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Parkinson's Disease UPDATE

A quarterly newsletter dedicated to awareness about the latest research, resources, advances and treatments for Parkinson's disease.

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PARKINSON'S DISEASE EARLY SIGNS AND CAUSES

Parkinson's disease is a movement disorder that affects the nervous system. Its symptoms occur because of low dopamine levels in the brain. Early signs include tremor, a loss of a sense of smell, and coordination problems.

Experts do not know why Parkinson's disease develops, but they currently believe that genetic changes and exposure to environmental factors, such as toxins, play a key role.

Read on to find out more about the early signs of Parkinson's disease and what causes it.

Early Signs

The symptoms of Parkinson's disease develop gradually. They often start with a slight tremor in one hand and a feeling of stiffness in the body. Over time, other symptoms develop, and some people can experience dementia.

Some early signs of Parkinson's disease may include:

- movement changes, such as tremors
- coordination and balance impairments that can cause a person to drop things or fall over
- a loss of sense of smell
- gait changes, so a person leans forward slightly or shuffles when walking
- fixed facial expressions due to changes in the nerves that control face muscles
- a voice tremor or softer voice
- more cramped and smaller handwriting
- sleep problems resulting from restless legs and other factors
- rapid eye movement sleep disorder may be a powerful predictor, according to a 2015 study.

Movement symptoms may start on one side of the body and gradually affect both sides.

Other common symptoms include:

- mood changes, including depression
- difficulty chewing and swallowing
- fatigue
- constipation
- skin problems
- dementia, delusions, and hallucinations that can develop in time

Having these symptoms does not mean a person has Parkinson's disease. Various other conditions can have similar symptoms, such as:

- Parkinsonism
- head trauma
- encephalitis
- stroke
- multiple system atrophy
- progressive supranuclear palsy

Causes

Parkinson's disease is a neurological disorder that develops when changes occur in the brain. Precisely why it happens is unclear, but scientists have identified some variations that occur.

Low dopamine levels

Parkinson's disease symptoms mainly result from low or falling levels of dopamine, a neurotransmitter. It happens when cells that produce dopamine die in the brain.

Dopamine plays a role in sending messages to the part of the brain that controls movement and coordination. Therefore, low dopamine levels can make it harder for people to control their movement.

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Featured Articles

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As dopamine levels continue to fall, symptoms gradually become more severe.

Low norepinephrine levels

Parkinson's disease may also cause damage to the nerve endings that produce another neurotransmitter, norepinephrine, which contributes to blood circulation and other automatic body functions.

Low levels of norepinephrine in Parkinson's disease may increase the risk of both motor and nonmotor symptoms, such as:

- stiffness and rigidity
- postural instability
- tremor
- anxiety
- difficulty focusing
- dementia
- depression

This may explain why people with Parkinson's disease commonly experience orthostatic hypotension. This refers to when a person's blood pressure changes when they stand up, leading to lightheadedness and a risk of falling.

Lewy bodies

A person with Parkinson's disease may have clumps of protein known as alpha-synuclein, or Lewy bodies, in their brain.

The accumulation of Lewy bodies can cause a loss of nerve cells, leading to changes in movement, thinking, behavior, and mood. It can also lead to dementia.

Lewy body dementia is not the same as Parkinson's disease, but people may have both as the symptoms are similar.

Genetic factors

Experts have identified changes in several genes that appear to have links with Parkinson's disease, but they do not consider it a hereditary condition.

Genetic factors appear to cause only 10% of cases, mostly among people with early onset disease.

Autoimmune factors

In a 2017, scientists found a possible genetic link between Parkinson's disease and autoimmune conditions, such as rheumatoid arthritis.

In 2018, researchers investigating health records in Taiwan found that people with autoimmune rheumatic diseases had a 1.37-higher chance of also having Parkinson's disease.

Risk factors

Several environmental factors may increase the risk of developing Parkinson's disease.

These include:

- Past traumatic brain injury: Head injuries from contact sports, for example, may increase the risk of the condition.
- Toxin exposure: Such as pesticides, solvents, metals, and other pollutants.
- Gender: Males are 50% more likely to develop the condition than females, although one 2016 study suggests the risk for females may increase with age.
- Age: The condition often appears from the ages of 60 years.
- Some drugs and medications: Certain medicines can lead to Parkinsonism, where a person has tremors and other symptoms but does not have Parkinson's disease.

