My Parkinson's Compendium - 2020

This document is comprised of publicly available material from a variety of Parkinson's Disease related sources.

The material has many different formats and this detracts from the overall look of the document.

It has been created to facilitate the rapid location of information pertinent to Parkinson's Disease, its treatment, the medications used in that treatment.

And so, we went for function over form. The document looks messy, but it works for us.

It has a Table of Contents that links to the material in the document.

The document was created in October - November 2020.

Feel free to download if you wish a copy for your own use.

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Table of Contents

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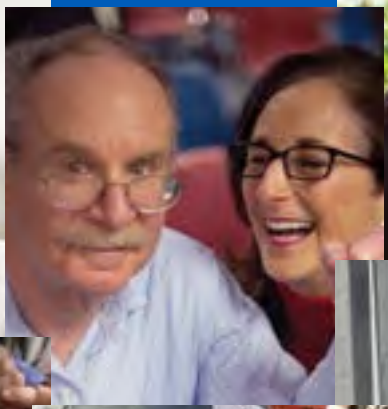
AMERICAN PARKINSON DISEASE ASSOCIATION

Strength in optimism. Hope in progress.

Parkinson's Disease HANDBOOK



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WHAT IS PARKINSON'S DISEASE?

So what exactly is Parkinson's disease (PD)? PD is a type of **movement disorder*** that can affect the ability to perform common, daily activities. Although PD is associated with a wide range of symptoms, there are features of PD that most people with the condition will experience. These symptoms are typically divided into those that affect movement (**motor symptoms**) and those that do not (**non-motor symptoms**).

The most common motor symptoms of PD are **tremor** (a form of rhythmic shaking), stiffness or **rigidity** of the muscles, and slowness of movement (called **bradykinesia**). A person with PD may also have trouble with posture, balance, coordination, and walking. Common non-motor symptoms of PD include sleep problems, constipation, anxiety, depression, and fatigue, among others. You will learn about the motor and non-motor symptoms of PD in greater detail in the next chapter.

It is important to note that, although there are common symptoms of PD, they can vary greatly from person to person. Moreover, how these symptoms change over time and whether other symptoms of PD emerge differ from person to person. Most people who develop the symptoms of PD do so sometime after the age of 50, but PD can affect younger persons as well. There are an estimated 1 million Americans living with PD and more than 10 million people worldwide.

*Note: Bolded terms are defined in the glossary at the back of this booklet

How PD Affects the Brain

PD is a **neurodegenerative disease**. There is a loss of **neurons** (nerve cells) in certain areas of the brain, including a region called the **substantia nigra** (sub-STAN-she-uh NYE-gruh), Latin for "black substance." The neurons in this region (which appear dark under a microscope) produce a **neurotransmitter** (a chemical messenger that allows neurons to communicate) called **dopamine**. Dopamine helps to regulate movement. As the number of cells in the substantia nigra decreases, there is less dopamine available in the brain. Dopamine is important to maintain normal movement patterns. This loss of dopamine is the reason that many treatments for PD are intended to increase dopamine levels in the brain. Treatment for PD will be explained in more detail in Chapter 4.

Loss of neurons in other parts of the brain also occurs in PD, and accounts for some of the non-motor symptoms of the disease.

In addition to decreases in dopamine and the cells that make dopamine, you might also read or hear about a protein called **alpha-synuclein** (AL-fa-sin-NUKE-lee-un). Studies suggest that alpha-synuclein normally helps neurons communicate with each other. In PD, the protein clumps up in microscopic aggregates called **Lewy** (LOO-ee) **bodies**. Researchers believe that alpha-synuclein build-up contributes to the development of PD, and that it may be possible to develop new treatments that reverse this build-up. Future research will hopefully tell us more about this protein.

Theories About Cause

The cause of most cases of PD is still unknown, although scientists believe that both genetics and environment interact to cause PD in most people who have it. Currently, there is an enormous amount of research directed at producing more answers about what causes PD and how it might be prevented or cured. When physicians diagnose PD, they often describe it as **idiopathic** (ID-ee-oh-PATH-ik). This simply means that the cause of PD is not known.

Genetic Factors

There are several genes that, when mutated, can increase the risk of PD. One of these, called LRRK2, is particularly frequent in families of North African or Ashkenazi Jewish descent. Mutations in the alpha-synuclein gene have also been found to trigger PD, but these are quite rare. Other genes that contribute to PD include the GBA gene, the parkin gene and the DJ-1 gene. However, in the large majority of cases, no primary genetic cause can be found. As studies of PD continue, it is likely that more genetic risk factors will be discovered. In addition, as medications are developed that target specific gene mutations, it will become increasingly important for individuals with PD to understand their particular genetic profile.

Environmental Factors

Certain environmental factors, such as significant exposure to pesticides or solvents and repeated head injuries, can increase the risk of PD. Most people do not have a clear environmental cause for their PD, and because many years can pass between exposure to an environmental factor and the appearance of PD symptoms, the connection is often difficult to establish. However, it seems likely that environmental factors do influence the development of PD, perhaps particularly in people who *also* have a genetic susceptibility.

Some environmental factors are associated with a lower risk of PD, such as exposure to caffeine and exercise (more on exercise later).

Other Risk Factors

There are other things that put an individual at higher risk for developing PD. The main risk factor is age, because PD is more common in older adults (>50 years of age). Men also have a higher risk of PD than women. PD seems to affect Caucasians more often than African Americans or Asians. The actual links between any of these factors and PD are not completely understood.

Now that you know a bit more about what PD actually is, the following chapter will provide greater detail about what to expect in terms of symptoms.

TIPS FOR UNDERSTANDING MORE ABOUT PD

Every day we learn more about the causes of and treatments for PD as results from new research emerge. APDA currently funds a diverse research portfolio and supports Centers for Advanced Research across the country.

To learn more about APDA's research programs, visit apdaparkinson.org/research.

SYMPTOMS

This chapter describes the most common symptoms of PD. Remember once again that, although there are typical symptoms of PD, these can vary greatly from individual to individual—both in terms of their intensity and how they progress. Motor symptoms generally involve movement, while non-motor symptoms do not.

Motor and Related Symptoms of PD

There are five primary motor symptoms of PD: tremor, rigidity, bradykinesia (slow movement), postural instability (balance problems), and walking/**gait** problems. Observing one or more of these symptoms is the main way that physicians diagnose PD.

Tremor

The characteristic tremor in PD is a slow, rhythmic tremor that typically starts in one hand, foot, or leg and can eventually affect both sides of the body. Tremor can also occur in the jaw, chin, mouth, or tongue. The classic tremor of PD is a **resting tremor**, which is strongest when the affected limb is at rest, and may become less apparent or even disappear during a purposeful movement. An **action tremor** (a tremor that occurs with intentional movement) may also be a feature of PD. In addition, some people with PD can experience a feeling of **internal tremor**, which is not necessarily noticeable to others.

Essential tremor is a neurologic movement disorder in which tremor is the major symptom, where the tremor is typically an action tremor, rather than the resting tremor of PD. Essential tremor is a different disorder than PD, but is sometimes mistaken for it, especially early in the disease.

Because resting tremor is a hallmark of PD, its presence (at least in some form) is a strong clue for the diagnosis of idiopathic PD. However, there are other types of tremors that can be easily mistaken for the tremor of PD and conversely, about 30% of people with PD never develop a tremor. It is also important to note, that if a person experiences symptoms of PD other diagnoses may be possible, including other movement disorders, especially if he/she *does not* exhibit the characteristic tremor of PD. Disorders that have some of the motor signs and symptoms of idiopathic PD are called **parkinsonian syndromes** or parkinsonism. Therefore, it is crucial to consult with a physician who has specialized training in neurologic movement disorders to assess the quality of any recurrent or persistent tremor.

Rigidity

Rigidity refers to a tightness or stiffness of the limbs or torso. Rigidity, especially in the early stages of PD, may be wrongly attributed to arthritis or orthopedic problems, such as a rotator cuff injury.

Bradykinesia

Greek for "slow movement," bradykinesia is a frequent symptom of PD and related movement disorders. In addition to a general slowness of movement, the bradykinesia of PD is typically demonstrated by a reduced or mask-like expression of the face (**hypomimia**), a decreased blink rate of the eyes, and problems with fine motor coordination (for example, difficulties buttoning a shirt). Having trouble turning over in bed and slow, small handwriting (**micrographia**) are other signs of bradykinesia.

Postural Instability

More pronounced in the later stages of PD, postural instability includes the inability to maintain a steady, upright posture or to prevent a fall. Such balance problems in PD are associated with a tendency to list or fall backward (**retropulsion**); in fact, a light push can cause the individual with PD to continue stepping

backward or to even fall down. Prominent postural instability early in the disease may indicate that the correct diagnosis is one of the other parkinsonian syndromes rather than PD.

Walking or Gait Difficulties

Bradykinesia and postural instability both contribute to walking, or gait, difficulties in PD, particularly as the disease progresses. A common, early symptom of PD is a decrease in the natural swing of one or both arms when walking. Later, steps may become slow and small, and a shuffling gait may appear. Gait problems in PD can also include a tendency to propel forward with rapid, short steps (**festination**). People with advanced PD may experience episodes of **freezing**, in which the feet feel as though they are glued to the floor.

Vocal Symptoms

In addition to the core motor symptoms of PD, changes in the voice are common. Generally, these are believed to be at least partly due to bradykinesia. In PD, the voice may become softer, or it may start off strong and then fade away. There may be a loss of the normal variation in volume and emotion in the voice, so that the individual may speak in a monotone. In more advanced PD, speaking may become rapid, with the words crowded together, or stuttering may occur. It is beneficial to see a speech language pathologist (SLP) in order to address any emerging communication difficulties as early as possible. You can find an SLP by visiting this website www.asha.org/slp and/or by speaking to your neurologist.

LSVT LOUD is an effective voice treatment program that involves retraining of vocal use and increasing the voice volume. For more information visit www.lsvtglobal.com.

Symptoms of PD can vary greatly from individual to individual—both in terms of their intensity and how they progress.

Non-Motor Symptoms of PD

Because PD is a type of movement disorder, the associated non-motor symptoms can be overlooked. However, there are several common symptoms of PD that do not primarily involve movement. Some of these non-motor symptoms such as decreased smell, depression, sleep disorders, and constipation can precede motor symptoms by years or even decades.

Disturbances in the Sense of Smell

A reduced sensitivity to odors (**hyposmia**) or a loss of smell (**anosmia**) is often an early symptom of PD.

Sleep Problems

Sleep problems are commonly experienced by people with PD. The inability to fall asleep, or **primary insomnia**, is less common than the inability to stay asleep, or **secondary insomnia**. Some people with PD disrupt the normal sleep-wake cycle by taking catnaps throughout the day; doing this may lead to an inability to sleep at night. Other individuals with PD have vivid dreams, although these are more typically due to side effects of medications for PD. People with PD may also talk or thrash in their sleep, particularly during the rapid eye movement (REM) sleep stage (**REM sleep behavior disorder**).

Depression and Anxiety

Depression is a fairly common non-motor symptom of PD. It can range in severity and may improve with PD treatment, anti-depressant medications, or psychotherapy, such as **cognitive behavioral therapy** (CBT). Group or family therapy may also help alleviate depression.

Anxiety occurs in PD as well and, like depression, can be mild or severe. In some cases, anxiety may require medication. As with depression, psychotherapy such as CBT can help to address anxiety.

Fatigue

Fatigue is a complex symptom of PD that is not fully understood. It is known, however, that fatigue is significantly associated with depression and sleep disorders.

Cognitive Decline

Particularly in more advanced PD or in older people with PD, problems with thinking, word finding, and judgment are common. Many individuals report difficulties in multitasking and organizing daily activities. Confusion may also be a side effect of some PD medications.

Weight Loss

Loss of weight is a common symptom of PD, particularly in the later stages of the illness. If weight loss is significant and unintended, your physician should perform an examination to exclude other medical causes of weight loss. While there can be a great deal of weight loss with PD, it will typically level off. There are different causes of weight loss in patients with PD, including decreased appetite (**anorexia**), swallowing difficulties, gastrointestinal problems such as chronic constipation, or depression. The constant motion of an advanced resting tremor or involuntary movements may burn many calories and can also be the cause of weight loss.

Gastrointestinal Issues

Disturbances of the gastrointestinal system are common in PD. Constipation, in particular, occurs frequently because PD may slow the automatic movement of the digestive system; however, side effects of medications may also contribute to constipation. Reduced swallowing and associated drooling or collection of saliva are often seen in PD. Nausea and vomiting occur occasionally in untreated PD, but more often these symptoms are related to medication side effects. Nausea and vomiting are most frequent when treatment for PD first begins.

Lightheadedness

Separate from the balance problems of postural instability but contributing to gait problems, lightheadedness or a faint feeling occurs often in PD. This symptom is related to the body's inability to quickly regulate blood pressure, particularly when sitting up from a lying position or standing from a sitting position. This phenomenon is known as **orthostatic or postural hypotension**. Feelings of lightheadedness may also be increased by certain medications for PD. When severe, lightheadedness may cause black-outs or fainting.

Urinary Issues

Urinary frequency (the need to urinate often) and **urinary urgency** (the feeling that one must urinate right away, even if the bladder is not full) are other possible symptoms of PD. These symptoms occur because the normal reflex mechanisms that control the bladder are disrupted. Urinary problems may be worse at night, when a person is lying flat. There may also be problems with initiating a urine stream (**urinary hesitancy**), slowness of urination, and overfill of the bladder. It should be noted that urinary symptoms in older men specifically may be caused by an age-related enlargement of the prostate gland and not PD.

Sexual Concerns

Changes in sexual desire, or **libido**, is another non-motor symptom of PD that is often under-recognized. Sexual desire may be reduced in some cases because of complex psychological issues. In other cases, a reduced libido can be a direct effect of PD. Treatment with PD drugs frequently improves sexual desire and, in some cases, even increases it to a troublesome level. In men, the inability to achieve or maintain an erection (**impotence**) can occur; however, impotence may also be related to other age-related changes in the body or other conditions.

Sweating

Excessive sweating is a relatively common sign of PD, particularly if the disease is untreated. It happens most often in the upper body.

Melanoma

Individuals with PD may have an increased risk of melanoma, a serious type of skin cancer. As a result, people with PD should undergo annual skin examinations with a dermatologist. If you notice any troubling skin lesions, be sure to talk to your physician about them.

Most people with PD will experience both motor and non-motor symptoms. As the disease progresses, most people will begin to experience more symptoms, though exactly which ones, and how severe they are, will vary from person to person. Talk with your physician about new symptoms as they arise to determine the best treatment.

The next chapter will provide more information on how PD is diagnosed.

PRIMARY MOTOR SYMPTOMS OF PD

- **Tremor**
- **Rigidity**
- **Bradykinesia (slowness of movement)**
- **Postural instability (balance problems)***
- **Walking or gait difficulties***

**May be more apparent in the later stages of illness*

DIAGNOSIS

PD is usually diagnosed clinically, meaning that a physician looks for the presence or absence of the possible symptoms of PD by interviewing the patient and performing a detailed neurologic examination.

PD can often be identified by a **general neurologist**, who is trained to diagnose and treat neurologic disorders. To avoid misdiagnosis, consultation with a movement disorder specialist is recommended. A **movement disorder specialist** is a physician who has undergone additional, subspecialty training in the diagnosis and treatment of movement disorders, such as PD, after training in general neurology.

What to Expect at the First Physician Visit

When you or someone you know first visits a physician for the evaluation of possible PD symptoms, it is helpful to know what to expect. During the first visit, the physician should:

- Take a complete and careful medical history
- Take your blood pressure while you sit and stand
- Assess your thinking (or **cognitive**) skills
- Examine your facial expression
- Look for tremor in your face, hands, arms, and legs
- Examine whether there is stiffness in your arms, legs, torso, or shoulders
- Determine whether you can get up easily from a chair, especially without using your arms
- Examine your walking pattern
- Assess your balance as you stand

Typically, a trained physician will only consider the diagnosis of

PD if the person being examined has at least two of the three core motor symptoms of PD, namely tremor, bradykinesia, and rigidity. At the end of your visit, the physician should discuss with you why you may or may not have PD and the level of certainty about the diagnosis. This determination is based on your medical history and examination at this visit.

Tools to Aid Diagnosis

In addition to taking a history and performing a detailed neurologic examination, physicians can sometimes use brain imaging to help support a diagnosis of PD in particular situations. However, imaging studies have their limitations in the diagnosis of PD and are typically used only in select patients. Brain imaging is *not* routinely performed by neurologists or movement disorder specialists when they are considering the diagnosis of PD, especially if the person's symptoms strongly suggest to the physician that idiopathic PD is the correct diagnosis.

Rather, use of imaging is most helpful when the diagnosis is uncertain, or when physicians are looking for changes in the brain that are more typical of one of several parkinsonian syndromes (and not idiopathic PD) and other conditions that can mimic PD. Imaging studies that may be used include **magnetic resonance imaging** (MRI), which examines the structure of the brain, and **DaTscan**, an imaging test that measures dopamine function in the brain. Although there are no specific features on MRI that confirm a PD diagnosis, certain features on MRI can suggest that the diagnosis is a parkinsonian syndrome other than PD. DaTscan is approved by the Food and Drug Administration (FDA) to help differentiate idiopathic PD from other disorders with similar symptoms, such as essential tremor. Essential tremor is occasionally difficult to distinguish from PD in its earliest stages. Because other parkinsonian syndromes may also have abnormal dopamine function, DaTscan cannot reliably distinguish between PD and other parkinsonian syndromes. Most physicians' offices will have access to MRI; however, DaTscan imaging may only be available at larger hospitals or medical centers.

Other imaging studies that can be done, but that are not used routinely in the clinic, include **positron emission tomography** (PET), which can measure certain brain functions. Although PET can be used as a tool to assist with the diagnosis of PD and parkinsonian syndromes, it is largely reserved for research purposes at this point.

In the case of idiopathic PD, there is typically a positive, predictable response to PD medication; in the case of other parkinsonian syndromes, the response to medication may not be particularly robust, or it may be absent entirely (the next chapter will talk more about PD treatments).

A DaTscan may be particularly useful for the refinement of a diagnosis if a person with PD symptoms does not respond to the usual PD medications.

Unfortunately, there are no standard biological tests for PD, such as a blood test. However, researchers are actively trying to find a PD **biomarker** or measurable characteristic in the body which indicates that disease is present. A biomarker could be any test that could help confirm the diagnosis of PD and follow disease progression.

The Healthcare Provider Team

In addition to a general neurologist or movement disorder specialist, you or someone you know with PD symptoms or a PD diagnosis may encounter several other healthcare providers. In fact, a team approach to the management of PD usually provides the best outcomes in the long term.

Key members of the PD healthcare team include nurses, physician assistants, physical therapists, dieticians, social workers, occupational therapists, neuropsychologists, and speech therapists, among others. All of these individuals can play important roles in the successful management of PD, although their input may not be immediate or necessary throughout the entire course of PD. Also, seeing your primary care physician (a family physician or general internist) is important to regularly assess, maintain, and monitor your general physical and mental health.

HOW TO PREPARE FOR YOUR FIRST PHYSICIAN VISIT

- Bring your complete medical and surgical history. If you have medical records from other physicians, particularly if these records are extensive, have copies of them forwarded to the neurologist or movement disorder specialist before your visit. Be sure to include results from any brain imaging studies that you may have undergone.
- Bring a complete list of medications (prescription and over-the-counter) you take. Also include any nutritional or vitamin supplements that you take regularly. Because some medications can produce or exacerbate the symptoms of PD, it is crucial to provide a complete list of medications and supplements that you are currently taking or have taken within the last year or so.
- Know your family medical history, particularly with respect to any first-degree relatives with tremor or other symptoms resembling those of PD.
- Be prepared to share any history related to alcohol use, tobacco use, or the use of illicit drugs.
- Be prepared to discuss your living situation, social support system, and employment (if relevant), and how you are coping with your symptoms, both physically and mentally.
- Because a first-time office visit can feel overwhelming, particularly one at a larger medical center, bring along a trusted family member or friend for support and assistance. Among other benefits, this person is extremely useful for helping you gather and remember information. Ask this person to take notes during your visit. Sometimes the physician may allow you to record the conversation.

If It's Not Idiopathic PD, What Could It Be?

There are several other conditions that might produce symptoms that can be mistaken for PD. Here are some possibilities:

- Medication side effects: Certain drugs can produce or exacerbate the symptoms of PD.
- Essential, or familial, tremor: This is a relatively common cause of tremor. A general neurologist or movement disorder specialist is the best physician to help differentiate between essential tremor and PD.
- A parkinsonian syndrome: The symptoms of several neurologic conditions are similar to those of idiopathic PD, but they are often managed differently and often do not respond to the typical medications for PD. Parkinsonian syndromes include multiple system atrophy, progressive supranuclear palsy, and corticobasal degeneration.
- Toxicity from exposure to certain metals or carbon monoxide

Remember: Only a general neurologist or movement disorder specialist can tell you with reasonable certainty if you have idiopathic PD. If for some reason you are not comfortable with the results of your first physician visit, getting a second opinion from another general neurologist or movement disorder specialist is always an option. It is important that you feel comfortable with your physician to ensure the best possible outcome for you.

Once you receive a diagnosis of PD, it is time to discuss treatment options with your physician. The next chapter will discuss current treatments for PD.

TREATMENTS

Once you are diagnosed with PD, your focus should be on improving your symptoms and maintaining an active and positive lifestyle. Although there is currently no cure for PD, it is possible to successfully manage symptoms through healthy choices, medications, and, in some cases, surgery.

Treatment needs change over the course of the disease. At every stage, it is important to maintain physical activity, eat a healthy diet, and pay attention to your mental health. Early treatment with medication can help most people with PD maintain an active lifestyle and continue working. Medications are adjusted throughout the course of the disease, in order to maintain the best control of symptoms and avoid major side effects. Adjusting medications can be complex, and is one of the best reasons to be seen by a movement disorders specialist.

LIVING WITH PD

Living with PD involves addressing symptoms through:

- **Lifestyle, including regular exercise and a healthy diet**
- **Medications and other treatments**
- **A supportive social network**
- **A strong partnership with your healthcare team**

Daily Living

Exercise and Daily Activity

In the management of PD, your lifestyle is one of the first things on which you will want to focus. Starting or continuing a schedule of regular exercise can make a big difference in your mobility, both in the short and long term. In fact, several research studies have shown that regular exercise routines of walking, strength training, or **Tai Chi** can help to maintain, or even improve, mobility, balance, and coordination in people with PD. People with PD also report the physical (and mental) benefits of swimming, cycling, dancing, and even non-contact boxing. Whatever you enjoy to stay mobile is the best activity for you, as you will be more likely to stay committed to it. Generally speaking, in the case of PD, the more active you are, the more active you'll stay.

If you did not exercise regularly before your diagnosis, or if you are unsure about your level of fitness or stamina, talk to your primary care physician first. It's important to have your overall health, and specifically your cardiac status, evaluated before starting any new exercise regimen. Also, a physical therapist is a great resource for finding out what your body can tolerate and what you can do safely on a regular basis. Your primary care physician or neurologist can provide you with a referral to a physical therapist. Regardless of your level of fitness, an early evaluation by a physical therapist can be very valuable. Among other benefits, a physical therapist can help you individualize your exercise regimen to suit your needs and capabilities.

The APDA Rehabilitation Resource Center at Boston University was established to help people with PD access information on exercise recommendations. This center provides callers an opportunity to speak with a licensed physical therapist who can answer questions about exercise and resources in the caller's area. Find out more at **www.bu.edu/neurorehab/resource-center**.

In addition to physical therapists, occupational therapists can help people with PD better manage their daily activities, particularly as the disease progresses. Occupational therapists can help you make the most of your mobility with any number of daily activities—whether it's writing, typing, cooking, driving, bathing, dressing, or grooming. Modifications for work and to the workplace environment also fall under the expertise of the occupational therapist.

A speech and language pathologist will evaluate and treat changes in voice volume and speech patterns. The Lee Silverman Voice Treatment (LSVT) program, an evidence-based therapy to increase loudness, is provided by many practitioners. A symptom that may develop as PD advances is **dysphagia** (dis-FAY-jyah), or difficulty swallowing. This requires careful assessment and treatment to avoid complications due to swallowing problems. Speech-language pathologists can help treat swallowing difficulties.

Diet

There is no one diet that is recommended for PD, but healthy eating in general is always a good choice. For example, eating several servings of fruits and vegetables a day increases fiber intake and can help alleviate constipation, in addition to promoting general health. Also, drinking plenty of water or other non-alcoholic and caffeine-free beverages ensures adequate hydration and may reduce the likelihood of low blood pressure and constipation.

There is evidence that the Mediterranean diet is heart- and brain-healthy and may be a good place to start when deciding on food options. This diet is characterized by vegetables, fruits, whole grains, legumes and nuts, moderate amounts of low-fat proteins such as chicken and fish and fats centered around olive oil.

Registered dieticians are great resources for reviewing your diet and making recommendations about healthy foods and daily calorie counts. A balanced diet should ensure that you get the

recommended daily supply of vitamins to maintain your overall health. There is currently no evidence resulting from a well-designed trial in PD patients that a specific vitamin or nutritional supplement is useful in the management of PD, but research is actively ongoing in this area. Depending on your bone health, however, your primary care physician may recommend vitamin D and/or calcium supplements.

There has been much attention given to the possibility that **antioxidants** prevent or slow the progression of PD. Antioxidants are substances that remove toxic **free radicals**, which are produced by cells in the body during injury or stress. In cells, these free radicals promote something called **oxidative stress**, a condition associated with cell loss and aging. The overproduction of free radicals and oxidative stress may also contribute to the development of PD. Antioxidants, such as vitamin E and coenzyme Q10, remove free radicals to reduce the effects of oxidative stress. However, a large study published in the early 1990s showed that supplemental vitamin E did not slow the progression of PD; in fact, people with PD who took supplemental vitamin E fared worse than those who did not. As a result, supplemental vitamin E is not recommended for people with PD. In addition, another study showed that coenzyme Q10 did not provide any clinical benefit to people with PD over a placebo (sugar pill). Nevertheless, antioxidants obtained through your diet may still be beneficial, and research in this area continues.

AN EYE ON ANTIOXIDANTS

The following "super foods" contain high levels of antioxidants and other important vitamins:

- **Grapes**
- **Blue and red berries**
- **Nuts**
- **Dark green vegetables, such as spinach, broccoli, and kale**
- **Sweet potatoes and carrots**
- **Tea, especially green tea**
- **Whole grains**
- **Beans, such as soybeans, lentils, and black-eyed peas**
- **Fish, such as tuna, salmon, and sardines**

Depending on your prescribed medications, you may need to adjust your diet further. Your physician and pharmacist will tell you if your medications need to be taken at certain times of day or with or without certain foods or beverages. In some people with PD, dietary protein (e.g. yogurt, meat, etc.) may affect the absorption of **levodopa** (LEE-voe-DOPE-ah), a common treatment for PD. In addition, if you are taking medications that include levodopa, you may need to adjust the time that you take iron supplements (if you take them), because these supplements can affect the absorption of levodopa from the gastrointestinal tract.

Medications for the Motor Symptoms of PD

Although there is no cure for PD, there are several classes of medications available for the successful treatment of motor symptoms throughout the course of the disease. Be sure to talk with your general neurologist or movement disorder specialist about your most troubling symptoms and your goals for medical therapy. Some medications work better than others for specific symptoms of PD. Make sure you provide your physicians with a complete list of medications (both prescription and over-the-counter) and any vitamin or nutritional supplements that you may be taking.

The benefits of medications can only be obtained if you have access to them and take them as directed. Some medications for PD are available in generic forms or through special programs, so that they are more affordable. Some medications for PD are available in extended release or other forms, which allows for less frequent or easier dosing. Talk to your general neurologist or movement disorder specialist about your situation as well as any preferences for obtaining and taking your medications. Remember that it is important to review with your prescribing physician or pharmacist the side effects of all of your medications, both prescription and over-the-counter, and how they may interact with your other medications or alcohol. Nurses, physician assistants, and pharmacists are also extremely valuable sources of information regarding all of your medications, including how they should be taken, their side effects, and how they may interact with other medications.

A Word About Motor Complications

Motor complications refer to disease-related and treatment-related difficulties that typically develop after several years of uncomplicated treatment of PD. As the disease progresses, a person with PD may begin to develop **"off" time**, when their medications are not sufficient to maintain good symptom control throughout the day. Doses and timing can usually be adjusted, and new medications added, to reduce off time.

In advanced disease, off periods may become unpredictable and less responsive to medication changes.

Levodopa treatment increases the risk for development of **dyskinesias** [dis-keh- NEE-zhee-ahs]), which are uncontrolled movements, especially at the time of peak symptom control from a levodopa dose. Dyskinesias may not be troublesome, and many people with PD report they prefer some dyskinesia with good symptom control to no dyskinesia with less complete symptom control. Sometimes, however, dyskinesias can be socially distressing and/or disabling. Development of significant dyskinesias is often the point at which surgery is considered.

Wearable technology refers to devices worn by a patient that capture movement information. These devices can help monitor motor fluctuations and help with medication management.

Carbidopa-levodopa **(Sinemet®, Rytary®, Parcopa®, Inbrija®, generics)**

The most effective treatment for PD is the combination medication of **carbidopa-levodopa** which is intended to increase brain levels of dopamine, that are deficient in people with PD. Levodopa, which is converted to dopamine in the brain, increases brain levels of dopamine. Levodopa reduces tremor, stiffness, and slow movement in people with idiopathic PD. Carbidopa prevents levodopa from being broken down in the body before it reaches the brain. Therefore, the addition of carbidopa allows levodopa to get into the brain more efficiently. Available in various strengths and delivery systems, carbidopa-levodopa is typically started at a low dosage to avoid nausea and vomiting, which can occur when the dose is increased too rapidly. The dosage is then increased over time as tolerated and until optimal therapeutic benefits are experienced. Carbidopa-levodopa is available in the United States as an immediate-release tablet (Sinemet® and generic), two types of extended-release formulations (carbidopa/levodopa ER available only in the generic version and Rytary®),

and an orally disintegrating tablet (Parcopa®). Levodopa alone is also available in an inhaled version (Inbrija®), to be used as needed if medication effects wear off between oral doses of carbidopa-levodopa.

Side effects of carbidopa-levodopa treatment include nausea, orthostatic hypotension, sleepiness (which can be sudden, called sleep attacks), impulse control behaviors, hallucinations, and confusion. Levodopa also contributes to the development of dyskinesias.

Carbidopa-levodopa Infusion **(Duopa™)**
An alternative form of carbidopa-levodopa (Duopa™) was approved by the FDA in 2015. It is intended for people with more advanced disease, whose symptoms are no longer responding well to oral carbidopa-levodopa. Instead of taking a pill, people with PD can receive carbidopa-levodopa in a gel form through an infusion pump. The pump delivers the medication directly into the small intestine through a surgically placed tube. The advantage of a continuous infusion of the carbidopa-levodopa is less immobility or "off" time from levodopa.

The side effects of the carbidopa-levodopa infusion are similar to those of oral carbidopa-levodopa, but may be associated with a higher incidence of peripheral neuropathy (numbness or loss of sensation in the fingers or feet).

Dopamine Agonists: Pramipexole **(Mirapex®, Mirapex ER®),** ***Ropinirole*** **(Requip®, Requip XL®),** ***Rotigotine*** **(Neupro®),** ***Apomorphine*** **(Apokyn®)**
Dopamine agonists are a little different from carbidopa-levodopa in that, instead of increasing dopamine levels in the brain, they mimic the activity of dopamine. They can be given alone in the early stages of PD, or as an adjunct to carbidopa-levodopa or other PD medications later on. Dopamine agonists are available in immediate-release as pramipexole (Mirapex®) and ropinirole (Requip®) or extended-release pramipexole (Mirapex ER®) and extended-release ropinirole (Requip XL®) formulations. One of the dopamine agonists, rotigotine

(Neupro®), is available as a skin patch. As with carbidopa-levodopa, dopamine agonists are typically begun at a low dosage and titrated upward as tolerated and until optimal therapeutic benefits are experienced.

Apomorphine hydrochloride injection (Apokyn®) is a dopamine agonist, but its effect is very quick and brief. A so-called rescue medication, Apokyn® is reserved for people with advanced PD who have trouble with severe immobility or "off" periods during levodopa therapy. Apokyn® is given as an under-the-skin injection, often by a **care partner**.

The side effects of dopamine agonists are similar to those of carbidopa-levodopa, although impulse control disorders and sudden onset of sleepiness can be more pronounced. Apokyn® in particular can cause severe nausea, so it must be given with a medication that reduces or prevents nausea.

COMT Inhibitors: Entacapone **(Comtan®),** ***Tolcapone*** **(Tasmar®)**

COMT inhibitors are sometimes used with carbidopa-levodopa. Like carbidopa, they prevent the breakdown of levodopa before it reaches the brain. The result is that a more reliable supply of levodopa enters the brain, where it can be converted to dopamine. COMT (catechol-O-methyltransferase) inhibitors are typically prescribed to treat frequent "off" times with levodopa therapy. The COMT inhibitor entacapone (Comtan®) is available as a combination pill with carbidopa-levodopa (Stalevo®).

Sometimes COMT inhibitors can increase the side effects associated with levodopa therapy. Other common side effects of COMT inhibitors are abdominal pain, diarrhea, and discolored bodily fluids such as urine. Regular blood tests for liver function are required with the use of tolcapone (Tasmar®).

Selective MAO-B Inhibitors: Rasagiline **(Azilect®),** ***Selegiline*** **(Eldepryl®, Zelapar®),** ***Safinamide*** **(Xadago®)**

Selective MAO-B inhibitors block the MAO-B enzyme in the brain, which breaks down dopamine. This is another way to

increase dopamine levels in the brain. MAO-B inhibitors can be used alone or with other PD medications. Selective MAO-B inhibitors may be prescribed to complement carbidopa-levodopa therapy, particularly if individuals experience "wearing-off" symptoms while taking levodopa. The selective MAO-B inhibitors for PD are available as a swallowed pill rasagiline (Azilect®) and selegiline (Eldepryl®) or an orally disintegrating tablet of selegiline (Zelapar®). Safinamide (Xadago®) is approved as an add-on therapy to carbidopa/levodopa for the treatment of "off" time. It is an MAOB inhibitor, but has other mechanisms of action such as inhibition of glutamate release.

Side effects of selective MAO-B inhibitors include mild nausea, dry mouth, lightheadedness, constipation, and, occasionally, hallucinations and confusion. Previous restrictions on the intake of foods containing tyramine (for example, aged cheeses, red wine, and draft beers) with selective MAO-B inhibitors have been relaxed by the FDA. However, MAO-B inhibitors can interact with other medications, such as certain antidepressants, nasal decongestants, and narcotic pain medications. Your physician or pharmacist can help you to understand these potential interactions.

Anticholinergics: Benztropine **(Cogentin®),** ***Trihexyphenidyl*** **(Artane®)**

Anticholinergics are often used for the management of PD as adjunct medications to other PD therapies. Anticholinergics are frequently prescribed to reduce the characteristic tremor of PD or to ease the problems associated with the wearing off of levodopa therapy.

Common side effects of anticholinergics include confusion, hallucinations, constipation, dry mouth, and urinary problems. As a result, the use of anticholinergics is typically limited to younger people with PD (under the age of 70). These anticholinergics should also be avoided in combination with antihistamines, certain psychiatric drugs, and alcohol.

Amantadine Formulations

Also used to prevent or treat influenza, **amantadine** (Symmetrel®) has been observed to ease the tremor of PD as well as muscle rigidity. It is typically used as an adjunct medication to other therapies for PD. In addition, it is used to decrease dyskinesia or involuntary movements caused by levodopa. Common side effects include lightheadedness, dry mouth, constipation, vivid dreams, lacy rash, typically on the legs, and swelling of the ankles. Amantadine dosing needs to be decreased in those with kidney disease. It may also interact with or enhance the side effects of anticholinergics and levodopa therapy. Amantadine is available in pill and syrup forms.

Two amantadine extended-release formulations are available. Gocovri® is taken once daily at night and is indicated for the treatment of levodopa-induced dyskinesias. It also has been shown to reduce "off" time. Osmolex ER™ is taken once daily in the morning and is indicated for the treatment of PD motor symptoms.

Adenosine inhibitors: Istradefylline (Nourianz™)

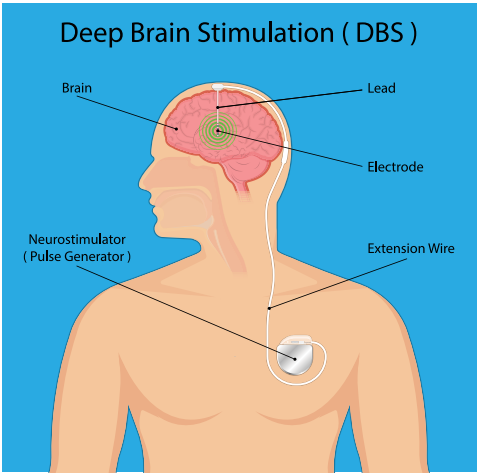
Adenosine inhibitors block the effects of the adenosine receptor. Like dopamine, adenosine is a neurotransmitter that works in the basal ganglia, the deep structures of the brain that are affected in PD. However, to some degree, adenosine and dopamine have opposite effects, so that *inhibiting* the adenosine receptor improves motor function. Istradefylline is indicated for use as an add-on treatment to carbidopa/levodopa for those experiencing "off" episodes.

