medicines like tamsulosin, pain medicines like opioids and tizanidine, tricyclic and other antidepressants, and medications for erectile dysfunction like sildenafil.

Increase water and salt intake: Many studies have evaluated how drinking water influences blood pressure. Drinking at least 1½ liters a day will help increase plasma volume and reduce OH symptoms. Increasing salt ingestion can also increase plasma volume as water chases salt into the bloodstream.



Stockings and abdominal bands: Compression stockings and abdominal bands can help oppose blood pooling in the limbs when you stand up. Abdominal bands have been shown to be more effective and have better compliance than stockings. A band can increase blood pressure by as much as 12 mmHg.

Pharmacological

Pharmacological approaches will be considered if OH symptoms persist after nonpharmacological methods have been tried, or if the patient has pronounced OH symptoms that need to be addressed to prevent complications like falls or injuries. The medications prescribed for OH are used to increase blood pressure by increasing the blood volume (fludrocortisone) or increasing blood-vessel narrowing (midodrine or droxidopa). A combination of pharmacological and nonpharmacological strategies usually yields better results than does a single approach.

Kenny Tan, MD, is a movement disorders fellow at the Feinberg School of Medicine. Danny Bega, MD, is an assistant professor in the movement disorders division of the Department of Neurology at the Feinberg School.



PARTNERING WITH NPF

The Northwestern Medicine Parkinson's Disease and Movement Disorders Center, recognized by the National Parkinson Foundation as a Center of Excellence, collaborates with NPF on events such as conferences for caregivers and the annual Moving Day Chicago fundraising event.

The PDMDC uses support from NPF to sponsor patient and caregiver symposia and to offer support groups and classes for Parkinson's patients in communities with limited clinical and educational services. In turn, Northwestern assists the foundation in implementing NPF programs in Illinois.

Founded in 1957 and headquartered in Miami, the National Parkinson Foundation is a premier international organization funding research and providing support services, education, outreach, and advocacy for people with PD and their loved ones. Its Centers of Excellence must provide the highest quality in patient care, implementation of best practices, leadership in developing targeted research to extend knowledge of PD, and innovative models of education, service, and outreach.

Northwestern and NPF work together to deliver high-quality patient care, make a difference, and form a united front against Parkinson's.



LEARN AND MOVE SERIES

The National Parkinson Foundation Chicago is hosting a new bimonthly program focused on outreach in the city's South and West Sides.

Learn and Move is a free educational program for Parkinson's patients, caregivers, and family members. The inaugural session's educational focus was "PD 101," an overview of the disease and its causes, symptoms, treatments, and more. The movement portion featured an exercise demonstration of Rock Steady Boxing, a noncontact, boxing-inspired fitness routine proven to dramatically improve symptoms of people with Parkinson's.

The Learn and Move program is offered every other month from 10 to 11:30 a.m. at the Kroc Center, 1250 West 119th Street, Chicago.

Registration is required. For dates of upcoming meetings and to register, call Jessica Bartsch at 630-709-4258.

Support Groups, Programs, and Events

Support groups allow people diagnosed with Parkinson's disease and their care partners to

- share experiences
- meet new people
- receive support and understanding

For more information on support groups, call 312-503-4397.

Parkinson's Support Group—Chicago

First Tuesday of the month (no group in July)

10:30 a.m.–2 p.m.

251 East Huron Street, Feinberg Pavilion, conference room A

Women with Parkinson's Support Group—Chicago

May 13, August 26, October 21, December 9

11 a.m.–12:15 p.m.

251 East Huron Street, Feinberg Pavilion, NM Academy 2-715

Art and Yoga—Chicago

Tuesdays (except the first Tuesday of each month)

1–3 p.m.

250 East Superior Street, Prentice Pavilion, conference room Q

Early Onset/Young Diagnosis—Chicago

May 13, August 26, October 21, December 9

9–10:15 a.m.

251 East Huron Street, Feinberg Pavilion, NM Academy 2-715

Parkinson's Wellness Programs at JCC Chicago

New Sessions: May 1–August 2

Cost: \$10/class, with a free J Fit membership

to the facility included

Bernard Horwich JCC

3003 West Touhy Avenue

Stay Fit Exercise Classes

Strength and Balance (Level 2)

Mondays, 3–4 p.m.

Power Flow (Level 1)

Mondays, 4–5 p.m.

Chair Class: Seated Strength and Stretch (Level 3)

Wednesdays, 3–4 p.m.