Symptoms usually appear from the age of 60 years. However, 5-10% of people with the disease have early onset Parkinson's, which starts before the age of 50 years.

Do racial factors affect the risk?

In the past, statistics have suggested that Parkinson's disease is less likely to affect Black people than other people of other ethnicities in the United States.

However, experts now say this may be due to a lack of awareness about how the disease can affect Black individuals and a higher chance of misdiagnosis due to inequities in health provision.

Prevention

It is not possible to prevent Parkinson's disease, but some lifelong habits may help reduce the risk.

Avoiding toxins

People should take precautions when using potentially toxic chemicals, such as herbicides, pesticides, and solvents.

Where possible, individuals should take the following steps:

- avoiding the unnecessary use of pesticides and herbicides
- using alternatives to products containing known toxins, such as paraquat
- taking precautions, such as wearing protective clothing, when it is not possible to avoid them

Avoid head trauma

For protection from a traumatic brain injury, people can take the following steps:

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- wearing protective headgear during contact sports
- wearing a helmet when cycling or motorcycling
- using a safety belt when traveling by car
- seeking medical attention for concussion and avoiding future risks until a doctor says it is safe to do so

Exercise

Regular physical exercise may help prevent or treat Parkinson's disease, according to a 2018 review. The authors note that physical activity can help maintain dopamine levels in the brain.

Dietary factors

Some dietary choices may also help reduce the risk of Parkinson's and other diseases. Research has shown that the following may help:

- Turmeric: A mild spice people can add to curries, soups, teas, and other foods. It contains curcumin, an antioxidant ingredient. According to one laboratory study, it may help reduce the risk of Parkinson's disease by preventing oxidative stress and the clumping of alpha-synuclein protein.
- Flavonoids: Research suggests this antioxidant may lower the risk of developing Parkinson's disease. Berries, apples, some vegetables, tea, and red grapes contain flavonoids.
- Avoiding aldehydes: Heating and reusing some cooking oils, such as sunflower oil, may cause aldehydes to form, which are toxic chemicals to Parkinson's and other diseases. Research from 2020Trusted Source suggests that potatoes fried in previously used cooking oils could have high levels of aldehydes.

Summary

Parkinson's disease is a lifelong condition involving neurological changes in the body.

Experts do not know why Parkinson's disease occurs, but genetic and environmental factors may play a role. Specifically, experts have found strong links with past traumatic brain injury and exposure to toxins.

Exercise, a healthy diet, and avoiding toxins may all help prevent Parkinson's disease, but there is no current evidence to confirm the specific cause.

Resources

https://www.medicalnewstoday.com/artcles/323396 (medicalne

No Pills, No Surgery, No Electrodes for Parkinson's Disease?

Minimally invasive devices to drip dopaminergic drugs edge closer to market

by John Gever, Contributing Writer, MedPage Today April 26, 2023

BOSTON – Several technologies for delivering levodopa-carbidopa in a more physiologically natural fashion than is possible with ordinary oral versions for Parkinson's disease took center stage here at neurology's leading scientific conference.

In plenary sessions and late-breaking abstract presentations at the American Academy of Neurology (AAN), researchers provided updates on two subcutaneous delivery systems -- one of which could gain FDA approval almost any time -- and another with a unique oral drip system.

Many neurologists see this type of treatment as a potential bridge for patients no longer controlled adequately with oral medications but whose disease is not so far advanced that surgical procedures such as thalamotomy, or implantation of deep brain stimulation systems, appear necessary. If dopaminergic stimulus could be provided continuously, instead of intermittently as is the case for oral drugs, it's believed that so-called "on" time could be prolonged and "off" time reduced, helping patients get through the day comfortably without undergoing risky surgeries.

AbbVie is the leader in the race to bring such systems to market. In fact, it already sells a continuous-delivery system for levodopa-carbidopa. Called Duopa, it pumps a levodopa-carbidopa gel directly into the intestinal tract for 16 hours per day. But it is far from non-invasive -- it requires a surgeon to create an abdominal stoma for quasi-permanent port placement.