Surgery

Deep Brain Stimulation

Deep brain stimulation (DBS) is a neurosurgical procedure for people with advanced PD who retain a good response to levodopa, but who have developed significant motor fluctuations including dyskinesias. DBS may also be used to treat medication resistant tremor. By stimulating specific points in the motor control circuits in the brain, DBS "rebalances" the circuits, restoring normal movement control to some degree. In most cases, this allows the person with PD to reduce their dosage of levodopa, and thus reduce their dyskinesias, while maintaining good symptom control.

DBS involves the implantation of permanent, thin electrodes into selected deep parts of the brain. A battery-operated pulse generator, much like a cardiac pacemaker, is implanted under the skin of the chest or abdomen. The pulse generator is connected to the stimulator electrodes via wires, which are tunneled underneath the skin of the scalp and neck (see image below). The DBS procedure is associated with a small chance of infection, stroke, bleeding, or complications associated with anesthesia.



The equipment is not visible underneath the clothes, and causes no discomfort in daily use. The electrodes are programmed by a remote computer for maximum symptom control, and the batteries can be replaced by an outpatient procedure when necessary, typically after several years.

DBS technology is constantly evolving with the development of rechargeable batteries which last much longer than a traditional battery, as well as more sophisticated programming options to maximize symptom control. The newer DBS systems are also MRI-conditional and can be placed in MRI-mode for the duration of an MRI, making the process of getting an MRI with a DBS system in place much simpler than with older systems.

Focused Ultrasound

Focused ultrasound (FUS) is a procedure that uses targeted ultrasound waves to heat up and lesion a precise location in the brain. By destroying a very specific area of the PD brain, the normal circuitry in the brain can be restored. Focused ultrasound is currently approved for treatment of tremor in PD.

Treatments for Non-Motor Symptoms of PD

People with PD commonly experience non-motor symptoms, including orthostatic hypotension, cognitive difficulties, hallucinations, depression, anxiety, sleep problems, or other difficulties. If you are experiencing any of these problems, be sure to discuss them with one or more members of your healthcare team. Additional therapies or medications (beyond those that treat the motor symptoms of PD) may be useful and can be taken in conjunction with your PD medications.

Medications Approved for Non-Motor Symptoms of PD

Droxidopa (Northera™) is specifically indicated to treat the orthostatic hypotension of neurologic diseases like PD. It should be used with caution in people with cardiac disease, as it may aggravate certain cardiac conditions. Common side effects include headache, dizziness, nausea, hypertension, fatigue, fever, and confusion. In addition, high dosages of carbidopa-levodopa may interfere with the activity of droxidopa. Other medications used to treat orthostatic hypotension are **fludrocortisone** (Florinef®) and **midodrine** (ProAmatine®).

Pimavanserin (Nuplazid™) is approved to treat hallucinations and delusions that may develop in advanced PD. It can cause swelling of the ankles, constipation, and confusion. Those with heart rhythm disturbances should avoid taking this medication.

Rivastigmine (Exelon®) is approved for dementia associated with PD. It can cause nausea, vomiting, and loss of appetite.

Complementary Therapies for PD

A vast array of complementary treatments for PD are available including meditation, massage, acupuncture, music therapy, and art therapy. Many of these therapies have been studied formally in PD, although usually in only small groups of people. Therefore, much is unknown about whether these therapies are truly effective and if so, how they work and how to maximize their benefit. Nevertheless, you may find them beneficial in addition to **evidence-based** medicines approved for PD. You should discuss the possible pros and cons of these options with one or more members of your healthcare team.

Many states have legalized medical marijuana and PD patients have tried it for relief of some of the motor and non-motor symptoms of PD. There is limited research however, investigating which PD symptoms respond to medical marijuana, as well as what type, delivery system, and dose should be used. There are also side effects of medical marijuana that must be considered including dizziness and low blood pressure. You should discuss the use of medical marijuana with your healthcare team as you would any other medication.

Research in PD is ongoing, and new treatments are on the way. The final chapter discusses the latest in research, potential treatments on the horizon, and clinical trials. Also provided are additional resources for people with PD and their families.

GLOSSARY

Action tremor: a tremor that occurs with intentional movement

Alpha-synuclein: a protein that builds up in certain nerve cells in certain brain regions of people with PD and related conditions

Amantadine: medication used to prevent or treat influenza that is also used to ease the tremor and rigidity of PD

Anorexia: decreased appetite

Anosmia: loss of the sense of smell

Anticholinergics: a class of drugs often used for the management of PD, typically as adjunct medications to other, standard PD therapies; used to reduce the tremor of PD or ease the problems associated with the wearing off of levodopa therapy

Antioxidants: substances found in certain foods and supplements that may remove toxic free radicals from the body

Biomarker: measurable characteristic in the body which indicates that disease is present

Bradykinesia: slowness of movement; a common motor symptom of PD

Carbidopa-levodopa: a combination medication commonly used to treat PD; intended to increase dopamine levels in the brain

Care partner: a person, such as a close family member or friend, who supports an individual with a chronic medical condition

Clinical trials: studies conducted in humans, often involving a drug or some other type of treatment

Cognitive: pertains to thought processes, such as memory, attention, concentration, and judgment

Cognitive behavioral therapy (CBT): a form of psychotherapy used to treat depression that focuses on challenging unrealistic thoughts and replacing them with more realistic ones

COMT inhibitors: drugs that block catechol-O-methyltransferase (COMT), an enzyme that breaks down dopamine and levodopa; used in PD to prevent the breakdown of levodopa therapy before it reaches the brain

DaTscan: FDA-approved imaging test used to detect dopamine function in the brain; can help differentiate essential tremor from idiopathic PD and other disorders that cause tremor

Deep brain stimulation (DBS): involves the use of embedded pulse generators to suppress the motor symptoms of PD, thereby allowing for a reduction in medication; surgical option for people with advanced PD who have tried a number of different medication regimens for their motor symptoms

Dopamine: a brain chemical (neurotransmitter) that enables movement; brain levels of dopamine fall in certain brain regions in people with PD

Dopamine agonists: drugs that mimic the action of dopamine

Droxidopa: FDA-approved drug used to treat the orthostatic hypotension of neurologic diseases like PD

Dyskinesias: fragmented or jerky movements of the limbs or torso; often apparent at peak times of levodopa therapy in more advanced PD

Dysphagia: difficulty moving food from the mouth to the esophagus

Essential tremor: a neurologic movement disorder in which tremor is the major symptom. Tremor is typically an action tremor, rather than the rest tremor of PD.

Evidence-based medicine: use of the best scientific evidence from clinical research to optimize clinical decision-making

Festination: a shuffling manner of walking associated with small steps and slowness of movement (bradykinesia)

Fludrocortisone: medication used to treat orthostatic hypotension

Free radicals: toxic substances that are produced by cells in the body during injury or stress

Freezing: 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

Gait: pattern of walking

General neurologist: a physician who is trained to diagnose and treat neurologic disorders

Hypomimia: a reduced or mask-like expression of the face

Hyposmia: reduced sensitivity to odors

Idiopathic: of unknown cause

Impotence: the inability to maintain or achieve an erection

Internal tremor: sensation of vibration inside the body

Lewy bodies: clumps of protein (alpha-synuclein) found in the nerve cells in certain brain regions of people with PD and related conditions

Libido: sexual desire

Magnetic resonance imaging (MRI): imaging technique that allows physicians to see the structure of the brain

Micrographia: slow, small handwriting

Midodrine: medication used to treat orthostatic hypotension

Motor complications: disease- and treatment-related complications, including off periods, dyskinesias, and other phenomena, that develop after several years of treatment

Motor symptoms: symptoms that primarily involve movement

Movement disorder: a neurological condition that affects movement

Movement disorder specialist: a physician, typically a neurologist, who has undergone further training to diagnose and treat movement disorders

Neurodegenerative disease: a disease in which neurons (brain cells) die. Neurodegenerative diseases include Parkinson's disease and Alzheimer's disease

Neurons: nerve cells, which form the structure for interconnected, intercommunicating networks in the brain

Neurotransmitter: a brain chemical that allows neurons to communicate with one another

Non-motor symptoms: symptoms that do not primarily involve movement

Off time: periods when treatments are not providing control of symptoms

Orthostatic or postural hypotension: the body's inability to quickly regulate blood pressure, particularly when sitting from a lying position or standing from a sitting position

Oxidative stress: a destructive condition in which free radicals damage cells; associated with cell loss and aging

Parkinsonian syndromes: movement disorders that are not idiopathic PD but have some overlapping symptoms, such as rigidity and slowness of movement (bradykinesia)

Positron emission tomography (PET): imaging technique that can measure certain brain functions

Primary insomnia: the inability to fall asleep

Rapid eye movement (REM) sleep behavior disorder: a particular type of sleep disorder that may be associated with talking or thrashing in one's sleep

Resting tremor: a tremor that occurs when still; a hallmark of PD

Retropulsion: the tendency to fall backward

Rigidity: stiffness of the muscles

Secondary insomnia: the inability to stay asleep

Selective MAO-B inhibitors: drugs that selectively block the enzyme monoamine oxidase B (MAO-B) in the brain; MAO-B breaks down dopamine

Substantia nigra: meaning "black substance" in Latin, a region in the base of the brain that contains dopamine-producing neurons, which appear dark under a microscope; people with PD experience cell loss in this region

Tai Chi: a form of exercise developed in ancient China that can help with posture and balance

Tremor: a form of rhythmic shaking

Urinary frequency: the need to urinate often

Urinary hesitancy: difficulty initiating a urine stream

Urinary urgency: the feeling that one must urinate right away, even if the bladder is not full

Wearable technology: devices worn by a patient that capture movement information

Apathy and Parkinson's Disease

Why do some people with Parkinson's disease (PD) experience reduced interest, motivation or enthusiasm? It could be apathy. In Parkinson's the same changes in brain chemistry that can cause movement symptoms can also affect a person's mood, energy and motivation.

A recent study found that about 40 percent of people with PD experience apathy, a motivational disorder in which people have trouble getting interested in daily activities. Until recently, apathy was largely misunderstood as a form of depression. Today the medical community defines apathy and depression as distinct syndromes with overlapping features.

It is important that people with PD, their care partners and their health teams be able to distinguish between apathy and depression. Medications used for depression can actually make apathy worse. Both apathy and depression can intensify the movement and cognitive symptoms of PD. Treating apathy is critical to improving health and well-being. Continue reading to learn about apathy — how it differs from depression and how people with PD can cope with its effects.

What is Apathy?

Apathy is defined as a lack of motivation. In PD, it shows up in three forms:

- **Cognitive**. Loss of interest/curiosity in new things.
- **Emotional**. A lack of passion or reaction to news or situations that normally would evoke an emotion.
- **Behavioral**. Trouble initiating activity, a need for others to prompt one to complete tasks.

In one study, people with PD who also had apathy spent almost no time pursuing hobbies and spent twice as much time watching TV as those without apathy. People with apathy may find themselves less able to take care of themselves independently and less able to manage their PD effectively. For example, a person with apathy may not be motivated to take medications on time. Apathy in PD can be stressful for care partners and family members who may be unaware of apathy and may instead view the person with PD as lazy or stubborn.

Diagnosis

Care partners may be the first to notice signs of apathy, although they may have trouble differentiating it from depression or sleep issues. Care partners often play an important role in urging the person with PD to seek a diagnosis. There is no universal test for diagnosing apathy. The one most widely used is the Apathy Scale, a questionnaire that people with PD fill out in the doctor's office. Another is the Lille Apathy Rating Scale, which is administered as an interview between the person with PD and a medical professional.

Is It Apathy or Depression?

Both apathy and depression can lead people to lose pleasure in daily life and enthusiasm for their usual interests. Given this overlap, how can we tell if a person has apathy or depression? In short: sadness, guilt and being worried or hopeless all point to depression, not apathy. By contrast, the inability to "get up and go" may point to apathy. It is possible to experience both and finding ways to cope with each is important to living successfully with PD.

Treatment

The first thing a person with PD and his or her care partner should do upon experiencing apathy is to consult the movement disorder specialist to ensure that PD medications are working optimally. The primary goals for treating apathy are similar to those used for treating PD movement symptoms: increase dopamine in the brain and improve the effect of anti-PD medications. There is no one-size-fits-all therapy for apathy, but research provides some insights.

For example:

- A trial comparing the two most commonly-used dopamine agonists found pramipexole (Mirapex®) to be more effective for apathy than ropinirole (Requip®).
- A study found that the rivastigmine (Exelon®) "patch," a treatment for Alzheimer's, was effective for treating apathy in people with PD who did not have dementia.
- Another study of repetitive Transcranial Magnetic Stimulation (rTMS) showed that people who received the experimental treatment and those who received a placebo both improved dramatically. The act of participating in the study itself may have boosted motivation.

Better Understanding Apathy

The Parkinson's Foundation is committed to better understanding how to help people with PD overcome Apathy. In 2017, we funded Nabila Dahodwala, MD, at University of Pennsylvania to study goal-directed behavior in Parkinson's. This study will test a new way of measuring goal-directed behavior in Parkinson's. It will also use brain imaging to observe brain changes that occur when people experience apathy and cognitive impairment. The hope is that the study will shed light on the mechanisms underlying apathy and cognition in PD and help in more easily diagnosing them. This knowledge will ultimately allow for the development of targeted PD treatments.

TIP

Coping with Apathy

There are also many non-drug approaches that may help a person with PD who is experiencing apathy to get motivated. The key for success is to set concrete and obtainable goals. A person with PD who is experiencing apathy may find it helpful to try dance therapy, music therapy, exercise, crafts, outings or cognitive challenges (e.g., computer games, crossword puzzles, bingo or card games). If you're a care partner, provide positive feedback when goals are achieved, but also be prepared for setbacks.

How can a person with PD get motivated to do these activities? The key is to have goals that are SMART.

- ✓ **Specific: when and where will the person with PD do the chosen activity? How often will he or she do it?**
- ✓ **Measurable: track your progress.**
- ✓ **Attainable: you don't have to go fast, you just have to go.**
- ✓ **Relevant: focus on the most pressing needs — like getting up and moving or not missing a doctor appointment — above less necessary tasks.**
- ✓ **Timely: set a schedule with reminders.**

Call our Helpline for more information at 1-800-4PD-INFO (473-4636).

Anxiety

Like people with other chronic diseases, people with Parkinson's disease (PD) often struggle with mental health difficulties. While the illness is known to impair many aspects of movement, research from the *Parkinson's Outcomes Project* has found that two non- motor symptoms — depression and anxiety — play a key role in the disease as well and its effect on people's quality of life.

Feeling worried is an understandable reaction to a Parkinson's diagnosis. But when feelings of constant worry or nervousness go beyond what is understandable, a person may be experiencing anxiety, which is more serious.

Anxiety is a common non-motor symptom of PD. It is important to note that anxiety is not simply a reaction to the diagnosis of Parkinson's, but is instead a part of the disease itself, caused by changes in the brain chemistry of the brain. **As many as two out of five people with PD will experience one of these forms:**

- **Generalized Anxiety Disorder:** Generalized anxiety disorder (GAD) is characterized by feelings of nervousness and recurring thoughts of worry and fear. This worrying is in excess of what would normally be expected given the situation and often leaves the person feeling out of control. Physical symptoms that may accompany these feelings include butterflies in the stomach and nausea, trouble breathing or swallowing, racing of the heart, sweating and increased tremors.
- **Anxiety Attacks:** Anxiety, or panic, attacks usually start suddenly with a sense of severe physical and emotional distress. Individuals may feel as if they cannot breathe or are having a heart attack. They may feel they are experiencing a medical emergency. These episodes usually last a few minutes to an hour, particularly when associated with "off" periods, though they can last for longer periods of time.
- **Social Avoidance:** Social avoidance, or social anxiety disorder, involves avoiding everyday social situations because of a fear of embarrassment at having Parkinson's symptoms, such as tremor, dyskinesias, or trouble walking noticed in public. Exposure to social situations can lead to severe anxiety in these individuals, which goes away when the person is removed from or completely avoids the situation.
- **Obsessive-Compulsive Disorder:** People with obsessive-compulsive disorder (OCD) may be plagued by persistent, unwelcome thoughts or images (obsessions), and by the urgent need to engage in certain rituals (compulsions) to try to control or rid themselves of these thoughts. As an example, they may be obsessed with germs or dirt, and wash their hands over and over. Performing these so-called rituals, however, only provides temporary relief, and not performing them markedly increases anxiety.

Anxiety is not tied to disease progression — it can begin before a PD diagnosis or develop much later on. Additionally, while some people with PD experience anxiety on its own, many are diagnosed with anxiety along with

depression. While anxiety is less well-studied than depression, it may be just as common. If left unchecked, anxiety can worsen a person's overall health condition.

Causes of Anxiety

Psychological Factors

Common fears and worries that go along with PD may trigger anxiety. One is a fear of being unable to function independently, particularly during a sudden "off" period (the time of day when medication is not working). This can lead to a fear of being left alone. Another is a concern about being embarrassed—often related to interacting with others in public.

Biological Factors

Many of the brain pathways and chemicals affected by Parkinson's are the same as those affected by anxiety and depression. People with Parkinson's have abnormal levels of the brain chemical GABA. Similarly, anxiety and depression are linked to low levels of this neurotransmitter as well, and can be treated with one class of anti-anxiety medications designed to increase these levels. In some cases, anxiety is directly related to changes in motor symptoms. Specifically, patients who experience "off" periods can develop severe anxiety during these states sometimes to the point of full-blown anxiety attacks.

How Is Anxiety Diagnosed?

Anxiety is usually diagnosed by a primary care physician, or a mental health professional, who will ask questions about certain symptoms. The doctor will talk with the patient about mood changes and behaviors. For people with an anxiety disorder, their symptoms become so intense that they are unable to function normally in life. Overall, it is easier to diagnose anxiety than depression in PD, because symptoms of anxiety and PD do not overlap as much.

In general, symptoms of anxiety may include:

- Excessive fear and worry

- Uncontrollable or unwanted thoughts
- Sudden waves of terror
- Nightmares
- Ritualistic behaviors
- Problems sleeping
- Pounding heart
- Cold and sweaty hands
- Dizziness
- Nausea

In people with Parkinson's, a diagnosis of an anxiety disorder is made only if the symptoms involve a clear change in a patient's previous behavior and are not easily confused with motor symptoms. For example, even though a patient may have a legitimate concern that a tremor or change in walking ability may be noticed in public, a diagnosis of social avoidance is only made if the patient realizes that the concern is excessive, the social situation is avoided, and it causes interference in the person's social or work life.

What Are Treatment Options for Anxiety?

There are two main types of treatment options for anxiety: medications and psychological counseling (psychotherapy). Depending on the severity of symptoms, psychotherapy can be used alone or combination with medication. Care should be tailored to each person's individual needs.

Medication Therapy

SSRIs (antidepressants)

A newer class of antidepressant drugs called selective serotonin reuptake inhibitor (SSRIs) are typically the first-line treatment for depression and anxiety disorders. They include:

- fluoxetine (Prozac®)
- sertraline (Zoloft®)
- paroxetine (Paxil®)
- citalopram (Celexa®)
- escitalopram (Lexapro®)

For patients with anxiety attacks, very low dosages should be used at first. Evidence shows these medications can increase attacks when first started at higher dosages. An added benefit of using SSRIs is that they also work for depression, which often occurs simultaneously.

Benzodiazepines (anti-anxiety medications)

An older class of medications called benzodiazepines is used to treat anxiety disorders and target the brain chemical GABA. They include:

- diazepam (Valium®)
- lorazepam (Ativan®)
- clonazepam (Klonopin®)
- alprazolam (Xanax®)

These medications can be very effective for anxiety, sometimes working better than antidepressants. They take effect very quickly, often providing some relief after a single dose. Also, they can help with other symptoms of PD, including certain types of tremor, muscle cramping and sleep changes. Major drawbacks include memory difficulties, confusion, increase in balance problems and tiredness. These medications should not be stopped suddenly, as patients can have serious withdrawal symptoms such as seizures and severe stiffness called spasticity.

NOTE: Benzodiazepines should be used with caution in older patients with Parkinson's or in those with dementia. If used regularly, they should never be stopped suddenly to avoid serious withdrawal symptoms.

Psychotherapy

Psychotherapy or "talk therapy" refers to many varieties of counseling. This type of treatment can help people diagnosed with an anxiety disorder understand their illness and better manage their symptoms. Mental health professionals who provide therapy include psychologists, social workers, psychiatrists, licensed professional counselors, and specially-trained nurses. The first step is to find a compatible therapist. Quality therapy can be beneficial because:

- Cognitive behavioral therapy (CBT) is very effective at helping people change negative thinking patterns and behaviors to solve their

problems and engage in life.

- CBT encourages patients to develop more positive thoughts about themselves, the environment around them and their future: in this case the outcome related to their illness.
- Counseling sessions can provide vital support, understanding and education. Patients may be seen alone, as a couple or family, or in a group.
- Psychotherapy offers two advantages: no drug side effects and coping skills that can be used over the long term.

Non-Conventional Therapies for Anxiety

- Relaxation techniques
- Massage therapy
- Acupuncture
- Aromatherapy
- Various forms of meditation
- Music therapy

For information on therapies, licensing and certification, visit the website of the National Center for Complementary and Alternative Medicine at the National Institutes of Health. Anyone considering non-conventional treatment for an anxiety disorder should be sure to discuss the following options with their doctor.

Tips for Living with Anxiety

- Educate yourself about PD and its symptoms, including anxiety.
- Keep a diary of your moods, your medications and your PD symptoms.
- Figure out what sets off anxiety for you.
- Talk with your doctor about anxiety, so you can get medical help.
- Tell your care partner and family members how you are feeling, so they can understand your emotions better and help you find ways to cope.
- Find a support group for people with PD.
- Be flexible in your approaches to coping with anxiety; try different approaches.

- Understand that symptoms change; if a coping strategy stops working, try a new approach.
- Like other PD symptoms, each individual experience anxiety differently.

Bradykinesia (Slowness of Movement)

Bradykinesia means slowness of movement, and it is one of the cardinal symptoms of Parkinson's. You must have bradykinesia plus either tremor or rigidity for a Parkinson's diagnosis to be considered.

In Parkinson's, this slowness happens in different ways:

- Reduction of automatic movements (such as blinking or swinging your arms when you walk)
- Difficulty initiating movements (like getting up out of a chair)
- General slowness in physical actions
- The appearance of abnormal stillness or a decrease in facial expression

This translates into difficulty performing everyday functions, such as buttoning a shirt, cutting food or brushing your teeth.

Bradykinesia can be particularly frustrating because it is often unpredictable. One moment you can move easily, while in the next moment you may need help.

Managing Slowness of Movement

Levodopa is the medication most commonly given to control the movement symptoms of Parkinson's. Dopamine agonists, MAO-B inhibitors, and amantadine can also be used alone or in combination

with other medications to improve slowness, as well as stiffness and tremor.

If you experience **"off" periods** – changes in your ability to move, usually related to medication timing – when bradykinesia and other symptoms are worse, adjusting the dose or schedule of your medication could help. Talk to your healthcare provider before making any changes to your medications.

In addition to medications, **exercise** should be part of your treatment plan for all Parkinson's symptoms.

Research also suggests that music therapy can reduce bradykinesia.

Breathing & Respiratory Difficulties

Some people with Parkinson's disease (PD) may experience shortness of breath. There is no clear cause underlying respiratory dysfunction in PD, its frequency or the effect that medications have on respiration. Several reasons for shortness of breath in PD include:

- **"Wearing off"** is a common experience among people with PD who have been taking levodopa for several years. These occur when the medication benefit wears off and PD symptoms (including shortness of breath) return before the next dose.
- **Respiratory dyskinesia** refers to an occurrence of irregular and rapid breathing when levodopa medications reach their peak effect. These may accompanied by involuntary body movements, typically experienced as dyskinesia.

- **Anxiety** is a common symptom of PD that may also exacerbate shortness of breath, whether by itself or as a consequence of wearing off of the medication.
- **Aspiration pneumonia** is a pneumonia that develops after food or liquid "goes down the wrong pipe." Advanced PD can increase the risk of swallowing difficulties, choking and aspiration pneumonia.
- **Non-PD health issues** include conditions such as asthma, allergies, lung disease, heart disease and other conditions that may cause shortness of breath.

Therapies

Treating breathing difficulties in PD depends on identifying their cause. There is no specific therapy for shortness of breath among people with PD and tests may show that everything is normal. Still, it may help to discuss your medications with your doctor.

Tips for Coping with Breathing Difficulties

- Work with your doctor to identify and treat any non-PD causes of shortness of breath, such as lung disease, heart disease or lack of physical conditioning and endurance.
- Exercise as much as possible. Shortness of breath may lead a person to move less. Less physical activity reduces the ability to take deep breaths. Staying active improves pulmonary function.
- Take steps to cope with anxiety. Talk with your doctor to figure out what sets off anxiety and find treatments (medications, exercise, lifestyle changes) and techniques that work for you.
- Speak to your doctor about getting an evaluation performed by a speech-language pathologist (SLP) who can help you address issues related to swallowing.
- Give up smoking.

Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

I Am A Carer

HOW TO COMMUNICATE? | LOOKING AFTER YOURSELF | RESOURCES

Carers play an important role in the care and support of someone with Parkinson's. They are often partners and family members, but could also be friends or neighbours. Many carers who provide care and support will not view themselves as a "carer". First and foremost they will view themselves as a wife, a husband, son, daughter or partner.

Caring for someone with Parkinson's can be a very long and difficult journey and people may react quite differently to the challenge. Make sure you take time to look after yourself as much as possible.

It depends on many factors such as:

- Your relationship with the person prior to them developing Parkinson's;
- Your own lifestyle prior to this diagnosis;
- Your own health and needs; and
- The level of support that you have from other people.

To be a good carer you need:

- an understanding of some of the special difficulties associated with Parkinson's;
- to learn when to help and when not to;
- to allow time for the person to do things for him or herself, without hurrying;
- to not take over (e.g. do not speak for them);
- knowledge about who to go to for help in such things as aids to daily living (e.g. eating problems);
- to have survival strategies (i.e. adopt a day by day approach); and
- to be honest in your relationship.

Carers can suffer from:

- frustration and even anger
- depression
- sleep disorders

Carers need:

- information and support
- encouragement
- a listening ear
- recognition
- opportunity to express frustrations
- good communication with health professionals
- quality time away and access to respite care
- a good night's sleep (too many broken night's sleep is one of the biggest problems with which carers of people with PD have to contend)
- to look after themselves and their own health
- a sense of humour

- pampering from time to time

Communication

Communication is key to caring for anyone.

As a carer, you are not likely to be the only person involved in that person's Parkinson's journey so developing good relationships with all key stakeholders involved in their care is paramount. Some of the people you may need to connect with to provide best quality care are:

- Family & Friends
- Specialists (Neurologist, Gerontologist, etc), General Practitioners, Nurses
- Allied Health Professionals e.g. Physiotherapists, Occupational Therapists, Speech Therapists, Social Workers, Psychologists, Dietitians etc.

You may come across communication barriers the person you are caring for is having with their own communication because of their Parkinson's. Some of these communication barriers and symptoms you may see are detailed on the Communication & Parkinson's information sheet.

A few other tips that may be helpful to carers of people living with Parkinson's:

1. Have patience

2. Speak to a person with clear tone and timing. You do not need to speak louder (unless you are aware that they have a known hearing impairment)

3. Speak slowly enough for that person. Repeat their turn of phrase to also help them slow their speech down

4. Provide time for them to respond to any questions

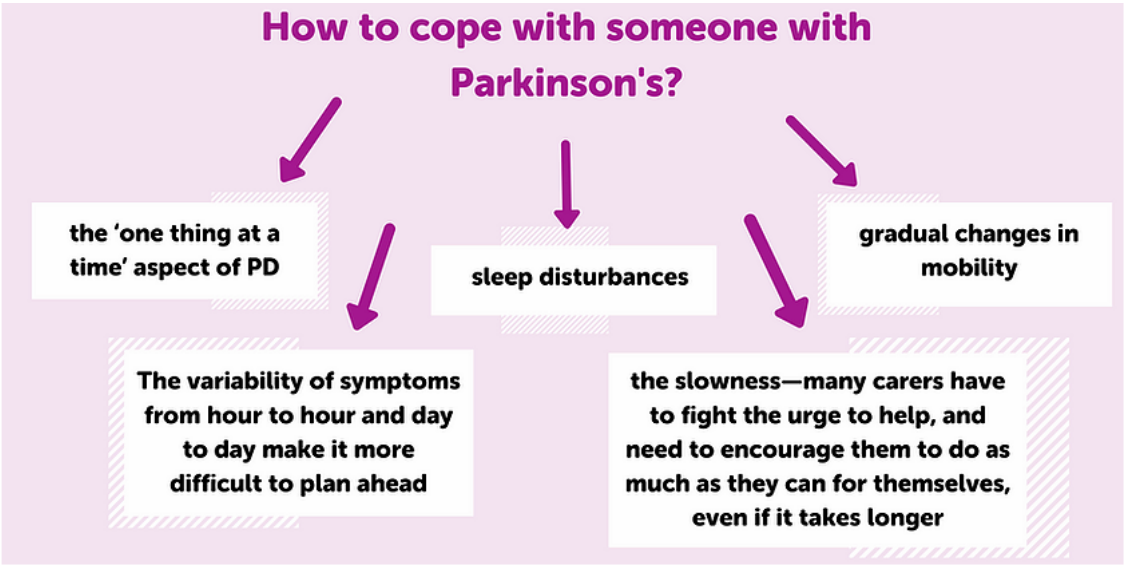
5. Encourage them to use single words or short word phrasing so their message is clearly conveyed

6. Provide empathy as often communicating for a person living with Parkinson's may leave them with a loss of confidence in addition to being frustrating and exhausting

7. Where appropriate, try asking closed-ended questions where people can answer simple "yes and no" answers

8. Always acknowledge when you have understood their questions and communication (e.g. nodding your head and saying "thank you")

9. Provide time for the person to finish their conversation and/or question.



HELPING YOU HELP OTHERS

Carerhelp

Carerhelp aims to empower carers to cope with the hard times as well as they can, and to make space for good times as well. When carers feel ready for their role, everybody benefits. Here are some of the key things carers can get from the Carerhelp website:

- Access to high quality information and resources that support them in the carer role
- Knowledge of the services available to carers
- A greater sense of control over their role
- Better communication with the health care team, family and friends
- Greater well-being

Carer Support Groups

Joining a carer's support group is one way to fulfil some of these needs. A support group consists of people who join together to give and get support and assistance in coping with a common problem. They are not a substitute for medical advice, nor are they fund-raising groups. They are simply voluntary gatherings of people who share common situations and problems and who, by sharing their experiences, support and help each other.

You can get information on whether there is a carer support group near you by ringing the Parkinson's Info Line on 1800 644 189.

Carers Fact Sheets

Carer's Australia has produced an excellent online resource called Surviving the Maze with over 60 fact sheets to assist carers to navigate the service system of community support.

Palliative Care Training

The Australian Healthcare and Hospitals Association have re-launched the Palliative Care Online Training Portal, funded by the Australian Government.

The Portal provides free, non-clinical, interactive training to carers, community & aged care workers, students, volunteers, family members and clinicians who want to build their skills if they are caring for someone with a life-limiting illness.

To date this training has been delivered to over 35,000 people and covers topics such as:

- the needs of people and their families as they approach end-of-life;
- assessment skills;
- end-of-life conversations;
- self-care and building resilience;
- pain management;
- and recognising deteriorating patients.

The Palliative Care Online Training Portal is available at www.pallcaretraining.com.au

Registration is free and there are no time restrictions for completion of the modules.

Aged Care Training

Parkinson's Australia's Aged Care Training Package called Caring for People with Parkinson's is now available. It is designed to educate and inform all the staff of Residential Aged Care Facilities to improve the quality of care provided for residents living with Parkinson's.

The training package is evidence based, with clearly stated and measurable learning outcomes, while incorporating the principles of best practice in care and utilizes a person-centred approach.

Learning Outcomes

1. Increase the awareness and knowledge of the signs, symptoms and treatments of Parkinson's disease.
2. Increase the understanding of the needs of someone living with Parkinson's.
3. Increase the capacity of staff in providing care for someone living with Parkinson's.

This training package is run through the state/territory Parkinson's organisations. Contact your state/territory organisation (click on website links top right of this page) for further details or phone 1800 644 189.

Cognitive Changes

Some people with Parkinson's disease (PD) experience mild cognitive impairment. Feelings of distraction or disorganization can accompany cognitive impairment, along with finding it difficult to plan and accomplish tasks.

It may be harder to focus in situations that divide your attention, like a group conversation. When facing a task or situation on their own, a person with PD may feel overwhelmed by having to make choices. They may also have difficulty remembering information or have trouble finding the right words when speaking. These changes can range from being annoying to interfering with managing household affairs.

To some degree, cognitive impairment affects many people with PD. The same brain changes that lead to motor symptoms can also result in slowness in memory and thinking. Stress, medication and depression can also contribute to these changes.

Symptoms of mild cognitive impairment (MCI) often do not interfere with home and work life. They may not even be noticeable, but can be detected through testing. Doctors used to believe that cognitive changes did not develop until mid- to late-stage PD, but recent research suggests that mild changes may be present at the time of diagnosis.

Tell your doctor if you have concerns about cognitive changes. You may need to change your medication or see a neurologist or neuropsychologist for assessment. An occupational therapist can also help you find strategies for adapting and coping with these symptoms. A speech therapist can help with language difficulties.

In general, mental and motor decline tend to occur together as the disease progresses. Significant cognitive impairment in PD is often associated with:

- Caregiver distress
- Worse day-to-day function
- Diminished quality of life
- Poorer treatment outcomes
- Greater medical costs due to nursing home placements
- Increased mortality

Cognitive impairment is different from dementia, which is when cognitive impairments occur in more than one area of cognition, leading to more severe loss of intellectual abilities that interferes with daily, independent living. While approximately 50 percent of people with PD will experience some form of cognitive impairment, not all lead to a dementia diagnosis.

Two recent long-term studies suggest that many people with PD will eventually develop a mild form of dementia as the disease progresses, usually many years after their initial diagnosis. One medication, Exelon® (rivastigmine tartrate), can treat dementia in PD. Other medications are being studied.

What causes cognitive changes in people with PD?

One cause is a drop in the level of dopamine, the neurotransmitter that is involved in regulating the body's movements. However, the cognitive changes associated with dopamine declines are typically mild and restricted.

Other brain changes are likely also involved in cognitive decline in PD. Scientists are looking at changes in two other chemical messengers — acetylcholine and norepinephrine — as possible additional causes of memory and executive function loss in Parkinson's.

Effects of Cognitive Changes

The cognitive changes that accompany Parkinson's early on tend to be limited to one or two mental areas, with severity varying from person to person. Areas most often affected include:

Attention

- Difficulty with complex tasks that require person with PD to maintain or shift their attention.
- Problems with mental calculations or concentrating during a task.

Speed of Mental Processing

- Slowing in thinking is often associated with depression in PD.
- Signs include: a delay in responding to verbal or behavioral stimuli, taking longer to complete tasks and difficulty retrieving information from memory.

Problem-solving or executive function

- Trouble planning and completing activities.
- Difficulties in generating, maintaining, shifting and blending different ideas and concepts.
- More concrete in approach to tasks.
- Loved ones can help the person with PD by providing cues, reminders and greater structure of activity.

Memory deficits

- The basal ganglia and frontal lobes of the brain (both help the brain organize and recall of information) may be damaged in PD.
- Difficulty with common tasks such as making coffee, balancing checkbook, etc.
- People with dementia can experience both short-term and long-term memory impairment. (Read about the relationship between dementia with Lewy bodies and PD dementia on the Lewy Body Dementia Association site.)

Language abnormalities

- Issues with word-finding, known as "tip of the tongue" phenomenon.
- Difficulty with language when under pressure or stress.
- Difficulty comprehending complex sentences where the question or information is included with other details.
- Common to experience problems with production of language and dysarthria.
- Problems in naming or misnaming objects — more common in middle to late stages of PD.

Visuospatial difficulties

- During early PD stages: difficulty with measuring distance and depth perception, which may interfere with parking a car or remembering where the car is parked.
- During advanced PD: in combination with dementia, problems with processing information about their surroundings or environment.
- Subtle visual-perceptual problems may contribute to the visual misperceptions or illusions.
- Increased chances of visual misperceptions or illusions in low-light situations (like night time) and if experiencing other visual problems (like macular degeneration).
- In severe cases, problems telling apart non-familiar faces or recognizing emotional expressions.

How are cognitive deficits diagnosed?

Common ways to assess and diagnose cognitive disorders:

- Interview the person with PD.
- Ask family members or caregivers about their observations.
- Administer cognitive screening tests such as the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MOCA). The neurologist will ask questions that evaluate the person's understanding of where and who they are, the date and year, attention, memory, language and problem-solving skills.
- Neurologist may suggest seeing a clinical neuropsychologist for a more detailed assessment.
- Neuropsychological assessment can be an important diagnostic tool for differentiating PD from other illnesses such as Alzheimer's disease, stroke or dementia.

How are cognitive changes in PD different than Alzheimer's disease?

Overall, dementia produces a greater impact on social and occupational functioning in PD than with **Alzheimer's** due to the combination of motor and cognitive impairments.

