About this book

**Glossary**
Definitions for all words underlined in blue can be found in the glossary starting on page 36. In addition, hovering over glossary terms with your cursor will reveal the definition. A comprehensive Parkinson’s disease glossary can be found at www.parkinson.org/glossary.

**Index**
An index of key words and topics can be found on page 40.

**Hyperlinks**
In addition to glossary words underlined in blue, words underlined in grey can be clicked to go directly to that page or link.

**Tip Sheets**
Certain pages include tip sheets with practical pointers for managing motor fluctuations. You can also view and download these in our PD library at www.parkinson.org/library.

**Videos**
Visit www.parkinson.org/videos and watch the “Managing Parkinson’s Mid-Stride” playlist for tips on how to work with your doctor to manage motor fluctuations.

**Navigation**
Click on the home icon on any page to return to the Table of Contents. The Contents items can also be clicked to go directly to the beginning of that chapter.
Every person’s Parkinson’s disease (PD) journey is unique. No two people have exactly the same symptoms or progression, let alone lifestyle and genetics. However, it is common that once you begin a treatment regimen after diagnosis, you can live life for a while with nearly complete relief from symptoms and few side effects. Eventually, though, after several years of being treated with levodopa, many people with PD notice that controlling symptoms becomes more difficult and requires more medication. At this point, motor fluctuations (also called “on-off” fluctuations) may begin to appear.

This book explains what motor fluctuations are, why these changes might happen, and how to treat and cope with them. The information, tips, and stories included here will provide answers, help you organize thoughts and questions for your medical team, and remind you that you are not alone on this Parkinson’s journey.
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Acknowledgements

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This book has been made possible through the generous donations of thousands of individuals affected by Parkinson's and grants from:

Design: Ultravirgo
If you’re reading this book, you are probably already familiar with Parkinson’s disease, but here are some basics: Parkinson’s is a neurodegenerative disorder that affects about one million people in the United States and 10 million people worldwide. It is called a movement disorder because of the tremors, slowing, and stiffening movements it can cause, but its symptoms are diverse and usually develop slowly over time.

Parkinson’s disease is not diagnosed with a test or a scan; instead it is diagnosed by your doctor, who asks you questions about your health and medical history and observes your movement. Your doctor may want you to have some tests, such as imaging, to rule out other possibilities. The goal of treatment is to help you manage your symptoms. Good symptom management can help you stay healthy, exercise, and keep yourself in tip-top shape. Although there is no way now to correct the brain changes that cause Parkinson’s, we know that exercise can help you fight the disease and that staying healthy can prevent setbacks that make PD progress faster. Great care is the key to living your best life with Parkinson’s.
Lack of dopamine — a neurotransmitter, one of several chemicals your brain cells use to send signals to each other — in people with Parkinson’s was first described in the 1960s. Soon after, dopamine-replacement therapy using levodopa became — and remains — the gold standard treatment. However, just as your doctor looks at tremors as a sign of changes in your brain, neuroscientists know that the reduction in dopamine in the brain is a sign of changes happening in brain cells. Neuroscientists think of Parkinson’s as a disease linked to several things in brain cells, from mitochondria, the power plants of the cell, to lysosomes and proteasomes, the garbage disposals of the cell. You might also hear that Parkinson’s is linked to a protein in the human brain called alpha-synuclein (α-synuclein). The exact way that all these pieces fit together remains unknown, but researchers continue to study how cells and brain networks are affected in Parkinson’s to improve our understanding of the disease and potential for treatments. We also know that dopamine is not the only neurotransmitter to be affected by Parkinson’s. The disease process also disrupts other brain chemicals like serotonin, norepinephrine, and acetylcholine, and this can cause changes in mood, behavior, and thinking (cognition).
You probably experienced a range of emotions upon hearing the words, “You have Parkinson’s disease.” In addition to fear, confusion, or anger, relief might have been one of them. For months, if not years, you might have been nagged by the question, “What’s going on with my body?” You or a loved one probably noticed a tremor, slowness, or stiffness and spoke to a doctor about it. The doctor – or maybe it took several doctors – probably referred you to a neurologist. Now you have treatment options to improve your symptoms. You and your health care provider might have decided to start medication right away, or you might have waited a bit, focusing on exercise to manage your symptoms.
After beginning treatment, whatever symptoms and complaints that led you to the doctor in the first place probably improved greatly. In these first few years of treatment, usually with easy-to-take Sinemet (carbidopa-levodopa pills) or other medications, people generally enjoy nearly complete relief from symptoms with minimal side effects. During this time, you have smooth transitions between doses. It is necessary to rely on a clock to tell you when it is time to take the next dose of medication because there is no return of symptoms between one dose of levodopa and the next. Medications allow you to go about your life, participating in work, hobbies, and social activities as you did before Parkinson’s.

After several years of being treated with levodopa, many people with PD notice that controlling symptoms becomes more difficult and requires more medication, but you can still live a good life.

What Are Motor Fluctuations and Dyskinesias?

**Motor Fluctuations**

Motor fluctuations are changes in your ability to move. They are also called “on-off” fluctuations. When levodopa begins to take effect, you experience periods of good symptom control ("on" time), when you can move and function well. As levodopa begins to lose its effect ("wearing off"), you may have periods in which symptoms are suddenly much more noticeable and movement becomes more difficult ("off" time). You might even have periods in which peak medication levels produce involuntary movements (dyskinesias). If you experience these various states throughout the day, you are said to have motor fluctuations.