The drawbacks being obvious, AbbVie has been pursuing an alternative: a subcutaneous delivery system temporarily named ABBV-951 that uses prodrugs for levodopa and carbidopa in liquid form. Primary results from a phase II trial were published several months ago, showing that the foslevodopa-foscarbidopa system extended "on" time without troublesome dyskinesia (a standard endpoint for Parkinson's disease drugs) by some 2 hours relative to immediate-release oral levodopa-carbidopa.

FDA approval is expected, but in late March, the agency told AbbVie that it had questions about the system's mechanical pump (though not about the system's efficacy or safety). No new clinical studies were requested and AbbVie promised to resubmit its application "as soon as possible."

The company presented several follow-up studies at the AAN meeting, including one comparing ABBV-951 with Duopa for pharmacokinetic parameters. Mean levodopa blood levels were virtually identical over 24-hour evaluations. Ratios of areas under the receiver operating characteristic curve indicated that levodopa availability was about 8% higher with the new system versus Duopa, and differences between maximum and minimum concentrations were somewhat lower.

The regulatory delay may give an alternative subcutaneous system a chance to catch up. Called ND0612, the product is under development by California-based NeuroDerm, now a unit of Mitsubishi Tanabe Pharma, and is designed to release regular liquid levodopa-carbidopa around the clock. The infusion device is placed primarily on sides of the abdomen and on the lower back.

At the AAN meeting, Alberto Espay, MD, of the University of Cincinnati, presented results from the product's pivotal phase III trial, called BouNDless. It randomized 259 Parkinson's disease patients to use ND0612 or ordinary oral levodopa-carbidopa medications for 12 weeks.

BouNDless began with two sequential run-in periods of 4-6 weeks each, beginning with standard oral therapy followed by ND0612, during which dosing regimens for the two types of treatment were optimized for each participant individually. When ND0612 was in use, patients could also receive immediate-release levodopa-carbidopa to maximize symptom control.

Of 381 patients initially enrolled, 259 completed the run-in phase -- no specific reason was given for most of the dropouts, although 6% of patients using the subcutaneous system during the run-in quit because of infusion-site reactions.

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The remaining 259 were then randomized to ND0612 (plus supplementary oral medications as needed) or to standard oral levodopa-carbidopa for 12 weeks in a double-blind, double-dummy format. ND0612 provided up to 720 mg of levodopa and 90 mg of carbidopa per 24-hour period.

Mean patient age was about 64, and just under two-thirds were men. Time since initial diagnosis was 10 years, with motor fluctuations first appearing a mean 5 years previously.

Prior to the run-in, "on" time without troublesome dyskinesia averaged about 9.4 hours/day, rising to about 12 hours with ND0612 during the run-in phase. "Off" time at that point averaged 3.5 hours. After randomization, "on" time remained near that level through the 12-week treatment period among patients assigned to the subcutaneous system. The oral-therapy control group, on the other hand, saw "on" time slip back to near baseline. At week 12, the net difference in "on" time favoring ND0612 was 1.72 hours (95% CI 1.08-2.36).

"Off" time showed the reverse pattern: at week 12, it stood at 1.90 hours with oral therapy, versus 0.50 hours with ND0612 ($P<0.0001$). Other outcome measures, including Unified Parkinson's Disease Rating Scale part II scores and patients' and clinicians' global impressions, also significantly favored ND0612.

Infusion-site reactions remained a problem, Espay acknowledged. Some 13% of patients using the system complained of moderate irritation and one patient considered it severe. Seven patients assigned to the system dropped out because of treatment-emergent adverse effects, compared with four in the oral-therapy group. Skin irritation, he said, "is the Achilles heel of all SQ [subcutaneous] based therapies." He said rotating the application site to different parts of the body appears so far to be the best way to minimize the problem.

Preliminary results with a third approach were also reported at the AAN meeting. This involved a plastic oral appliance similar to the retainers that orthodontics patients often wear for maintenance, but with a small pump attachedopens in a new tab or window that drips a levodopa-carbidopa paste onto the back of the tongue, where it is then swallowed with saliva. Called DopaFuse, the system was developed by a company called SynAgile, based in Wyoming. Its chief medical officer, C. Warren Olanow, MD, formerly of the Icahn School of Medicine at Mount Sinai in New York City, presented findings from a small, 2-week phase II trial.