- There is some overlap between symptoms and biological changes seen in Alzheimer's and PD. However, it is less likely for both disorders to occur at the same time.
- Development of dementia in people with PD represents progression of the disease, usually after several years of motor impairment.
- Dementia may or may not occur in people with PD. According to recent research, 30 percent of people with Parkinson's do not develop dementia as part of the disease progression
- See 10 Signs of Alzheimer's.

What co-existing conditions affect thinking and memory?

There are other factors that can have a negative impact on a person's cognitive skills, such as disorders of mood, anxiety and sleep. In some cases,

these factors can make memory and thinking deficits worse as well as directly affect a person's quality of life.

Depression

- Up to 50 percent of people with PD experience some form of depression during the disease.
- More likely to occur in people who experience severe cognitive impairment.
- Successful treatment of depression with medication and psychotherapy can improve cognitive symptoms.
- Can make it difficult to control motor symptoms (such as tremor and balance problems) in PD.
- Tends to be more severe in people with worse motor symptoms.

A combination of medications and behavioral strategies is usually the best treatment for cognitive problems in PD.

Anxiety

- May be as common as depression in Parkinson's.
- While less studied, up to 40 percent of people with PD experience some form of anxiety.
- Can interfere with memory storage, disrupt attention and complex task performance. For example, most people remember going blank on a school exam when feeling anxious.
- Negative impact on social life. People with poorly controlled anxiety often avoid social situations, which can impact family and work relationships.
- May experience anticipatory anxiety in situations where they have to use cognitive skills.
- Similar to depression, successful treatment can lead to improvement of cognitive problems related to anxiety.

Sleep disturbance

- The impact of poor sleep on attention, alertness and memory are well-known.

- Problems with falling and staying asleep are common in PD, especially as the disease progresses.
- Mild reductions in sleep can directly impair attention, judgment and the ability to multi-task because people with PD have a lower cognitive reserve or resistance of the brain to stressors.
- Undergoing a sleep study examines sleeping patterns and how often sleep is disrupted.
- Sleep problems are often addressed with medication and behavioral treatments. As sleep improves, its impact on thinking and memory is reduced.

Four types of sleep problems have been reported in PD:

1. Issues staying asleep and early morning awakening (insomnia).
2. Involuntary movements and pain that interrupt sleep.
3. Increased nighttime urination.
4. Nighttime agitation, vivid dreams and visual misperceptions or hallucinations.

Fatigue

- Just as fatigue can cause problems with movement and walking in PD, it can also impair thinking and memory. For example, a person with PD may have difficulty performing a complex cognitive task (like working on taxes over extended periods).
- Maximize attention and energy resources by diving tasks into more manageable 10 to 15-minute sections. This helps minimize fatigue and keep you on task.
- Be aware that as the day wears on, people with PD may begin to fatigue — physically and cognitively.
- Medications can help improve energy and alertness (methylphenidate (Ritalin®) and modafinil (Provigil®)), but many have yet to be studied extensively for PD and fatigue.

Some medications used to treat PD have also been shown to have stimulating effects on thinking and energy levels (like selegiline (Eldepryl®) and amantadine).

Seeking Help for Cognitive Changes

Cognitive change is a sensitive issue. In fact, the doctor is often as hesitant to address this subject as the person with PD is to ask about it. Sometimes, the doctor will delay discussing cognitive impairment out of concern for the person who is still coping with the shock of a new PD diagnosis or struggling with motor symptoms.

For this reason, the person with PD often needs to be the one to initiate the conversation. Tell your doctor if you or your loved one is experiencing problems that upset the family or cause interruptions at work.

Cognitive issues are never too mild to address with your care team. A doctor can provide ways to help, often, referring psychiatrist, neuropsychologist, speech or occupational therapist for further evaluation and assistance. The neuropsychological evaluation can be particularly useful, especially in the early stages of a cognitive problem. Having this baseline test can help the doctor determine whether future changes are related to medications, the progression of the PD itself or to other factors such as depression.

When reporting symptoms of mild cognitive impairment, the doctor will first want to rule out causes other than PD, such as Vitamin B-12 deficiency, depression, fatigue or sleep disturbances. It should be noted that PD does not cause sudden changes in mental functioning. If a sudden change occurs, the cause is likely to be something else, such as a medication side-effect.

If cognitive symptoms are traceable to PD, there are drug therapies available. Though developed for Alzheimer's, these medications have been found to have some effect in PD. These include rivastigmine (the only medication approved by the FDA for dementia in PD), donepezil and galantamine. In addition, a person with attention difficulties that are due to daytime sleepiness may benefit from stimulants.

How are cognitive problems treated?

Much remains to be learned about the basic biology that underlies cognitive changes in PD. Researchers work towards the development of diagnostic tests to identify people who seem to be at greatest risk for cognitive changes and to differentiate cognitive problems in people with PD from

those that occur in another disorder — related but different — known as dementia with Lewy bodies.

Cognitive Remediation Therapy

For those with milder cognitive deficits, c**ognitive remediation therapy** is a treatment that emphasizes teaching alternative ways to compensate for memory or thinking problems. In this treatment, the clinician uses information from neuropsychological testing to identify cognitive strengths that can be used to help overcome weaker areas of thinking.

- While widely used in the treatment of cognitive problems resulting from brain injury or stroke, there has been less use of this technique in people with PD.
- Does not reverse or cure cognitive disorders, but instead teaches strategies that can help with daily functioning and coping with cognitive problems.
- Depending on the severity of cognitive impairment, many can use these skills independently.
- In cases where the person is more impaired, caregivers or family members can help apply these strategies.
- Usually conducted by a neuropsychologist or speech-language pathologist, who is specially trained in these techniques and can provide a supportive environment for the person with PD to express concerns and frustrations over changes in mental functioning.
- Works best with milder forms of cognitive deficits, as it requires insight into the person's own memory and thinking problems.

Behavioral Management

In this type of treatment, changes in the environment can be made to help minimize memory, visual-perceptual or orientation difficulties.

- Strategies include simplifying the décor of the living area to reduce excessive stimuli may help with confusion and using a nightlight or low-level lighting to reduce visual misperceptions and confusion at nighttime.
- Behavioral strategies can help deal with other problems such as impulsivity, wandering, poor initiation and problems with

communication.
- Many benefit from a regular routine in their day-to-day activities and feel more comfortable with a clear, structured schedule.

Tips for Caregivers

- Offer help only when asked.
- Prompt the person — for example, instead of asking, "Did anyone call?" ask, "Did Linda call?"
- Say the name of the person and make eye contact when speaking to gain and hold attention.
- Put reminder notes and lists in a prominent place.
- Keep things in routine places.
- To ensure medications are taken on time, provide a dispenser, perhaps with a built-in alarm.
- Use photos on cell phone contact entries to prompt face-name association.
- If the person is searching for a word, provide a cue, such as, "the word you are looking for probably begins with 'd'."
- Do not finish the sentences of a person who needs more time to put them together.
- When presenting the person with a list of actions, first verbalize them, then write them down.
- Ask questions to moderate the conversation pace and allow catch up and reinforcement.

Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

What Is Parkinson's?

Causes

information

COMMUNICATION AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Communication involves both verbal (speech) and non-verbal skills (facial expression, body language and writing). Parkinson's has the potential to affect all aspects of communication and in turn impact on inter-personal relationships.

Verbal Communication

It is estimated that 50% of people with Parkinson's will develop speech changes due to changes in coordination and reduced activity of the muscles involved in speech mechanism. The most common changes experienced include:

- Microphonia (reduced volume)
- Monotone
- Huskiness of voice
- Festination (similar to stuttering)
- Dysarthria (slurred speech)
- Rapid speech pattern
- Slow speech pattern

All of the above changes in speech will be challenging for people with Parkinson's, family members and health professionals. Patience and understanding are essential.

Strategies and Treatment Options

- Give conscious attention to the volume and rate of speech
- Take a deep breath before starting to speak in order to maintain volume to finish the sentence
- Rehearse mentally what you wish to say
- Reduce background noise if possible

The input of a speech pathologist experienced in Parkinson's will be of benefit. Therapy options include the Lee Silverman Voice Treatment (LSVT) which primarily addresses microphonia and monotone. This is an intensive course of treatment and is available in most Parkinson's-specific treatment facilities.

Voice quality may become husky, breathy or strained. This is often due to "bowed vocal folds". Speech therapy may assist.

In cases of festination a simple strategy is to remind the person with Parkinson's to concentrate on the key word. In some cases a pacing board may be useful.

Dysarthria may respond to speech therapy.

If increased rate of speech is a problem conscious attention on slowing the speech pattern in addition to the use of a pacing board can be helpful.

Slow speech pattern is not simply a speech problem but in fact originates from a slowing of thought process (bradyphrenia). This is out of the control of the person with Parkinson's and may be misinterpreted as confusion or dementia. An attempt to hurry their thinking, or interrupting them, may result in "blocking" or "freezing" thoughts.

Telephone use may be challenging due to the above verbal changes in addition to the impact of tremor or dyskinesia (involuntary movement). It may be helpful to sit while using the phone and consider the use of a hands-free receiver.

COMMUNICATION AND PARKINSON'S

Non-verbal Communication

Muscle rigidity, slowness of movement and the effect of Parkinson's on automatic gestures and skills result in the more visible manifestations of the condition. These include:

- Masked expression
- Reduced blink rate
- Reduction in body language
- Micrographia (reduced handwriting size) and tremor related changes

Strategies and Treatment Options

Facial exercises will help maintain flexibility of facial muscles. A conscious effort to smile and express emotions is essential to avoid misunderstanding of cognition or intellect.

Similarly, conscious attention to blinking will address the stare-like expression and maintain adequate eye lubrication.

Parkinson's affects all automatic repetitive skills and gestures leading to a gradual reduction in body language, and subsequent immobility. This may be misinterpreted as intentional. Prolonged periods of immobility (of lower limbs) may result in postural oedema (swelling).

Micrographia occurs in most cases and may be an early indicator of Parkinson's. Cursive writing is a learned and automatic skill. With the development of Parkinson's the handwriting becomes smaller, cramped and less legible as the person writes. The use of lined paper may address this problem.

Tremor may impact on handwriting, the use of a keyboard and mouse, resulting in information technology challenges. Software is available to minimise these problems, and input from an occupational therapist experienced in Parkinson's may be of benefit in all aspects of written communication.

It is important to remember that each case of Parkinson's is unique to the individual; therefore there will be variations in communication changes. It is vital to allow the person with Parkinson's adequate time to respond when engaged in conversation. There may be a tendency for partners, family members or carers to respond on behalf of the person with Parkinson's which may add to the frustration already experienced. However, there may be times when this is appropriate, with consent.

Open and honest communication regarding all areas of Parkinson's will assist in coping with the impact of living with Parkinson's.

For further information contact
your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

IN THIS TOGETHER
parkinson's
AUSTRALIA

information

CONSTIPATION AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Constipation is a common problem for many people with Parkinson's. At first glance, constipation may seem more of a nuisance than a real concern. Constipation adds to the challenge of having Parkinson's and has a negative effect on the person's quality of life.

It is important that you seek help in managing your constipation because the good news is that it can be managed and it should not be allowed to interfere with your enjoyment of life. Discuss it with your GP or phone the National Continence Helpline for advice 1800 33 00 66.

What is Constipation?

Constipation is the infrequent passage of hard, dry bowel motions that are difficult to pass. The myth that you must use your bowels every day is simply not true. There is a wide variation in frequency from three times per day to three times per week.

The normal bowel motion is soft formed and easy to pass and you should feel like you have completely emptied your bowel. If you are straining to empty your bowels or your bowel motion is hard and dry, you may be constipated and you need to take action.

Why is Constipation a Problem for People With Parkinson's?

There are four main ways Parkinson's may cause constipation:

- The muscles of the bowel can be affected, altering how food moves through the bowel
- Medication used to treat Parkinson's can slow down the bowel
- Chewing and swallowing difficulties may affect the ability to eat an adequate diet and drink an adequate amount of fluid
- The muscles used for walking and exercise programs can be affected and decreased levels of adequate exercise can affect bowel activity

Parkinson's can affect the muscles of the bowel, causing slowness and rigidity. The bowel is further robbed of stimulation if your mobility is reduced. This results in the bowel motion (faeces) not being propelled quickly enough through the bowel, which can cause constipation.

Emptying the bowel can be more difficult because of poor coordination of the back passage (anal) muscles. These muscles may contract instead of relaxing, making it difficult to pass the bowel motion completely.

Medicines used to treat Parkinson's may be a factor in constipation – either by directly affecting the bowel by slowing it down, or by affecting appetite.

Chewing and swallowing difficulties can affect you eating sufficient fibre on a daily basis. Fibre is found in fruit, vegetables and grains and is important in keeping the bowel action formed and soft. Drinking sufficient fluid is essential in preventing constipation. You may find this difficult if your swallowing is affected. Talk to your treating doctor if you are experiencing chewing and swallowing difficulties. You may benefit from a referral to a dietician.

CONSTIPATION AND PARKINSON'S

Constipation Needs to be Treated

Constipation, if left untreated, can lead to several problems. You may feel unwell, lethargic and nauseated, worsening the constipation as you do not feel like eating and drinking adequately. Severe constipation can mimic diarrhoea with loose bowel motions, which is caused by the hard motion irritating the bowel wall. The loose bowel motion can result in bowel incontinence (involuntary leakage from the bowel).

Constipation can also disturb your bladder causing you to pass urine more frequently and more urgently, and may even result in you being incontinent (involuntary leakage of urine). Constipation may make it more difficult for you to empty your bladder and this may result in urinary tract infections.

What You Can do to Prevent and Manage Constipation

There are four simple steps that prevent constipation and the same four steps are key to the management of constipation.

Eat well

Eat a healthy diet rich in dietary fibre. We need at least 30gms of fibre each day. The following is a daily guide to getting enough fibre:

- 2 serves of fruit
- 5-6 serves of vegetables
- 3-6 serves of grain (cereal) foods – use wholemeal or wholegrain breads, high fibre breakfast cereals, brown rice and wholemeal pasta more often than white or refined choices
- Legumes, nuts and seeds are also excellent

It is important to get the right balance between adequate fibre in your diet and drinking sufficient fluid to avoid further problems with constipation.

Drink well

Drink 1.5 – 2 litres (6-8 glasses) of fluid daily unless advised otherwise by your doctor. Limit caffeine, alcohol and sugary drinks as they can cause bladder irritation. Remember that cola, chocolate and some energy drinks are high in caffeine. The best drink is water.

Exercise regularly

Keep moving. Aim to exercise for 30 minutes most days. Walking is a great exercise.

Practice good toilet habits

Go to the toilet when you get the urge to use your bowels, as this is the most effective time to completely empty your bowels. Most people get the urge first thing in the morning or following a meal when eating food has stimulated the bowel

Get into the correct sitting position on the toilet – sit on the toilet, elbows on knees, lean forward and support your feet with a footstool. Relax and bulge out your tummy, relax your back passage and let go – don't hold your breath. When you have finished, firmly draw up your back passage.

If you have tried these four steps for about three weeks and your constipation has not improved, seek help. The following health professionals will be able to offer you advice regarding your next steps:

- Treating Doctor or GP
- Practice Nurse or Community Health Nurse
- The National Continence Helpline 1800 33 00 66

CONSTIPATION AND PARKINSON'S

A Word About Laxatives

Laxatives are medicines that help you pass a bowel motion. Laxatives will make the motion softer and easier to expel, or will increase the motility of the bowel. Laxatives are not the first step in the treatment of constipation but may be necessary if the four steps above do not work. The laxative that best suits you will vary depending upon your degree of mobility, your fluid and fibre intake and your bowel function. Talk to your treating doctor or neurologist before starting any of these medicines.

Seek Help

Constipation is a common problem for people with Parkinson's. It impacts negatively on your quality of life. It should not be dismissed as a trivial problem. Seek help if constipation is an issue for you. It can be cured or better managed. Don't let constipation interfere with your enjoyment of life.

For more information

Speak to your doctor or contact the National Continence Helpline 1800 33 00 66. The Helpline provides free information about bladder and bowel control problems as well as advice about continence products and clinics, and has a wide range of free information and resources available.

The National Continence Helpline is an Australian Government initiative managed by the Continence Foundation of Australia. For further information visit continence.org.au

Where to Get Help and Further Advice

National Continence Helpline: 1800 33 00 66

Continence Foundation of Australia: continence.org.au

Parkinson's Australia: parkinsons.org.au

Bladder and Bowel website: bladderbowel.gov.au

Public Toilet Map: toiletmap.gov.au

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The Continence Foundation is the Australian peak body for awareness, education and advocacy for those with incontinence and their carers.

Continence Foundation of Australia

For further information contact your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

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Delaying Mobility Disability in People With Parkinson Disease Using a Sensorimotor Agility Exercise Program

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This article introduces a new framework for therapists to develop an exercise program to delay mobility disability in people with Parkinson disease (PD). Mobility, or the ability to efficiently navigate and function in a variety of environments, requires balance, agility, and flexibility, all of which are affected by PD. This article summarizes recent research identifying how constraints on mobility specific to PD, such as rigidity, bradykinesia, freezing, poor sensory integration, inflexible program selection, and impaired cognitive processing, limit mobility in people with PD. Based on these constraints, a conceptual framework for exercises to maintain and improve mobility is presented. An example of a constraint-focused agility exercise program, incorporating movement principles from tai chi, kayaking, boxing, lunges, agility training, and Pilates exercises, is presented. This new constraint-focused agility exercise program is based on a strong scientific framework and includes progressive levels of sensorimotor, resistance, and coordination challenges that can be customized for each patient while maintaining fidelity. Principles for improving mobility presented here can be incorporated into an ongoing or long-term exercise program for people with PD.

Most people who are diagnosed with Parkinson disease (PD) do not consult with a physical therapist until they already have obvious mobility problems. However, it is possible that a rigorous exercise program that focuses on anticipated problems, which are inevitable with progression of the disease, may help patients who do not yet exhibit mobility problems. Although there are excellent guidelines for physical therapists to treat patients with PD who exhibit mobility problems in order to improve or maintain their mobility,[1,2] there is little research on whether exercise may delay or reduce the eventual mobility disability in patients diagnosed with PD.

The major cause of disability in people with PD is impaired mobility.[3] Mobility, the ability of a person to move safely in a variety of environments in order to accomplish functional tasks,[4] requires dynamic neural control to quickly and effectively adapt locomotion, balance, and postural transitions to changing environmental and task conditions. Such dynamic control requires sensorimotor agility, which involves coordination of complex sequences of movements, ongoing evaluation of environmental cues and contexts, the ability to quickly switch motor programs when environmental conditions change, and the ability to maintain safe mobility during multiple motor and cognitive tasks.[5,6] The types of mobility deficits inevitable with the progression of PD suggest that the basal ganglia are critical for sensorimotor agility.[2] Critical aspects of mobility disability in people with PD, such as postural instability, are unresponsive to pharmacological and surgical therapies,[7] making preventative exercise an attractive option. As yet, there is no known ongoing exercise program for people diagnosed with PD that focuses on maintaining or improving their agility to slow or reduce their decline in mobility.

This article uses the known sensorimotor impairments of PD that affect balance, gait, and postural transitions to develop a conceptual framework to design exercises that aim to delay disability and maintain or improve mobility in people with PD. This framework is based on the current knowledge of the neurophysiology of PD and the inevitable constraints on mobility resulting from basal ganglia degeneration. The scientifically based principles presented here, which are focused on mobility disorders in people with PD, can be incorporated into an existing therapy program for people with PD.

Based on this framework, this article also presents an example of a novel sensorimotor agility program that we are currently testing in a clinical trial. This program is unique in that it encourages a partnership among physical therapists, exercise trainers, and patients to set up, progress, and reevaluate an exercise program that ultimately can be carried out independently in the community. It is likely that a mobility program, such as the one presented here, would need to be sustained and modified throughout the course of the disease to maintain maximal benefit.

Why Exercise May Prevent or Delay Mobility Disability in People With PD

Exciting new findings in neuroscience regarding the effects of exercise on neural plasticity and neuroprotection of the brain against neural degeneration suggest that an intense exercise program can improve brain function in patients with neurological disorders. Specifically, animal studies have demonstrated neurogenesis,[8] an increase in dopamine synthesis and release,[9] and increased dopamine in the striatum following acute bouts of exercise.[10] Such changes in the brain may affect behavioral recovery as a result of neuroplasticity (the ability of the brain to make new synaptic connections), neuroprotection, and slowing of neural degeneration.[11,12] Studies with parkinsonian rats have suggested that chronic exercise may help reverse motor deficits in animals by changing brain function. Specifically, rats that ran on a treadmill showed preservation of dopaminergic cell bodies and terminals[11,13] associated with improved running distance and speed,[12] indicating a neuroprotective effect of exercise. Conversely, nonuse of a limb induced by casting in parkinsonian rats increased motor deficits as well as loss of dopaminergic terminals.[11] Aerobic exercise, such as treadmill training and walking programs, has been tested in individuals with PD and has been shown to improve gait parameters, quality of life, and levadopa efficacy.[14–16] However, it is not clear whether aerobic training, by itself, is the best approach to improving *mobility*, which depends upon dynamic balance, dual tasking, negotiating complex environments, quick changes in movement direction, and other sensorimotor skills affected by PD. It is possible that treadmill training, for example, could be even more effective for addressing complex mobility issues for people with

PD if the therapist could incorporate tasks such as dual tasking, balance training, and set-switching into a treadmill program.

There currently are many untested exercise programs available for people with PD[17–19] as well as several randomized controlled studies that test specific exercises, such as strength (force-generating capacity) training or gait training.[20–29] The approach presented in this article is focused on exercises that challenge sensorimotor control of dynamic balance and gait to improve mobility in people with PD. There are many other aspects of PD that also must be addressed in rehabilitation.

Drive Neuroplasticity With Task-Specific Agility Exercise

Studies in rats have demonstrated that task-specific agility training (eg, acrobatic, environmental enrichment-type, high-beam balance course) results in larger improvements in motor skills as well as larger changes in synaptic plasticity than simple, repetitive aerobic training such as running on treadmills.[30–35] Task-specific exercise also has been shown to be more effective than aerobic or general exercise to improve task performance in patients with stroke.[36,37] Task-specific exercises targeted at a single, specific balance or gait impairment in patients with PD have been shown to be effective. For example, exercises targeted at improving small step size, poor axial mobility, difficulty with postural transitions, small movement amplitude, or slow speed of compensatory stepping have individually been shown to be effective in improving each particular aspect of mobility.[18,22,38–42] We have borrowed singular techniques from several successful programs and combined them with task-specific components of mobility and systematic sensorimotor challenges into a comprehensive exercise program directed at delaying and reducing mobility problems in individuals with PD.

Reduce Mobility Constraints With Exercise

People with mild or newly diagnosed PD often do not have obvious muscle weakness or poor balance.[43] Nevertheless, the literature suggests that muscle weakness, secondary to abnormal muscle activation associated with bradykinesia and rigidity, can be present at all stages of PD.[44–47] Similarly, balance and mobility problems may be present in people with mild PD but only become apparent when more-complex coordination is required under challenging conditions.[48,49] For example, mobility problems may only be apparent when an individual with PD is attempting to walk quickly in a cluttered environment while talking on a cell phone. As the disease progresses, balance problems become more apparent, just as patients begin to show impaired kinesthesia and inability to quickly change postural strategies.[50,51] The basal ganglia affect balance and gait by contributing to automaticity, self-initiated gait and postural transitions, changing motor programs quickly, sequencing actions, and using proprioceptive information for kinesthesia and multisegmental coordination.[52–54] During the progression of PD, mobility is progressively constrained by rigidity, bradykinesia, freezing, sensory integration, inflexible motor program selection, and attention and cognition.[2] Table 1 summarizes constraints on mobility due to PD, the impact of these constraints on mobility, and the goals of exercises that could potentially reduce the impact of each constraint.

Constraints Affecting Mobility in People With PD, With Implications for the Sensorimotor Agility Program

Rigidity

Parkinsonian rigidity is characterized by an increased resistance to passive movement throughout the entire range of motion, in both agonist and antagonist muscle groups.[55–57] The functional outcomes of rigidity, in general, include a flexed posture,[58] lack of trunk rotation,[59,60] and reduced joint range of movement during postural transitions and gait.[56,61] Electromyography studies have shown that people with PD have high tonic background activity, especially in the flexors, and co-contraction of muscles during movement, especially in the axial muscles.[56,57] In addition, antagonist muscle activation is larger and earlier, resulting in coactivation of muscle groups during automatic postural responses.[61]

Another characteristic of parkinsonian rigidity is axial rigidity, which results in a loss of natural vertebral, pelvis/shoulder girdle, and femur/pelvis flexibility and range of motion that accompanies efficient postural and locomotor activities.[60,62] Wright et al[55] found that rigidity in the neck, torso, and hips of standing subjects was 3 to 5 times greater in subjects with PD than in age-matched control subjects when measuring the torsional resistance to passive movement along the longitudinal axis during twisting movements. Levodopa medication did not improve their axial rigidity.[55] The high axial tone (velocity-dependent resistance to stretch) in patients with PD contributes to their characteristic "en bloc" trunk motions, which make it difficult for them to perform activities such as rolling over in bed or turning while walking.[62]

Table 1.
Parkinsonian Constraints Affecting Mobility and Exercise Principles Designed to Reduce These Constraints[a]

Constraints	Impact on Mobility	Exercise Principles
I. Rigidity	Agonist/antagonist co-contraction Flexed alignment of trunk Reduced trunk rotation Reduced joint range of movement High axial tone (stiffness)	Trunk rotation Reciprocal movements Rhythmic movements Erect alignment Large CoM movements Increase limits of stability
II. Bradykinesia	Slow, small movements Narrow base of support Lack of arm swing	Fast, large steps CoM control Large arm swings
III. Freezing	Poor anticipatory postural adjustments Abnormal mapping of body and movement Abnormal visual-spatial maps Divided attention affects mobility	Improve weight shifting Understand role of external cues Exercise in small spaces Practice dual tasks
IV. Inflexible program selection (sequential coordination)	Poor rolling, sit-to-stand maneuvers, turns Difficult floor transfers Inability to change strategy quickly	Plan task in advance Quick change strategies Sequencing components of task
V. Impaired sensory integration	Inaccurate without vision Imbalance on unstable surface Poor alignment with environment	Kinesthetic awareness Decrease surface dependence Flexible orientation
VI. Reduced executive function and attention	Difficulty with dual tasks and sequences of actions	Practice gait and balance with secondary task and sequences of actions (ie; boxing, agility course)

[a] CoM=center of mass.

Schenkman et al[63] showed that exercise can increase trunk flexibility in people with PD. We propose an agility program that includes movements that minimize agonist-antagonist muscle co-contraction (ie, reciprocal movements), promote axial rotation, lengthen the flexor muscles, and strengthen the extensor muscles to promote an erect posture. Rigidity can potentially be addressed with kayaking, an exercise in which the person counter-rotates the shoulder and pelvic girdle; tai chi, a set of exercises that focuses on the individual's awareness of postural alignment during postural transitions; and pre-Pilates, a series of exercises aimed at increasing spinal mobility and lengthening flexor muscles groups. In addition, the program should include strategies for turning and transitioning from a standing position to sitting on the floor and back again that emphasize trunk and head rotation (Tabs. 2 and 3).[18]

Bradykinesia

Bradykinesia is most commonly defined as slowness of voluntary movement,[43] but it also is associated with slow and weak postural responses to perturbations and anticipatory postural adjustments. Reactive postural responses to surface translations[61,64] and anticipatory postural movements prior to rising onto toes[65] and prior to step initiation[66] are bradykinetic in patients with PD. Bradykinetic voluntary stepping and postural compensatory stepping are characterized by a delayed time to lift the swing limb, a weak push-off, reduced leg lift, a small stride length, and lack of arm swing.[61,64,66,67] Bradykinesia also is apparent in reduced voluntary and reactive limits of stability, especially in the backward direction.[64,68] The characteristic narrow stance of patients with PD may be compensatory for bradykinetic anticipatory postural adjustments prior to a step, at the expense of reduced lateral postural stability.[67,69] Bradykinetic postural responses in people with PD generally are not improved by antiparkinsonian medications, highlighting the need for an exercise approach to this constraint on mobility.[6] Bradykinesia also is seen in postural transitions such as turning[70] and the supine-to-stand manuever,[59] as well as in single-joint movements[71] and multi-joint reaching movements[72] in people with PD.

Bradykinesia is evident in slowed rate of increase and decrease of muscle activation patterns.[73] Reduction in muscle strength in people with PD has been attributed primarily to reduced cortical drive to muscles because voluntary contraction, but not muscle response to nerve stimulation, is weak in these individuals.[74,75] Electromyographic activity in bradykinetic muscles often is fractionated into multiple bursts and is not well scaled for changes in movement distance or velocity.[71] Years of bradykinesia from abnormal, centrally driven muscle control and abnormal, inefficient pat-

Table 2.
Representative Agility Exercise Program, With Progressions

Exercise	Actions	Progressions
I. Tai chi: Increase limits of stability, improve perception of posture and coordination of arms and legs and backward and lateral large steps	Prayer wheel: anterior-posterior slow, rhythmical weight shifts coordinated with large arm circles Cat walk: slow and purposeful steps, with diagonal weight shifts Cloud hands: slow lateral steps, with trunk vertical Part the wild horse's mane: coordination of arms and legs while walking forward Repulsing the monkey: deliberate slow, backward walking, with diagonal weight shifts	Learn one action per week, starting with weight shifting and leg placement and progressing to coordinated arm, neck, and torso motion
II. Kayaking: Trunk rotation, segmental coordination, speed	Kayaking stroke: diagonal trunk rotation, with reciprocal forward arm extension and backward arm retraction	Speed, surface, resistance, vision, dual task
III. Agility course: Agility, multisegmental coordination, quick changes in direction, and mobility in tight spaces	High knees: high-amplitude stepping, with hand slapping knees Lateral shuffle: quick, lateral steps Tire course: wide-based, quick and high steps, with turns Grapevine cross: over coordinated steps	Speed, dual task, quick change in directions, tight and cluttered spaces, vision
IV. Boxing: Anticipatory postural adjustments, postural corrections, fast arm and foot motions, backward walking, timing, sequencing actions	Jab: short, straight punch from shoulder Cross: power punch, with trunk rotation, leading arm crosses midline Hook: short, lateral punch, with elbow bent and wrist twisted inward, trunk rotation Combinations: 2 or more punches delivered quickly after one another	Speed, dual task, walking forward, walking backward, turns, remembered sequences of action
V. Lunges: Big steps, stepping for postural correction, limits of stability, quick changes in direction, internal representation of body	Postural correction: lean until center of mass is outside base of support, requiring a step; all directions Single multidirectional steps (clock stepping) Dynamic multidirectional lunge walking	Surface (up and down stool), external cues, vision, resistance, dual task (add arm movements or cognitive task)
VI. Pre-Pilates: Improve trunk control, axial rotation and extension, functional transitions, sequencing actions	Cervical range of motion, sit-to-stand maneuver Floor transfer, supine (bridging) Rolling (prone lying, progress to spinal extension exercises) Quadruped (bird-dog, cat-camel, thread the needle) Half-kneeling to stand	Improve form and speed

terns of muscle recruitment limit functional mobility and eventually may result in focal muscle weakness.

Because bradykinesia is due to impaired central neural drive, rehabilitation to reduce bradykinesia should focus on teaching patients to increase the speed, amplitude, and temporal pacing of their self-initiated and reactive limb and body center-of-mass (CoM) movements. Table 2 presents representative exercises aimed at reducing bradykinesia for mobility. These exercises may promote weight-shift control and postural adjustments in anticipation of voluntary movements such as lunges, kicks, and quick boxing movements. Patients also practice taking large, protective steps while tilting past their limits of stability and in response to external displacements associated with hitting or punching a boxing bag. To reduce bradykinesia, patients should be encouraged to "think big"[42] while increasing the speed and amplitude of large arm and leg movements throughout agility courses and during multidirectional lunges and boxing (Tabs. 2 and 3). Walking sticks may help patients attend to the large, symmetrical arm swing that is coordinated with strides during gait.

Freezing

Freezing of gait manifests as a movement hesitation in which a delay or complete inability to initiate a step occurs.[76] Freezing not only slows walking, but it also is a major contributor to falls in people with PD.[77] It is a poorly understood phenomenon that is associated with executive disorders in people with PD.[76,78] Freezing during gait occurs more often when a person is negotiating a crowded environment or narrow doorway, when making a turn, or when attention is diverted by a secondary task.[77,79] Jacobs and Horak[80] recently found that freezing or "start hesitation" in step initiation is asso-

Table 3.
Progressions for Each Activity

A. Kayaking: Kayaking focuses on counter-rotation of shoulder and pelvic girdle and axial trunk rotation.				
Level	**Surface**	**Vision**	**Resistance**	**Dual Task**
1	Sit on a chair	Normal, well-lit room	Holding pole	Counting
2	Sit on DynaDisc[a]	Sunglasses	3-lb pole	Verbal: make a list
3	Stand on firm surface	No-body glasses	6-lb pole	Verbal/cognitive: math

B. Agility course: The agility course includes turns, doorways, hallways, and small areas. The tasks include high knees walking with hands touching knees, skipping, lateral shuffles, grapevine, and tire course. Advanced individuals may add agility on an inclined surface and bouncing or tossing a ball.			
Level	**Speed/Agility**	**Dual Task**	**Arms and Trunk (High Knees and Tire Course Only)**
1	Self-paced	Count steps out loud	Self-selected
2	Increase speed	Motor task: toss ball between hands	Reciprocal arms
3	Quick changes in direction, pace, stop and go	Cognitive task: math	Add head and trunk rotation

C. Boxing: The boxing task includes simple to complex combinations involving jabs, hooks, and crosses.			
Level	**Plane of Movement**	**Speed**	**Dual Task**
1	Lateral stance to the bag	Self-paced	Count punches
2	Pivot with back foot	Bursts of speed: combo punches for 15 s	Name punches (hook, jab, cross)
3	Walk backward around bag	Bursts of speed: combo punches for 30 s	Cognitive task while maintaining pattern

D. Lunges: Three types of lunges use these progressions: (1) lunges for postural correction, (2) clock stepping (multidirectional, in-place) lunges, and (3) dynamic lunges during locomotion.						
Level	**Surface**	**External Cue**	**Vision**	**Resistance**	**Dual Task**	**Arms and Trunk (Dynamic Lunges Only)**
1	Firm surface	Rubber discs designate foot placement	Well-lit room	None	None	None
2	One foot on compliant surface (DynaDisc/ foam mat)	Decrease disc size or number	Sunglasses	Weight vest (start with 10% of body weight)	Motor task: trunk	Use arms reciprocally
3	Foam mat (both feet)	No discs	No-body glasses	Increase vest weight, 5% of body weight increments	Verbal or cognitive	Lift arms over head while holding ball

[a] DynaDisk manufactured by Exertools Inc, 320 Professional Center Dr, #100, Rohnert Park, CA 94928.

ciated with repetitive, anticipatory, lateral weight shifts and that people who are healthy can be made to "freeze" when they do not have time to preplan which foot to use when initiating a compensatory or voluntary step. Therefore, freezing may be related to difficulties in shifts of attention, preplanning movement strategies, or quickly selecting a correct central motor program.

To help people in the early stages of PD reduce their chances of being affected by freezing, agility exercises should be performed in environments in which freezing typically occurs. As shown in Tables 2 and 3, exercises that involve high stepping, skipping, or taking large steps in different directions through doorways and over and around obstacles, such as between chairs placed shoulder-width apart, could potentially reduce freezing episodes. Quick turns should be practiced in corners and near walls. Individuals with PD could perform these exercises in the home or gym, where obstacle courses have been set up that require turning quickly, negotiating narrow and tight spaces such as corners, ducking under and stepping over obstacles, picking up objects while walking, and quickly changing directions and foot placement. Once a person successfully performs the agility exercises on an obstacle course, more-advanced progressions could be introduced, such as performing dual cognitive tasks while maintaining form and speed on agility tasks.

Inflexible Program Selection and Poor Sequential Coordination

Research suggests that the basal ganglia play an important role in task switching, motor program selection, and suppression of irrelevant information before executing an action.[52] The inability to quickly switch motor programs has been demonstrated in individuals with PD by an inability to change postural response synergies in the first perturbation trial after a change in support, change in instructions, or change in perturbation direction.[51,81] Dopamine replacement does not improve inflexible program selection.[82,83] The difficulty with switching motor programs manifests in difficulty maneuvering in new and challenging environments and in changes in postural transitions, such as turning, standing from a sitting position, and rolling over.[84] In addition to difficulty switching motor programs, people with PD have difficulty sequencing motor actions.[65,85,86] Patients with PD show a delay between their anticipatory postural adjustments and voluntary movements, such as rising onto toes[65] or a voluntary step.[66] These findings suggest that mobility in people with PD is constrained by poor coordination among body parts and between voluntary movements and their associated postural adjustments, as well as by difficulty in switching motor programs appropriate for changes in task constraints.

Consequently, an exercise program should include complex, multisegmental, whole-body movements and should include tasks requiring quick selection and sequencing of motor programs such as practicing postural transitions (eg, moving from stance to the floor, rolling, and arising from the floor to stance). As shown in Table 2, one such exercise approach is tai chi, which helps patients to learn increasingly complex sequences of movement and to focus on smooth timing and synchronization of whole-body movements. Incorporating boxing actions into a remembered sequence is another way to practice the quick selection and sequencing of complex motor programs for mobility. To address problems of quick program selection, lunges and agility exercises also provide practice changing motor strategies during stopping, starting, changing direction, changing stepping limb, and changing the size and placement of steps.