Usually, when you first develop wearing off, the switch from “on” to “off” happens gradually. “Off” periods initially are predictable and occur near the end of each medication dose. For example, when they first begin treatment, many people are placed on a regimen of carbidopa-levodopa three times a day. Early on, as we described above, the medication lasts dose to dose, but over time the medication may begin to wear off 30 minutes to an hour before the next dose. At this point, you notice a gradual return of symptoms. As Parkinson’s progresses, levodopa stays effective for shorter periods of time. This means you have to take more frequent doses, and “off” episodes may become more sudden and/or unpredictable.
For some people the first sign of an “off” period is a return of motor symptoms—tremor, stiffness, or slow movement. For others, non-motor symptoms might creep in. This could include a range of complaints, such as pain, anxiety, fatigue, mood changes, difficulty thinking, restlessness, sweating, or drooling (from decreased swallowing). Since non-motor symptoms can be subtle in the beginning, it may be difficult at first to link them to a change in the effect of your PD medication.

**Dyskinesia**

Dyskinesias are involuntary movements: they are often fluid and dance-like, but they may also cause rapid jerking or slow and extended muscle spasms. Any part of the body may be involved, including the face, arms, legs, and trunk. The most common kind of dyskinesias are “peak dose.” These occur when the concentration of levodopa in the blood is at its highest—usually one to two hours after you take it. This typically matches up with when the medications are working best to control motor symptoms.

Sometimes, instead of at peak dose, dyskinesias can occur as you are just beginning to turn “on” and again as you begin to turn “off.” This is known as diphasic dyskinesia, or the dyskinesia-improvement-dyskinesia (D-I-D) syndrome. Diphasic dyskinesias are associated with relatively low doses of levodopa and, unlike peak-dose dyskinesias, tend to improve with higher doses of levodopa.

Dyskinesias may be mild and non-bothersome, or they can be severe. Most people with PD prefer to be “on” with some dyskinesias rather than “off” and unable to move well. However, for some people dyskinesias can be severe enough that they interfere with normal functioning.

*John was diagnosed with Parkinson’s in 1997, and in early 2002 he had his first episode of dyskinesia. I usually describe it to people as a rapid misfiring of his nerves, and in John’s case, it caused very violent shaking and misfiring. We could watch the clock and after exactly four hours, it would subside. Initially, it only happened every couple of months. Then it increased to once a week, then once a day, then sometimes a couple of times a day. As his wife, it was alarming to watch.*

— Donna
Other Common Issues

**Dystonia**

Dystonia is when your muscles continuously contract, causing parts of your body to twist. This leads to repetitive movements or abnormal postures and can cause great pain and discomfort. Many times it starts when you try to perform an action with the involved body part. For example, if you have dystonia of the foot, you may be fine when seated, but if you start to walk, you may develop toe curling or foot inversion (turning in of the foot or ankle). Dystonia can also be present when you are not using the involved body part; in the example above, you could have toe curling even when sitting.

In Parkinson’s disease, dystonia can occur at different times. In young people with PD, a common initial symptom is cramping or curling of the toes and feet after activity. Like dyskinesia, dystonia may occur at peak dose (when the medication is working at its best), and it is sometimes the earliest sign of dyskinesia. More commonly, dystonia occurs when dopamine levels are the lowest (“off” periods) or when the medications are just starting to kick in. This means some people experience dystonia first thing in the morning, as nighttime medications are wearing off and before they take their first daytime dose. Sometimes dystonia can persist intermittently throughout the day, and may not correlate with timing of medications at all.

It is important to keep track of when dystonia occurs, to figure out if there is a relationship between the onset of dystonia and the timing of your medication. Talk to your doctor. If there is a pattern (keep track using the Parkinson’s Symptoms Diary on pages 18–19), adjusting the dose or frequency of medication may help.
Freezing
As Parkinson’s advances, it may bring with it a variety of symptoms that are uncommon in early stages, such as problems with walking (gait abnormalities) and poor balance (postural instability). Some people experience “freezing,” the temporary, involuntary inability to move. This can occur at any time – for example, you want to walk forward but your feet feel stuck to the ground (called “freezing of gait”), or you may be unable to get up from a chair.

Some freezing happens when you are due for the next dose of dopaminergic medication. This is called “off” freezing. Usually, the freezing episodes lessen after taking your medication.

_The first time I froze, I fell. I couldn’t believe it. It was like I had cement boots on and couldn’t raise my feet. I reported it to my doctor, and she added a dopamine agonist to my regimen. I still have freezing episodes from time to time, but not as much. When I have an episode, I try to shift my weight from leg to leg. This helps. Also, I always turn in a square instead of trying to do a pivot turn. I also notice that I’m more likely to freeze at doorways when the floor surface changes, so I’m extra careful then._ — Erika

**TIPS FOR CAREGIVERS**

Freezing (feet glued to floor) is a significant cause of falls.

Freezing often happens while turning around in close quarters. Try to avoid tight turns whenever possible. Instruct the person with Parkinson’s to make wider turns.

If the person has a freezing episode while trying to walk, encourage him or her to stop, straighten posture, and shift weight to one foot before beginning to step with the other.

To help with freezing, count or clap a rhythmic beat.

Some people who experience freezing episodes do better with a visual cue, such as “step over my foot.”
Motor fluctuations and dyskinesias tend to develop at about the same time in the disease course. Early in the disease, the benefits of levodopa can last for several hours. The length of effect depends on the half-life of the drug (the time it takes for your body to process the drug in your blood) and other individual factors like body composition and dietary intake. For carbidopa-levodopa, the half-life is about 60–90 minutes, but “on” time can last much longer. This is most likely because some levodopa is still stored in the remaining dopamine-producing brain cells. So, when you first start on levodopa therapy, you take it only a few times a day and can smoothly transition from one dose to the next without a return of symptoms in between doses.
As Parkinson’s progresses, more dopamine-producing brain cells die, and the benefits from a dose of levodopa do not last as long. Your brain eventually reaches a point where it stops producing dopamine in any significant amount, so it must rely on medicine to replace dopamine, such as levodopa and dopamine agonists. When this happens, scientists think that two things are going on:

- First, the cells in your brain lose the ability to store some of the levodopa, and you don’t get a benefit when it is not present in your blood (i.e., after 60-90 minutes); and
- Second, the cells in your brain become more and more sensitive to both higher and lower concentrations of levodopa, making you more likely to experience “off” time when your blood levels are low and to experience dyskinesia when your blood levels are high.