Like BouNDless, the trial had a somewhat complicated design. On study day 1, patients came into the clinic and received standard oral levodopa-carbidopa that day, with frequent blood sampling and clinical tests that day. On day 2, still in clinic, patients then used the DopaFuse system and underwent the same testing. On day 3, patients (also still in clinic) took one dose of regular oral medication and then used DopaFuse for the rest of the day. From day 4 to 14, patients repeated the day 3 procedure at home, and on day 15, they returned to the clinic for further testing.

Sixteen patients participated. Some patients found the device uncomfortable: a total of eight instances of abrasion or laceration inside the adjacent cheek were reported. All but one was considered mild, however, and all resolved after one day. No adverse events were considered serious and none of the patients discontinued on account of them.

Pharmacokinetic parameters indicated that the device was working as intended. Motor fluctuations while using DopaFuse on day 3 were smaller by about half relative to day 1 when patients received regular oral therapy. "On" time without severe dyskinesia was extended by about 1.5 hours relative to regular oral treatment, as was "on" time without any dyskinesia. "Off" time was reduced with DopaFuse to a corresponding degree.

The key clinical issue with all of these systems is, once approved, where they would fit in the treatment landscape. This came up after Espay's presentation when a session moderator posed the question directly. Espay responded, "The way in which we at the moment conceive this therapy is in adapting it into the early phase of advanced treatment, for individuals who are experiencing more fluctuations, for whom [conventional] dose optimization is not quite effective."

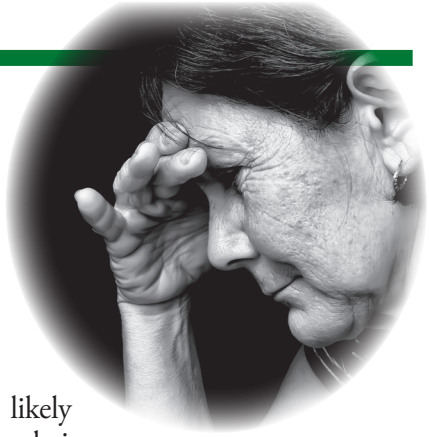
It would be an option, he added, "for individuals currently being considered for deep brain stimulation, for instance." Asked later whether one might introduce a continuous-infusion therapy earlier in the disease process, Espay agreed that it might indeed be warranted, but for now it remains only a "theoretical" possibility that needs more research. "We have not the data yet to demonstrate that it would in fact pan out," he said.

Source Reference: Rosebraugh M, et al "Foslevodopa-foscarbidopa subcutaneous infusion maintains similar levodopa exposure to levodopa-carbidopa intestinal gel delivered to the jejunum when infused for 24 hours" AA

Resources

https://www.medpagetoday.com/meetingcoverage/aan/104206

What's the Life Expectancy for Parkinson's Disease?



What is Parkinson's disease?

Parkinson's disease is a progressive brain disorder that affects mobility and mental ability. If you or a loved one has been diagnosed with Parkinson's, you may be wondering about life expectancy. According to some research, on average, people with Parkinson's can expect to live almost as long as those who don't have the condition.

Is it fatal?

While the disease itself isn't fatal, related complications can reduce life expectancy by 1 to 2 years. A small 2018 study suggests the survival rate of people with Parkinson's is highly dependent on the type of parkinsonian disorder they have. Patients with idiopathic Parkinson's disease (meaning the disease has no cause) and normal cognitive function appear to have a mostly normal life expectancy. People with atypical Parkinsonism including dementia with Lewy bodies (LBD), progressive supranuclear palsy, and multiple system atrophy have increased mortality compared to the general population. There's also a correlation between mortality rate and the existence of parkinsonian symptoms (except for tremors) and olfactory dysfunction, or problems related to your sense of smell. Gender could also play a role in mortality. Multiple studies suggest a higher mortality rate among those assigned female at birth.

Symptoms and Stages

Parkinson's disease is classified by stages, ranging from 1 to 5. Stage 5 is the most advanced. Advanced stages may increase the risk of health complications that can reduce lifespan.

The symptoms of Parkinson's are gradual and sometimes unnoticeable in the early stages of the disease. They may include: tremors, loss of balance, slowing of movements and spontaneous, uncontrollable movements.