Sensory Integration

There is strong evidence that the basal ganglia are critical for high-level integration of somatosensory and visual information necessary to form an internal representation of the body and the environment.[87,88] Despite clinical examinations of patients with PD revealing only inconsistent, subtle signs of abnormal sensory perception,[89,90] an increasing number of studies are showing abnormal kinesthesia and use of proprioception in people with PD. For example, Wright et al[55] and Horak et al[64] found that individuals with PD have an impaired ability to detect the rotation of a surface or the passive rotation of the torso and that this poor kinesthesia is worsened by levodopa medication. Individuals with PD also show impaired perception of arm position and movement and decreased response to muscle vibration.[91–93] The poor use of proprioceptive information and decreased perception of movement are associated with over-estimation of body motion (bradykinesia) and over-dependence on vision.[50,94]

To facilitate use of proprioceptive information and reduce over-reliance on vision, an agility program should progress balancing and walking tasks by: (1) wearing dark sunglasses to reduce visual contrast sensitivity and (2) use of "no body" glasses to obscure the bottom half of the visual field so the body cannot be seen. In addition, many of the exercises can be performed on a variety of surfaces to require adaptation to altered somatosensory information from the surface. External feedback and sensory cues from the therapist regarding quality and size of the movements should be used initially and progressively decreased as patients develop a more accurate internal sense of body position. As shown in Table 3, the sensorimotor agility program used as an example in this article progresses with traditional progressive challenges[95] (increasing resistance, speed of gait, endurance, and so on) and with sensorimotor challenges (dual tasking and changes in base of support, visual input, and surface conditions).

Cognitive Constraints

The inability to simultaneously carry out a cognitive task and a balance or walking task has been found to be a predictor of falls in elderly people.[96] It is even more difficult for a person with PD than age-matched elderly people to perform multiple tasks,[86] possibly because the basal ganglia are responsible for allowing automatic control of balance and gait and for switching attention between tasks.[52,86] Postural sway increases most in individuals with PD who have a history of falls when a cognitive task is added to the task of quiet stance.[97] These findings suggest that the ability to carry out a secondary cognitive or motor tasks while walking or balancing is a critical element of mobility that is a particular challenge in people with PD.

An agility program could progress task difficulty by adding cognitive or motor tasks that teach patients with PD to maintain postural stability during performance of secondary tasks. Table 3 presents exercises in which it is safe and appropriate to add a dual cognitive or motor task. The exercises at level 1 have no dual tasks, level 2 has a motor task (eg,

bouncing a ball) added to the basic exercise such as an agility course, and level 3 has a cognitive task (eg, performing math or memory problems) added to the same basic exercise. The progression of adding secondary tasks to gait and balance tasks serves as a training device as well as a tool to help patients understand the relationship between safe mobility and secondary tasks in everyday life.

A Sensorimotor Agility Program for People With PD

In this article, we propose a novel sensorimotor agility program targeted at constraints on mobility in people with PD. The expertise that contributed to the program includes an internationally recognized neurologist specializing in movement disorders for more 35 years and 5 physical therapists experienced in treating people with PD, including 3 with PhDs with a focus on PD. Six certified athletic trainers who regularly work with people with PD also were helpful in designing the program. We propose that the exercise program outlined in Table 2 could last 60 minutes, with about 10 minutes for each category of exercise. The exercises in the 6 categories were selected to target one or more of the constraints on mobility (Tab. 1).

Although not all people with PD have all of the constraints addressed in this article, it may be that exercise should target all of these constraints, as each constraint generally is associated with the progression of PD and eventually has a marked effect on mobility. Addressing constraints early may delay the onset of related mobility deficits. Category I, "tai chi," is a whole-body exercise that focuses on developing a sense of body kinesthesia, improving postural alignment, and sequencing of whole-body movements that move the CoM. Category II, "kayaking," focuses on trunk and cervical rotation and speed, with large, coordinated arm movements. Category III, "agility course," focuses on quickly changing motor programs such as quick turns, sequencing actions, and overcoming freezing. Category IV, "boxing," focuses on building the patient's agility and speed, backward walking, and components of anticipatory and reactive postural adjustments in response to a moving bag. Category V, "lunges," helps patients with PD practice large CoM movements, multidirectional limits of stability, and steps for postural correction. Category VI, "pre-Pilates," is a set of exercises that help patients with PD extend and strengthen the spine, as well as practice postural transitions such as sit-to-stand maneuvers, floor transfers, and rolling.[18]

The sensorimotor progressions of exercises II through V follow 3 levels of difficulty (Tab. 3). Progressions include: (1) reducing the base of support, (2) increasing surface compliance to reduce surface somatosensory information for postural orientation, (3) increasing speed or resistance with weights, (4) adding secondary cognitive tasks to automate posture and gait, and (5) limiting visual input of the body with "no body" glasses or of the environment with dark sunglasses to increase use of kinesthetic information. Category I (tai chi) and category VI (pre-Pilates) exercises progress by increasing the length of remembered sequences and improving the form of each subcomponent of the movements. All of these sensorimotor progressions were chosen specifically to target the predictable constraints on mobility due to PD, and testing of the program is currently under way.

Summary

We present a progressive sensorimotor agility exercise program for prevention of mobility disability in people with PD. The program is based on the role of the basal ganglia in posture and gait, the principles of neural plasticity, and the inevitable constraints of PD that ultimately affect dynamic balance and mobility. These principles of the program include a focus on self-initiated movements, big and quick movements, large and flexible CoM control, reciprocal and coordinated movements of arms and legs, and rotational movements of torso over pelvis and pelvis over legs. Flexible, rotational axial motion of trunk and neck are stressed to achieve erect postural alignment, strengthening of extensors, and lengthening of flexors. Our program is designed to facilitate sensory integration for balance, emphasizing the use of somatosensory information to move the body's CoM quickly and effectively for balance and mobility. Secondary cognitive tasks are added to mobility tasks to automatize control of balance and gait. This sensorimotor agility approach to mobility training is intended for prevention of mobility disability but may be modified for patients at later stages of PD progression to improve their mobility.

Both authors provided concept/idea/project design, writing, and project management. Dr Horak provided fund procurement, facilities/equipment, institutional liaisons, and consultation (including review of manuscript before submission).

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information

DEMENTIA AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Common cognitive changes which occur with Parkinson's and are often mistaken for dementia are:

- Anxiety
- Apathy
- Bradyphrenia (slowness of thinking)
- Concrete thinking
- Masked expression
- Obsessive compulsive disorder

If sudden onset confusion with or without hallucinations occurs it is essential that reversible causes such as infection are addressed.

Dementia is a term used to describe the symptoms of a large group of neurological illnesses which cause a progressive decline in a person's functioning. It is a broad term used to describe a loss of memory, intellect, rationality, social skills and what would be considered normal emotional reactions. Not all people with Parkinson's will develop dementia.

It is estimated that dementia occurs in 30-60% of people affected by Parkinson's. Two types of dementia commonly associated with Parkinson's are Parkinson 's disease dementia (PD-D) and Lewy Body Dementia (LBD). Risk factors for the development of PD-D are:

- Increased age
- Diagnosis of Parkinson's at an older age
- Longer duration of condition
- Non-tremor predominant Parkinson's

Problems with planning, sequencing, decision making and visuospatial awareness are frequently seen in PD-D and suggest a subcortical dementia. In addition visual hallucinations may occur. These changes may be seen several years after the initial motor symptoms and diagnosis of Parkinson's.

Long-term use of Parkinson's medications may result in confusion and hallucinations. Frequent monitoring by the treating specialist is essential. The decision to introduce treatment for dementia must be made on an individual basis.

LBD commonly presents earlier in the progress of the condition. Symptoms suggestive of LBD are:

- Shorter duration of condition
- Early onset hallucinations
- Fluctuating cognitive changes

Often a diagnosis of Parkinson's may be changed to LBD following the onset of the above symptoms.

People with LBD may be very sensitive to Parkinson's medications and medications used in the treatment of dementia.

Regular review by a specialist is essential.

Alzheimer's Australia (1800 100 500) offers respite, education and support services to carers and those living with these conditions.

For further information contact your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

IN THIS TOGETHER parkinson's AUSTRALIA

Dizziness or Fainting

Orthostatic hypotension (OH) is a drop in blood pressure that happens when you go from a seated position or lying down to standing. Certain medications (including those for high blood pressure), dehydration and conditions such as heart disease increase this risk.

When orthostatic hypotension is related to a neurologic disorder like Parkinson's, it's called **neurogenic OH, or nOH**. Damage caused by nervous system disorders, including Parkinson's, can result in the nervous system not being able to make or release norepinephrine, a chemical that constricts blood vessels and raises blood pressure. This causes dizziness or lightheadedness.

nOH Symptoms

- Lightheadedness
- Dizziness
- Weakness
- Difficulty thinking
- Headache
- Blurred or dimmed vision

Neurogenic OH tends to be underdiagnosed. It is usually identified because people get dizzy or start to black out when they stand up. Early in the PD progression, you might not notice the dizziness, but you may experience the foggy thinking or memory problems.

Managing nOH

If you become lightheaded upon standing, report it to your doctor. In general, asking your doctor to screen you for nOH once a year is a good idea. This is done by taking your blood pressure while lying down and then standing. A drop of 20 points in the top number (systolic) or 10 points in the bottom number (diastolic) indicates nOH.

If you receive a diagnosis of nOH, talk to your doctor about reducing or eliminating certain medications (such as anti-hypertensives and some dopaminergic medications).

There are also several lifestyle strategies you can try:

- Drink more fluids to keep hydrated.
- Consume more salt and caffeine.
- Wear thigh-high support stockings. Compression garments such as antigravity stockings can be effective in preventing OH.
- Monitor your **blood pressure**.
- Sleep with your head elevated between 10 and 30 degrees.
- Change positions slowly, especially when rising from a seated to a standing position. Pause for several seconds between each move.
- Be aware of behaviors and circumstances that can make nOH worse:
- Exposure to heat
- Fever
- Prolonged standing
- Vigorous exercise
- Drinking alcohol
- Straining while going to the bathroom
- Meals high in carbohydrates

If these strategies do not help, there are several medications available to treat nOH. To learn more, call our Helpline at 1-800-4PD-INFO (473-4636) or read our book *Parkinson's Disease: Medications*. Then talk to your doctor about your options.

Drooling

Excessive drooling, called sialorrhea, is a common symptom of Parkinson's and can cause awkwardness in social situations. It ranges from mild wetting of the pillow during sleep to embarrassing outpourings of saliva during unguarded moments. For example, this can happen when the head is down, the mouth is held open involuntarily (as happens in advanced PD) or when a person is engaged in an activity and is distracted from the need to swallow automatically.

Drooling, along with speech and swallowing issues, is included among non-movement symptoms even though the root cause is motor: decreased coordination, slowness of movement (bradykinesia) and rigidity of the muscles of the mouth and throat.

Parkinson's causes a reduction in automatic actions, including swallowing, creating an inability to manage the flow of saliva in and around the mouth. In PD, usually the amount of saliva your body produces is normal, but swallowing difficulties – swallowing less often or not completely – lead to saliva pooling in the mouth.

When severe, drooling is an indicator of more serious difficulty with swallowing (also known as dysphagia), which can cause the person to choke on food and liquids and can even lead to aspiration pneumonia.

Managing Drooling

If you are having problems with drooling, you might consider an appointment with a speech-language pathologist. These professionals

can perform a swallow test to diagnose any difficulties and can also give you some strategies to help with drooling.

One trick is to suck on hard candy or chew gum, preferably sugarless. Candy and gum activate the jaw and the automatic swallowing reflex and can help clear saliva, providing temporary relief from drooling.

Another tactic is to wear a sweatband on your wrist. This can be used to discretely wipe the mouth as necessary and is a relatively inconspicuous accessory.

If these lifestyle strategies are not effective, adjusting anti-PD medications may make it easier to swallow. There are also some other prescription medication options:

- **Glycopyrrolate and other oral anticholinergic medications** (trihexyphenidyl, benztropine, hycosamine): Oral anticholinergic medications, as a class, decrease the production of saliva. Usually this is perceived as a side effect (dry mouth), but in this case it is an advantage. Other anticholinergic side effects may be seen, including drowsiness, confusion, vomiting, dizziness, blurred vision, constipation, flushing, headache and urinary retention. Anticholinergics can also have mental side effects, so their use should be carefully considered.
- **Scopolamine patch**: This patch offers anticholinergic medicine that slows production of saliva as it is absorbed into the entire bloodstream. The side effects are similar to those seen with use of oral anticholinergic medications.
- **1% atropine eye drops** (an anticholinergic): This treatment is given as 1-2 drops under the tongue per day to dry the mouth. Systemic side effects are much less likely with this local treatment.
- **Botulinum toxin A**: Botulinum toxin weakens muscles. 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. Injection of botulinum toxin A into the salivary glands of the cheek and jaw decreases production of saliva without side effects, except for thickening of oral mucus secretion. Botox is not always effective, but when it works the benefit can last for several months before it wears off and re-

injection is necessary. Botulinum toxin A can be an effective treatment for severe drooling, although pills, the patch and mouth drops should be tried first in the interest of cost saving. Botulinum toxin should probably be avoided when oral secretions are already deep and thick. Botulinum toxin B causes dry mouth when used for dystonia, but it is not approved by the FDA for drooling.

Depression

Mental health is extremely important in PD. Although common in other chronic diseases, research suggests that depression and anxiety are even more common in PD. It is estimated that at least 50 percent of those diagnosed with PD will experience some form of depression during their illness, and up to 40 percent will experience an anxiety disorder.

The Parkinson's Foundation *Parkinson's Outcomes Project* found that taken together, mood, depression and anxiety have the greatest impact on health status, even more than the motor impairments commonly associated with the disease.

While everyone feels sad from time to time — and while people with PD may experience grief in reaction to a PD diagnosis — depression is different.

Sadness is temporary, but depression is persistent, lasting for weeks or longer. Depression is a part of PD itself, resulting from changes in the chemistry of the brain. Specifically, PD causes changes in areas of the brain that produce dopamine, norepinephrine and serotonin — chemicals that are involved in regulating mood, energy, motivation, appetite and sleep.

A person may experience depression at any time in the course of PD, even before diagnosis. In addition, the symptoms of depression may come and go. It's important to know that depression can intensify both the motor and cognitive symptoms of PD. Researchers have found that people with PD who experience depression begin PD medications for motor symptoms earlier. Treating depression can improve quality of life and movement.

Depression, while common in PD, is often overlooked and undertreated. It is important to be aware of its symptoms, so that if you experience it, it can be treated effectively. Treating depression is one of the most significant ways to decrease disability and improve quality of life. Fortunately, there are effective treatments for depression. In this section, we explore depression and how it is diagnosed and treated.

Recommendations for People with PD

- Get screened for depression at least once a year.
- Discuss changes in mood with their healthcare professional and doctor.
- Bring a family member to doctor's appointments to discuss changes in their mood.

What Causes Depression?

Depression is a mood disorder in which overwhelming feelings of sadness, loss and hopelessness interfere with a person's ability to function at home or work. There are many causes of depression, including psychological, biological and environmental factors. Those with PD have an imbalance of certain neurotransmitters (brain chemicals) that regulate mood which is thought to play a major role. Like tremors and other motor symptoms of PD, depression can be improved with medications. The following factors can contribute to the development of depression.

Psychological factors

- **Negative thoughts** in addition to attitude about living with a chronic illness can lead to feelings of sadness, helplessness and hopelessness. Dwelling on these feelings may make a person more vulnerable to depression.
- **Social isolation** or the lack of a supportive social network that results from a more restricted lifestyle. Things such as early retirement or loss of independence make depression more likely.

Biological Factors

- **History of mental health issues.** Research suggests many people with PD experience depression or anxiety two to five years before the diagnosis of PD, which may mean that depression is not simply a psychological reaction to the illness, but a part of the underlying disease process.
- **Changes in the brain.** PD and depression affect the same physical parts of the brain involved in thinking and emotion. Also, both conditions affect the levels of three important neurotransmitters (dopamine, serotonin and norepinephrine) that influence mood and movement.

Environmental Factors

- **Severe stress.** People diagnosed with a chronic illness often get depressed. For some people, the ongoing distress of coping with such a life crisis triggers the disorder.
- **Side effects from drugs.** Certain prescription drugs can cause symptoms that mimic depression.

What are symptoms of depression?

Symptoms of depression will differ from person to person and can range in severity from mild to severe. Although people experience depression in differently, there are common symptoms including:

- Persistent sadness
- Crying
- Loss of interest in usual activities and hobbies
- Decreased attention to hygiene, medical and health needs

- Feelings of guilt, self-criticism and worthlessness
- Increased fatigue and lack of energy
- Change in appetite or eating habits (either poor appetite or over-eating)
- Loss of motivation
- Complaints of aches and pains
- Feelings of being a burden to loved ones
- Feelings of helplessness or hopelessness
- Reflections about disability, death and dying
- Sleep difficulties (too little or too much)
- Poor attention and concentration problems
- Feeling slowed down or restless inside
- Thoughts of death or suicide

How Is Depression Diagnosed?

Most people with PD will go undiagnosed or undertreated for depression; therefore, being diagnosed is a critical first step towards effective treatment and recovery. To be diagnosed with depression, a person must experience one of the following symptoms most of the time over the previous two weeks:

- Depressed mood
- Loss of interest or pleasure in activities once enjoyed

In addition, some of the following symptoms must be present:

- Changes in sleep or appetite
- Decreased concentration or attention problems
- Increased fatigue
- Feeling slowed down or restless
- Feeling worthless and guilty
- Suicidal thoughts or a wish for death

Difficulties in Diagnosing Depression in Patients with Parkinson's

- Certain symptoms of depression overlap with symptoms of PD — for example, sleep problems and feeling slowed down occur in both

conditions.

- Some experts think that depression in PD often involves frequent, shorter changes in mood versus a constant state of sadness daily.
- Many people with PD express less emotion due to the effect the disease has on the muscles of the face. This symptom, called facial masking, makes a person unable to express emotion through facial expressions.
- Many people with Parkinson's do not seek treatment because they often do not recognize they have a mood problem or are unable to explain symptoms. For these reasons, it is helpful to ask a caregiver or loved one if he or she has noticed any changes commonly reported in depression.

What are the treatment options for depression?

Just as the symptoms and causes of depression can differ from person to person, so too can suitable treatment approaches. There are two main types of treatment options for depression: antidepressant medications and psychological counseling (psychotherapy).

The Parkinson's Foundation recommends a holistic, comprehensive approach to depression. Although antidepressants are often effective in reducing symptoms, they should seldom be used alone. In most cases, the best approach is a combination of antidepressant medication, counseling, exercise and social support.

How can you ease depression in PD? First, share your concerns with your doctor. Many movement disorders specialists now include questions about depression in their exams. If your doctor does not, raise the topic. He or she may recommend medical or nonmedical coping strategies, including the following:

- With your doctor, evaluate your PD medications. People with PD who experience uncontrolled "on-off" periods and freezing episodes are more prone to depression. It is important to talk with a doctor to ensure your PD is being treated optimally — both motor and nonmotor symptoms.
- Many commonly-prescribed antidepressants are effective for people with PD. Different drugs work in different ways, thus the approach

needs to be tailored to each person. Be aware that some medications for depression may interact with PD medications.
- Consider psychological counseling, specifically an approach called cognitive behavioral therapy (CBT). This therapy helps people recognize and change patterns of thought and behavior to ease depression and anxiety.
- Be aware of anxiety and ensure it is treated, since it is so often diagnosed alongside depression.
- Exercise — walking, yoga, gardening or any exercise that appeals to you can help to ease symptoms of depression.

Medication

Most people with depression are treated with a class of drugs called selective serotonin reuptake inhibitors (SSRIs). These may include:

- Fluoxetine (Prozac®)
- Sertraline (Zoloft®)
- Paroxetine (Paxil®)
- Citalopram (Celexa®)
- Escitalopram (Lexapro®)

In addition, there are several non-SSRI antidepressants used to treat depression. These may include:

- Venlafaxine (Effexor®)
- Mirtazapine (Remeron®)
- Buproprion (Wellbutrin®)
- Tricyclic antidepressants (Amoxapine)

These medications work equally well, though their side effects and interactions with other medications slightly differ. Each person does not react the same way to these drugs, so if one *antidepressant* medication fails, another medication or combination of medications, as well as complementary treatments, should be tried until symptoms are under control. It can take some trial and error to find the right treatment.

Psychotherapy

Psychotherapy is a broad term used to refer to the many varieties of counseling or talk therapy available today. This is an important treatment option for people with depression and is often used in combination with medication.

Research from the Parkinson's Foundation Parkinson's Outcome Project found that rates for depression were lowest among patients receiving care from clinics with the most active approach to counseling.

Ways therapy can be beneficial:

- **Cognitive behavioral therapy** (CBT) has been shown to be effective. It helps people change negative thinking patterns and behaviors to reduce symptoms of depression. Learning these skills helps people cope better and think positively for the long term.
- **Counseling sessions** can provide vital support, understanding and education. Patients may be seen alone, as a couple or family or in a group.
- **Psychotherapy** offers an alternative to antidepressants. Some people with PD may not tolerate, respond fully or want to take an antidepressant.

Electroconvulsive Therapy

Electroconvulsive therapy (ECT) is a standard treatment option for people with severe or non-responsive depression, meaning no other treatments work. Although in the past movies and other media have portrayed it in a frightening way, it is a relatively safe and effective treatment available for severe depression. It also temporarily improves motor symptoms in PD. Major drawbacks include: time involved in getting the treatment, the need to undergo general anesthesia and possible memory problems or confusion as a complication. It is contraindicated for those with deep brain stimulators.

Exercise

Exercise has been found to be a simple therapeutic approach for improving mood and depression. It can include walking, stretching, yoga, Tai-chi and all basic forms of physical activity.

Non-Conventional and Complementary Therapies for Depression

- Light therapy
- Relaxation techniques
- Massage therapy
- Acupuncture
- Aromatherapy
- Meditation
- Music therapy
- Parkinson's support group

Tips for Coping with Depression

- Educate yourself about PD and its symptoms, including depression.
- Ask for help — it takes courage, but it also puts you in control of finding a way to feel better and overcome feelings of helplessness.
- Keep an open mind. Depression is not a personal failing or a sign of weakness, it is a chemical imbalance in the brain.
- Plan short-term goals that you can achieve daily. Makes plans to walk, do a chore or talk to a friend. Small accomplishments contribute to a feeling of self-worth.
- Maintain social ties. Plan to connect with a friend once a week or take on volunteer work.
- Plan something to look forward to. Think about things you can do to enhance your quality of life and plan how to achieve them in small steps.
- If you have stopped or cut back on leisure activities because of PD, try to resume one that you enjoyed or find a new one.
- Connect with the PD community. Compare notes on coping with depression with members of a support group.

Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

Dyskinesia

Dyskinesias are involuntary, erratic, writhing movements of the face, arms, legs or trunk. They are often fluid and dance-like, but they may also cause rapid jerking or slow and extended muscle spasms. They are not a symptom of Parkinson's itself. Rather, they are a complication from some Parkinson's medications.

Dyskinesias usually begin after a few years of treatment with levodopa and can often be alleviated by adjusting dopaminergic medications. Younger people with PD are thought to develop earlier motor fluctuations and dyskinesias in response to levodopa.

Dyskinesias may be mild and non-bothersome, or they can be severe. Most people with Parkinson's 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.

Peak-Dose Dyskinesia

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. In the earliest stages of Parkinson's, they are usually not bothersome, and you may not even notice these extra movements.

Diphasic Dyskinesia

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.

Managing Dyskinesia

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). Levodopa therapy is typically the cause of dyskinesias, but other drugs such as dopamine agonists, COMT (catechol-o-methyl transferase) inhibitors and MAO-B inhibitors can worsen dyskinesias.

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. There are currently two medications available to treat dyskinesia, and several in development.

- Amantadine may be added to your medication regimen to reduce dyskinesias without worsening "off" periods.
- The U.S. Food and Drug Administration has approved an extended-release formulation of amantadine (brand name Gocovri) specifically for the treatment of levodopa-induced dyskinesia in people with PD. Other amantadine formulations are sometimes used off-label for dyskinesia.

Read *Managing Parkinson's Mid-Stride: A Treatment Guide to Parkinson's* for more information about dyskinesia, the therapeutic

Dystonia in Parkinson's Disease

Dystonia is a continuous or repetitive muscle twisting, spasm or cramp that can happen at different times of day. Curled, clenched toes or a painful, cramped foot are telltale signs of dystonia. Dystonia can occur in different stages of Parkinson's disease (PD). For example, dystonia is a common early symptom of Young Onset Parkinson's, but it can also appear in middle to advanced stages of Parkinson's.

What is Dystonia?

Dystonia often happens when the person with PD tries to perform an action with the affected body part. For example, if you have dystonia of the foot, you may feel fine when sitting, but you may develop toe curling or foot inversion (turning in of the foot or ankle) when trying to walk or stand. Dystonia can also happen when you are not using the involved body part. Some dystonia happens unrelated to an action or movement — like toe curling while sitting.

People with PD often experience a painful dystonia on the side of their body with more Parkinson's symptoms. This frequently happens first thing in the morning when dopamine levels are at their lowest, or as nighttime medications wear off, or may come and go throughout the day. This painful cramp may go away after the first daily dose of Parkinson's medications or may not relate to timing of medication at all.

Foot dystonia is one of the most common sources of dystonic pain, specifically in early PD, but dystonia can affect other body parts. In addition to cramping, it can cause forceful twisting movements. A common example is when a person's arm feels pulled behind their back or their head is pulled to the side or toward the chest. Severe and painful spasms also can occur in the neck, face or throat muscles.

These movements are different from the flowing, writhing movements of dyskinesia (involuntary, erratic, writhing movements of the face, arms or trunk) which are not usually painful.

Although dystonia can be a Parkinson's symptoms, people can experience dystonia without having Parkinson's. Whether or not a person with dystonia has Parkinson's, it is often treated with the same medications.

Parts of the Body Affected by Dystonia

- **Arms, hands, legs and feet:** Involuntary movements, spasms or twisting and "curling"
- **Neck:** May twist uncomfortably, causing the head to be pulled down or to the side. This is called cervical dystonia or spasmodic torticollis
- **Muscles around the eyes:** May squeeze involuntarily, leading to a person to blink too much or to have difficulty opening the eyes. This is also called blepharospasm
- **Vocal chords and swallowing muscles:** May cause a person's voice to sound softened, hoarse or breathy
- **Jaw:** May open or close forcefully or there may be grimacing of the face
- **Abdominal wall:** May cause sustained contractions and involuntary, writhing movements of the abdominal wall

Managing Dystonia

It can be helpful to keep track of when dystonia occurs to find a relationship between the onset of dystonia and the timing of your medication. Your doctor may ask you some of the following questions to see if there is a pattern:

- Do you experience dystonia when levodopa (Sinemet) is at a peak (also known as an "on" period)?

- Do dystonia symptoms happen before the first dose in the morning or when medication is wearing off?

With your physician's direction, adjusting the dose or frequency of medication may help relieve dystonia. Those with morning dystonia (before the first dose of levodopa kicks in), may be advised by their doctor to add a bedtime dose of controlled-release carbidopa-levodopa or a long-acting dopamine agonist.

Therapies to Manage Dystonia

Physical and occupational therapy are also options for managing dystonia. It may be difficult to exercise when you are in pain. However, if you are in pain while moving and suddenly stop, the pain can get worse. A physical or occupational therapist can recommend exercises or techniques to target the source of your pain and to stretch and strengthen the body parts most affected by dystonia.

Botulinum Toxin Injections

If various therapies fail and your dystonia is not helped by altering medication timing, you and your healthcare provider may consider Botulinum toxin.

(BOTOX®) injections. Botulinum toxin weakens muscles, which helps calm the overactivity caused by dystonia. By targeting the overactive muscles, your physician can decrease the discomfort and pain caused by dystonia. It can take several injections to work well and it may not always be effective. When it does work, the benefit can last for several months before it wears off and re-injection is necessary.

Botulinum toxin A (BOTOX®): Can be used to treat dystonia as it stops unnecessary nerve signals from firing. It can also be used to decrease saliva production for people who have issues with drooling.

Botulinum toxin B (Myobloc): Primarily used to treat dystonia. Botulinum toxin B can cause dry mouth when used for dystonia, but unlike Botulinum toxin A, it is not approved by the U.S. Food and Drug Administration (FDA) for drooling.

Deep Brain Stimulation

Deep brain stimulation (DBS) surgery may also, in some cases, help dystonia in Parkinson's. DBS is a standard treatment for specific types of dystonia when it is not associated with Parkinson's. Its role as a treatment for dystonia in Parkinson's is being researched.

For dystonia, the electrical leads can be placed in the same brain regions used in Parkinson's disease. health practitioners are also trying to use new DBS technologies that better target Parkinson's symptoms.

Tips for Living with Dystonia

- ✓ **Learn about dystonia and treatment options in the Parkinson's Foundation book *Managing Parkinson's Mid-Stride*.**
- ✓ **Work with your doctor to find the best treatment for you.**
- ✓ **Meet with a physical and/or occupational therapist to identify strategies to strengthen and stretch the impacted area.**
- ✓ **Acknowledge the emotional impact of pain and consider seeking out support from a trained mental health professional or spiritual leader.**
- ✓ **Pursue activities you enjoy and pace yourself during social, physical and creative activities. Consider calming activities such as meditation, yoga or Tai Chi.**

*Connect with others who are living with Parkinson's and dystonia through online groups or support groups or through our online forum, **PDConversations.org.** Call the Parkinson's Foundation Helpline at 1-800-4PD-INFO (473-4636) if you need help finding a group near you or a referral to a PD specialist.*

Parkinson's Disease and the Gut (Part 1) | Pacific Neuroscience Institute

In Part 1 of this 3-part blog I cover questions or concerns that many of my patients with **Parkinson's disease (PD)** have that center around the gut.

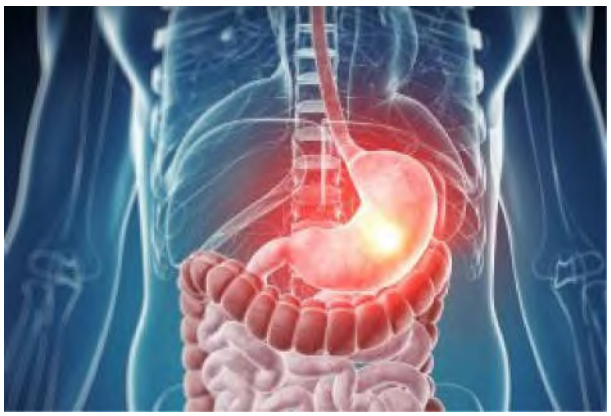
1. Constipation/delayed gastric emptying
2. Dietary recommendations for PD in general
3. Protein interactions with levodopa
4. Dietary interactions with MAO-B inhibitors
5. Connection of PD and the gut
6. Antibiotic impact on gut bacteria
7. The outlook for prevention or prevention progression for PD

1. Gastrointestinal symptoms of Parkinson's disease

Up to 70% of patients with PD have gastrointestinal symptoms, often beginning years prior to the onset of **motor symptoms**, along the entire length of the gastrointestinal tract. I will describe the issues that can arise from top to bottom, so to speak.

Symptoms of the mouth and throat include the slowing down and reduction of the swallow response, resulting in drooling or repeated swallows being required in early stages of PD. As the disease progresses, swallowing difficulty (known as dysphagia) may worsen, resulting in aspiration (going down the wrong pipe), which can be silent (not noticed) or associated with coughing, choking, or pneumonia. Dysphagia and aspiration should be evaluated by a swallow study, performed by a speech therapist. Treatment recommendations include chewing more slowly, clearing one's throat before taking another bite, eating while sitting up with the chin tucked, and changing the texture of the solids and liquids to be easier and safer to swallow.

The swallow response is a subconscious movement of the muscles of the mouth and pharynx and PD affects these subconscious movements. In the same way that the blink reflex reduces, the swallowing becomes less frequent. This results in drooling (known as sialorrhea) because the saliva is not being swallowed as frequently. Drooling can be treated with **botulinum toxin (e.g., Botox) injections** into the salivary glands to reduce saliva production.



Source: Pitara

Symptoms related to the stomach include bloating, indigestion, and early satiety, which typically reflect delayed stomach (gastric) emptying, sometimes known as gastroparesis. The gut movements (known as peristalsis) are coordinated by nerve cells surrounding the length of the gastrointestinal tract, and therefore may slow down or become uncoordinated the same way that movements of the limbs can be slowed or uncoordinated. This may be due to loss of enteric (gut-related) dopamine cells and degeneration of vagal nuclei (the nerve cells in the major nerve that controls the gut, the vagus nerve). A major issue of delayed gastric emptying is delayed action of levodopa (e.g., Sinemet or Rytary) because the **medications** move more slowly through the stomach and into the small intestine, where they are absorbed. This delay may be minimized by taking the medication on an empty stomach. Treatment of gastroparesis includes dietary modification (blenderized food) and monitoring of nutritional status. If the delayed gastric emptying is severe, there are medications that can help, such as domperidone and erythromycin. Please note that metoclopramide (Reglan) and prochlorperazine (Compazine), medications used for gastroparesis caused by diabetes, should not be taken by Parkinson's patients because they block dopamine and may make motor symptoms worse.

Symptoms related to the lower gut. A very common symptom of parkinsonism, which can be present years prior to onset of motor symptoms, is slow-transit constipation. The term slow-transit refers to constipation that is due to the gut slowing down as waste products move through. This is similarly due to slowed peristalsis as in the case of delayed gastric emptying. Sedentary lifestyles, lack of adequate hydration, and the Western diet (low fiber) exacerbate constipation.

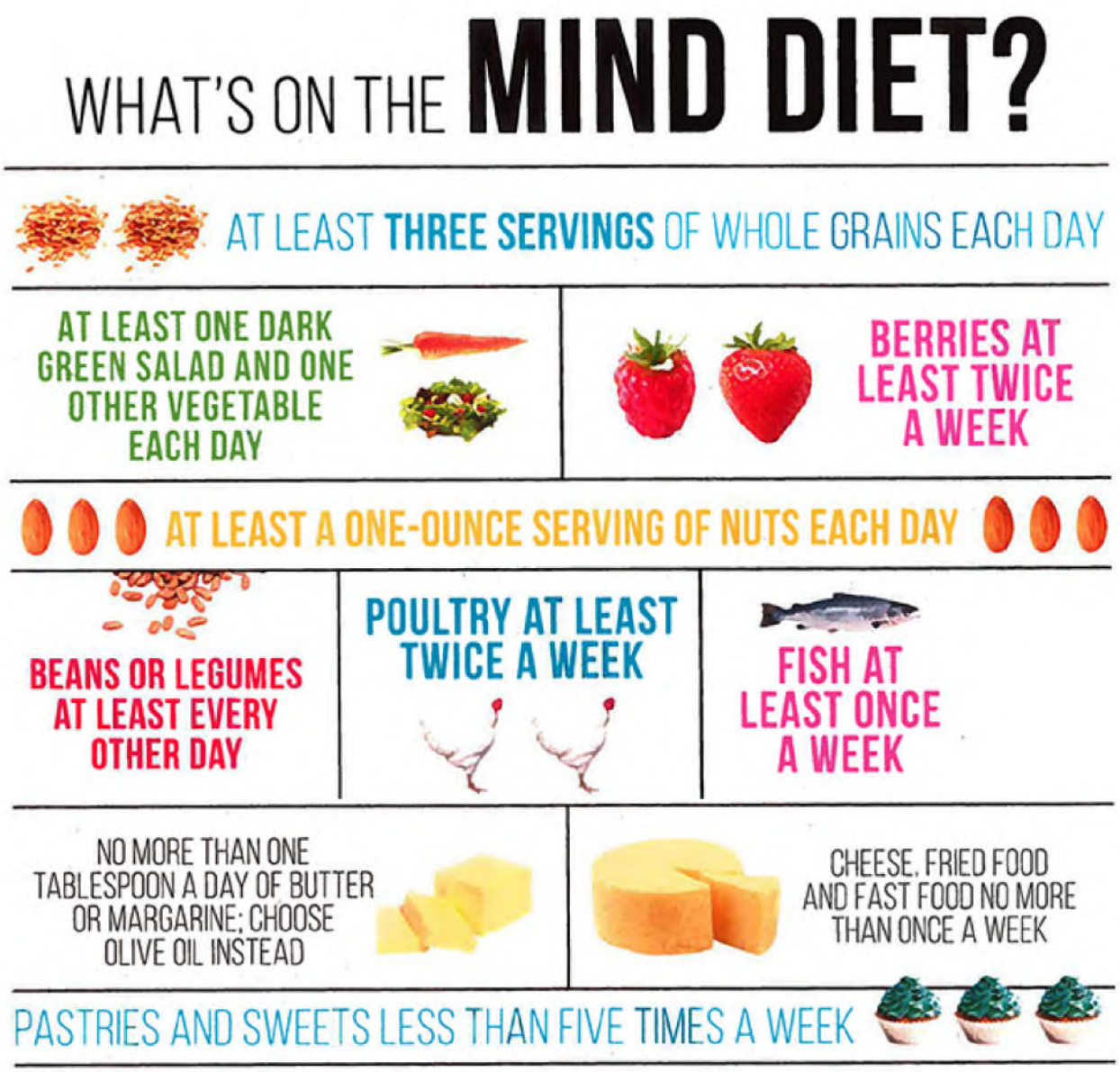
Chronic constipation is a major issue on many levels, but one of the main concerns from the day-to-day perspective is that constipation can worsen gastroparesis, thereby delaying the action of levodopa effect further. In addition, chronic constipation is associated with hemorrhoids, anal fissures (tears – ouch!), diverticulosis (weakening of colon wall which can cause bleeding and infections), and even up to a two-fold increased risk of colon cancer when

severe. Intermittent treatment of constipation (getting “stopped up” for several days, taking laxatives, then having multiple bowel movements each getting looser and looser) results in alternating constipation plus diarrhea, dubbed “constirrhea” by one of my patients. Therefore, it is best to stay on top of the bowel movements and use non-medication and medication options to stay regular, with a bowel movement every day or two.