So, as these changes happen in your brain, you will have to take more doses throughout the day to avoid the return of symptoms, such as tremor, slowness, and shuffling gait.

For a few years, my medication was working great! People didn’t even know that I had Parkinson’s. Then gradually my symptoms started to come back sooner than the time I was supposed to take my next pill. I was really anxious at first, but with some medication adjustments and increasing my dosages, my doctor was able to put me back on track. — Ken

How Will My Doctor Work with Me to Manage These?

The “therapeutic window” describes the period of time when a medication is effective. There is enough medication in your body to control your symptoms, but not too much so that side effects occur. Good medication response occurs within the window – outside the window, you might get motor fluctuations (not enough medication) or dyskinesias (too much). “Off” periods and dyskinesias tend to increase in frequency and severity as the disease progresses. See figures on next page.
The figures here, based on insights from NPF's *Parkinson's Outcomes Project*, the largest-ever clinical study of Parkinson's, illustrate how levels of dopamine in your brain change and how your body reacts to those changes as Parkinson's progresses.

**THE BASIC MODEL**

![Graph showing dopamine levels over time](image_url)

- **Medication Effect (blue line)**: The blue curve represents how we think the level of dopamine in the brain changes after you take medication: levels rise, you metabolize the drug, then levels decline.

- **Therapeutic Window (white area)**: The goal is to get dopamine levels into the "therapeutic window." When levels are here, you don't feel the absence of dopamine. However, you might still have symptoms, especially later in the disease.

- **Dyskinesia (dark blue area)**: If you get too much dopamine, you may experience dyskinesia: writhing motions that are difficult or impossible to control. Usually we say that these go away when you get back into the therapeutic window, but they might actually persist for a bit even after dopamine levels go down.

- **“Off” Symptoms (light blue area)**: After you take your pill(s), as your body metabolizes the dopamine at the end of the dose, you may experience "wearing off," leading to "off" episodes. This happens later in the disease.

**BEFORE PARKINSON’S**

- **Wide Therapeutic Window**: Natural (or "endogenous") dopamine levels stay within the therapeutic window.

**DOPAMINE LEVELS BEFORE PARKINSON’S**

- 7am 9am 11am 1pm 3pm 5pm 7pm 9pm 11pm
EARLY PARKINSON’S
Some “off” before first dose, with breakfast at 8 am. Second dose with lunch at noon, with no “off” experienced. A late dinner results in some mild afternoon “off” as the lunch dose is metabolized.

MID-STAGE PARKINSON’S
Early morning “off” is bad before first dose at 8 am. Some people set an early alarm to take pills before they get up for the day. You might also use an alarm to keep on schedule, which can work pretty well.

ADVANCED PARKINSON’S
Some people need a fast-acting “rescue” medication to jumpstart their day. Mid-day off Because the therapeutic window is so narrow, dosing intervals can be as short as 2 hours.

Natural dopamine levels (dark gray line) are below the therapeutic window (white area), resulting in “off” (light blue) without medications.

Natural dopamine levels (dark gray line) are well below the therapeutic window (white area), resulting in pretty severe “off” state (light blue area) without medications.

Natural dopamine (dark gray line) is low.
The goal of managing motor fluctuations and dyskinesias, like the goal for treatment of any symptom, is to help you remain as active and independent as possible. If your symptoms are mild and not bothersome, no changes need to be made to the medication regimen. But if these symptoms start to impact your daily functioning or quality of life, you can work with your physician to adjust medications. When people first begin to experience these complications, there is a relatively wide therapeutic window (see “Early Parkinson’s” on the previous page). Motor fluctuations can often be reversed by increasing the dose of levodopa or incorporating other Parkinson’s medications without inducing troublesome dyskinesias.

Management of Motor Fluctuations
Depending on what medications you are already taking, there are several approaches your doctor can take to help smooth out your response to medications to avoid or minimize fluctuations.

Your doctor can adjust your dose of levodopa, either by giving you a higher dose each time you take your medication, or by giving you the same dose or a smaller dose more frequently. Your doctor may add different medications to your current regimen. There are several medications that can be taken along with carbidopa-levodopa. These help keep levels of dopamine more consistent to avoid “off” time. All of these medications have the same end goal – increasing dopamine in the brain – but they work differently on the body and brain. For this reason, the options are not mutually exclusive and often can be tried together.

Treatment options include the following (see Appendix on page 34 for a list of typical Parkinson’s medications and a pronunciation guide):
• Increase the levodopa dose or frequency of administration
• Add a COMT inhibitor (i.e., entacapone or tolcapone)
• Add a dopamine agonist (i.e., ropinirole, pramipexole, rotigotine)
• Add an MAO-B inhibitor (i.e., selegiline, rasagiline)
• Switch from immediate-release (IR) carbidopa-levodopa to extended-release (ER) carbidopa-levodopa or to a combined preparation

NOTE
For more information, order your free copy of the book Medications from the National Parkinson Foundation by calling the NPF Helpline at 1-800-4PD-INFO (473-4636) or online at www.parkinson.org/books.
A controlled-release formulation of carbidopa-levodopa (Sinemet CR) is available. It was designed to extend the benefits you get from the same dose of carbidopa-levodopa and possibly decrease the number of pills needed per day. However, studies have shown that people who take the immediate-release version and those who take the controlled-release form have about the same number and frequency of motor complications. Furthermore, the CR version can take longer to take effect than regular carbidopa-levodopa and it is not always well absorbed into the blood. For these reasons, it is perhaps most valuable in treating wearing off effects that occur overnight.