Symptoms in later stages of Parkinson's may include: falling more frequently, trouble dressing and eating, severe stiffness in legs making it impossible to stand or walk, hallucinations or delusions, cognitive changes (problems with planning, language, attention, memory), dementia, lightheadedness, mood disorders, loss of sense of smell or taste, vision problems. sleep disorders and sexual problems

Your risk of falling increases as Parkinson's progresses to stages 3, 4, and 5, and motor balance worsens.

A 2016 study suggests that people with Parkinson's are about three times more likely to fall than the general population, and serious falls can result in concussions and broken bones. In rare cases, serious falls can be fatal. Pneumonia, particularly aspiaration pneumonia, is the leading cause of death for people with Parkinson's, accounting for 70 percent of Parkinson's deaths. Aspiration pneumonia happens when you inhale food, stomach acid, or saliva into your lungs. As Parkinson's progresses, swallowing can become more difficult, causing food and liquid to enter the lungs.

Treatment Options for Each Stage of Parkinson's

Parkinson's disease cannot be cured, but medications, supportive treatments, lifestyle changes, and even surgery can help manage your symptoms, particularly when started early.

Stage 1

Early treatment of Parkinson's typically includes physical therapy and regular exercise to help improve your balance, strength, and flexibility. In physical therapy, a physiotherapist will work with you to relieve muscle stiffness and joint pain through movement and exercise, with the goal of improving your walking and flexibility. Making dietary changes can also help improve early Parkinson's symptoms. For example, increasing the amount of fiber in your diet and drinking lots of water can help reduce constipation. Increasing the amount of salt in your diet and eating lots of small, frequent meals can help you avoid the dizziness that can accompany low blood pressure. You should only increase your salt intake if your blood pressure is low. Be sure to consult with your healthcare provider first. In early Parkinson's, your doctor might prescribe medications known as dopamine agonists, such as Ropinirole (Requip). These medications can provide short-term relief from symptoms and may delay the appearance and severity of motor-skill complications as the disease progresses.

Stage 2

If you're in this stage of Parkinson's, you may have trouble swallowing (dysphagia) and problems with your speech. A speech-language pathologist can provide exercises to help you with speaking and swallowing and provide assistive technology to help you communicate. You may also benefit from working with an occupational therapist who can help you come up with practical solutions to problems you encounter in your everyday life, such as difficulty getting dressed or showering. Your doctor may prescribe medications to help treat symptoms such as tremors and problems with movement. Options

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include: Carbidopa-levodopa (Sinemet, Rytary, Duopa): This medication, known as a dopamine precursor, is the most potent and effective medication for Parkinson's. Levodopa is absorbed by nerve cells in your brain and turned into the neurotransmitter dopamine, which helps replace the dopamine lost to Parkinson's. It is usually taken as a liquid or tablet and taken alongside other medications like benserazide or carbidopa that reduce the side effects of levodopa and prevent it from being broken down in the bloodstream before it gets to the brain.

Dopamine agonists: These drugs mimic dopamine's effects in the brain, helping relieve Parkinson's symptoms. Their effects are similar to levodopa but milder, and they can be taken less frequently than levodopa. Options include pramipexole (Mirapex), ropinirole (Requip), and rotigotine (Neupro).

MAO-B Inhibitors: These drugs stop the breakdown of dopamine in the brain and include rasagiline (Azilect), safinamide (Xadago), and selegiline (Eldepryl).

Amantadine (Gocovri). Amantadine is known as a NMDA antagonist, although the exact way it works in your body is not yet fully understood. It is prescribed to help treat dyskensias and "off episodes" in patients already taking levodopa-based medication. Dyskensia is a side effect of Parkinson's disease that causes involuntary movements. "Off episodes" occur when the medication you regularly take does not work as well as it usually does.

Other drugs: Catechol-O-methyltransferase (COMT) inhibitors are often prescribed to people in later stages of Parkinson's disease and help prevent levodopa from being broken down in the body. Anticholinergics can prevent tremors and treat movement disorders caused by Parkinson's.

You may want to use complementary therapies in all stages of Parkinson's to improve well-being and help manage stress. These include: yoga, tai chi, meditation, massage, music therapy and art therapy.

Stage 3

Treatments and therapies used in early stages of Parkinson's may still be used in stage 3. These treatments include: exercise, physical therapy, a balanced diet, speech-language therapy, occupational therapy, medications and alternative therapies.