For more on management of constipation, please see **Part 2** of this blog.

2. Dietary recommendations for patients with PD

There are no specific diets that have been shown to reduce progression of PD. However, there is good reason to believe that a well-balanced, nutritious diet (one that might be recommended for any person in the age range) would be best. Patients with coronary artery disease, kidney disease, and diabetes should consult their medical doctors and nutritionists as those conditions have other dietary restrictions or priorities. In those without other medical conditions, one might extrapolate from success in preventing Alzheimer’s disease with the use of the **Mediterranean-DASH Intervention for Neurogenerative Delay (MIND)** diet that there may be benefit in Parkinson’s as well since both are neurodegenerative diseases and involve cell dysfunction due to build-up of toxic proteins.



The MIND diet has 15 dietary components, including 10 “brain-healthy food groups”:

- Green leafy vegetables
- Other vegetables
- Nuts* (may recommend crushed or nut butters)
- Berries (especially blueberries and strawberries)
- Beans
- Whole grains
- Fish*
- Poultry
- Olive oil
- Red wine* — with caution – see below

The five unhealthy groups are:

- Red meats
- Butter and stick margarine
- Cheese
- Pastries and sweets
- Fried or fast food

The MIND diet includes at least three servings of whole grains, a salad and one other vegetable every day. It also involves snacking most days on nuts and eating beans every other day or so, poultry and berries at least twice a week and fish at least once a week. The MIND diet recommends limited eating of the designated unhealthy foods, especially butter (less than 1 tablespoon a day), cheese, and fried or fast food (less than a serving a week for any of the three).

However, because this diet has not been studied in PD, where patients may have balance issues which could worsen with alcohol, I DO NOT recommend a daily glass of wine. The supplement resveratrol may be taken instead. I also do not recommend as strict a limitation of cheese and butter, but I do recommend limiting excess sugars and processed foods. It seems to me that it would be more optimal for a patient to enjoy high-quality food of limited quantity, even (on occasion) rich foods or pastries, rather than having high quantities of low-quality, processed foods such as “diet” versions of food, which typically have higher sugar content when advertised as “fat-free” or may use more chemicals to substitute for flavor. For example, dark chocolate is known to have anti-oxidant qualities so it would seem that a small amount (an ounce for example) of good quality chocolate, enjoyed with thoughtfulness, would do better than abstaining altogether or attempting to abstain and then “breaking a diet” with binges of low-quality chocolate.

Regarding fish intake, I would recommend avoiding high-mercury fish:

- King Mackerel
- Marlin
- Orange Roughy
- Shark
- Swordfish
- Tilefish
- Ahi Tuna (albacore tuna has lower mercury content and can be had once a week).

Mercury content information is located at the **EPA website**.

Patients with Parkinson’s may have swallowing difficulties and dietary recommendations may vary depending on the severity of the condition. In general, high-risk foods to avoid in the context of swallowing include whole nuts, popcorn, hard candy, and tough meats. Some patients may be advised to maintain a dysphagia diet, which may recommend pureed foods or mechanical soft foods (e.g., meatloaf), and may recommend liquids to be thickened to

the consistency of nectar or honey. These diets are recommended in conjunction with a swallow evaluation by a speech/language pathologist (SLP, i.e., speech therapist). If a PD patient has coughing/choking with food, liquid or meds, even if only on occasion, it's important to notify the medical team to evaluate further.

3. Protein interactions with levodopa

Source: iStock

For patients who are taking **levodopa** (carbidopa-levodopa in the forms of Sinemet, Rytary, or Parcopa; or benserazide-levodopa, known as Madopar), protein in the gut inhibits absorption of levodopa. That is, taking the medication with or just after a meal makes the medication less effective, or delays the onset of action, or even may cause the medication not to kick in at all. For this reason, levodopa should be taken on an empty stomach. I recommend taking the medication AT LEAST 30 minutes prior to a meal, or AT LEAST 60 minutes after finishing a meal. This does not mean a meal has to be taken at that half-hour mark, just that there should be a delay prior to eating. Also if patients are taking medications 4 or 5 times per day, they may still eat only 3 meals, meaning that each dose does not have to be followed by a meal. The medications should be taken as consistently as possible at the same times per day but on occasion adjustments may be made if there is a late meal.

Please note that the only food that interferes with absorption of levodopa is protein (which is found in meat products, dairy products, beans, legumes and nuts, among other types of foods). Therefore, if a patient wants to have a small snack just before a dose of levodopa, there is no issue if the snack is protein-free (such as coffee and toast in the morning, berries and vegetables, etc.).

The total protein intake should be of moderate level – protein is still important for general health and maintenance of muscle. On average this is about 50-60 grams per day, or 2-3 servings of protein-rich food per day. Again, patients with kidney disease need to confer with their nephrologists about the optimal daily dose of protein. For patients with PD who do not have other protein-intake related considerations, the daily dose does not have to be limited, just the timing adjusted to reduce interference with levodopa intake. Patients with PD who are not taking levodopa do not need to be concerned about protein intake and meal timing.

4. Dietary adjustments with MAO-B inhibitors

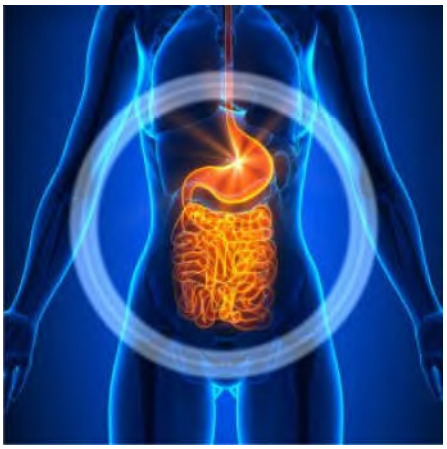
The medications rasagiline (Azilect), selegiline (Eldepryl, Emsam, Zelapar), and the new medication safinamide (Xadago) are **MAO-B inhibitors**. This means they reduce the metabolism of the brain's natural dopamine, thereby

causing more dopamine to be available for use.

The labeling on the medication advises patients to follow a low-tyramine diet. However, this dietary recommendation on the labeling is because MAO-B inhibitors are in the class of MAO inhibitors in general. Non-selective MAO inhibitors would also reduce the metabolism of the amino acid tyramine, which can cause elevated levels of tyramine, which would manifest with high blood pressure and other cardiovascular side effects.

When taken at the appropriate dose, there is no dietary restriction that is actually required. The doses that are FDA-approved for these 3 selective MAO-B inhibitors are shown to be specific for MAO-B, and therefore I do NOT limit metabolism of tyramine. Patients should NOT take doses higher than recommended (1 mg for rasagiline, 10 mg for selegiline). Tyramine is found in aged cheeses, sourdough bread, soy-based products, draft beer, red wine, fermented cabbage (such as sauerkraut and kimchi) and in cured meats. Of course, patients should not be taking an excess of tyramine-rich foods but when eaten in moderation, there is virtually no risk of the tyramine crisis.

5. Connection of PD and the gut



PD patients and normal control subjects have different types of gut bacteria, known as the gut microbiome. In addition, abnormal protein deposits of alpha-synuclein seen in the brains of patients with PD have also been found in the gut prior to development of motor symptoms, up to 20 years prior to diagnosis. There are a number of theories and studies that look into the connection that the gut may have with relation to the onset of Parkinson's disease. A detailed summary of research studies of the brain-gut connection in our understanding of Parkinson's disease can be found in **Part 3** of this 3-part blog series.

Source: abneyandbaker.com

6. Antibiotic impact on gut bacteria

Because antibiotic use is one of the main factors in changing natural gut bacterial profiles, I would also remind patients to exercise caution about antibiotics – both in their diet and in their own health care. There is a movement to limit the amount of antibiotics in meats and dairy products, and one should make efforts to seek out antibiotic-free products for home cooking and when eating in restaurants. Antibiotics should also be limited to use in conditions clearly caused by bacterial infection. Too often antibiotics are given for viral infections such as the cold or the flu, in some cases at the insistence of patients themselves. Overuse of antibiotics in both situations can result in antibiotic-resistant bacteria as well as the previously mentioned changes in gut flora. The limitation of unnecessary antibiotics is important for all people, not just those who have PD, in order to limit the rise of antibiotic-resistant superbugs.

7. The outlook for prevention or prevention of progression for Parkinson's disease

There is a lot of promising ongoing research to identify biomarkers for PD utilizing gut tissues such as saliva. In the future, these may serve to identify people at risk of developing PD, and/or help determine markers of progression for patients with PD. Many earlier stage patients may be assessed for risk and more timely assessments of disease could be made. Drug development could potentially target very early stage disease versus treating clinical progression.

In the meantime, there is no evidence to support the use of probiotics or pre-biotics to supplement the gut microbiome – yet. This is an area of early research for the management of gut-related symptoms such as constipation. The hopes of preventing disease progression may take larger and longer studies.

At this point, based on current evidence, I would encourage healthy eating as detailed above.

*Read **Part 2** and **Part 3** of this 3-part blog series.*

***Dr. Melita Petrossian** is Director of **Pacific Movement Disorders Center** and is a fellowship-trained neurologist with clinical interests and expertise in movement disorders such as Parkinson's disease, essential tremor, dystonia, gait disorders, ataxia, myoclonus, blepharospasm, hemifacial spasm, Meige syndrome, spasticity, tics, and Tourette's syndrome. She also specializes in Parkinson's-related conditions such as Dementia with Lewy Bodies, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration, primary freezing of gait, and Parkinson's disease dementia.*

Exercise Can Be a Boon to People With Parkinson's Disease Personal Health

By JANE E. BRODY JAN. 23, 2017 New York Times

Susan Sills, a Brooklyn artist who until recently made life-size cutouts on plywood using a power saw, long suspected she might be at risk for developing Parkinson's disease. Both her mother and grandfather had this neurological movement disorder, and she knew that it sometimes runs in families.

Credit Paul Rogers Cartoon

So she was not surprised when at age 72 she first noticed hand tremors and a neurologist confirmed that she had the disease. But to watch her in action three years later, it would be hard for a layperson to tell. She stands straight, walks briskly, speaks in clarion tones and maintains a schedule that could tire someone half her age.

She wisely put the power saw aside, Ms. Sills now makes intricately designed art jewelry. She is also a docent at the Brooklyn Museum, participates in a cooperative art gallery and assists her husband's business by entertaining customers.

Ms. Sills attributes her energy and well-being partly to the medication she takes but primarily to the hours she spends working out with a physical therapist and personal trainer, who have helped her develop an exercise regimen that, while not a cure, can alleviate Parkinson's symptoms and slow progression of the disease.

The exercises opened me up," said Ms. Sills, allowing such symptoms as small steps, slow movements and tiny, cramped handwriting to subside.

"The earlier people begin exercising after a Parkinson's diagnosis, and the higher the intensity of exercise they achieve, the better they are," Marilyn Moffat, a physical therapist on the faculty of New York University, said. "Many different activities have been shown to be beneficial, including cycling, boxing, dancing and walking forward and backward on a treadmill. If someone doesn't like one activity, there are others that can have equally good results."

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Unfortunately, Dr. Moffat added, "no one tells people with Parkinson's what they could and should be doing unless they get to a physical therapist." The typical delay in starting an effective exercise program also stems from the ability of medication to alleviate early symptoms, leaving patients with little incentive to exercise.

While everyone can benefit from exercise, it is especially important for people with a progressive movement disorder like Parkinson's that can result in weakness, stiffness, difficulty walking, poor balance and falls, as well as impaired cognitive processing. Regular exercise bestows increased levels of fitness; a greater sense of well-being; stronger muscles and bones; healthier joints; more efficient breathing; and better digestion and blood circulation. The result is enhanced physical, mental and cognitive health, all of which are especially important to people with a chronic ailment.

For Parkinson's patients in particular, regular exercise tailored to their needs can result in better posture; less stiffness; improved flexibility of muscles and joints; faster and safer walking ability; less difficulty performing the tasks of daily living; and an overall higher quality of life.

Patients who participate in exercise programs designed to mitigate symptoms and perhaps delay progression of Parkinson's "can function independently at a higher level, have stronger feelings of well-being, and are happier about their quality of life," said Dr. Moffat, who has witnessed major improvements in people she's worked with.

Among the many exercise options is an agility program that incorporates the principles of tai chi, kayaking, boxing, lunges and Pilates. It was developed and proved safe and effective by Laurie A. King and Fay B. Horak at Oregon Health and Sciences University. The agility course includes navigating turns, doorways, hallways and small areas; tasks like walking with knees high and hands touching them; skipping; and shuffling from side to side.

In a report on their work in Physical Therapy, the journal of the American Physical Therapy Association, Dr. King and Dr. Horak explained that intense exercise can improve "plasticity" of the brain, protect against nervous system degeneration, and even reverse motor deficits.

Exercise Can Be a Boon to People With Parkinson's Disease Personal Health

By JANE E. BRODY JAN. 23, 2017 New York Times

Another program, called Rock Steady Boxing, was founded by Scott C. Newman, a former prosecutor in Marion County, Ind., who developed Parkinson's at age 40. He reported significant improvements in his physical health, agility, daily functioning and quality of life shortly after he began high-energy workouts doing boxing moves a few years after his diagnosis.

Mr. Newman has pointed out that Parkinson's is not a muscle wasting disease. Rather, the brain forgets how to tell the muscles what to do. He believed it should be possible to teach the brain to get muscles to work more effectively, which is what Rock Steady Boxing and other exercise programs for Parkinson's disease seem to have achieved.

While it is best to begin a challenging exercise program early in the disease, Dr. Moffat and Mr. Newman say it can help at any stage. Rock Steady Boxing, for example, has created training programs suited to fitness levels at all stages of Parkinson's.

Another personal experience, by a cross-country cyclist, resulted in a tandem cycling program for Parkinson's patients. In a 200-mile trip across Iowa in 2003, Jay Alberts, a biomedical engineer at the Cleveland Clinic, pedaled in the lead position with a woman who has Parkinson's. The pace he set forced her to pedal a third faster than she would have done on her own. The woman's tremors disappeared while she was pedaling with Dr. Alberts, and he later showed in a controlled study that the ability of forced pedaling to suppress Parkinson's symptoms can persist for weeks afterward.

Dr. Alberts suspects that the high-intensity exercise changes how the brain processes movement, resulting in improved motor function over all. The benefits of tandem cycling can be achieved indoors and out, even without a biking partner.

The exercise program that has mainly helped Ms. Sills, called L.S.V.T. BIG, evolved from the Lee Silverman Voice Treatment program – L.S.V.T. LOUD — created to improve the speech of Parkinson's patients, who tend to talk more and more softly. Developed specifically to counter the unique movement impairments associated with Parkinson's, it trains patients to "make big strong movements, not little weak ones," Ms. Sills said, for example, taking big steps and swinging your arms widely when

Exercise Can Be a Boon to People With Parkinson's Disease Personal Health

By JANE E. BRODY JAN. 23, 2017 New York Times

you walk. "This is the normal way to walk, but not when you have Parkinson's, but it no longer feels strange to me," she said.

Other programs tailored to benefit Parkinson's patientsinclude ParkFit, which fosters a more active lifestyle; Dance for PD, which has classes in every New York City borough and many other countries; and Microsoft Kinect Adventures, which uses Xbox games geared to different stages of the disease.

Correction: January 23, 2017

An earlier version of this article misstated the affiliation of Laurie A. King and Fay B. Horak. They are at Oregon Health and Sciences University, not the Cleveland Clinic.

Table of Contents

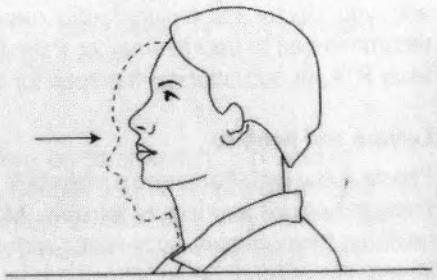
Therapeutic exercises

Regular exercise can help maintain flexibility, improve posture, keep muscles strong and joints supple. It can improve circulation to the heart and lungs. It can provide a sense of achievement and control over your condition and it can also enhance your mood.

The following pages outline some physical exercises that may be beneficial. It is important to establish a daily routine for these exercises and to stop them if you are tired. A physiotherapist is recommended to develop an individual exercise program.

Neck and shoulder exercises

- Shrug your shoulders up and down
- Rotate your shoulders up, back and down
- Repeat 10 times each



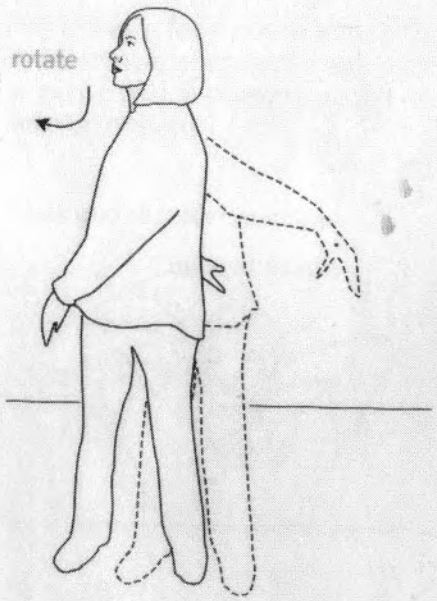
- Pull your head straight back keeping your jaw and eyes level
- Hold for 5 seconds
- Repeat 10 times

- First, take your right ear to your right shoulder, and then lightly grab the side of your head with your right hand while reaching behind your back with your left hand
- Feel a gentle stretch on the left side of your neck
- Hold for 10 seconds

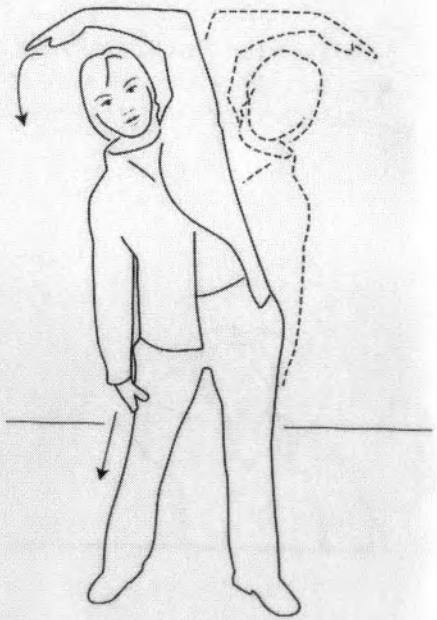
- Repeat on the other side
- Bend your head backwards
- Apply light pressure and push the back of your head forwards with your fingertips
- Hold for 10 seconds
- Repeat once

Trunk exercises

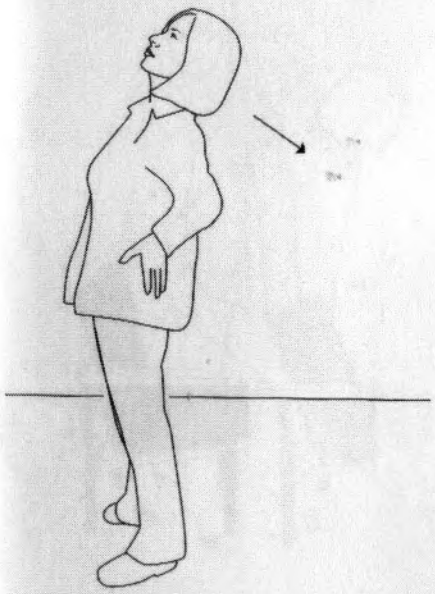
You may wish to hold a chair for support whilst doing all of these exercises.



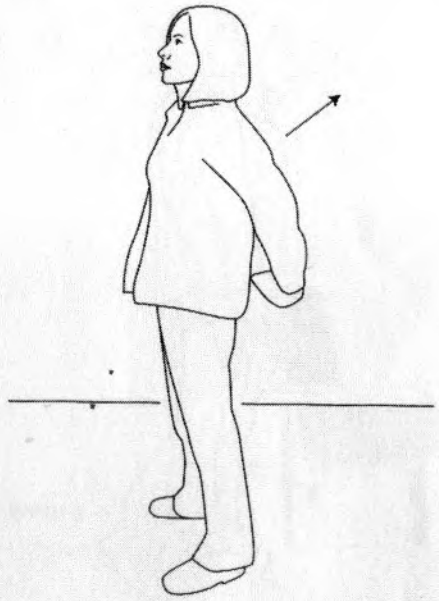
- Feet apart
- Rotate your head, shoulders and hips together (slowly) side to side
- Repeat 10 times



- Feet apart
- Stretch sideways
- Repeat 10 times



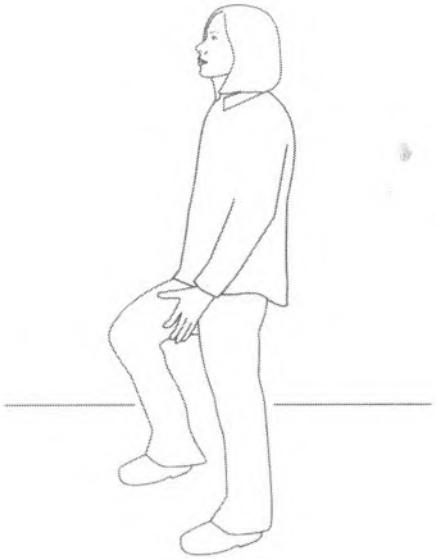
- Feet apart
- Rest hands on your lower back
- Bend backwards
- Hold for 10 seconds
- Repeat once



- Feet apart
- Lace fingers behind your back
- Squeeze your shoulder blades together
- Slowly raise your arms
- Hold for 10 seconds
- Repeat once

Leg exercises

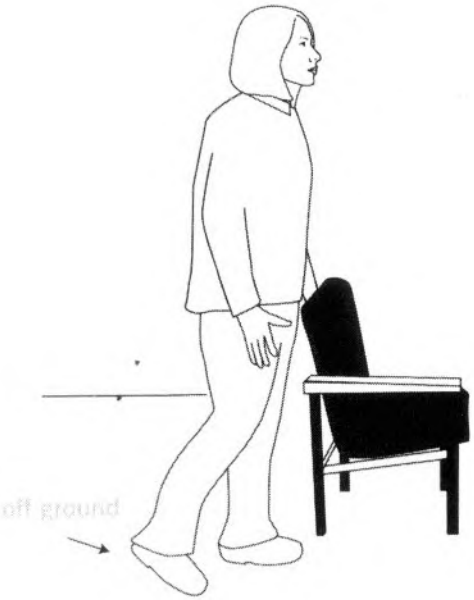
You may wish to hold a chair for support whilst doing all these exercises.



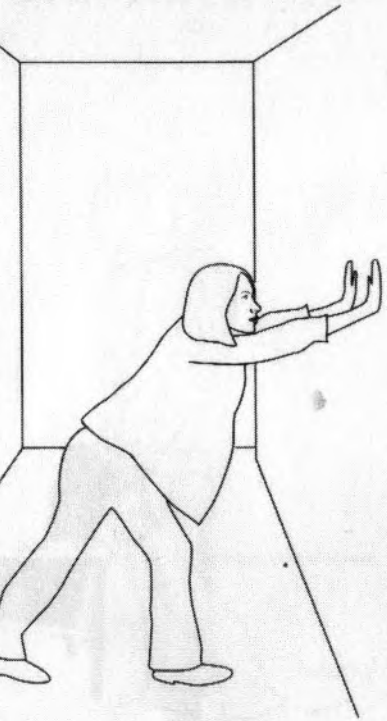
- March on the spot for 2 minutes
- Lift your knees as high as possible
- Swing your arms
- Hold a chair for support if necessary

- Following previous instructions for sitting and standing, however, push to stand using legs (if possible do not use arm rests)
- Repeat 10 times

- Slowly take a leg out to the side and return (lifting your foot off the ground)
- Repeat 10 times on each side



- Pull a leg straight back (lifting your foot off the ground) and return slowly. Squeeze buttocks
- Repeat 10 times each side



retch your calf keeping your heel
the floor. Keep your back leg
raight and your front knee bent
old for 10 seconds
epeat once on each side

- Place your foot on a stool
- Lean forward reaching down to your shin until a stretch is felt in the back of your thigh (hamstring)
- Hold for 10 seconds
- Repeat once on each side

Support, assistance and further information

Parkinson's organisations

In every state or territory you will find a Parkinson's organisation. Each organisation provides support, information and education. Support groups help people living with Parkinson's maintain control of their lives through activities, sharing experiences and contact with other people living with Parkinson's and their carers.

You can contact your state organisation by calling 1800 644 189 or visiting Parkinson's Australia:

www.parkinsons.org.au

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Facial Masking

When we think of muscles that can be affected by stiffness and slowness, the muscles people work out in the gym are probably the first to come to mind: legs, arms, maybe even abdominals! But the same stiffness and slowness that can impact your walking and other activities can have more subtle impacts, as well. One of these is reduced facial expression, also called hypomimia or facial masking.

When the muscles of the face are stiff or take longer to move, it can be hard to crack a smile, raise your eyebrows or otherwise express your feelings using your face, which is an important part of how we communicate. Combined with Parkinson's **speech changes**, such as low voice volume, facial masking can make it hard for others to interpret your mood and intentions. People might assume you're upset or depressed all the time, which can be frustrating if they constantly ask, "What's wrong?" when you are feeling fine. On the other hand, if you are experiencing symptoms of **depression**, talk to your doctor. Mood changes are common in Parkinson's disease, and treatable!

Managing Facial Masking

Medications to treat movement symptoms should help with facial masking, as they alleviate rigidity.

It is also a good idea to ask your doctor for a referral to a speech-language pathologist. He or she can teach you facial exercises that may help with masking, as well as other issues you may be having, including speech and swallowing problems.

Finally, if you are having more frequent cases of people misinterpreting your mood or not believing you when you say how you are doing, try explaining the difficulty with muscle control and expression. This may help people to better understand how you are feeling, and also increase their awareness of Parkinson's disease.

Parkinson's Disease Fact Sheet

About Parkinson's Disease

Parkinson's disease is a progressive, incurable neurological disorder associated with a loss of dopamine-generating cells in the brain. It is primarily associated with progressive loss of motor control, but it results in a complex array of symptoms, including many non-motor symptoms. Parkinson's impacts an estimated one million people in the United States.

Critical Clinical Care Considerations

- To avoid serious side effects, Parkinson's patients need their medications ***on time, every time*** — do not skip or postpone doses.
- Write down the exact times of day medications are to be administered so that doses are given on the same schedule the patient follows at home.
- Do not substitute Parkinson's medications or stop levodopa therapy abruptly.
- Resume medications immediately following procedures, unless vomiting or severely incapacitated.
- If an antipsychotic is necessary, use pimavanserin (Nuplazid), quetiapine (Seroquel) or clozapine (Clozaril).
- Be alert for symptoms of dysphagia (trouble swallowing) and risk of pneumonia.
- Ambulate as soon as medically safe. Patients may require assistance.

Common Symptoms of Parkinson's Disease

Motor

- Shaking or tremor at rest
- Bradykinesia or freezing (being stuck in place when attempting to walk)
- Low voice volume or muffled speech
- Lack of facial expression
- Stiffness or rigidity of the arms, legs or trunk
- Trouble with balance and falls
- Stooped posture
- Decreased ability to swallow (dysphagia) and drooling

Non-Motor

- Depression
- Anxiety
- Constipation
- Cognitive decline and dementia
- Impulse control disorders
- Orthostatic hypotension
- Pain
- Hallucinations and psychosis
- Sleep disturbances
- Sexual dysfunction
- Urinary dysfunction

Typical Parkinson's Medications

L-DOPA	Dopamine Agonist	MAO-B Inhibitors	Anticholinergics	COMT Inhibitors	Other
carbidopa/ levodopa (Sinemet or Sinemet CR) carbidopa/levodopa oral disintegrating (Parcopa) carbidopa/ levodopa/ entacapone (Stalevo) carbidopa/levodopa extended-release capsules (Rytary) carbidopa/levodopa enteral solution (Duopa)	ropinirole (Requip) pramipexole (Mirapex) rotigotine (Neupro) apomorphine (Apokyn)	rasagiline (Azilect) selegiline (l-deprenyl, Eldepryl) selegiline HCL oral disintegrating (Zelapar)	trihexyphenidyl (formerly Artane) benztropine (Cogentin) ethopropazine (Parsitan)	entacapone (Comtan) tolcapone (Tasmar) carbidopa/ levodopa/ entacapone (Stalevo) **has L-DOPA in formulation*	amantadine (Symadine, Symmetrel)

Medications That May Be Contraindicated in Parkinson's Disease

Medical Purpose:	Safe Medications:	Medications to Avoid:
Antipsychotics	pimavanserin (Nuplazid, FDA approved to treat Parkinson's disease psychosis), quetiapine (Seroquel), clozapine (Clozaril)	avoid all other typical and atypical antipsychotics
Pain Medication	most are safe to use, but narcotic medications may cause confusion/ psychosis and constipation	if patient is taking MAO-B inhibitor such as selegiline or rasagiline (Azilect), avoid meperidine (Demerol)
Anesthesia	request a consult with the anesthesiologist, surgeon and Parkinson's doctor to determine best anesthesia given your Parkinson's symptoms and medications	if patient is taking MAO-B inhibitor such as selegiline or rasagiline (Azilect), avoid: meperidine (Demerol), tramadol (Rybix, Ryzolt, Ultram), droperidol (Inapsine), methadone (Dolophine, Methadose), propoxyphene (Darvon, PP-Cap), cyclobenzaprine (Amrix, Fexmid, Flexeril), halothane (Fluothane)
Nausea/ GI Drugs	domperidone (Motilium), trimethobenzamide (Tigan), ondansetron (Zofran), dolasetron (Anzemet), granisetron (Kytril)	prochlormethazine (Compazine), metoclopramide (Reglan), promethazine (Phenergan), droperidol (Inapsine)
Antidepressants	fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa), escitalopram (Lexapro), venlafaxine (Effexor)	amoxapine (Asendin)

Special Alert: Drugs such as benzodiazepines, muscle relaxants, bladder control medications and other medications used for sleep and pain may lead to confusion, hallucinations and other symptoms.

Share This With Your Doctor

If you have a Deep Brain Stimulation device (DBS):

MRI Warning

- MRI should not be performed unless the hospital has MRI experience imaging a DBS device safely.
- MRI should never be performed if the pacemaker is placed anywhere other than the chest or abdomen.
- Under certain conditions, some DBS devices are safe for full-body MRI and do not need to be turned off. In other cases, devices should be turned to 0.0 volts and MRI should not be used to image structures of the body lower than the head, as dangerous heating of the lead could occur.
- Always check with your DBS team before having an MRI to make sure the procedure will be safe for you.

EKG and EEG Warning

- Turn off the DBS device before conducting EKG or EEG.
- Diathermy should be avoided.

Parkinson's Foundation

The Parkinson's Foundation's ***Aware In Care*** campaign aims to help people with Parkinson's get the best care possible during a hospital stay.
For more information please visit **Parkinson.org/awareincare** or call **1-800-4PD-INFO (473-4636)**.

Fatigue

Do you or a loved one with Parkinson's disease (PD) feel physically or mentally exhausted? This could be fatigue — a feeling of deep tiredness that does not improve with rest. About half of people with PD report fatigue is a major problem and a third say it is their most disabling symptom.

Fatigue is different from sleepiness. A person who is fatigued feels exhausted, however, does not necessarily feel like sleeping.

Fatigue is common early in the course of PD, but can occur at any point and can happen whether movement symptoms are mild or severe. It is sometimes confused with other symptoms that can make a person sleepy or tired, like sleep disturbances or pain. Fatigue is also a symptom of

depression, but a person can be fatigued without being depressed. Stress can make fatigue worse.

No specific cause has been shown to cause fatigue in PD. It is possible that motor symptoms like tremor and stiffness contribute to making muscles tired. But fatigue can have causes outside of Parkinson's, too. It is important to identify and treat illnesses or medications not related to PD that cause fatigue.

The extreme exhaustion that comes with fatigue can lead people to reduce hours at work or retire, or avoid social activities. Understanding fatigue as a symptom of PD and finding ways to cope with it are essential to maintaining a good quality of life.

Symptoms

- Physical fatigue: feeling deeply tired or weary; may worsen with "off" fluctuations.
- Mental fatigue: mental tiredness that makes it difficult to concentrate.

Therapies

- Few therapies have been tested for fatigue in PD. None have been proven effective against fatigue on its own. Therapies for movement symptoms do not seem to help fatigue.
- When fatigue is mixed with other symptoms, treating those symptoms may help people feel more energetic. For example, treating sleep disturbances can help a person sleep soundly through the night and treating depression may also help.
- Some therapies for motor symptoms may contribute to fatigue or make you sleepy. Adjusting doses of these medications may help solve the problem.
- Talk to your doctor about medications you take that are not for PD — these also may contribute to fatigue.
- Although little research has been done to evaluate stimulants like amphetamine salts, your physician may recommend trying a low dose.
- Work with your doctor to identify and treat any medical causes of fatigue besides PD, such as anemia.

- Talk with your doctor before taking any vitamins or supplements. These may interact with medications for PD or other disorders.
- In addition to your neurological appointments, have regular check-ups with your primary care doctor. Ask him or her to test for nutritional deficiencies such as vitamin B, potassium and more.

Tips for Coping with Fatigue

- Eat well.
- Stay hydrated.
- Exercise. Walk, do Tai Chi, dance, cycle, swim, do yoga or chair yoga — whatever you enjoy. Fatigue may make it hard to start exercising, but it may make you feel more energetic afterward. If you find it difficult to get going, consider exercising with another person or a group.
- Keep a regular sleep schedule. If you have difficulty sleeping because of tremor or stiffness, trouble rolling over or needing to use the bathroom, talk to your doctor about these issues.
- Take a short nap (10 to 30 minutes) after lunch. Avoid frequent naps or napping after 3:00 p.m.
- Stay socially connected.
- Pace yourself: plan your day so that you are active at times when you feel most energetic and have a chance to rest when you need to.
- Do something fun: visit with an upbeat friend or pursue a hobby.
- At work, take regular short breaks.

Note: Fatigue has been identified by the PD community as an unmet need. More research to understand and solve fatigue in PD is underway.

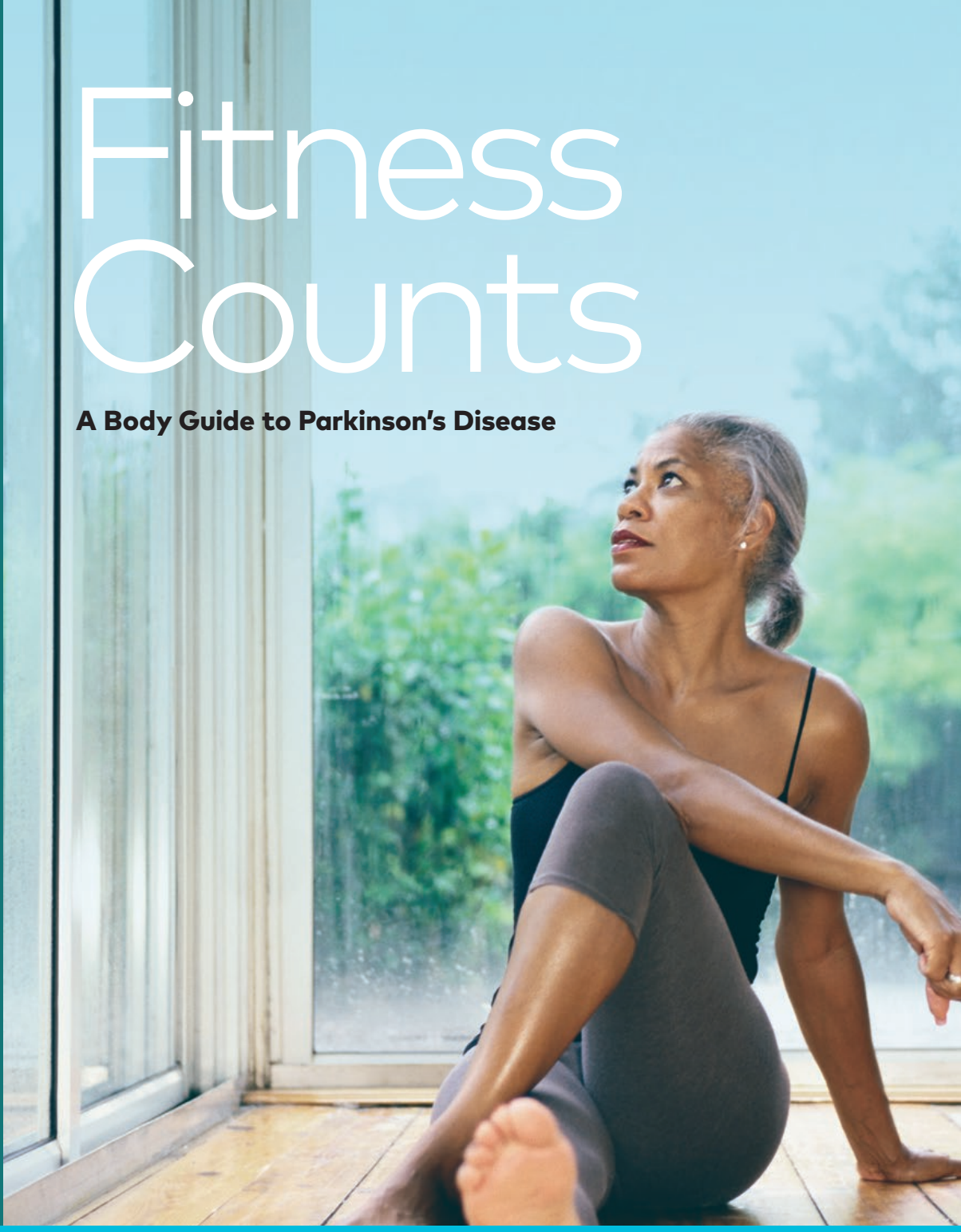
Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

What Is Parkinson's?