Extended-release carbidopa-levodopa capsules (Rytary) are a newer attempt to deliver levodopa so that it lasts longer. These capsules contain both immediate- and extended-release carbidopa-levodopa. This design allows rapid absorption of part of the dose but slower absorption of the rest and therefore maintains levodopa concentrations longer than immediate-release levodopa alone. This form of levodopa may reduce “off” time while requiring fewer medication administrations.

It is worth mentioning that carbidopa-levodopa can be obtained as an orally disintegrating (melt in your mouth) form (Parcopa). This can be useful if you struggle to swallow pills. As an alternative, Sinemet may be chewed (immediate-release only; do NOT chew controlled-release).

Another option, rather than adding more medications or taking medications more frequently, is to use an on-demand or as-needed approach. There are several short-acting dopamine replacement medication options available or in development that can be used as “rescue” therapy in people experiencing “off” episodes. They are designed to take effect quickly: within 15 minutes or less. Typically, the response is short, maybe an hour or two. It is called “rescue” therapy because it bridges gaps in other medication effectiveness. “Rescue” medications can be effective for people who struggle with morning akinesia (inability to move or slowness of movement) or who experience an unexpected or inconvenient “off” episode. At the time of this writing, there is only one such medication approved in the U.S., but others are on their way (see page 20).
**WORKSHEET**

**Parkinson’s Symptoms Diary**

Many symptoms of Parkinson’s can be bothersome and interfere with day-to-day quality of life. Patient and family observations can help the medical team make a care plan. Fill out this worksheet and share it with providers to see if there is a pattern to when Parkinson’s symptoms occur.

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List the symptoms you want to track - e.g., tremor, dyskinesia, anxiety - in the top row. When those symptoms occur, fill in the number that corresponds to the severity at that time. Write medication names and doses next to the times at which you take them. Put an X (or list foods) in the “Meal” column at mealtimes. Put an X in the “Sleep” column when you sleep.

0 = NONE  
1 = SLIGHT OR MILD  
2 = MODERATE, BOTHERSOME  
3 = SEVERE, VERY BOTHERSOME

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Current and potential “rescue” medications:

• Apomorphine (Apokyn) is an FDA-approved, short-acting dopamine agonist that can be used as “rescue” therapy. It is delivered via a subcutaneous injection, similar to an insulin shot or EpiPen, which allows for it to take effect quickly: within 3.5 to 12.5 minutes.
• A sublingual (absorbed under the tongue) strip of apomorphine is currently being studied.
• A powder aerosol inhaled formulation of levodopa (similar to inhalers used to treat asthma) is also being studied.

Management of Peak-Dose Dyskinesia
Peak-dose dyskinesias occur at the time when levodopa is working best – when levodopa is at its highest concentration in the blood. In the earliest stages, they are usually not bothersome, and you may not even notice these extra movements. Because they tend to occur at peak concentrations of levodopa, one management strategy is to reduce dopamine levels. This can be done with small decreases in levodopa dosage or by removing other dopaminergic medications (e.g., dopamine agonists, COMT inhibitors, or MAO-B inhibitors).

However, as Parkinson’s progresses, if you reduce the levodopa dose, your Parkinson’s symptoms will not be well controlled. Amantadine is a medication that may be added to your medication regimen to reduce dyskinesias without worsening “off” periods. At the time of this writing, there are several medications in development with the goal of improving management of dyskinesia.

Management of Dystonia
Depending on when dystonia occurs, your doctor may try different approaches to treatment. If you have morning dystonia, which occurs before your first dose of levodopa kicks in, your physician may add a bedtime dose of controlled-release carbidopa-levodopa or a long-acting dopamine agonist.

If dystonia is related to diphasic dyskinesia (i.e., as the medications are wearing off or before they begin working), increased doses of levodopa or smaller doses more frequently may be useful. On occasion, oral medications to treat spasms, such as anticholinergic medications, can be
tried, but these can cause significant mental and physical side effects, so their use should be carefully considered.

If other measures fail and your dystonia doesn’t correlate with levodopa timing, you and your health care provider may consider botulinum toxin injections. Botulinum toxin weakens muscles. By targeting the overactive muscles, your physician can improve both the abnormal position and the pain caused by dystonia. It can take several injections to optimize benefit and may not always be effective, but when it works the benefit can last for several months before it wears off and re-injection is necessary. Botulinum toxin A (Botox) is sometimes used to decrease saliva production for people who have issues with drooling; botulinum toxin B (Myobloc) is used to treat dystonia.

**What Next?**

With advancing disease, there is a further narrowing of the therapeutic window. For some people, it can become increasingly difficult to find a dose of levodopa that is both effective and does not cause dyskinesia. As we learned above:

- If you increase medications in an attempt to improve “off” time, it may lead to worsening dyskinesia.
- If you decrease medications in an attempt to improve dyskinesia, it may result in worsening of parkinsonian symptoms or more frequent “off” periods.

When faced with this paradox, your physician might suggest alternatives to better manage your symptoms. Fortunately, more options are becoming available for people who are significantly bothered by these fluctuations.

**Deep Brain Stimulation (DBS)**

There are several neurosurgeries that have been used to treat the symptoms of Parkinson’s. Today, the most common is deep brain stimulation. During DBS surgery, a special wire, called a lead (pronounced “leed”), is inserted into a specific area of the brain responsible for movement. The lead is connected to a pacemaker-like device that is typically implanted in the chest region, below the collarbone. This device (the neurostimulator, or pulse generator) creates electrical pulses that are
sent through the lead, which “stimulates” the brain and regulates abnormal brain cell activity. Stimulator settings can be adjusted periodically both by the DBS programmer (a doctor, nurse, physician assistant, or other qualified staff member) and by the person with Parkinson’s, within the parameters that the programmer sets.