Stages 4 and 5

Treatments often become less effective in the most advanced stages of Parkinson's. As the disease progresses, your doctor might switch up how your medication is delivered to make it more potent. For example, a patient taking dopamine agonist tablets may be switched to Apomorphine, a form of dopamine agonist injected under the skin or administered through a continuous infusion using a small pump carried on your person. If you're on levodopa drugs, your doctor may switch you to duodopa, a type of levodopa in the form of a gel that is continuously pumped into your gut through a tube inserted into your abdomen.

In late stages of Parkinson's, you may undergo surgical procedures such as deep brain stimulation (DBS), which involves implanting a pulse generator, similar to a pacemaker, into your chest wall. The pulse generator is then connected to fine wires placed under the skin and inserted into specific areas of the brain where electrical currents from the generator stimulate areas of the brain affected by Parkinson's. While surgery can't cure Parkinson's, it factors that affect life expectancy.

Parkinson's and Falls

Falls are a common secondary symptom of Parkinson's disease. The risk of falling starts increasing in stage 3 and is greater in stages 4 and 5. In these stages, you may not be able to stand or walk on your own. You're also prone to broken bones and concussions, and severe falls can be dangerous. A serious fall can reduce your life expectancy due to complications from the fall.

Age

Age is another factor in the diagnosis and outlook for Parkinson's disease. Most people will be diagnosed after age 70. Age can also make you more prone to falls and certain diseases even without Parkinson's disease. Such risks can increase for older adults with Parkinson's.

Gender

People assigned female at birth have a reduced risk of getting Parkinson's. People assigned male at birth are 50 percent more likely than those assigned female at birth to develop the disease. Researchers have not found the exact reasons for this. However, people assigned female at birth with Parkinson's may have a faster progression and reduced longevity. Symptoms in people assigned female at birth may be different from symptoms in people assigned male at birth. It's important to note that age can play a factor regardless of gender. Patients assigned female at birth and who are over age 60 may not fare as well as younger people of the same biological sex diagnosed with the disease.

Access to Treatment

Life expectancy has increased significantly due to advances in treatment. Medications, as well as physical and occupational therapy, are especially helpful in the earliest stages of the disease. These treatments can improve a person's quality of life.

Long-term outlook

Parkinson's is not a fatal disease, meaning one does not die from it. Early detection is the key to helping reduce complications that can shorten life expectancy. If you suspect that you or a loved one may have Parkinson's disease, see your doctor right away.

Resources

https://www.healthline.com/health/parkinsons/life-expectancy

"Help Us Help Others – Donate Today"

Without ongoing contributions from generous donors like you, the **PARKINSON RESEARCH FOUNDATION** would be unable to fund **EDUCATION**, **RESEARCH**, and **FREE SERVICES** for the millions of people living with Parkinson's disease around the world.

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Please give serious consideration to the designation of PRF in your Will, Charitable Trusts, Life Insurance, Appreciated Securities and Real Estate as this offers preplanned giving opportunities that will serve the Parkinson community for years to come. Please call Lynne Henry (941) 893-4389 at the Parkinson Research Foundation, today, for personal assistance in initiating this effort.

The following language has been reviewed and is deemed a legally acceptable form for including such a bequest in a will:

"I give and bequeath to the Parkinson Research Foundation,
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for discretionary use in carrying out its aims and purposes,
(the sum of $_____) OR (a sum equal to _____% of the value of my gross
estate at the time of my death under this will or any codicil hereto)."

The Parkinson Research Foundation Federal ID number is 20-0205035

Memorial and Honor Giving

Honor a family member, friend or special event by donating to PRF. Pay tribute to someone you love whose life has been impacted by Parkinson's disease. In lieu of flowers, please consider designating Parkinson Research Foundation as your charity of choice.

Workplace Giving: Launch a Giving Campaign

Please consider leading a team at work by encouraging your colleagues and staff to join together to help those living with Parkinson disease. Launch a workplace giving campaign today.

Ask about Matching Gifts

Many gracious employers double even triple charitable donations made by individual employees. Some companies will match gifts made by retirees and/or their spouses. Contact your employees for matching gift eligibility as this allows you to maximize your personal donation.

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