Causes

Fitness Counts

A Body Guide to Parkinson's Disease



Parkinson's Foundation

About this book

GLOSSARY

Definitions for all words underlined in blue can be found in the glossary starting on page 51. A comprehensive Parkinson's disease glossary can be found at Parkinson.org/Glossary.

INDEX

An index of key words and topics can be found on page 52.

PARKINSON'S FOUNDATION RESOURCES

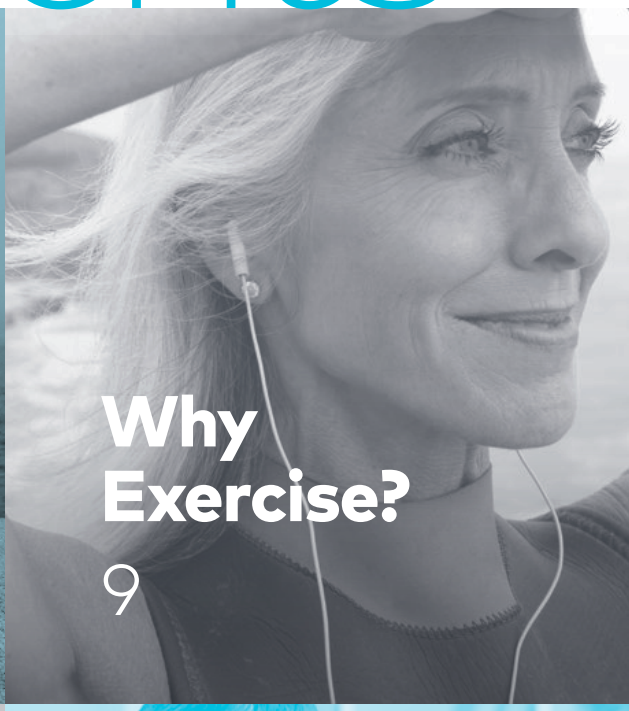
Several episodes of our podcast series, *Substantial Matters: Life and Science of Parkinson's*, focus on exercise and overall wellness. Check it out at Parkinson.org/Podcast.

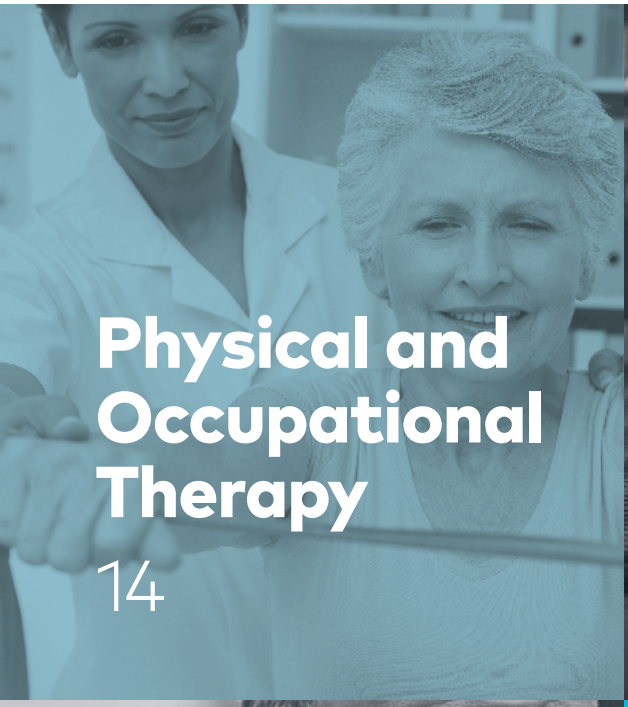
While medication has long been the most promising treatment available for Parkinson's disease (PD), a regular exercise program should always be part of managing PD. In fact, most movement disorder neurologists say that exercise is as important as any one of your medications. Though exercise is not a cure, it may help slow the progression of symptoms.

This book provides general exercise information and suggestions for all people living with PD. You may use it to help increase your fitness level and improve your ability to do everyday activities. In addition, this book includes resources for physical and occupational therapists who would like information regarding treatment options for people with PD.

Be creative with your fitness. Exercise indoors and out. Change your routine frequently. Dance. Use music. Try a new exercise. Exercise with a partner, child, friend or animal. Join an exercise program or group. Above all, challenge yourself and **have fun**!

Contents





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CHAPTER ONE

About Parkinson's Disease

To understand the role fitness plays in treating Parkinson's disease, we first need to understand the symptoms of the disease. If you are reading this book, you are probably already familiar with PD, but here are some basics: Parkinson's is a progressive, 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 "motor features" it can cause – tremors, slow movements, stiffness and muscle cramping. Symptoms are diverse and usually develop slowly over time. Parkinson's not only disrupts brain networks that control movement, but also those linked to mood, behavior and thinking (cognition).

Parkinson's disease is not diagnosed with a test or a scan; instead it is diagnosed by a neurologist, who asks you questions about your health and medical history and observes your movement. Your doctor may want you to have some tests or imaging; some, like an MRI, can help rule out other conditions, while others, like DaTScan, may help confirm a Parkinson's diagnosis if there is uncertainty. The goal of treatment is to help you manage your symptoms.

The symptoms of Parkinson's disease include more than just the motor features. Parkinson's impacts thinking: the disease can affect working memory, decision-making, staying attentive and concentration. Parkinson's is also linked to depression and anxiety, and it can affect behavior and disturb sleep.

From a biological perspective, Parkinson's results in low levels of the brain chemical dopamine, and this leads to the loss of effective communication between the higher brain structures on the surface of the brain (called the cortex) and the deep part of the brain that manages more basic functions (called the basal ganglia). The higher brain structures are where you think, and the deep structures are where those thoughts are translated into actions, particularly movement. 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 do know that the dopamine system is not the only one affected by Parkinson's. The disease process also disrupts other brain networks, including those linked to mood, behavior, and cognition (thinking).

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 help reduce setbacks that make living with PD more challenging. Great care is an important part of living your best life with Parkinson's.

NOTE

Before starting an exercise program, it is important to discuss your program with your doctor and/or physical or occupational therapist. They can address your fitness questions and concerns on a more personal level. These health professionals can also design a specific fitness routine for you and keep you updated on current Parkinson's research.
(See Chapter 3, Physical and Occupational Therapy, on page 14 for information on how to find a therapist near you.)

Parkinson's Symptoms

While you may not experience all the symptoms below, Parkinson's will affect many systems of the body. Parkinson's symptoms vary from person to person and change over time. Three telltale symptoms help doctors make a diagnosis:

1. **Slowness of movement (bradykinesia)**
2. **Tremor**
3. **Rigidity**

Bradykinesia plus either tremor or rigidity must be present for a Parkinson's diagnosis to be considered.

Other symptoms of PD are related to these movement challenges:

- Changes in walking
  - Difficulty turning
  - Festination or shuffling (quick, small, involuntary steps forward)
  - Retropulsion (quick, small, involuntary steps backward)
- Freezing episodes (an inability to perform a movement, or a feeling that your feet are stuck to the ground)
- Micrographia (small, cramped handwriting)
- Speech and swallowing changes

Another movement symptom, postural instability (trouble with balance and falls), is often mentioned, but it does not occur until later in the disease progression.

The **non-movement symptoms** of PD can also indirectly affect mobility:

- Bowel and bladder changes (constipation, urinary urgency and frequency, incontinence)
- Cognitive changes (attention, memory problems)
- Mood changes (anxiety, depression)
- Orthostatic hypotension (a drop in blood pressure and a feeling of lightheadedness upon standing)
- Sensory changes (pain, tightness, tingling, burning)
- Sleep disorders
- Visuo-spatial problems (difficulty detecting changes in the amount of space surrounding objects; e.g., detecting the correct height of a step)

PD is a Movement and Sensory Disorder

People with Parkinson's have difficulty regulating the size or speed of their movements. Movements are bradykinetic (too slow) and hypokinetic (too small).

Changes in the movement system (muscles) lead to challenges controlling movements, including the following:

- Starting and stopping movements
- Automatically controlling muscles
- Linking different movements to accomplish one task: for example, moving from sitting to standing
- Finishing one movement before beginning the next: for example, not completely turning around before sitting down

Changes in the sensory system also lead to challenges, particularly noticing and correcting movement and voice issues. Here are some other examples:

- Slowness or smallness of movements: for example, when told to make the movement bigger, a person with PD may feel the movement is now too big
- Lack of movement: for example, an arm that does not swing during walking
- Changes in posture
- Changes in voice volume: for example, when told to speak louder, a person with PD may feel they are shouting

TIP

Research from the Parkinson's Foundation *Parkinson's Outcomes Project*, the largest-ever clinical study of Parkinson's, suggests that people with PD do at least 2.5 hours of exercise a week for a better quality of life.

CHAPTER TWO

Why Exercise?

Research from the Parkinson's Foundation *Parkinson's Outcomes Project* shows that starting an exercise routine and consistently exercising have positive effects on self-reported health-related quality of life and mobility. It is better to start earlier, but it is never too late.

People with advanced PD who exercise show greater positive effects on health-related quality of life, so it is particularly important to keep exercising and find new ways to facilitate exercise as the disease progresses.

There are two main reasons that exercise is important when you have Parkinson's:

1. In addition to PD, your body is coping with the general effects of aging.
As we age, certain changes occur in our bodies:

- Loss of tissue elasticity (skin wrinkles, muscles can tighten)
- Mineral loss in bones (fractures can occur more readily)
- Loss of muscle mass (muscles are not as toned):
  We lose 1% of muscle mass per year over the age of 60!

If you combine normal, age-related changes with a sedentary lifestyle, you increase your risk of developing cardiovascular disease, osteoporosis, diabetes and cognitive impairment. Without regular exercise, our bodies and minds become weaker, stiffer and more likely to suffer an injury.

2. Research proves that exercise benefits people with PD.
Studies in both animals and humans have demonstrated the brain and body benefits of exercise for people with Parkinson's.

Exercise as Medicine

Ongoing research is clearly showing us that in addition to directly benefiting symptoms, exercise helps the brain compensate for changes that occur because of Parkinson's. Studies have shown that exercise and physical therapy can improve many aspects of Parkinson's by incorporating feedback, repetition, challenge, problem-solving, engagement and motivation. Aside from taking medications on time, exercise is the single most important activity you can do to manage Parkinson's and lead the best possible life.

Reported benefits of exercise include improvements in the following areas:

- Gait and balance
- Flexibility and posture
- Endurance
- Working memory and decision making
- Attention and concentration
- Quality of sleep

And reductions in the following concerns:

- Falls
- Freezing of gait
- Depression and anxiety

Exercise Effects on Cognition

About half of people with Parkinson's experience challenges with what doctors call *executive functioning*, which involves planning activities, keeping a schedule, staying organized and similar tasks. Executive dysfunction can appear as problems with working memory (measured by how many things you can keep track of at the same time) and problems keeping focused on a task and responding to changes.

The parts of the brain that perform executive function tasks are the same ones that help you adapt to changing environments. For example, you use your executive function centers when you go from walking inside the house to walking outside. You also use them when you learn a new skill or improve an old skill.

Aerobic Exercise

It is well-known that aerobic exercise makes your heart healthier and improves how your body uses oxygen. Studies also show that aerobic exercise can improve age-related changes in executive function. Scientists are studying if and how aerobic exercise works to slow Parkinson's disease and what the right "dose" of exercise is to get the best benefits. *(See page 26 for more information on aerobic exercise and examples of exercises you can try.)*

Skill-Based Exercise

Skill-based exercises focus on complex movements of the whole body, such as balance, hand-eye coordination and reaction time. Studies of skill-based exercise have been shown to improve motor function, but so far we don't know if aerobic or skilled-base exercise is better for PD. In fact, the answer may be doing both, especially for targeting cognition. Your physical therapist may incorporate skill-based and aerobic training by having you do exercises with specific goals. An example might be to walk a course through your neighborhood and finish in a pre-set time.

TIP

For more information on Parkinson's effects on thinking and memory, order your free copy of the book *Cognition: A Mind Guide to Parkinson's* by calling our Helpline at 1-800-4PD-INFO (473-4636) or online at Parkinson.org/Books.

Exercise and Neuroplasticity

You know that exercise improves muscle strength, flexibility, bone density and cardiovascular health. But did you know that this same exercise leads to changes in your brain? When you begin a new activity or exercise, your brain – not just your muscles – is *learning* the movements. This process of teaching your brain a new pattern (whether it is a movement, being comfortable in a new place or even learning a way to think) is called neuroplasticity.

Research has measured the following Parkinson's-fighting changes in the brains of animals that exercise:

- More effective use of dopamine by brain cells
- Growth of new blood vessels, which helps brain cells get the oxygen and nutrients they need to stay healthy and participate in the activities of thinking
- Improved use of energy by brain cells (better metabolism)
- Increased release of special proteins that strengthen connections (synapses) between brain cells, and growth of new connections
- Reduced potentially harmful effects of the immune system (less inflammation)
- Growth of new brain cells

All of this contributes to even better effects of the medicines you take to fight Parkinson's. So take advantage of the fact that by doing something enjoyable to make your body healthier, you are also making your brain healthier!

TIP SHEET

Tips

- **When you learn a new exercise skill (like tai chi, boxing, etc.) it helps both how you move and how you think.**
- **There is not one best exercise – you should do aerobic, strength and skill-based exercises to get the best benefits.**
- **Doing a variety of exercises, as well as pushing yourself to get better at the exercises you do, helps your brain cells grow new connections, resulting in learning.**
- **Exercise is a lifelong commitment.**
- **Exercise is medicine!**

Social and Emotional Benefits

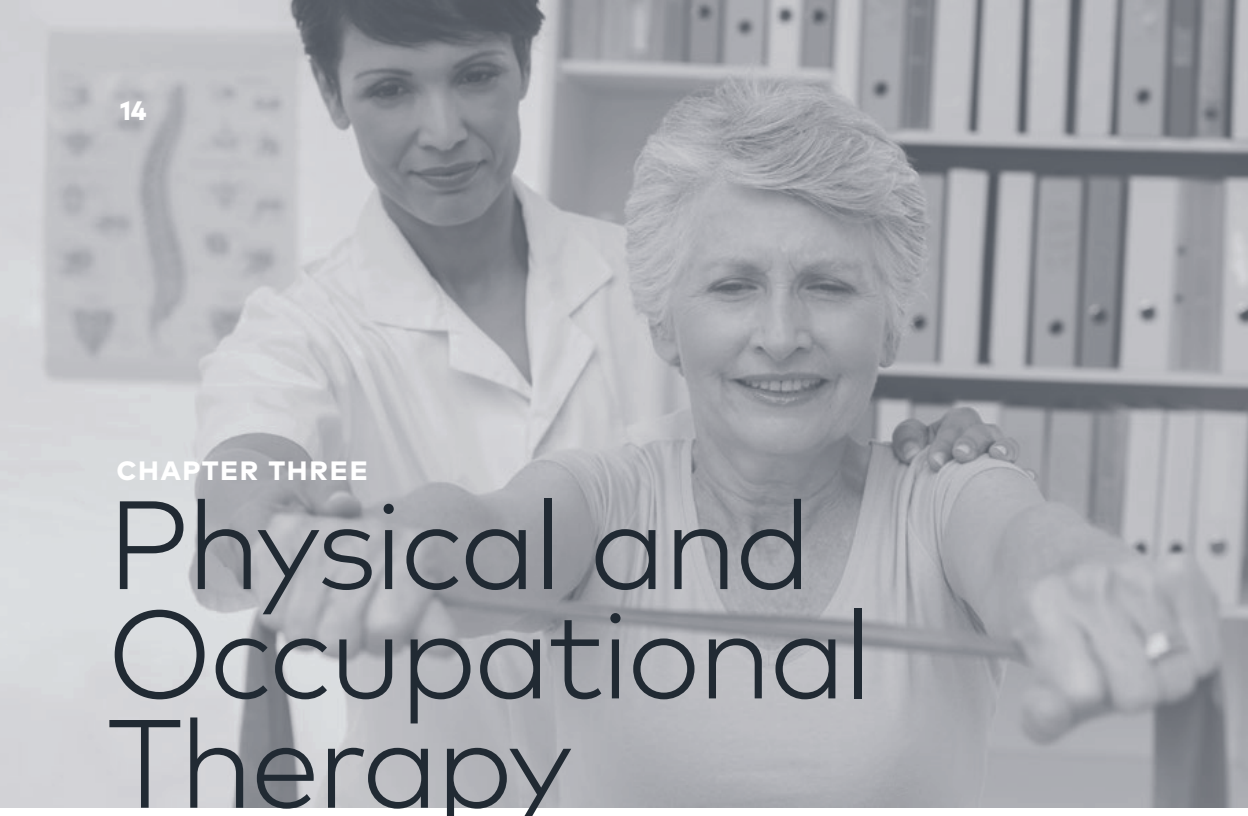
It is important to challenge yourself with exercise, but not to the point that you feel discouraged. Exercise is a daily achievement. You need to believe you can do it and feel that you're accomplishing something for yourself. If you are struggling with motivation or with believing in your own ability, ask your care team, friends or family for help. You might join a group fitness class or ask a friend to go for a walk with you. In this way exercise can provide social and emotional benefits, as well as physical and mental ones. The key is finding exercises and activities that you enjoy that also help you feel and move better.

TIP

Choose an exercise program that you will actually do! Don't design a great, Parkinson's-specific exercise program and then skip it because it is too hard or not fun.

TIP

Mixing exercises that are skill-based and/or aerobic increases the chance of getting both motor and cognitive benefits.



CHAPTER THREE

Physical and Occupational Therapy

Licensed rehabilitation specialists, including physical and occupational therapists, work in a variety of healthcare settings and play a vital role in the fitness and well-being of people with PD.

Physical therapists address balance, strength and range of motion related to a person's functional mobility (e.g., walking, getting in and out of chairs and changing position in bed). They can also design a personalized exercise routine.

Occupational therapists address performance skills related to tasks that occupy a person's time, such as activities of daily living (e.g., dressing, bathing, cooking), work, school, social/communication and leisure activities.

PTs and OTs who work with people with PD can do all of the following:

- Design or modify exercise programs
- Evaluate and treat mobility and walking problems
- Evaluate and treat joint or muscle pain that interferes with activities of daily living (ADLs)
- Help with poor balance or frequent falls
- Teach care partners proper body mechanics and techniques for assisting someone with PD
- Make referrals to movement and exercise programs in the community
- Recommend and teach the use of appropriate adaptive equipment and walking devices

Four Stages of Intervention

Physical and occupational therapy can be helpful throughout your journey with Parkinson's. Interventions generally occur in four stages:

Stage 1: Pre-habilitation
This stage is like prevention. You start working on a problem before you even experience symptoms. Begin an exercise program even if there are no noticeable difficulties with balance, stiffness or movement. You can ask for a referral to a physical therapist as soon as you receive a Parkinson's diagnosis.

Stage 2: Rehabilitation
At this point, you notice symptoms, but you can take steps to fix the problem. Continue your exercise program. Learn how to walk better, get up from bed or a chair, get out of a freezing episode and improve posture.

Stage 3: Preservation
Do your best to make sure you do not lose what you have. Stay active. Join a group, get physical and social and have fun!

Stage 4: Prevention
The stages come full circle. You do not want any new problems on top of existing challenges. Continue your exercise program. Learn about home modifications, care partner training and ways to stay strong.

How to Find a Physical or Occupational Therapist

Many states allow you to go directly to a physical or occupational therapist without a referral from a healthcare professional. However, depending on your health insurance plan, there may be limitations on where you can receive treatment or the number of visits that are covered.

For help finding a physical or occupational* therapist near you, particularly one with experience working with people with Parkinson's, try the options below. Recent research from ParkinsonNet, a collaborative network of medical and allied health professionals in the Netherlands, led by the medical director of a Parkinson's Foundation Center of Excellence, shows that people with Parkinson's who receive physical therapy from a specialized provider – someone with training and experience in PD – receive better benefits and achieve better health outcomes.

1. Call the Parkinson's Foundation Helpline.
Call our toll-free Helpline at 1-800-4PD-INFO (473-4636) or email helpline@parkinson.org to speak with a PD information specialist. When you call our Helpline, you can ask about exercise classes in your area. You can also find out if there is a physical or occupational therapist in your area who has completed our Allied Team Training for Parkinson's (ATTP®) program. This is a special training program for allied health professionals, including physical and occupational therapists, that helps them develop a deeper understanding and appreciation of the skills needed to help people living with PD.

2. Search the American Physical Therapy Association (APTA).
Visit www.apta.org. Click on "For the Public," then "For Patients" and finally "Choosing your PT." The search will note physical therapists who have specialized certifications; choose geriatric or neurological rehabilitation. You can also call 1-800-999-2782.

TIP

Ask for a referral to a physical or occupational therapist with geriatric or neurological experience. Explain that you are looking for someone who has experience working with people with Parkinson's.

3. Search the LSVT Global Directory.
Visit www.lsvtglobal.com to find LSVT BIG-certified physical and occupational therapists. Click on "Find a Clinician," choose "LSVT BIG" and follow the instructions. You can also call 1-888-438-5788. *See page 50 for information on LSVT.*

4. Call your local movement disorders center.
Movement disorders centers in the Parkinson's Foundation Centers of Excellence network are models of the team care approach to Parkinson's treatment. They have physical and occupational therapists on staff or allied health professionals in the community to whom they frequently refer their patients. If the referral is coming from the movement disorders center, it is likely that the provider has experience working with people with Parkinson's.

5. Call the department of physical therapy at the closest university.

6. Call your local hospital.

For a list of questions to ask your therapist to get the best possible care, visit the National Board for Certification in Occupational Therapy (NBCOT) at www.nbcot.com. Click on "Public," then "Why Certification Is Important," and scroll down to "Questions to Ask Your Therapist." These questions are useful as you find the right occupational or physical therapist for you.

* *The American Occupational Therapy Association (AOTA) does not have a general search function for occupational therapists near you on their website.*

TIP

It is ideal for every person diagnosed with PD to begin a fitness routine in the pre-habilitation stage. Data from the Parkinson's Foundation *Parkinson's Outcomes Project*, the largest-ever clinical study of Parkinson's, show that people with PD who start exercising earlier experience a significant slower decline in quality of life than those who start later. If you have Parkinson's and are not yet exercising, speak with your healthcare provider about beginning therapy. Establishing early exercise habits is an essential part of overall disease management. It's never too late to start!

CHAPTER FOUR

What Exercises Should I Do?

The general goals of exercise and physical and occupational therapy are to improve your symptoms and help you do activities you enjoy. Your therapist should design a program in which you practice skills to improve and maintain your mobility. These skills might include walking, balance and maintaining good posture.

Your program needs to push your brain as well as your muscles. Your therapist will help you challenge yourself by trying different exercises, setting goals for improvement and working harder (for example, by increasing repetitions). Scientists believe that learning this way will lead to better brain changes.

Working with Your Therapist

To improve your performance on a routine skill, like walking, your therapist might have you focus on a complex task, like walking while bouncing a ball or counting backwards. This is called dual-task practice, and it can help you target specific mobility impairments. Do you have difficulty getting up from a chair? Your therapist will likely work with you on muscle strength and ask you to practice sitting and standing with seats at different heights. But he or she may also have you perform this task while standing on a balance pad and answering questions.

Here are just a few of the many types of exercise that have been found to help people with PD:

YOGA	TAI CHI	BOXING
TREADMILL TRAINING	DANCE	AEROBIC EXERCISE
BALANCE	STRENGTH TRAINING	
AMPLITUDE TRAINING (MAKING MOVEMENTS BIGGER)		

TIP

Research has shown that everyone benefits from exercise. It is never too late to get started, but talk to your doctor before you begin and before changing the intensity of your exercise program. Also ask for help if you are struggling to stay motivated. Your PT or OT can help you find exercises that are challenging and enjoyable AND lead to improvements in mobility.

TIP

Try something new and different. Don't do the same exercise at the same intensity in the same way all the time.

Deep Breathing

Breathing deeply will help you relax, and relaxing will help you stretch. Do not hold your breath, strain or take shallow breaths while exercising. Shallow breaths overwork the upper chest muscles and upper parts of the lungs, leading to tension and fatigue. Full, deep breaths allow the diaphragm to lower and the lungs to expand deeply. This helps you take in more oxygen with each breath.

Proper Diaphragmatic Breathing

Lying comfortably on your back, place one hand on your chest and one hand on your abdomen.

Take in a slow, full breath (inhale) through your nose, and feel the hand on your abdomen rise as the lungs fill with air.

As you breathe out (exhale) through your mouth, feel the hand on your abdomen lower as your lungs empty.

Massage

Massage therapy has been shown to increase circulation, reduce muscle tension and promote relaxation. It can be particularly helpful if you have problems with rigidity, anxiety and/or stress.

Massage is not a substitute for regular movement and exercise, but it can be a wonderful addition to your overall exercise program. Self-massage and care partner-assisted massage can be helpful. Most drug or department stores sell items such as wooden rollers and hand-held electric massagers that you or your care partner can use.

If you want a professional massage, select a massage therapist who is certified by the American Massage Therapy Association (AMTA). To find one near you, visit www.findamassagetherapist.org or call 1-877-905-0577.

It is important to note that massage services are often not covered by health insurance.

Flexibility Exercises

Regular stretching is the first step in your exercise program, and it can be one of the most enjoyable. Stretching helps you fight the muscle rigidity that comes with PD. It also helps your muscles and joints stay flexible. People who are more flexible tend to have an easier time with everyday movements.

While there are no standard stretching exercises for people with PD, the American College of Sports Medicine and the American Heart Association recommend the following guidelines for everyone:

- Perform at least 10 minutes of stretching at a time.
- Perform stretches at least 3-4 times per week; daily is better.
- Hold stretches for 10-30 seconds.
- Perform 3-4 repetitions of each stretch.

The muscles that tend to become tight in PD are those that bend and rotate the joints. At a minimum, a flexibility program should focus on the following body areas:

1. Chest wall
2. Shoulders and elbows
3. Back of the thighs (hamstrings) and knees
4. Calves
5. Front of wrists and palms
6. Low back and neck

Stretching Tips

TIP SHEET

- **Your stretch should feel like a gentle pull. Do not stretch to the point of pain.**
- **Remain motionless while holding your stretch. Do not bounce while stretching. Bouncing can cause small tears in muscle fibers, and this can actually lead to less flexibility.**
- **Breathe evenly in and out during each stretch. Do not hold your breath.**

STANDING STRETCHES

Chest Stretch

1. Stand facing a corner, placing forearms and hands on each wall.
2. Lean forward into the corner.
3. Keep head up and feet flat on the floor

Back Stretch

1. Stand with feet hip-width apart.
2. Place palms on low back.
3. Gently lean trunk and neck back.

Shoulder Stretch

1. Stand tall with feet hip-width apart.
2. Clasp hands behind back.
3. Gently lift arms up and away from the back, keeping head up.

LYING STRETCHES

Shoulder Stretch

1. Lie flat on your back.
2. If you are using a pillow, place it only under your head, not under your shoulders.
3. Slowly lift your arms straight up and allow them to fall back overhead.

Rotation Stretch

1. Lie on your back with knees bent and feet flat. Arms should be outstretched at your side.
2. Rotate both knees to one side, keeping arms and upper torso flat. Turn head in opposite direction.
3. Repeat, rotating knees in the opposite direction.

SEATED STRETCHES

Neck and Chest Stretch

1. Sit tall in a chair with hands clasped behind back of chair.
2. Allow neck to gently fall back.

Hamstring Stretch

1. Sit tall in chair and place one leg straight out on another chair.
2. Keep toes pointed up, knees flat and back straight.
3. Gently reach for toes.
4. Only reach as far forward as you can without your knee bending.

Rotation Stretch

1. Sit tall with your right arm behind the chair.
2. Reach your left arm in front of you to grab the back of chair or the right armrest.
3. Turn your neck and look over your right shoulder.
4. Repeat on the other side.

Ankle Circles

1. Kick foot in front of you.
2. Move foot in slow, complete circles.
3. Repeat in both directions.

Overhead Stretch

1. Sit tall in a chair and lace fingers together.
2. Turn palms facing out and slowly lift arms overhead.
3. Gently allow neck to fall back.
4. Look up at hands.

Seated Side Stretch

1. Sit to one side of a chair that has armrests.
2. Keep your feet flat on the floor.
3. Reach your right arm down toward the floor.
4. Reach the left arm up and over toward the right.
5. Repeat on the other side.

Aerobic Exercises

Aerobic exercise is any activity that works the heart, lungs and muscles and helps the body burn calories. A range of national and international health organizations, including the Department of Health and Human Services, the American Heart Association, the World Health Organization and others, recommend that most adults get at least 150 minutes per week of moderate intensity exercise, or 75 minutes per week of vigorous exercise.

Data from the *Parkinson's Outcomes Project* confirms that 2.5 hours of weekly exercise is the target amount for people with Parkinson's to lead a better quality of life. This means 30 minutes of exercise five times a week. You can be creative and work around any physical limitations. For example, walk for 10 minutes three times a day instead of one 30-minute walk.

EXAMPLES OF AEROBIC EXERCISE

- Walking, jogging, running
- Swimming
- Dancing
- Water aerobics
- Chair aerobics
- Biking: indoor (stationary), outdoor, tandem or motor-powered (bikes that force movement at higher speeds than one would normally go)

TIP

For maximum benefit in people with PD, research suggests that aerobic activity should be at a moderately-high to high intensity or pace.

Target Heart Rate

Your target heart rate is the range in which your heart should be beating to give you the most benefit during exercise. Your target heart rate is important because it helps determine your fitness level when you start your exercise program and shows you how you are progressing.

CALCULATING YOUR HEART RATE

Calculate your maximum heart rate by subtracting your age from the number 220.

Your target heart rate should stay within 50-85% of your maximum heart rate. Take your pulse every so often while you exercise to make sure you stay within your range.

TARGET HEART RATE AND MAXIMUM HEART RATE AVERAGES

AGE	TARGET HEART RATE (50-85%)	MAX HEART RATE (100%)
30 years	95-162 beats per minute	190
35	93-157	185
40	90-153	180
45	88-149	175
50	85-145	170
55	83-140	165
60	80-136	160
65	78-132	155
70	75-128	150
75	73-123	145
80	70-119	140
85	68-115	135

Caution! If you take high blood pressure medications, be sure to check with your physician before calculating your target heart rate. Certain medications lower your heart rate and will affect your target rate. Also check with your physician if you have a pacemaker or atrial fibrillation.

Strengthening Exercises

Strong muscles are vital to maintaining and improving functional ability. While there are no specific guidelines for strength training in people with PD, muscles can be strengthened at any stage.

Strength training can take the form of lifting weights, using machines at the gym, using your own body weight for resistance or even using common household items like a milk jug filled with sand.

The American College of Sports Medicine and the American Heart Association recommend the following guidelines for everyone:

- Perform at least one set of each exercise, 10–15 times.
- Do strengthening exercises 2–3 days per week (but do not work out the same muscles on consecutive days; muscles need a day to rest before training again).

At a minimum, a strengthening program should include the following muscles, which help to combat posture and strength changes common in PD:

1. Core muscles (abdominals)
2. Thigh muscles (quadriceps)
3. Buttocks (gluteals)
4. Back muscles
5. Back of the arm muscles (triceps)

TIP SHEET

Strengthening Tips

- **Stop any exercise that causes pain.**
- **Concentrate on standing (or sitting) straight while doing the exercises.**
- **Keep movements smooth and even.**
- **Do not grip hand weights too tightly.**
- **Do not hold your breath. Breathe evenly throughout each exercise. As a rule, you should breathe out on the hardest part of the movement, and breathe in on the easiest part.**

STANDING STRENGTHENING EXERCISES

Wall Slides

1. Stand with feet 6-8 inches from the wall.
2. Rest your back and hands on the wall.
3. Slowly bend your knees and slide down the wall.
4. Do not let your knees move past your feet.
5. Hold this pose for a count of 5.
6. Slide back up the wall.

Quad Strengthening

1. Sit tall on the edge of a chair with your arms crossed on your chest.
2. Slowly lean forward and use your legs to push up to stand.
3. Stand for a moment.
4. Slowly lean forward again and lower yourself to sit.

SEATED STRENGTHENING EXERCISES

Shoulder Blade Squeeze

1. Sit tall on the edge of a chair.
2. Open arms out to the sides, fingers spread.
3. Pull arms back and squeeze shoulder blades together.

ON-THE-GROUND STRENGTHENING EXERCISES

Bridge

1. Lie on your back with knees bent and feet flat.
2. Raise hips and squeeze buttocks.
3. Hold this pose for a count of 5, then lower.

Quadruped

1. Begin on hands and knees. Keep your back flat.
2. Reach one arm straight forward.
3. Extend opposite leg straight back.
4. Hold for a count of 3-5.
5. Repeat on other side.

Back Extension

1. Lie on stomach.
2. Lift upper body off surface, supporting body weight on forearms.
3. Hold position for a count of 5-10.

NOTE: Remember, this is not a push-up. Your back muscles should be doing the work, not your arms.

Other Exercises

Yoga

Yoga increases flexibility, breathing and posture awareness and helps with relaxation and stress reduction. Yoga is a self-paced activity, which means that not everyone has to perform a pose in the same way or hold it for the same amount of time. Most poses can be modified depending on your needs. You can even practice yoga in a chair.

Yoga classes and private sessions are held at many fitness centers, senior centers and community recreation centers. Since there are many types of yoga, it is important to contact the instructor or the facility prior to starting a class. Search for an instructor in the Yoga Journal online directory at www.yogajournal.com/directory or the Yoga Alliance, www.yogaalliance.org 1-888-921-YOGA (9642). Finally, there are many books and videos on yoga for people with Parkinson's that you can order or view online.

Tai Chi

Tai chi is an ancient Chinese form of exercise that involves slow, gentle movements, each flowing into the next. Tai chi incorporates posture, mental focus and deep breathing as the body is in constant motion. Research has shown that tai chi can improve balance in people with PD. Many people with Parkinson's also report improvements in flexibility, strength and relaxation after doing tai chi. Fitness centers, senior centers and community recreation centers might offer tai chi classes. It is important to speak with the tai chi instructor to learn if the class will be beneficial for you.

You can learn more about tai chi and other therapies discussed in this chapter from the National Center for Complementary and Alternative Medicine at the National Institutes of Health: www.nccam.nih.gov.

Pilates

The Pilates method focuses on developing strong core muscles to help build strength and teach body awareness, good posture and graceful movement. The exercises can be performed using a floor mat and a variety of equipment. Pilates can help improve flexibility and agility and may also help with back pain.

Classes are often offered at fitness centers, senior centers and community recreation centers. It is important to first speak with the Pilates instructor to learn which exercises are best for you.

To learn more about Pilates or for help locating an instructor, visit the Pilates Method Alliance website at www.pilatesmethodalliance.org or call 1-866-573-4945.

Dance

Dance classes engage participants' minds and bodies in a social environment. Many people with PD who cannot walk well report they can still dance, and dance well! Studies show that dance can help with:

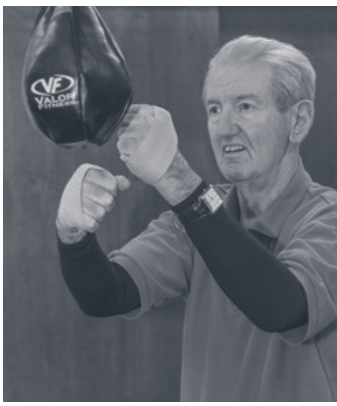
- Balance
- Walking ability
- Balance and walking confidence
- Movement initiation
- Quality of life and sense of well-being

There are many dance options for people with PD, including general dance therapy as well as specific types of dance, such as tango. Dance/movement therapists work with individuals and groups in a variety of settings. To locate a dance therapist, visit the American Dance Therapy Association at www.adta.org or call 410-997-4040.

Two programs that are popular across the country are Dance for PD® and Let Your Yoga Dance®. Learn more and find classes at www.danceforparkinsons.org and www.letyouryogadance.com, respectively.

Boxing

Non-contact boxing, when performed safely and in the proper setting, can be a fun and beneficial type of exercise. Programs like Rock Steady Boxing (which works exclusively with people with PD) provide training to instructors and links to classes in your area. Rock Steady Boxing classes combine many aspects of exercise that are important for people with PD – aerobic, strengthening, balance/agility, and dual-task practice. It challenges both the body and the brain. For more information go to www.rocksteadyboxing.org or call 1-888-217-0577.