The best candidate for DBS is someone who has a good response to levodopa, but experiences disability because of motor fluctuations and dyskinesias that cannot be satisfactorily controlled by oral medications.

**Carbidopa-Levodopa Intestinal Gel (Duopa)**
If frequent administration of oral medications doesn’t smooth out blood levels enough, your carbidopa-levodopa can be delivered in gel form, which is slowly and continuously pumped through a tube inserted surgically through the stomach into your intestine, similar to an insulin pump for diabetics. You wear the pump, and it smoothly delivers medication for up to 16 hours at a time.

This may be an option for people who are not candidates for DBS because of mild cognitive impairment or other issues. Lifestyle factors must be taken into account when choosing this therapy, as you must consider carrying the pump, potential for the tube to get dislodged, and other factors.

**Advanced Parkinson’s with Continuous Dopaminergic Stimulation**
This example shows using a fast-acting “rescue” medication in the morning to get started. A steady supply of medication delivered via a pump helps target the right dopamine levels.

Natural dopamine (dark gray line) is low.
I was diagnosed with Parkinson's in 2008 and underwent deep brain stimulation surgery for disabling dystonia in 2013. After the DBS surgery, I was able to walk without the need for a wheelchair or cane. In early 2015, with progression of the disease, my dystonia got worse and I needed a higher dose of levodopa. My doctor suggested that I was ready for the Duopa pump. Since levodopa is pumped directly into the small intestine, bypassing the stomach, I've found that there is less interaction with food, less wearing off, and less “off” time! I didn't realize how much of an adjustment it would be getting used to the tubing that carries the levodopa from the pump to the small intestine, but after a couple months, I got used to it. I feel a bit stronger than before, to the point that I actually feel like exercising and getting together with others again. Do I still need to budget my energy? Yes, I have Parkinson’s. But I can be less strict about it. The pump and DBS have been a great blessing to me and my husband, each in its own time and for its own reason, in this fight against Parkinson's disease. — Pam

On the Horizon

As we think about what's next, your doctor will be aware that dopamine is not the only neurotransmitter to be affected by Parkinson's. The disease process also disrupts other brain chemicals like serotonin, norepinephrine, and acetylcholine, and this can cause changes in mood, behavior, and cognition. Researchers are studying the impact of PD on the cholinergic system (the system of cells that use acetylcholine to send messages). There is some evidence that gait impairment (problems with walking) and falls in PD are related to dysfunction of the cholinergic system, and there may soon be treatments to help with this. The cholinergic system is also involved in controlling memory and sleep, and problems in these areas may respond to the same treatments. The cholinergic system is affected after the dopamine system, and ways to treat its dysfunction – from exercise to medications to electrical stimulation – are still being researched.
Parkinson’s is a progressive disorder – this means that symptoms develop slowly over time – and the disease progresses differently from person to person. There is a saying, “If you’ve met one person with Parkinson’s, you’ve met one person with Parkinson’s.” While there are many common experiences, each individual’s symptoms, progression, and overall journey with the disease will be unique.

Most people with Parkinson’s also have non-motor symptoms, though each person experiences them a little differently. No one has every symptom; you may experience them, or you may not. Like motor fluctuations, you can eventually have fluctuations in the frequency and severity of your non-motor symptoms.
Your doctor and other members of your care team can help you manage non-motor symptoms, which can include the following:

- Anxiety
- Apathy (lack of motivation or drive)
- Changes in speech and swallowing
- Cognition changes, such as slower thinking, difficulty keeping track of time, or difficulty focusing
- Constipation and other problems with digestion
- Depression
- Dyspnea (shortness of breath)
- Excessive sweating
- Hallucinations or paranoia
- Impulse control problems, or compulsive behaviors, which can appear as problems with shopping, gambling, or hypersexuality; anger management issues can also be a problem of impulse control
- [Orthostatic hypotension](#) (lightheadedness upon standing)
- Pain
- Seborrheic dermatitis
- Sexual dysfunction
- Sleep problems
- Urinary incontinence: having to go more frequently, having little or no warning before needing to urinate, or loss of control of urine
- Vision problems

In addition to non-motor symptoms of Parkinson’s disease itself, over time you may become more susceptible to certain side effects of medication. For instance, orthostatic hypotension may by worsened by certain medications, and cognitive side effects or hallucinations can be aggravated by medications that have been tolerated in the past. This change in susceptibility can influence which medication combinations work best and may drive the need to change medications, add medications (to combat hypotension, for example), or simplify your regimen to just carbidopa-levodopa in some cases.

These and other treatment and lifestyle adjustments can be made to successfully manage your symptoms. Make sure to tell your doctor if you are experiencing anything out of the ordinary, as early recognition and treatment can help you minimize symptoms. (You can use the Parkinson’s Symptoms Diary on pages 18–19 to track non-motor symptoms, too.)
Because of how Parkinson’s impacts movement, it is natural to move less and do less as the disease progresses. However, it’s a troubling cycle: PD itself causes symptoms like slowness and stiffness that make it hard to move, and a decline in ability to move may be due to reduced physical activity! For people with Parkinson’s, exercise is medicine.

It is well-known that exercise is good for the body: it can prevent problems due to inactivity and muscle weakening; help maintain joint flexibility, muscle strength, and tone; reduce inflammation; and improve circulation to the heart and lungs. In people with PD, there is clear evidence that exercise helps with both the motor and non-motor symptoms. Studies have shown that people with Parkinson’s who exercise fall less often and have fewer falls resulting in injury, and exercise leads to improvement in flexibility, strength, and balance.

Findings from the National Parkinson Foundation’s *Parkinson’s Outcomes Project*, the largest-ever clinical study of Parkinson’s, show that increasing physical activity to at least 2.5 hours a week can achieve what we can’t yet do with medicine: slow Parkinson’s progression. We don’t know for sure what is happening in the brain, but people who exercise experience a milder disease course and better quality of life, and people who start exercising...
find that their health improves. If you are not exercising at least 2.5 hours a week, start now!