Aerobic Dance (Level 2)

Wednesdays, 4–5 p.m.

Build Your Care Network

Care Partner Support Group

Wednesdays, 3–4 p.m.

SAFRA Spring Symposium

Sunday, May 21

9 a.m.–noon

Bernard Weinger JCC

300 Revere Drive, Northbrook

This event is free to attend. Continental breakfast will be served. For more information or to register, call **312-926-8400** or visit **classes.nmh.org**.

Recruiting for Clinical Trials

EARLY PD

SURE-PD3

This study is designed to test whether increasing levels of the antioxidant urate can slow the progression of early PD. In this study, blood urate levels will be raised with a drug called inosine, which the body converts into urate. You may qualify if you have been diagnosed with PD within the past three years, are not taking medication to treat PD (except for MAO-B inhibitors), and do not have a history of gout, recurrent kidney stones, heart attack, or stroke. [Funded by the Michael J. Fox Foundation and the National Institute of Neurological Disorders and Stroke.](#)

PD WITH MOTOR FLUCTUATIONS

Rescue Therapy

Cynapsus

A 24-week, prospective, multicenter, open-label Phase 3 study in levodopa-responsive patients with motor fluctuations ("off" episodes), designed to evaluate the long-term safety, tolerability, and efficacy of APL-130277. [Funded by Cynapsus Therapeutics.](#)

Infusion Therapies

Apomorphine

This is a multicenter, open-label Phase 3 safety and efficacy study of continuous infusion apomorphine in subjects with advanced PD who are unable to achieve adequate control despite optimized noninvasive therapy. [Funded by US World Meds.](#)

Neuroderm

The primary aim of this study is to assess the long-term safety (systemic and local) and tolerability of continuous subcutaneous infusion of NDO612 by adverse events, vital signs, and local tolerability. [Funded by Neuroderm.](#)

TOZ-PD

The purpose of this study is to test the effect of tozadenant tablets in patients using levodopa, whether tozadenant decreases end-of-dose wearing-off of levodopa, and what side effects can be expected with tozadenant. Participants will maintain an accurate record of on- and off-time in a home diary. Other symptoms that some patients experience will be evaluated during clinic visits. Requires 15 visits over 1½ years. [Funded by Biotie Therapies.](#)

PD NONMOTOR SYMPTOMS

Orthostatic Hypotension

Restore

This study will evaluate the time-to-treatment intervention in patients with PD, multiple system atrophy, pure autonomic failure, nondiabetic autonomic neuropathy, or dopamine beta hydroxylase deficiency who have been previously stabilized with droxidopa therapy for symptoms of neurogenic orthostatic hypotension (dizziness, light-headedness, or feeling that they are about to black out). [Funded by Lundbeck NA.](#)

Cognitive Dysfunction

Synapse

This study will assess the efficacy of a fixed dose of SYN120 on cognition in patients with Parkinson's disease dementia. Requires 6 visits over 24 weeks. [Funded by Biotie Therapies.](#)

Surgical

INTREPID

This study will evaluate the safety and efficacy of bilateral stimulation of the subthalamic nucleus as an adjunctive therapy for improving the number of waking hours per day with good symptom control and without troublesome dyskinesia. Subjects are adults with advanced, levodopa-responsive bilateral PD that is not adequately controlled with medication. Requires 14 clinic visits and a phone call over 5½ years. [Funded by Boston Scientific Corporation.](#)



OBSERVATIONAL STUDIES

PPMI

This study will identify clinical, imaging, and biologic markers of PD progression for use in clinical trials of disease-modifying therapies. The five-year study is recruiting PD subjects who do not require therapy for at least six months, as well as non-PD subjects. Funded by the Michael J. Fox Foundation.

Biorepository

The objective is to collect pertinent genetic, biologic, and clinical information from subjects with PD and healthy control subjects evaluated at the Parkinson's Disease and Movement Disorders Center. Funded by the Northwestern Medicine Parkinson's Disease and Movement Disorders Center.

NPF QII

The purpose is to determine the long-term effects of PD and related conditions on quality of life. Funded by the National Parkinson Foundation.

For more information about Parkinson's disease research at Northwestern, visit parkinsons.northwestern.edu/clinical_trials.html, call **312-503-0755**, or email PDclinicaltrials@northwestern.edu.

Parkinson's Disease and Movement Disorders Center

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Northwestern Medicine's Parkinson's Disease and Movement Disorders Center is proud to be a National Parkinson Foundation Center of Excellence.

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