*Some centers offer classes for different stages of PD – be sure to ask about which class is best for you.

Certified Personal Trainers

Certified personal trainers generally work at fitness centers, senior centers, private gyms and in the home. Certification is available through a number of national organizations. Make sure your trainer is certified and ask about their knowledge and experience working with people with PD. Working with a trainer is a good way to continue with your exercise routine once you are no longer receiving physical or occupational therapy. Encourage your therapist to review and explain your program to your trainer to ensure a smooth transition.

Music

Many people with PD are aware of the positive effect that music has on them. Now researchers are taking notice of these benefits. Studies show that music can reduce stress, improve breathing and voice quality and promote self-expression. In addition, music therapy can help with many aspects of PD:

- Improving bradykinesia
- Improving movement quality
- Acts as a rhythm for movement
- Improving quality of life

Music therapists work in a variety of settings, and some insurance companies will pay for their services. Music therapists work with individuals or groups through the use of some of the following:

- Singing
- Interpreting music through movement
- Using music for relaxation
- Using music to help initiate movement
- Song writing
- Lyric discussion
- Imagery
- Performing music
- Therapeutic drumming

For more information on music therapy, visit the American Music Therapy Association at www.musictherapy.org or call 301-589-3300.

CHAPTER FIVE

Walking, Turning and Falls Prevention

Problems with walking and balance are common in people with Parkinson's. However, the right combination of exercises and new ways of moving can improve balance, limit or prevent falls and put confidence back into your stride. Most people do not think about their walking. They can walk and talk and carry bags, purses and plates of food without difficulty. Arms swing naturally, and feet land on the heels with each step. Individuals with PD, on the other hand, lose their automatic movements. Feet begin to shuffle, and performing two tasks at once becomes more difficult. Turning becomes challenging, often leading to a freezing episode and sometimes a fall.

NOTE: Freezing of gait is the sudden inability to move the feet. You might feel stuck in place, completely unable to move, or legs may tremble in place.

There are many PD-related walking changes:

- Smaller steps
- Slower speed
- Less trunk movement (especially rotation)
- A narrow base of support (feet too close together)
- Less or absent arm swing (on one side of the body or both)
- Feet that land flat on the floor with each step instead of on the heel (this leads to shuffling, which can cause tripping and/or falling)

Managing Changes in Your Walking

Along with exercise, focusing on each movement helps improve the quality of walking.

TIP SHEET

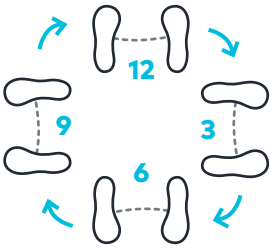
Walking Tips

- **Tell yourself to land heel first. You can do this by thinking of each step as a big kick.**
- **Focus on the size of your steps rather the speed of your steps.**
- **Avoid carrying things while walking. People with PD have difficulty performing more than one task at a time.**
- **The moment you begin to shuffle or freeze, try to come to a complete stop. Take a breath, stand tall and start again, focusing on making that first step a big step.**
- **Stand tall and look out in front of you; do not look directly down at your feet.**
- **Use a cane or walker/rollator if recommended by your therapist or doctor.**

NOTE: The golden rule of using a walking device is this: if you need to reach out and touch furniture, walls or people when you are walking, then you most likely need a device.

Turning Tips

- When beginning a turn from a stopped position, lead with your foot, not your upper body. Planting your feet and turning your upper body frequently leads to a freezing episode.
- If you want to turn right, shift your weight to the left foot and step out with the right foot. To turn left, shift your weight to the right and step out with the left foot.
- Try not to pivot when you turn. Instead, focus on how you lift your feet.



To turn in a small area, or when you are stopped and must turn, try the "clock turn" technique: start at 12:00, take two slow steps to 3:00, etc.

To turn in an open area, use large steps and make a U-turn.

TIP

Individuals with PD must "tell" their feet how to move. By thinking about what you are doing, you use a different part of your brain than the part affected by PD. You re-route the message from the brain to the feet.

Freezing Tips

FREEZE "TRIGGER"	FREEZE REDUCTION STRATEGY
Answering the phone	Never rush to answer the phone. Keep a cordless phone within easy reach. Keep pathways open; rearrange furniture to keep floors free of clutter. Use an answering machine.
Walking onto/off of an elevator, train or bus	Allow everyone else to get on or off first. Announce that you have PD and ask people to be patient. Walk up to the threshold, stop, then focus on stepping over it.
Walking through a doorway	Tell yourself not to focus on the doorway; instead focus on how your feet hit the ground. Guess how many steps it will take to walk from where you are through the doorway, then count your steps as you move through to see how close you were to your guess. Look through the doorway at an object inside, and focus on approaching the object. Walk up to the threshold, stop, then focus on stepping over it. Place colored tape in horizontal stripes in front of and through the doorway, and focus on stepping over the tape. You can also place colored tape on the threshold itself, so you focus on stepping over it. Keep areas around doorways well lit and free of clutter.
Walking in crowds	Try to walk near walls. Take slow, deep breaths and focus only on how your feet are moving, not on the people around you. Alternate between walking a few feet and stopping.
Starting to walk	Stop all movement and take a deep breath. Make sure weight is even on both feet. Visualize stepping over or kicking an object. Shift weight to the side and step with the unweighted foot. March in place before stepping. Have your care partner place their foot ahead of your foot and step to it.

Note: For all strategies in the table above, focusing on the task is important. Rushing, carrying objects, talking with others or even looking away for a moment may limit how well the strategy works.

Falls and Balance

People with Parkinson's are two times as likely to fall compared to the general older population. Once falls begin, they are likely to continue. Falls lead to injuries, fractures, pain and fear of falling. Ultimately, falls can cause a decline in mobility, strength and cardiovascular health – all things to be avoided.

Causes of Falls

- Slowed reaction time
- Freezing of gait
- Leg weakness
- Dizziness
- Shuffling steps that lead to tripping
- Poor safety awareness
- Difficulty doing two things at once
- Balance difficulties

Preventing Falls

A physical or occupational therapist can recommend specific exercises, equipment and techniques to improve balance and mobility inside and outside the home.

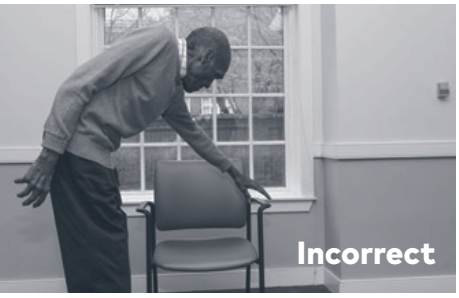
BALANCE EXERCISE

Single Leg Stand

1. Stand with a bed or couch behind you and a sturdy chair next to you.
2. Shift your weight onto one leg, lifting the other leg up for a few counts.
3. Switch to the other leg and repeat.

NOTE: You can hold the chair to steady yourself as needed. To make the exercise more challenging, place two large soup cans or heavy containers on the floor in front of you and try to tap the can/container one or more times with your lifted foot before you put your foot down.

Safe Movement Techniques



Sitting Down in a Chair

When sitting, turn all the way around so that the backs of both legs touch the chair.

Reach back with both arms to slowly lower yourself down.

NEVER reach forward for the chair first and then turn to sit. This can lead to landing sideways on the end of the chair, landing too hard in the chair or missing the chair and falling to the floor.

Standing Up from a Chair

When moving from sitting to standing, do not push yourself straight up out of the chair. This frequently leads to falling back on to the chair. Instead, do the following:

1. Move to the front of the chair.
2. Place legs wide apart.
3. Bend knees so feet are under you.
4. Place hands on chair rail.
5. Lean forward so your weight is on the balls of your feet and your bottom begins to lift off the chair ("nose over toes").
6. Push to stand.

TIP SHEET

Reaching Tips

There are many strategies you can use to make reaching safer.

- Stand in the "power stance" with feet wide apart and staggered. This allows you to shift your weight side to side and front to back.
- Stand directly in front of the object you are reaching for.
- Place one hand on the counter, wall or other stable object while you reach with your other hand.
- Avoid reaching for an object that is farther than arm's length.
- Never lean your center of gravity (near the belly-button area) too far forward. If you reach for an object and your weight moves up onto the balls of your feet or your toes, you are too far from the object.

TIP SHEET

Tips for Preventing Backward Falls

- Avoid stepping backward. Instead, step sideways. Make a safe turn, then walk forward.
- Do not stand directly in front of the oven door, refrigerator door, microwave or other appliance you are trying to open. Instead, stand slightly to the side and use a "power stance," with one hand on a stable surface.

This stance can lead to retropulsion or falls.

This technique is safer. Note the "power stance" position of the feet.

Getting up from a Fall

Begin to bend your knees.

Once your knees are bent and your feet are flat on the floor, reach one arm out to the side.

Reach the arm that was out to the side across your body while allowing your knees to fall over so that you can roll onto your side.

Push yourself up to a side sit.

Push yourself up onto your hands and knees.

Crawl to a sturdy piece of furniture, like a chair.

- Hold onto the chair with both hands.
- Bring your strongest leg up in front of you so that your foot is flat on the floor under your knee.
- Be sure your legs are wide apart.

Push up with your strong leg. Bring your other leg up so that the foot is flat on the floor. Pause here for a moment to be sure you are not lightheaded.

Slowly push your trunk up to stand tall.

General Tips for Preventing Falls

For a complete safety review of your home, contact a physical therapist, occupational therapist or certified aging-in-place specialist (CAPS). You can locate a CAPS by contacting the National Association of Home Builders at 1-800-368-5242.

Recommendations

- Remove throw rugs.
- Keep areas well lit.
- Install grab bars in the bathroom.
- Install handrails on all stairs.
- Avoid clutter.
- Avoid rolling chairs.
- Use nightlights.
- Do not be afraid of change.

When a Fall Occurs

1. Remain calm. Feel and look for any pain or possible injuries before you try to get up. Plan your strategy carefully.

2. Use a heavy piece of furniture to assist you in getting up. If you doubt your ability to safely get up alone, crawl or scoot to a phone and call for help.

3. If you are someone who frequently falls, it is recommended that you enroll in a home emergency response system.

CHAPTER SIX

Posture

Your mother was right. You do need to sit up straight! Even without Parkinson's, it is easy to fall into the habit of bad posture. Many of our daily activities contribute to bad posture:

- **Sitting and watching TV for too long**
- **Leaning over to work on the computer**
- **Sitting for too long while driving or riding in the car**
- **Looking down while reading or texting**
- **Propping your head against the headboard while lying down in bed**

The following tips are helpful for maintaining good posture in all positions.

Sitting

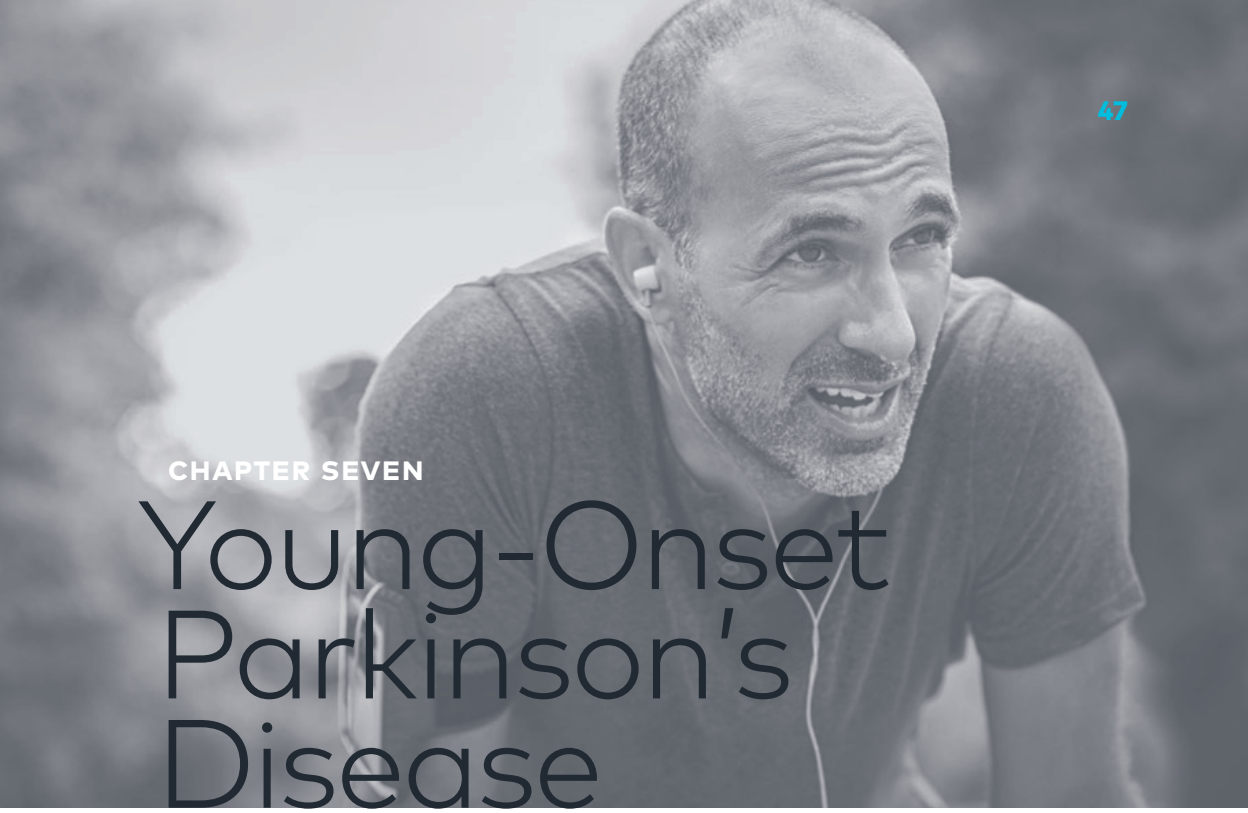
- Sit so that your back is fully in contact with the chair back.
- Use a back support or pillow along your low back, especially for long car and plane rides and in the theater – it will help you to sit tall.
- Keep the computer screen and TV at eye level to minimize neck & eye strain.
- While reading, use a bookstand or rest your elbows on a pillow or a table. This allows you to look directly ahead at the pages.
- When reading in bed, sit with your entire back resting on the headboard, not just your head and neck.
- Maintain eye contact during conversation. This holds the head erect.
- Avoid sitting in chairs without back support or armrests.
- Avoid recliners. They promote rounding of the neck, shoulders and head, as well as tightness in the hips.
- Avoid low, soft couches and chairs. The height of your chair should allow for your hips and knees to be level with one another.

In Bed

- Act like Goldilocks. Avoid using too many pillows or a pillow that is too thin under the head.
- The best position for sleeping is lying on your side with a pillow between the knees.
- Avoid sleeping in a chair. Lie down on a bed to nap.

More Tips

- Perform frequent neck and shoulder stretches to relieve muscle tension.
- Place written reminders on commonly used items like the bathroom mirror, computer screen and television: “STAND TALL.”



CHAPTER SEVEN

Young-Onset Parkinson's Disease

Everyone with PD will experience their disease in different ways. However, individuals with young-onset Parkinson's disease (YOPD) face unique issues relating to employment, body image, children, and long-term planning for finances and health care.

Fortunately, individuals with YOPD generally have fewer functional difficulties early in the disease. This is in part because they tend to have fewer medical issues to deal with as compared to older adults with PD.

If you have YOPD, empower yourself through knowledge, support and exercise. It is important that you begin a fitness routine as soon as possible to potentially slow the course of your disease and limit functional disabilities.

Research shows that:

- younger brains have greater potential for neuroplasticity (brain change)
- when an exercise program is challenging, intense, and works toward specific goals - greater gains are made for those with PD
- seeing a physical therapist seems to be more effective than just performing a generic exercise program
- high intensity biking and treadmill training are safe (once cleared by your doctor), can be easily performed, and can improve gait and balance

Take control of your disease and start a fitness plan now. Do not wait until you start to have pain or problems with your movements to begin taking care of yourself. Your fitness program should also address nutrition, stress management, leisure activities, and time management.

Your ideal fitness routine should:

- be something you enjoy doing
- not add extra stress to your life
- fit in to your daily routine
- challenge you physically and mentally
- include moderate to high aerobic activity, core strengthening, flexibility and balance exercises
- be directed toward a goal or goals

KEY POINT

Remember that simply exercising may not be enough for everyone with PD. Issues related to diminished or lost arm swing will not improve by biking. This is why physical and occupational therapists are so important. Therapists will advise you on what exercise and functional training are best for you to regain or prevent loss of movements.

Appendix

TRAINING THE THERAPISTS AND TRAINERS

This section provides resources for physical & occupational therapists and other fitness professionals. Show this to or copy these pages for your fitness teams.

Parkinson's Foundation Trainings

Allied Team Training for Parkinson's (ATTP®)
ATTP is a unique curriculum in which healthcare professionals from diverse disciplines learn the best techniques in Parkinson's disease care through a dynamic, team-based approach. The interactive training program includes care strategies for all stages of Parkinson's, interdisciplinary training to foster stronger care teams and continuing education credits.

Through online modules and a three- to four-day in-person training, participants receive in-depth knowledge of how to assess and treat persons with Parkinson's disease in an interdisciplinary setting. Trainees practice integrated care planning in teams, using case study vignettes and videos of actual persons with Parkinson's. Trainees practice integrated care planning in teams and meet persons with Parkinson's disease to hear first-hand the impact of PD on people's lives.

Physical Therapy Faculty Program
The Parkinson's Foundation Physical Therapy Faculty Program is an accredited "train the trainer" program improving Parkinson's physical therapy care by training faculty leaders across the U.S. so they can, in turn, educate physical therapy students. This intensive course allows physical therapy educators to immerse themselves in learning the latest evidence-based findings in Parkinson's research and care.

For more information about these programs, call the Parkinson's Foundation Helpline at 1-800-4PD-INFO (473-4636) or visit Parkinson.org/ProfessionalEducation.

Online Courses for Allied Health Professionals
The Parkinson's Foundation offers multi-module online courses for physical and occupational therapists, nurses, and speech-language pathologists and provides continuing education units (CEUs) for course completion.

Boot Camp for Parkinson's Training

The Brian Grant Foundation
Boot Camp training teaches physical and occupational therapists, group exercise instructors and personal trainers how to develop an evidence-based group exercise program. Visit www.briangrant.org for more information.

Other Trainings for Health Professionals

There are many certification programs available for allied health professionals to enhance their ability to care for people with Parkinson's disease, including the following:

LSVT Global: LSVT LOUD® and LSVT BIG®
LSVT Global, Inc. provides specialized training and certification to speech-language clinicians (LSVT LOUD), and physical and occupational therapy clinicians (LSVT BIG) in clinically-proven methods to help improve communication and movement in individuals with Parkinson disease and other neurological conditions. Visit www.lsvtglobal.com or call 888-438-5788 from more information.

PWR!® (Parkinson Wellness Recovery)
PWR! provides training and certification opportunities for physical and occupational therapists and fitness professionals in Parkinson's-specific, learning-principled exercise programs. Visit www.pwr4life.org or call 520-591-5346 for more information.

Information Resources

Association of Physiotherapists in Parkinson's Disease Europe
APPDE initiates and supports knowledge transfer between physiotherapy clinicians, researchers, educators, members of the multidisciplinary team, people with Parkinson's, families, policymakers and healthcare providers to promote best practice physiotherapy for people with Parkinson's across Europe. *Visit www.appde.eu for more information.*

EUROPEAN PHYSIOTHERAPY GUIDELINE FOR PARKINSON'S DISEASE
www.appde.eu/european-physiotherapy-guidelines.asp
This link from their site is particularly helpful for PTs.

TIPS AND TRICKS FOR PEOPLE WITH PARKINSON'S
www.appde.eu/coping-strategies.asp

Glossary

Glossary terms are identified with a blue underline the first time they appear in this book.

A **ADL** Activities of Daily Living

B **Bradykinesia** Slowness of movement

D **DatScan** Ioflupane I 123 injection, also known as phenyltropane, is a radiopharmaceutical agent which is injected into a patient's veins in a procedure referred to as SPECT imaging.

F **Festination** Quick, short steps

Freezing Temporary, involuntary inability to take a step or initiate movement; when it refers to walking, it is called "freezing of gait"

M **Micrographia** Small, cramped handwriting

N **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

O **Orthostatic hypotension** A drop in blood pressure upon changing position from lying down or sitting to standing; also called "postural hypotension" and can cause fainting; when related to a neurological disorder like Parkinson's disease, called "neurogenic orthostatic hypotension," or nOH

R **Retropulsion** The tendency to walk and fall backwards

Index

ABOUT THE PARKINSON'S FOUNDATION

The Parkinson's Foundation makes life better for people with Parkinson's disease by improving care and advancing research toward a cure. In everything we do, we build on the energy, experience and passion of our global Parkinson's community. A wealth of information about Parkinson's and about our activities and resources is available on our website, 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: Parkinson.org/Feedback

YOUR GENEROSITY MAKES THIS PUBLICATION POSSIBLE.

The Parkinson's Foundation is proud to provide this booklet and other educational materials at no cost to people around the globe. If you found this book helpful, please consider a gift so that we may continue to fight Parkinson's on all fronts: funding innovative research, providing support services and offering educational materials such as this publication. Thank you for your support.

DONATE ONLINE: Parkinson.org/Donate

DONATE BY MAIL: Parkinson's Foundation
200 SE 1st St, Suite 800
Miami, FL 33131

DONATE BY PHONE: 1-800-4PD-INFO (473-4636)

TAX ID: 13-1866796

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MIAMI, FLORIDA 33131

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HELPLINE:
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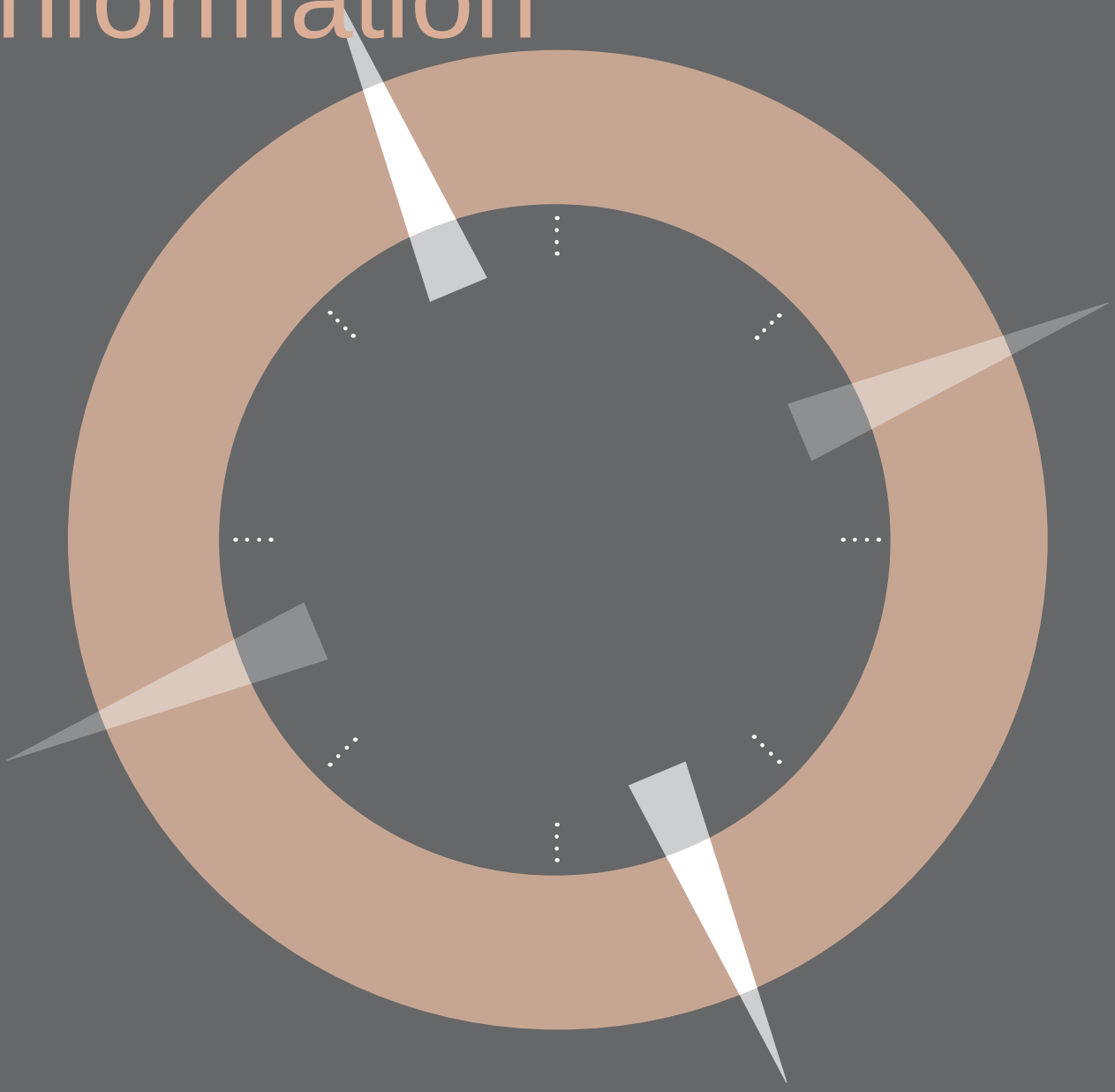
PARKINSON.ORG

PARKINSON'S General Information



Real Talk
for Patients
and Families

Table of Contents

How (and How Not) *to Use This Book*

Every person diagnosed with Parkinson's disease (PD) embarks on a unique journey. No standard trajectory or path exists, and for many, this proves to be among the most challenging aspects of the disease. Since The Michael J. Fox Foundation's earliest days, we have received countless requests from people and families living with PD for candid, trustworthy and understandable information about what to expect as Parkinson's progresses — and for resources to chart the best course.

The goal of this book is to help you anticipate and navigate the clinical, emotional and social aspects of Parkinson's that often correlate with different phases of the disease. It's not intended to impose an artificial timeline upon the course of PD, nor to place a highly individualized disease into abstract categories. Each person's Parkinson's — the particular symptoms, impact and progression — is distinct. There is no way to predict any one individual's path; you and your doctor will get a sense of how it unfolds with time. Recognizing the personalized nature of PD, though, we know that specific symptoms and transitions are more likely to arise at certain times as your life with Parkinson's moves forward. We want to give you the opportunity to face these potential pivot points with extra assurance and identify with others' shared experiences.

We've set out to create a practical and appealing guide, one you and your loved ones will want to read and return to as you go through life with PD. Use it to spark conversations at home or in the doctor's office and refer to it for actionable tips.

As with any resource, take from it what resonates with you and move away from anything that feels overwhelming. Skim the chapters, digest a few pages at a time or scan the patient profiles. Don't read it cover to cover and imagine that a life with Parkinson's has been condensed into a short book. Put it down if it upsets you or you find yourself obsessing over the content, placing labels on your disease or fearing the worst about your Parkinson's. Remind yourself that you have your own version of Parkinson's. Some people prefer to concentrate on the "here and now" of their disease whereas others want to plan for a possible — not inevitable — road ahead. Whichever camp you fall into, this book contains information for you. Focus on what speaks to you.

This guide tries to lend structure to a highly variable disease by painting a broad picture around the most common experiences people tell us they encounter along the way. Remember, you won't have all the experiences in this book. Not everyone will reach the middle or later stages of PD or have the same degree of symptoms.

You'll find the information arranged in the following manner:

» **Getting to Know Parkinson's Disease**: the emergence of symptoms, initial diagnosis and early years of living with disease.

» **Paving a Path with Parkinson's Disease**: the progression of symptoms (to different degrees in different people); perhaps continued adjustment to life with PD; and, for some, when medication is started for symptom management (although this can, of course, be earlier or later).

» **Looking Ahead with Parkinson's Disease**: the advancing years of Parkinson's in which symptoms may be fairly significant and medication complications could be present. Not everyone with Parkinson's reaches this stage; even those who do won't experience everything that's discussed.

People living with PD today have reason for great optimism about their own futures with Parkinson's and that of the entire Parkinson's community. Research is rapidly moving forward, bringing us closer to a deeper understanding of the disease, concrete ways to diagnose and measure PD, better symptomatic therapies and ultimately, a cure. New symptomatic medications are making it through the drug development pipeline to pharmacy shelves. Therapies that could potentially modify the course of disease are in clinical trials. Parkinson's surgical procedures and devices are improving. Options are continually expanding to support you and your ability to live life with Parkinson's to the fullest at every step of your journey.

We hope this guide (and its accompanying website and video suite at michaeljfox.org/PD360) inspires you to get (or stay) actively involved in your care, engage in new ways with the PD community and live well with Parkinson's for many years to come.

HOW THIS BOOK WAS CREATED

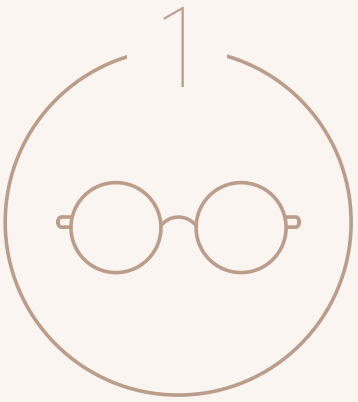
This book and the accompanying multimedia materials arose from conversations that repeatedly identified a need to broaden understanding of Parkinson's disease, including options for living well for those newly diagnosed or navigating new symptoms as the disease progresses, as well as those caring for a loved one with the disease. While we strive to capture the diversity of living with Parkinson's, we know we cannot represent every experience of this complex and varied condition.

Content development was led by Rachel Dolhun, MD, a movement disorder specialist, board-certified neurologist and vice president, medical communications at the Foundation.

We are grateful to Claire Henchcliffe, MD, D.Phil., of Weill Cornell Medicine for her expert medical review of the book and to Karen Jaffe, MD, and Soania Mathur, MD, members of the Foundation's Patient Council, for their evaluation of the book as people living with Parkinson's.

Special thanks to the four members of the Parkinson's community who lent their challenges, hopes, images and journeys with Parkinson's disease to this project: Lisette Ackerberg, Jimmy Choi, Michael S. Fitts and Richie Rothenberg.

Seven Tenets for Life with Parkinson's Disease



There is no "one size fits all" description of Parkinson's disease.

Your symptoms and progression are not like anyone else's. Monitor your own Parkinson's, educate yourself on the disease, and become the top expert on you.

Isolation can worsen symptoms.

You don't have to manage this disease on your own. A team-based approach (including a movement disorder specialist and allied care professionals) can help you stay physically and emotionally strong. Keep open lines of communication with loved ones and consider joining a support group.

Don't settle.

Parkinson's disease varies, and so do treatment options. Designing a regimen that feels comfortable and effective for you will take time and, likely, more than one try. Keep working with your doctor and care team until you get there. Make changes to address progression as needed.

Hone your news instinct.

The latest research is the latest hope, but in our 24/7 media environment, there's a learning curve to interpreting science news. Find experts you trust, seek out credible updates and commentary, and let go of the rest. Being news-savvy can help you maintain peace of mind.

Parkinson's is a non-linear disease.

You can have good days, weeks and months even during trying times. Exercising, eating well and staying involved with your social circle, community and activities you enjoy can have a major influence on your Parkinson's path.

Get engaged.

There are as many ways to contribute to better outcomes for yourself and others as there are people with Parkinson's. Participating in research studies or advocacy, raising funds, starting a blog or support group — however you choose to get involved — can give you a sense of control and help bring us all closer to a world without Parkinson's.

Be prepared.

Parkinson's diagnosis or not, we all face certain issues in our later years. Make sure your family understands your wishes for end-of-life care, and put your will and estate in order. Having challenging conversations at the beginning of your journey with Parkinson's can help lighten the burden as the disease advances.

"I feared Parkinson's most when I least understood it — the early days, months, and years after I was first diagnosed. It seems strange to say it, but I had to learn to respect Parkinson's disease." — MICHAEL J. FOX

01.
Getting to Know Parkinson's Disease

The diagnosis of Parkinson's is life-changing and takes time to process. Everyone works through this in his or her own way, and each approach will be different. Most people are able to keep living in much the same manner as prior to diagnosis — there is no need for sudden career changes or shifts in living arrangements. For many, however, now is an opportune time to plan for the possibility of adjustments in the workplace, at home and in relationships.

The Here and Now:

Parkinson's-related Changes You May Notice in the Beginning

In early Parkinson's, symptoms come to attention and diagnosis is confirmed by a physician, on the basis of three cardinal motor symptoms:

- Resting tremor: a rhythmic shaking that occurs in (typically) one finger, hand or arm when relaxed, and disappears when the appendage is being used
- Rigidity: muscle stiffness detected on examination by a doctor
- Bradykinesia: slowness of movement — may be experienced as reduced walking speed or arm swinging while walking, slowed rate of blinking or decreased facial expression

At the time of diagnosis, bradykinesia plus at least one of the first two symptoms (resting tremor or rigidity) is typically present on one side of the body. Although a resting tremor is the most common symptom at diagnosis, not everyone experiences it. Balance and walking problems — unsteadiness or changes in gait pattern and/or pace — may also be seen early on but, if they do occur, they are more likely to develop in later stages of disease. Dystonia, an involuntary muscle contraction that causes an abnormal sustained posture (such as inward turning of the foot), may be present at diagnosis, especially in younger people, but can occur throughout the course of disease as well.

The diagnosis of Parkinson's is based on a person's medical history and physical examination. No laboratory (blood, urine or spinal fluid) test or brain scan can confirm that a person has the disease. These exams often are done to exclude other conditions that can look like Parkinson's, but they alone cannot make the diagnosis. (Such tests will become possible with the discovery, still under pursuit by our Foundation and multiple research groups, of a so-called "biomarker" — an objective measurement that reveals the risk, presence or progression of disease. A good example of a biomarker is high blood pressure in heart disease.) With that said, in 2011 the U.S. Food and Drug Administration (FDA) approved a new type of brain imaging called DaTscan, which can help physicians evaluate movement disorders including Parkinson's disease. DaTscan can't diagnose Parkinson's on its own, but it can be a helpful adjunct to the clinician's diagnostic evaluation, particularly in differentiating essential tremor (an involuntary shaking of the hands, head or voice) from tremor due to Parkinson's disease or Parkinson's-related disorders.

Non-motor symptoms, which sometimes precede the onset of motor symptoms, also may support the diagnosis. Constipation, smell loss and certain sleep disorders are common, but other potential non-motor symptoms include fatigue, memory or thinking problems, and mood disturbances, including depression. A few people won't experience any non-motor symptoms, but most encounter one or more over the course of their disease.

In the earliest years, symptoms (with the possible exception of fatigue or depression) may not significantly interfere with your work or physical or social activities. Because of this, and the fact that the available Parkinson's medications ease symptoms but don't alter the underlying disease process, many patients feel medications are optional for them during this time. Nonetheless, everyone experiences symptoms differently and when they impact quality of life — regardless of how long it's been since diagnosis (one day, one year or one decade) — medications should be considered. Don't save medication for a later date because you fear it may stop working or believe that the sooner you start, the sooner you'll have complications. While these concerns are understandable, not everyone experiences them and they are due to a complex mix of factors.

Since Parkinson's disease is unique to each individual, the rate and extent of its progression will vary from person to person.

"IT'S THE MIDDLE OF SUMMER. WHY DID YOU ASK IF I'M COLD?" *"YOUR HAND IS SHAKING."*

Michael S. Fitts looked down at his hand and back at his friend. "Yeah, that's been doing that every now and then."

Michael's journey to diagnosis proved to be a frustrating one. He often sat at his computer, researching his mysterious symptoms. At first, his primary care physician shrugged off the concern of the otherwise healthy man in his late 30s. A referral to a neurologist finally led to his Parkinson's diagnosis.

Unlike many people with Parkinson's, Michael found medication necessary early on to manage his symptoms, but the right treatment proved elusive. A first therapy left him feeling "out of his mind." He experienced depression to the point that he was unable to get out of bed for work each morning. He worried about becoming a burden to family.

He found a support group, but at first that was a tough fit too. He sat in his first meeting feeling like the odd one out, the only patient without white hair and the only African American. But he kept attending, and now he credits the group — along with his church and family — with helping him stay engaged with favorite hobbies, such as photography, and forge connections within the Parkinson's community. Now he has made it his personal mission to introduce Parkinson's resources to people of color who often go undiagnosed or undertreated.

WATCH MORE OF MICHAEL'S STORY AT
MICHAELJFOX.ORG/PD360.

Emotional and Social Aspects:

What People with Parkinson's Say It Feels Like Early On

In many ways, the emotional aspects of receiving a Parkinson's diagnosis may be more profound than the earliest clinical symptoms, which typically are highly manageable.

Prior to diagnosis, uncertainty and anxiety are common. Symptoms may be attributed to normal aging or other medical conditions, such as arthritis or a sports or overuse injury. During this time, you might have been hiding symptoms and concerns from family and friends so they wouldn't worry. Learning that in fact you have a chronic, progressive disease can feel abrupt, if not surreal.

» For some, the diagnosis — having an explanation for their symptoms — brings a sense of relief. Others experience shock and disbelief. Those who are younger or lack a family history of PD may have more prominent denial and doubt responses. People who have maintained healthy lifestyles may wonder how Parkinson's is even possible when they "did everything right."