I’ve always been active, and two years prior to my diagnosis, I began working out regularly, lifting weights and cardio training three to five days a week. I felt good. Exercise gave me the strength and energy I needed to keep up with my toddler. After I was diagnosed, I was put on a trifecta of PD drugs. Then I read how exercise was THE ONLY THING proven to slow the progression of PD. So, I began training much harder than I ever had. I’ve experienced the benefits of exercise in my sleep. My PD therapy is doing weights or running the track. I have more energy, stamina, and strength than many men my age. — Alison

Exercise Effects on Cognition

There is also evidence that regular exercise is good for the mind: exercise has a positive effect on mood and overall sense of wellbeing, reducing stress and increasing a sense of control over your Parkinson’s symptoms. Now, we understand that these benefits go even further: exercise can increase brain adaptability. NPF-funded studies show that exercise facilitates neuroplasticity (the adaptability of your brain to new challenges) and might even be able to reverse executive function deficits (e.g., problems with focused attention and planning) in people with PD. All exercise is good for Parkinson’s, and researchers are studying if any one exercise approach is better than another for improving cognitive function in people with PD. Researchers are also studying the effects of novelty – trying new exercises – as there is some evidence that learning new exercises can actually lead to brain cell growth.

Types of Exercise

Research has shown that people with Parkinson’s often need to work on the sequencing or timing of motions and on compensating for the effects of the disease (and the effects of aging!) on the brain’s ability to accurately judge distances. Doctors refer to this as improving temporal and spatial accuracy.

So, while all exercise programs should include aerobic, strengthening (resistance), and stretching activities, you should talk to your neurologist and work with a physical therapist to design an exercise program that focuses on practicing skills linked to rehabilitation of or compensation for common PD motor deficits. These skills might include walking, along with
maintaining good posture and balance. Your care team will help ensure that the exercise program you design together includes the following elements:

- **Feedback**: So that you will know if you are doing the motion correctly;
- **Correction**: Adjustments of your motion to improve performance;
- **Problem-solving**: Exercises and activities that challenge your limits and require thought;
- **Intensity**: You should challenge yourself with goals for improvement and repetition.

You can get to the problem-solving element by mixing up the way you are learning a motor skill and trying different exercise types. Such variability helps push your brain as well as your muscles. Different types of exercise that have been found to help people with PD include biking, running, tai chi, yoga, weight training, non-contact boxing, dancing, and more.

The most important recommendation is this: **Choose an exercise program that you will actually do!** Don’t design a great, Parkinson’s-optimized exercise program and then skip it because it is too hard or not fun.

The second most important recommendation is that you should do something new and different. Pushing yourself to improve is like doing something new, so that is okay, but don’t stagnate. Don’t just do the same exercise at the same intensity in the same way all the time.

It is always important to check with your health care team to make sure the type of exercise you are considering is safe and appropriate for you.

Don’t forget the emotional aspects of exercise. You need to both find fulfillment in it and believe you can do it! If you are struggling with motivation or with believing in your own ability, ask your care team, friends, or family for help. You will likely feel a great sense of accomplishment after each session.

**NOTE**

For more information on the benefits of exercise and guidance on exercises you can do, visit www.parkinson.org/exercise and request your free copy of the publication *Parkinson's Disease: Fitness Counts* by calling the NPF Helpline at 1-800-4PD-INFO (473-4636).
In the early days after your diagnosis, you likely were able to continue with your activities – work, hobbies, errands, travel – as you did before “Parkinson’s disease” entered your vocabulary. But as time goes on and symptoms start to break through, it is common for people with Parkinson’s to stop socializing as much as they used to. Sometimes the person with Parkinson’s and the primary caregiver isolate themselves, withdrawing gradually from participation in the community and prior social life. This can happen for a variety of reasons including fear of stigma or a lack of confidence to interact with others or perform in social situations. It can be hard to get around, or you may feel uncomfortable about attracting attention and having to explain your Parkinson’s. It is normal to feel that way, but if you are open to talking about it, you’ll find out you are not alone.
It’s sad to see people with Parkinson’s struggling to get the care and understanding they need. It’s why I strive to be the best caregiver possible. I saw firsthand how my mother hesitated to go out in public because her tremors and dyskinesia caused people to stare. — Emilia

Sharing about Parkinson’s can make it easier to comfortably socialize. Talking about it is easy for some people but can be difficult for others. You do not have to tell everyone – start with a few trusted family members and friends, and get ahead of the questions through education.

First, it is important to understand the disease yourself. The National Parkinson Foundation offers several options to help you and your family learn all about Parkinson’s disease, from warning signs and diagnosis through symptoms, treatment, and living well. Explore [www.parkinson.org](http://www.parkinson.org) for information on any PD topic, and call the NPF Helpline at 1-800-4PD-INFO (473-4636) with any questions. You may even share this book to help people understand what you’re going through.
CHAPTER SEVEN

Hope

You have many reasons to hope for a bright future with Parkinson’s. You can find hope in at least three important places:

RESEARCH  Every day, scientists are discovering new things about Parkinson’s and new therapies and strategies that we hope will make a difference for everyone affected by PD. Research doesn’t just mean developing new drugs: over the past decade, our understanding of the importance of exercise has helped change lives. New developments in deep brain stimulation and other approaches to quieting harmful signals in the brain or enhancing helpful ones are being tested every day. Many new drugs are on their way to becoming part of day-to-day treatment, and researchers are studying the most effective way to organize a Parkinson’s clinic to ensure you get today’s best care.

Launched in 2009, the National Parkinson Foundation’s Parkinson’s Outcomes Project, the largest-ever clinical study of Parkinson’s, is leading the way in many of these and other research areas. With almost 10,000 patients and 6,000 caregivers enrolled from four countries, we are looking at patterns in treatment and care to change the course of the disease.
YOUR PARKINSON’S CARE TEAM  You are in charge of putting together a care team that works for you! First of all, it is important to see a neurologist: people with Parkinson’s who seek expert care have better outcomes. Each year in the U.S. alone, neurologist care saves about 4,600 lives, and better access to care could prevent the deaths of another 7,000 people with PD. Neurologists who have extra training in Parkinson’s and similar conditions are called movement disorder specialists. The best neurologist for you might be someone from your community, or it could be a scientist who has a clinic at the university hospital. Your neurologist will make sure that you are taking the right medications and have access to physical, occupational, and speech therapists who have experience treating people with PD.

While seeing a neurologist is important, it is likely your primary care provider who will manage your overall health. Find the health care professional who is the best fit for you – this might be a knowledgeable gerontologist, internal medicine doctor, family physician, or nurse practitioner – and work with that person to get the very best care. Your primary care provider or neurologist should be able to help you find a social worker, counselor, or other mental health professional who can help you with problems often associated with having a chronic illness. All these members of your care team can help you develop strategies for what to do if you have an urgent problem or an emergency: who to call, who to notify, and what to tell any doctor who helps you. Don’t forget that you and your care partner, if you have one, are also integral members of the care team!

YOUR OWN SELF-CARE  Most important of all, and likely your greatest source of hope, is what you and your family can do. You take your medications, you exercise, you challenge yourself, and you achieve your own victories. Get engaged in the fight against Parkinson’s! Look to other people living well with Parkinson’s for inspiration. Set goals that you can achieve, and then achieve them! Many people with PD recognize that a Parkinson’s diagnosis is not the end of their life, but a turning point. Work with your loved ones to figure out what this change means for you. Many people find that the hope they gain from taking charge of their own life with Parkinson’s is more visceral and tangible than the hope that a researcher somewhere will achieve a breakthrough. There are things you can do today to give yourself a better life with PD. Empower yourself to take charge!
Your Partner in Care

Over its history, the National Parkinson Foundation, a division of the Parkinson’s Foundation, has invested millions of dollars in research, education, and services, with a central focus on improving the lives of people with Parkinson’s today. The foundation never focused on the distant future, but instead ushered in revolutions in therapy, social work, and team care. NPF was there for the launch of levodopa in the 1960s, and NPF was supporting the care teams who said, days after the breathtaking power of levodopa had sunk in, “Let’s get moving on the next breakthrough!”

Today’s best care is far superior to today’s average care, and NPF believes that every person with Parkinson’s deserves the best. You deserve the best. Through efforts such as the Parkinson’s Outcomes Project, NPF is investing in pushing the limits of what we can do to help everyone affected by Parkinson’s.

By reading this book, you are taking a step towards achieving your best life with Parkinson’s.

The NPF Aware in Care kit contains information to give to hospital providers about Parkinson’s and what medications are safe for people with PD. Call the NPF Helpline at 1-800-4PD-INFO (473-4636) to request your free Aware in Care kit, or order one online at www.parkinson.org/store. Review the materials when you receive the kit, so you will be ready to advocate for yourself or your loved one if he or she is hospitalized, whether it’s a planned visit or an emergency.
### TYPICAL PARKINSON’S MEDICATIONS

**L-DOPA**
- carbidopa-levodopa (Sinemet® or Sinemet CR®)
- carbidopa-levodopa orally disintegrating (Parcopa®)
- carbidopa-levodopa entacapone (Stalevo®)
- carbidopa-levodopa extended-release capsules (Rytary™)
- carbidopa-levodopa enteral solution (Duopa™)

**Dopamine Agonist**
- ropinirole (Requip®)
- pramipexole (Mirapex®)
- rotigotine (Neupro®)
- apomorphine (Apokyn®)

**MAO-B Inhibitors**
- rasagiline (Azilect®)
- selegiline (l-deprenyl, Eldepryl®)
- selegiline HCL orally disintegrating (Zelapar®)

**Anticholinergics**
- trihexyphenidyl (formerly Artane®)
- benztropine (Cogentin®)
- ethopropazine (Parsitan®)

**COMT Inhibitors**
- entacapone (Comtan®)
- tolcapone (Tasmar®)
- carbidopa-levodopa-entacapone (Stalevo®)
  *has L-DOPA in formulation*

**Other**
- amantadine (Symadine®, Symmetrel®)
### PRONUNCIATION KEY

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pronunciation</th>
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<tbody>
<tr>
<td>Levodopa</td>
<td>lee-voe-<em>doe</em>-pa</td>
</tr>
<tr>
<td>Carbidopa</td>
<td>Car-bee-<em>doe</em>-pa</td>
</tr>
<tr>
<td>Sinemet</td>
<td>Sin-uh-met</td>
</tr>
<tr>
<td>Rytary</td>
<td>Rih-<em>tar</em>-ee</td>
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<tr>
<td>Duopa</td>
<td>Due-<em>oh</em>-pa</td>
</tr>
<tr>
<td>Ropinirole</td>
<td>Row-<em>pin</em>-er-ole</td>
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<tr>
<td>Pramipexole</td>
<td>Pram-ih-<em>pex</em>-ole</td>
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<tr>
<td>Rotigotine</td>
<td>Row-<em>tig</em>-oh-teen</td>
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<tr>
<td>Apomorphine</td>
<td>Ae-poe-<em>more</em>-feen</td>
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<tr>
<td>Rasagiline</td>
<td>Rah-<em>saj</em>-ah-teen</td>
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<tr>
<td>Selegiline</td>
<td>Sell-<em>edge</em>-ah-teen</td>
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<tr>
<td>Entacapone</td>
<td>En-<em>tah</em>-cuh-pone</td>
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<tr>
<td>Tolcapone</td>
<td>Toll-cuh-pone</td>
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<tr>
<td>Amantadine</td>
<td>Uh-<em>man</em>-ta-deen</td>
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Glossary terms are identified with a blue underline the first time they appear in this book.

**Acetylcholine**  A chemical messenger (see neurotransmitter) released by cholinergic nerves; involved in many brain functions, such as memory and control of motor activity

**Akinesia**  Inability to move or slowness of movement

**Alpha-synuclein**  A protein in the human brain that is associated with the development of Parkinson's; it is the main component of Lewy bodies

**Anticholinergic**  The earliest medications used in Parkinson's, these medications block brain receptors for acetylcholine; they can cause significant mental and physical side effects, so they are most useful in young people with tremor-predominant PD; some antihistamines and sleeping agents (e.g., Benadryl) are anticholinergics

**Cholinergic system**  The system of cells that use acetylcholine to send messages

**Deep brain stimulation (DBS)**  A surgical option for treatment of some Parkinson’s symptoms

**Diphasic dyskinesia**  Dyskinesia that occurs as you are beginning to turn “on” and again as you begin to turn “off”; associated with relatively low doses of levodopa and tend to improve with higher doses of levodopa

**Dopamine**  A chemical messenger (see neurotransmitter) that is primarily responsible for controlling movement, emotional responses, and the ability to feel pleasure and pain; in people with Parkinson’s, the cells that make dopamine are impaired or die
**Dopamine agonist (DA)**  A class of drug used to treat motor symptoms of Parkinson’s; DAs are chemicals that have been manufactured to act similarly to dopamine – that is, attach to the same cells in the brain (receptors) that dopamine activates to produce its effect.

**Dyskinesia**  Abnormal, involuntary movement of muscles.

**Dyskinesia-improvement-dyskinesia (D-I-D) syndrome**  See diphasic dyskinesia.

**Dystonia**  A disorder in which your muscles contract uncontrollably, causing parts of your body to twist, resulting in repetitive movements or abnormal posture; can be very painful.

**Freezing**  Temporary, involuntary inability to move; frequently “freezing of gait,” where the person with Parkinson’s wants to walk forward but their feet feel stuck to the ground.

**Half-life**  The time taken for the concentration of a drug in the bloodstream to decrease by one half; drugs with a shorter half-life must be taken more frequently.

**Levodopa**  The medication most commonly given to control the motor symptoms of Parkinson’s; it is converted in the brain into dopamine.

**Motor fluctuations**  Changes in the ability to move, often related to being in the “off” medication state, when Parkinson’s symptoms reemerge; also called “on-off” fluctuations.

**Motor symptom**  A symptom of Parkinson’s that affects movement, including tremor, rigidity, bradykinesia (slow movement), and postural instability.

**Movement disorder specialist**  A neurologist with extra training (usually a one- or two-year fellowship) in Parkinson’s and other movement disorders.
Neurodegenerative disorder  A disease characterized by the loss of cells of the brain or spinal cord, which over time leads to dysfunction and disability; Parkinson’s disease, Alzheimer’s disease, and Lou Gehrig’s disease are all examples.

Neuroplasticity  The brain’s ability to reorganize itself by forming new connections; this allows the brain to compensate for injury and disease and to respond to new situations and changes in the environment.

Neurotransmitter  A chemical messenger, such as dopamine or acetylcholine, that transmits nerve impulses from one nerve cell to another, allowing them to communicate with each other.

Non-motor symptom  A symptom of Parkinson’s that affects something other than movement, such as sleep, mood, behavior, sensory function (sense of smell, vision, pain), or autonomic function (urinary, gastrointestinal, and sexual function); typically does not respond to dopamine-replacement therapy.

Norepinephrine  A chemical messenger (see neurotransmitter) that is released in response to stress; known as the “stress hormone,” it raises blood pressure; it is also involved in regulation of mood.

“Off” time  When medication is not working as well; symptoms become more noticeable and movement becomes more difficult.

“On-off” fluctuations  See motor fluctuations.

“On” time  When medications are working and you experience good symptom control.
Orthostatic hypotension  The tendency for blood pressure to decrease significantly when you rise from seated or lying to standing, causing dizziness, lightheadedness, headache, blurred or dimmed vision, or fainting; called neurogenic orthostatic hypotension when it is the result of a neurologic disorder such as Parkinson’s

P  Peak-dose dyskinesia  The most common kind of dyskinesia in Parkinson’s; happens when the concentration of levodopa in the blood is at its highest, usually one to two hours after you take it

R  “Rescue” therapy  Fast-acting (<15 minutes) but short-lasting (1–2 hours) dopamine replacement medication used by people experiencing “off” episodes to bridge the gap in other medication effectiveness; may be delivered as an injection, orally, using an inhaler, or other techniques

S  Serotonin  A chemical messenger (see neurotransmitter) that is involved in regulation of mood, pain perception, gastrointestinal (digestive) function, sleep, and other physical functions

T  Therapeutic window  The period of time when a medication is effective, when there is enough medication in your body to control symptoms, but not too much so that side effects occur

W  Wearing off  The time period when levodopa begins to lose its effect and symptoms start to become more noticeable
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About the Parkinson's Foundation
At the Parkinson's Foundation we make life better for people with Parkinson’s through expert care and research. Everything we do helps people with Parkinson's actively enjoy life. We continue to bring help and hope to the estimated one million individuals in the United States, and 10 million worldwide, who are living with Parkinson's disease. A wealth of information about Parkinson’s and about NPF’s activities and resources is available on our website, www.parkinson.org.

Your feedback matters!
We'd like to know what you think of our publications and programs. Please take a few moments to fill out our online feedback form. Your answers will be used to improve our resources and will benefit people with Parkinson's, caregivers, families, and others in the Parkinson's community. Thank you for your help.

Online form:  www.parkinson.org/feedback

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