» Anxiety about unexplained symptoms can transform into worry about what a future with PD looks like. Feelings of depression may arise in reaction to diagnosis, but these also can be clinical symptoms of Parkinson's. Depression is treatable but can be hard to recognize when you're going through it. Pay attention to what you hear from your family and friends — they may see changes in your mood or behavior before you do.

» Many people report feeling a sense of loss — a loss of control, and a mourning for what the future could have been — dreams, aspirations and events yet to come. At the same time, they may withdraw, either purposely or unintentionally, from social activities and interactions.

Most people probably go through a combination of feelings and responses. Adjusting to and accepting a diagnosis of Parkinson's can seem overwhelming. But Parkinson's disease is not a death sentence. Most experts would say people die with, not from, PD. It is entirely reasonable to expect many of the years with Parkinson's to be as happy and productive as what came before. As patient authors of an early Michael J. Fox Foundation guide for the newly diagnosed wrote: "The initial reactions to diagnosis are stepping stones on the way to acceptance. When acceptance is reached, many look back at the period after diagnosis and realize that they were living in fear of a tragic future that never materialized."

At this stage you also may grapple with decisions about disclosure — how, when and whom to tell about the diagnosis. If you are undecided about sharing your Parkinson's diagnosis, consider outlining a strategy in advance. Having a solid plan in place for deciding whether and when to disclose, delivering your news and navigating possible responses will allow you to be proactive and control the flow of communication. Taking time to consider your various "audiences" — family members, friends and professional colleagues — can help you find a comfortable way to integrate Parkinson's into the different areas of your life.

Young-onset Parkinson's disease (YOPD) — usually defined as diagnosis at age 50 or younger — may prompt additional considerations about how to handle ongoing obligations to a workplace or young family. (See sidebar, Young-onset Parkinson's Disease, page 15.)

ACTIONS TO CONSIDER NOW

1 Learn about Parkinson's disease.

Information is the best antidote to worry. With knowledge about the disease, available treatment options and ongoing research, you can better evaluate your own symptoms, find the right clinician(s) and develop a treatment plan tailored to your needs. Some people are satisfied with only the basics (or less); others want to wrap their arms around everything there is to know. No matter where you fall on this spectrum, ask your doctor and other people with Parkinson's which sources of information they have found to be the most useful, credible and reliable. Give yourself permission to avoid sources that leave you feeling doubtful, fearful or anxious. And remember: No one else knows exactly how your particular Parkinson's journey will unfold.

REMEMBER TENET #4:
HONE YOUR NEWS INSTINCT.

2 Build a flexible support system that reflects what you need now.

Different people gravitate to different kinds of support (one-on-one vs. group settings, sharing vs. observing, in-person vs. online). Support systems can evolve over time but they are usually a mix of family, friends, healthcare professionals and, in some cases, paid caregivers, each of whom can be called on as needed at various points in your course with Parkinson's.

3 Assemble the care team that's right for you.

It can be very helpful, at least at the time of initial diagnosis, to see a movement disorder specialist (MDS). Even if you love your primary care physician or general neurologist, seeing an MDS intermittently throughout the course of your Parkinson's disease can be valuable. Because they see more people with Parkinson's, specialists are more attuned to optimizing a care regimen and aware of cutting-edge research that may benefit you. A movement disorder specialist also can help you assemble a care team tailored to your specific needs. For example, if you are having trouble with walking, balance or falls, you might be referred to a physical therapist; home safety issues might lead your doctor to order an occupational therapy home visit; speech therapists can help alleviate voice problems that affect communication; a social worker can help identify supportive resources in your community.

THINK ABOUT TENET #2:
ISOLATION CAN WORSEN SYMPTOMS.

4 Participate in clinical research.

While you may not have given much (or any) thought to clinical trials before diagnosis, research participation is an especially important consideration during the early years of Parkinson's. Trials focused on disease modification or biomarker identification, in particular, often need recently diagnosed individuals who are not yet taking medication. The world of clinical research has expanded to include not only traditional trials at clinical centers but also many opportunities to participate virtually, through online portals, smartphone apps and wearable devices. You'll find lots of information to get started in our Clinical Research Participation Guide at michaeljfox.org/PD360.

5 Consider the pros and cons of genetic testing.

Our Foundation often fields questions

"I had to build a new life when I was already pretty happy with the old one."

— MICHAEL J. FOX

from people with Parkinson's on genetic testing (learning whether you carry genetic changes correlated with increased risk for Parkinson's disease). While genetic testing isn't routinely performed during the evaluation and management of PD, it is an integral part of Parkinson's research and drug development. At the current time, having a PD-associated genetic change won't alter your course of treatment. It may, however, encourage you to make — or continue — healthy lifestyle changes and connect with clinical trials. (Several genetic trials are ongoing and more are expected to begin within the next few years.) As a part of this collective, your information can be invaluable: An increased understanding of Parkinson's genetics have informed the majority of research breakthroughs made in the past decade. Genetic testing (with the specific goal of learning this information) and genetics research are two different things, though, and if you choose to participate in the latter but don't want to know your status for personal or family-related reasons, you can choose not to.

Thinking about delving into your genetic makeup may stir up emotions for you and your family. Talk with your doctor and a genetic counselor about these feelings as well as what Parkinson's genetic testing can and can't tell you. Ask about the presently available options for testing — through your provider's office, an online service or participation in a clinical trial, — the cost (if any) to you, and what the results could mean for you and your family. Find a fuller discussion of Parkinson's genetics and information about genetic trials at michaeljfox.org/PD360.

6 Exercise regularly.

Exercise offers benefits for everyone. In Parkinson's specifically, exercise can help sustain mobility and motivation, and improve overall well-being and quality of life. Group exercise can foster social interactions and a sense of community, too. No single form of activity is universally recommended — many types of exercise, at both high and low intensities, done alone or with others, are beneficial for people with PD. The best exercise is the one you will do regularly, so choose something you like and will stick with. To learn about exercises that are popular among people with Parkinson's and may target specific symptoms, check out our Exercise Resource Guide at michaeljfox.org/PD360.

7 Eat well.

Just as our activity levels impact general health and well-being, so does what we eat. Doctors encourage people with Parkinson's to follow a well-balanced diet — one rich in vegetables, fruits and healthy fats (found in foods like nuts, avocado and olive oil). Other than that, no specific diet is recommended for Parkinson's. Once medications are started, though, some considerations around diet may be necessary. (Learn more on page 42.)

Young-onset Parkinson's Disease

Young-onset Parkinson's disease (YOPD) is generally defined as Parkinson's diagnosed at age 50 or younger. (Average age at diagnosis is around 60.) Distinctive features of YOPD are related to:

Cause.

For every individual with Parkinson's, genetics and environmental factors likely contribute to different degrees to cause disease. In younger people, especially those who have multiple family members with Parkinson's, genetics may play a larger role. If you have YOPD (and particularly if you have a family history of Parkinson's), you might consider genetic testing to see if you carry one of the known mutations that increase risk of PD. Discuss this testing with your family, doctor and genetic counselor — the results might not only be of personal interest to you and your family, they also could offer valuable insights to the Parkinson's research community. (Read more about genetic testing in Actions to Consider Now, page 12.)

Path to Diagnosis.

The diagnosis of YOPD may be missed or delayed — physicians and younger people are not typically expecting Parkinson's, and early PD symptoms, especially arm or shoulder stiffness, often are attributed to arthritis, sports injuries or other medical conditions. Attaining a diagnosis may bring feelings of relief, but those with YOPD may be vulnerable to feelings of stigma and alienation. Parkinson's is commonly viewed as an "older person's" disease, and younger adults' symptoms are more likely to be misinterpreted or misunderstood in the day-to-day.

Symptoms and Progression.

People with YOPD are less likely to experience balance problems or considerable memory and/or thinking problems (dementia), but are more prone to dystonia — an involuntary muscle contraction that causes an abnormal sustained posture, such as inward turning of the foot. In general, symptoms of YOPD tend to progress more slowly over time.

Medications and Side Effects.

Younger people may delay starting medication and/or begin with drugs other than levodopa, especially if symptoms are mild. This is in part because they are more likely to encounter dyskinesia — involuntary, uncontrolled movements, often writhing or wriggling — as a complication of long-term levodopa use combined with prolonged course of disease. Treatment instead may begin with an MAO-B inhibitor, amantadine, a dopamine agonist or, when tremor is particularly prominent, an anticholinergic drug. (Learn more about Parkinson's medications on page 42.)

Special Considerations.

» Career/Employment.
Whether and when to share a diagnosis in the workplace are nearly universal concerns. (For more on this topic, check out our guide to disclosing a PD diagnosis at work at michaeljfox.org/PD360.) Depending on specific symptoms and occupation, many people are able to continue working for a significant period of time. Regardless, having a back-up plan, which could include changing schedules or even careers, or seeking early retirement, is worthwhile.

» Finances.
Financial planning may take on a new light, especially factoring in regular doctor visits and medications. It's a good idea to explore long-term care insurance and disability options, even though they may never become necessary.

» Family Planning.
Although the data on pregnancy and PD is limited, plenty of women with Parkinson's disease have successfully carried healthy babies to term. The use of birth control pills doesn't exclude one from taking any PD drugs, but doses may need adjustment. Couples living with Parkinson's might therefore wish to consider other forms of contraception.

» Parenting.
Parents may worry about caring (both physically and financially) for young children, whether their children are at increased risk for developing the disease, and how to tell them about the diagnosis. Parents in the MJFF community have found it helpful to convey the facts using words directed to the child's level of education, express optimism where possible and offer reassurance on the situation.

Motor and non-motor symptoms may pose logistical challenges when raising children. It may be useful to establish a group of family, friends and neighbors who can help when necessary — such as with babysitting or carpooling — and think about restructuring household roles and responsibilities.

People in midlife may find parenting issues compounded if they are part of the "sandwich generation," caring for or supporting their own parents as well as their children. Social workers can be a good resource to lay out options for these types of situations.

» Relationships and Marriage.
Parkinson's can impact relationships with significant others and spouses. Talking openly and honestly about present and future concerns, as well as addressing symptoms and issues (especially those related to sexual health) as they arise, can be helpful. Cooperation and flexibility — important in any partnership — become even more critical when managing life with Parkinson's together.

02.
Paving a Path with Parkinson's Disease

You may be well into your journey with Parkinson's, but could feel as though you're blazing your own trail. Parkinson's is uncharted territory for every individual; it comes without a map to follow or a standard timeline of progression to refer to. PD can be an unpredictable daily companion. It may require you to "roll with the punches" or take your life in directions you may not have planned. But while nobody would ever ask for the diagnosis, many with Parkinson's reflect positively on the relationships it fosters and opportunities it reveals that otherwise would not be possible.

The Here and Now:

Changes You May Notice as Disease Unfolds

After living with Parkinson's for a while, your symptoms might be affecting some of your physical activities, social interactions or work.

It may be that stiffness and slowness are making morning routines more challenging, or your tremor might be too pronounced to hide, leading you to feel self-conscious. Or, walking and balance problems may develop or intensify. Non-motor symptoms, such as constipation or mood changes, may appear or become more pronounced, even aggravating motor symptoms or impacting the effectiveness of treatments for them. (See sidebar, Non-motor Symptoms of Parkinson's, on page 24.) On the other end of the spectrum, symptoms could be highly manageable and have no significant effect on any part of your life.

If symptoms, for whatever reason, get in the way of doing what you want or need to do, taking medication is an option. Which medication to begin and when are personal decisions that should be made in conjunction with your doctor. A wide variety of Parkinson's drugs exists to choose from; figuring out the ideal one(s) often requires time and effort on the part of both the patient and physician. There is no one-size-fits-all approach. You and your doctor should take into account your symptoms, age, any medical needs and prescriptions you may have outside of Parkinson's, work situation (if applicable) and unique life circumstances, alongside potential benefits and side effects of PD medications.

REMEMBER TENET #3:
DON'T SETTLE.

Almost any of the Parkinson's medications can serve as an initial therapy. For mild symptoms, many people opt for an MAO-B inhibitor, amantadine or an anticholinergic, whereas others elect to start levodopa or a dopamine agonist. Regardless of which drug is chosen, it is prescribed at a low dose and increased slowly until benefit is seen, intolerable side effects occur or a set target dosage is reached. (See the Guide to Medications for descriptions of these and other PD drugs, on page 42.)

If MAO-B inhibitors, amantadine and anticholinergics are no longer adequate for symptom control, levodopa or a dopamine agonist (or increased dosages if they are already being taken) becomes necessary. These drugs can be taken on their own or in combination with other Parkinson's medications, including each other. As disease progresses, medication regimens often must be adjusted to address evolving non-motor and motor symptoms as well as any drug-associated complications that appear. Over time, levodopa may seem less effective: Individual dosages may fail to kick in, gradually wear off before the next dose is due, or stop working unexpectedly, leading to more "off" time (periods when symptoms are not optimally controlled). Levodopa also can contribute to dyskinesia, which are uncontrolled, involuntary movements, often writhing or wriggling in nature.

If significant "off" time and/or dyskinesia occur, a variety of management options may be relevant. These include modifications of the drug regimen, enrollment in a clinical trial testing a therapy for these symptoms or deep brain stimulation (DBS) surgery. Many people with moderate Parkinson's have experienced a dramatic improvement in symptoms and quality of life after DBS. While this therapy can make a real difference, it is not for everyone, and even good candidates for the procedure still must grapple with the significant decision of whether to undergo invasive treatment. (Find a deeper discussion of DBS on page 36.)

Medical and surgical therapies remain only one component of a Parkinson's treatment program. Regular exercise is a crucial part of the management strategy, especially as symptoms progress. Physical activity and dietary adjustments can help lessen symptoms and maximize medication benefits. (See: Actions to Consider Now on page 22.) Some people also find non-pharmacological interventions, including complementary and alternative medicine, to be helpful in managing their disease. (Check out our Guide to Complementary and Alternative Medicine on page 46.)

"BEING OPEN AND BEING ABLE TO TALK ABOUT PARKINSON'S IS REALLY ALSO A PART OF HEALING."

Jimmy Choi runs across the marathon finish line. As he walks toward the volunteers handing out medals and water, his body begins to register the nearly four hours of exertion he's undertaken. But running is when Jimmy, who has lived with Parkinson's disease for 13 years, feels most in control.

His athletic ability stands in contrast to his everyday challenges, from buttoning shirts to opening jars. Regular visits to his movement disorder specialist help him manage medications so that "off periods" are shorter and he is more productive during the day. His sleep averages four to five hours a night — "very light sleep," he notes ruefully.

When he was diagnosed at 27, Jimmy shared his condition only with his wife Cherryl and a handful of family members. His physical activity slowed, he gained weight and he began walking with a cane. One day while carrying his infant son, he tumbled down the stairs. Only Jimmy suffered bruises, but he knew it was time to make a change. He began walking, then running, and soon entered his first 5K race.

Today, Jimmy has completed 12 marathons, 76 half marathons (and counting), along with countless shorter races in support of research efforts, the PD community and his own well-being.

WATCH MORE OF JIMMY'S STORY AT
MICHAELJFOX.ORG/PD360.

Emotional and Social Aspects:

What People with Parkinson's Say It Feels Like Over Time

Life with Parkinson's disease can be an emotional rollercoaster.

As symptoms begin to impact social, occupational or physical activities, you may relive emotions you experienced when you were first diagnosed. Starting medication can trigger a wave of new feelings and a jarring recognition that Parkinson's will remain with you for the rest of your life.

As medication begins to take effect and symptoms ease, though, many people report regaining a sense of control and empowerment. Those who have been hiding their diagnosis now may feel ready to share their news within and outside of immediate family and close social circles. Many go further, taking on an active role in the Parkinson's community. This may mean telling their story to lessen stigma and others' fears about disclosing a diagnosis, getting involved in policy and advocacy, participating in clinical trials, or launching a community fundraiser to support research or patient service organizations. Pre-eminent journalist — and Parkinson's patient — Michael Kinsley calls this the "confrontation" approach, but admits he prefers denial: "If you're ever entitled to be selfish, I thought (and still think), it's now. So I see good doctors, take my pills most of the time, and go about my business. I couldn't tell you some of the most basic things about Parkinson's and how it works."

Regardless of how involved you wish to be in your local Parkinson's community, technology has created a host of opportunities to discuss your experiences, connect with others like you (in online support groups, for example), track symptoms and progression, and contribute to Parkinson's research (through smartphone apps and web-based clinical trials). As you enter new communities and forge new partnerships, online or in real life, it's not out of the ordinary to discover yourself assuming new identities and your previous relationships changing shape.

Parkinson's symptoms may or may not interfere with your occupation at this stage, but the potential for this is a common concern, especially among those with young-onset PD. Questions of if, when and how to tell an employer and coworkers about a diagnosis invariably arise. (Check out our guide to disclosing a Parkinson's diagnosis at work at michaeljfox.org/PD360.) These are personal decisions based on many factors. Although there is no obligation to bring Parkinson's into the workplace, the stress of hiding it can exacerbate symptoms, and those who reveal their diagnosis often say they wish they'd done it sooner. A general understanding of the Americans with Disabilities Act (ADA) may be useful should accommodations be required to keep working in the future. Like most massive works of policy, the ADA unfortunately doesn't lend itself to skimming; seek out books or knowledgeable people who can help you make sense of the legislation and get what you need out of it. In short, the ADA protects those who are "disabled," inform their employers of such and request a "reasonable accommodation" to continue performing their job satisfactorily. The determination of disability is made by individual states according to federal guidelines and requires that a person be impaired in a way that affects daily life. Not everyone with Parkinson's, especially those in early and mild stages, will meet the criteria.

Even when current employment status can be maintained — irrespective of disclosing diagnosis — it's wise to have an alternate plan, whether that means adjustments to your schedule, a change of jobs or early retirement.

CONSIDER TENET #6:
GET ENGAGED.

"Sure, Parkinson's may be one step forward and two steps back, but I've learned that what is important is making that step count." — MICHAEL J. FOX

ACTIONS TO CONSIDER NOW

1

Modify diet for optimal medication effectiveness.

Once medication is started, dietary modifications may be required to ensure those medications work optimally and to avoid interactions between drugs and certain foods. Levodopa competes with dietary protein for absorption in the small intestine, so taking it with a high-protein meal may reduce how much of the drug gets into your system and how well that particular dose works. When disease is mild, levodopa typically doesn't require separation from meals, but in later stages this may be beneficial. MAO-B inhibitors increase tyramine, and combining them with foods high in tyramine — usually aged cheese and cured meats — could raise blood pressure. These foods don't need to be eliminated from the diet altogether, but should be eaten only in moderation.

2

Continue exercising and adapt as necessary.

As Parkinson's progresses, exercise becomes even more important. Physical activity, along with regular stretching, can lessen motor and non-motor symptoms. Exercise can help to maintain or improve general movement and flexibility, decrease stiffness and improve coordination, gait and balance. It also can ease depression and anxiety, enhance sleep and lessen constipation, apathy and fatigue. Both independent and group activities are beneficial, but the latter has the added benefit of social interaction and even a support system. For examples of exercises that many people with Parkinson's engage in, check out our Exercise Resource Guide at michaeljfox.org/PD360.

3

Add allied healthcare services as needed.

In addition to regular exercise, structured therapy programs designed for people with Parkinson's can help you target specific symptoms. Lee Silverman Voice Treatment (LSVT) BIG physical therapy concentrates on gait and balance issues. SPEAK OUT! and LSVT LOUD speech therapy programs can help counteract loss of vocal volume and clarity. Occupational therapy focuses on ways to help you more easily and safely perform regular daily activities, such as bathing and dressing.

4

Manage financial affairs.

At a certain age it becomes well-advised for everyone to put his or her financial house in order. With that said, living with a chronic disease can add complexity to this process and interfere with your peace of mind. Conferring with a financial planner, accountant, attorney or other professional adviser can help ensure that you and your family have a solid plan in place to meet whatever financial needs may arise.

Non-motor Symptoms of Parkinson's Disease

Not everyone experiences all non-motor symptoms, but over the course of disease (and even before diagnosis) you may live with one or more. Each non-motor symptom can be present at different times and to different degrees.

Sleep disturbances frequently are experienced by people with Parkinson's. Motor and non-motor symptoms, side effects of some Parkinson's medications and conditions associated with PD — restless legs syndrome and REM sleep behavior disorder — can cause difficulty falling asleep, staying asleep or both. **Restless legs syndrome** (RLS) is an uncomfortable sensation in the legs, occurring mainly at night, which resolves only with moving the legs or walking. It may be caused by Parkinson's, the medications used to treat it or a separate medical condition (low iron levels, for example). **REM sleep behavior disorder** (RBD), which often precedes the onset of motor symptoms and diagnosis of PD, causes a person to act out dreams because the normal suppression of muscle activity is impaired. Those with RBD may kick, punch, yell or get out of bed unknowingly during sleep. If RBD poses a safety risk or interrupts a person's or their partner's sleep, Klonopin (clonazepam) or melatonin (an over-the-counter hormonal supplement) is typically recommended. For other sleep disturbances, treatment is targeted at the underlying issue. If nighttime motor symptoms or restless legs are a problem, Parkinson's medications may be adjusted. If depression interferes with sleep, an antidepressant may be prescribed. To maximize sleep in general, it's recommended that you exercise regularly (but not too close to bedtime) and keep a regular schedule where you go to bed and wake up at the same time every day.

Mood disturbances are likely due to both brain chemical changes caused by PD and reactions to physical and mental symptoms of Parkinson's. **Depression** may cause decreased mood and energy, as well as less interest in previously enjoyable activities. Treatment options include counseling and/or antidepressant medications; regular exercise often is beneficial as well. Most antidepressants can be used in conjunction with any of the available Parkinson's medications, but dosages may need adjustment if MAO-B inhibitors are taken concurrently. **Anxiety** can occur on its own or accompany depression. It might cause uncontrollable worry or feelings of restlessness or being "on edge." A relatively stable level of anxiety often can be managed with antidepressants and/or talk therapy, but for sudden spells of anxiety or panic attacks, anti-anxiety medications, such as benzodiazepines, are sometimes prescribed to use as needed.

Fatigue and **excessive daytime sleepiness** may be a product of sleep and/or mood disturbances, but can be distinct non-motor symptoms of Parkinson's or medication side effects. Treatments may include limiting medications that can cause daytime drowsiness, such as dopamine agonists. In some situations, sedating medications may be added to induce sleep at night or stimulant-type medications prescribed to increase alertness during the day. A strict schedule with a regular bedtime, daytime activities and avoidance of napping (or restriction to short scheduled naps in the early afternoon) is helpful but can be difficult to stick to.

Constipation is part of the underlying disease process. It can predate a diagnosis and worsen as disease progresses. Not only is it uncomfortable, it also can impact medication absorption and effectiveness. Constipation can be decreased with exercise and dietary modifications, such as adding fiber and probiotic-containing foods, increasing water intake and drinking warm liquid in the mornings to stimulate bowel movements. In some cases, stool softeners, laxatives and/or prescription medications are necessary. Certain medications — anticholinergics and opioid pain medications, for example — can cause constipation, so it is worthwhile to review your list of prescribed medications and make changes where possible.

Low blood pressure when changing positions, or orthostatic hypotension, can be due to Parkinson's and/or the medications used to treat it. It causes lightheadedness, dizziness or fainting. Regular exercise (without excessive sweating) and certain dietary adjustments — increasing fluid (namely water) consumption to six to eight 8-ounce glasses per day and salting

food (if heart and kidneys are healthy); avoiding hot or alcoholic beverages; and eating multiple small meals throughout the day (rather than three large ones) — may help. When dietary and lifestyle adjustments aren't enough, drugs may be prescribed to treat orthostatic hypotension. (Read more in the Guide to Parkinson's Medications, page 42.) Some medications — such as diuretics (fluid pills), bladder medications and certain antidepressants — can contribute to low blood pressure and should be decreased or discontinued if possible.

Speech disturbances may include changes in the rhythm, rate, tone and/or volume of speech. Words could become slurred or mumbled. Speech therapy programs can teach exercises and tactics to help you speak louder and clearer and certain devices can improve or amplify communication. Some provide a stimulus to alert you when vocal volume decreases; others feature microphones or tablets for writing or pointing to letters, numbers and symbols.

Drooling may occur in some people in the later stages because saliva is swallowed less frequently. It can be embarrassing and prevent social engagement. Management options may include postural adjustments (keeping the chin up and mouth closed), sugar-free hard candy (to stimulate swallowing), or botulinum toxin injections (Myobloc or Botox) into the salivary glands or prescription medications to decrease the production of saliva.

Cognitive impairment, a disturbance of memory, thinking and/or language abilities, varies widely in Parkinson's, but generally manifests differently from the memory loss and confusion associated with Alzheimer's disease. It primarily impacts what are known as "executive skills" (organizing, planning, problem solving, etc.), but also can affect attention and concentration,

visuospatial function (interpreting where objects are in space), and, to a lesser extent, short-term memory. It can lead to slower thought processing, trouble finding words or difficulty multitasking. Cognitive problems can range from subtle changes detectable only on formal clinical testing to mild problems that are more than expected with aging but that don't interfere with daily activities (mild cognitive impairment) all the way to significant problems that affect everyday routines, job performance and/or social activities (dementia).

Mild cognitive problems don't always worsen, but if they do, it is more likely to happen in the later stages of Parkinson's. No medications are currently available to treat mild cognitive symptoms, but there is some evidence to support the idea of "exercising your brain" to maintain cognitive fitness. Take an expansive approach: Attending a get-together where you'll have to remember the names of new acquaintances and make sparkling conversation about current events can be every bit the cognitive workout a crossword puzzle is, and has the added benefit of keeping you social. Regular exercise and a healthy diet also are recommended for brain health. (Find further discussion of Parkinson's disease dementia on page 28.)

Hallucinations and delusions can be associated with Parkinson's. If they do occur, it is more likely to happen in advancing stages. Visual hallucinations (seeing things that aren't there) and delusions (firmly held, false, often paranoid, beliefs) are the typical manifestations of what is known as Parkinson's disease psychosis. Psychosis may be due to Parkinson's disease itself and/or the medications used to treat it. (Learn more about psychosis on page 29.) Decreasing or discontinuing certain Parkinson's medications may help, but this is often at the expense of worsening motor symptoms. If medication adjustments are inadequate or symptoms of psychosis are especially severe, antipsychotics may be prescribed. (See the Guide to Medications, page 42.)

03. Looking Ahead with Parkinson's Disease

The passing of time brings natural changes and life transitions for everyone (Parkinson's or not). For people with PD, these shifts may occur earlier than expected or be more challenging. If you've had Parkinson's for quite a while, you've likely gotten to know your symptoms — and also often the best management strategies — well. As time marches on, symptoms may change or progress. Be confident in your past experiences overcoming challenges and take heart in the knowledge that treatment options are expanding for symptoms at all stages of the disease.

The Here and Now:

Parkinson's Changes that Can Emerge with Time

Some people who have had Parkinson's for several years still work, raise families and run marathons.

You could be bothered by tremor but have no walking problems or vice versa. Each individual's symptoms, as well as the severity and rate of progression, remain distinct throughout PD's course. That being said, after years or decades with PD, you may experience a need for varying levels of assistance. Help could come in the form of your spouse buttoning your shirt because poor dexterity makes dressing tedious or a decision to move to an assisted-living facility. These considerations could come up earlier in the course of disease for some and never arise for others. What's important is to stay in tune with your own symptoms and situation. Stay on your own path. Someone else's course doesn't dictate yours.

REMEMBER TENET #1:
THERE IS NO "ONE SIZE FITS ALL" DESCRIPTION OF PARKINSON'S DISEASE.

Some people may experience different degrees of **balance or walking problems**. Imbalance causes unsteadiness, which makes walking a straight line tricky. Walking changes can include shuffling, difficulty getting started (hesitation), a sudden inability to move (freezing) or short, accelerating steps that are hard to stop (festination).

Difficulties with walking and balance can increase the risk of falls, which in turn could cause injuries, hospitalization or, eventually, the loss of independence (in other words, the need for living arrangements other than one's own home). Unfortunately, these symptoms are tough to treat — for most, they don't significantly improve with the current medications and surgical therapies. Yet, they can be managed by optimizing Parkinson's drug regimens, exercising regularly, learning fall-prevention strategies and using assistive devices (such as a cane or walker) if necessary. Participating in physical or occupational therapy, specifically with a therapist who has expertise in neurological disease, can make a substantial difference as well. (Find a detailed discussion of gait and balance issues at michaeljfox.org/PD360.) Occasionally, changes in balance or walking are due to conditions other than Parkinson's, which require a different treatment course. Don't automatically assume everything you experience is part of your PD — discuss all symptoms and any worsening with your movement disorder specialist, who can determine what's part of Parkinson's and what might be something else.

For some people, issues related to swallowing also could arise. **Swallowing difficulties** may manifest in several ways — coughing or choking while eating or drinking, throat clearing or a sensation of food getting "stuck" while going down. If these occur, a speech-language pathologist can check how well you tolerate solids and liquids of different consistencies and your doctor can order imaging tests, such as a videofluoroscopy, or a modified barium swallow study, to determine where problems are happening (such as in the mouth while chewing or in the throat while swallowing) and if liquids and/or foods are going into the lungs instead of the stomach (if you are "aspirating"). Based on these results, dietary modifications and adaptive strategies can be recommended to lessen the risk of aspiration, which could otherwise potentially lead to pneumonia. If you experience frequent episodes of aspiration pneumonia or have severe weight loss, a feeding tube may be suggested. But just because you have a problem swallowing does not mean you will need a feeding tube. Since swallowing disturbances could pose choking risks and the Heimlich maneuver can be life-saving, care partners may want to learn this technique.

Non-motor symptoms also may be noticed. One particular symptom that some, but not all, people encounter after living with Parkinson's for many years is **Parkinson's disease dementia** (PDD). If mild cognitive impairment worsens over time, it can (but doesn't always) morph into PDD, which causes memory, thinking and/or language problems significant enough to interfere with daily life at home, work or in social circles. Like milder cognitive impairment in Parkinson's, PDD can impact executive skills (such as organizing, multitasking and problem solving), visuospatial function (interpreting where objects are in space), attention and short-term memory, but to a more considerable extent. It also may cause behavioral, mood and motivational changes. If PDD occurs, it's typically after a person has had Parkinson's for many years. When dementia arises at the same time as or within

a year of the onset of motor symptoms, it could instead be due to Lewy body dementia (LBD), a form of atypical parkinsonism. (Learn more about atypical parkinsonism at michaeljfox.org/PD360.) In addition to Parkinson's motor symptoms and dementia, LBD can be characterized by fluctuating levels of alertness and visual hallucinations (seeing things that aren't there).

Visual hallucinations might be associated with LBD and PDD, but they can occur in the absence of dementia — either as a side effect of Parkinson's (or other prescription or over-the-counter) medications or as a distinct symptom of the disease, known as **Parkinson's disease psychosis**.

Psychosis, if it does occur, is more common in advancing disease and in conjunction with significant cognitive changes. In addition to hallucinations, this aspect of Parkinson's can include illusions (misinterpreting things that are there), a false sense of presence (feeling as though someone or something is nearby) or delusions (strongly held false beliefs, usually expressed as paranoia or suspicion about financial issues or spousal infidelity).

It's important to stress this is a symptom of Parkinson's disease and does not mean a person is "going crazy." Symptoms are treatable. Doctors will first adjust medications, reducing or withdrawing those that are most likely to contribute to psychosis, such as dopamine agonists and anticholinergics. If motor (and other) symptoms worsen significantly as a result of these modifications, adding antipsychotic drugs may be necessary. Nuplazid (pimavanserin), the first drug approved specifically to treat hallucinations and delusions due to Parkinson's disease psychosis, hit the U.S. market in 2016. Other antipsychotics, including Seroquel (quetiapine) and Clozaril (clozapine), were used prior to Nuplazid and may still be prescribed in certain situations. (Read more about all of these drugs in the Guide to Medications on page 42.)

"I DON'T STOP LIVING BECAUSE OF PARKINSON'S."

Lisette Ackerberg lived with Parkinson's disease for a decade before telling her family and friends. She had watched her grandfather and her father live with Parkinson's for years, and never wanted loved ones to look at her with sympathy. So when she finally made her announcement, she did it with bravado at her 60th birthday party.

Her concerns about others' perceptions, along with her symptoms, have shifted over the the nearly three decades she has lived with PD. Today, symptoms and medication side effects can make shopping or other daily tasks difficult. An inability to anticipate dyskinesia has curbed her spontaneity. But through it all, she remains positive. "You have to know that this disease isn't a death sentence. It just means you alter your life. You change it so it works."

In 2004, within a single month, Lisette lost her father to Parkinson's and her husband to multiple sclerosis. The immense stress seemed to catapult the disease, but now she credits that time with helping her define her personal formula for managing her PD: sleep, strong exercise, good food and a conscious effort to stay positive.

She took up walking, and walked in a 5K for Parkinson's on her 75th birthday, "in the hail," as she recalls. "I was very proud of that." But as she approaches her eightieth birthday, Lisette no longer feels any pressure to prove herself. "I exercise everyday but I don't walk those distances."

And with that, she left her interview to continue planning another birthday party, this time for her mother's 98th.

WATCH MORE OF LISETTE'S STORY AT **MICHAELJFOX.ORG/PD360**.

Emotional and Social Aspects:

What People with Parkinson's Say It Feels Like After Many Years

Parkinson's disease will include periods of challenging adjustment and transition; this realization alone can increase your creative coping skills.

Making changes in routine or treatments could go a long way toward helping you live well. Avoid isolating yourself. Engaging with others is critical to ensuring both mind and body well-being; talk with your doctor about any symptoms that are preventing you from enjoying activities with family and friends so you can work together to address them. It's normal to feel frustrated, especially if you begin to experience symptoms that interfere with socal interactions, but you needn't feel hopeless.

REMEMBER TENET #5:
PARKINSON'S IS A NON-LINEAR DISEASE.

Depending on which symptoms are present, different types and levels of support may be necessary. Some people may need help with household duties like laundry, grocery shopping or bill paying. Others might require help with showering and dressing, or preparing and eating meals.

Within the home, spouses or live-in partners usually supply the majority of assistance. If finances allow, you might consider hiring a home health aide or certified nursing assistant to help with certain tasks, such as transferring out of bed or bathing. (A social worker can direct you to the right resources and necessary paperwork.) If you as a caregiver simply need a chance to run errands, do household chores, socialize with friends or get some exercise, you could ask a friend or family member to come over a few times a week. In some cases the support of a skilled medical professional is necessary. After a hospitalization or fall, for instance, a nurse might monitor blood pressure to guide medication adjustments or a therapist may teach rehabilitation exercises to help you regain strength and mobility. Insurance usually covers a set number of these professional visits each year.

Growing care needs or certain symptoms — such as walking or balance issues that increase risk of falls, cognitive problems, or hallucinations or delusions — may affect a person's ability to continue living alone or at home. In these instances, assisted-living or skilled-nursing facilities may provide alternative solutions. Assisted-living varies, but often includes meals, medication administration and some personal care. Skilled-nursing facilities provide full medical care and 24-hour supervision if greater levels of attention are required.

Medication adjustments may be necessary to meet evolving non-motor and motor symptoms as well as any drug-associated complications that appear. An expanding repertoire of treatments now exists that can be transformative for people throughout the course of Parkinson's. Relatively recently approved treatments include new formulations of levodopa, one of which is delivered continuously into the intestine via a surgically-implanted tube. (Learn more about this in our Guide to Medications on page 42.) More research than ever before is actively under way to develop therapies capable of meeting the needs of Parkinson's patients at every stage of disease (and to find treatments that would prevent the disease from advancing into the later stages in the first place). "The latest research is the latest hope," says Michael J. Fox. Keeping hope alive is vital to wellness for everyone with PD, especially those who may be in the later years of disease.

ACTIONS TO CONSIDER NOW

1 Keep up with exercise.

Regular exercise remains an important tool for managing progressing Parkinson's. No matter what symptoms are present and how significant they may be, some form of exercise likely can be done. Your doctor and physical therapist can help create a program to suit your fitness level and symptoms. If balance is an issue, stretching exercises can be performed on a floor mat; many physical activities — yoga, dancing and cycling — can effectively be done while seated. (There's more information on exercise at michaeljfox.org/PD360.)

2 Continue adjusting diet as needed.

For constipation and low blood pressure, increased water intake and other dietary adjustments (typically along with pharmacological management) are recommended. Swallowing dysfunction may dictate changes in diet consistency (thickening liquids or softening solids, for example). The increasing occurrence of "off" time (periods when medication doesn't work optimally to control symptoms) may signal the need to take levodopa separate from meals, particularly those high in protein, which can interfere with the drug's absorption and effectiveness. In these cases, take levodopa on an empty stomach (30 to 60 minutes before or after a meal) or with a small carbohydrate snack (such as crackers, oatmeal or toast). Another option is to save higher amounts of protein for the end of the day, when symptom control may not be as critical. Some people adopt vegetarian eating habits, but depending on the content (beans, nuts, cheeses, etc.), these diets can still be high in protein.

3 Keep your financial house in order.

Some healthcare and life insurance policies cover a portion of costs related to caregiving (a certain number of home visits from skilled medical professionals or a percentage of assisted-living or skilled-nursing facility costs, for example). Disability policies don't cover any of these expenses and long-term care plan benefits vary. Individuals and their families are therefore ultimately responsible for meeting the majority of caregiving costs. Many turn to savings, reverse mortgages, annuities or trusts.

End-of-life financial planning shouldn't be overlooked. A power of attorney for property can be appointed to manage money, investments and businesses. A written will can ensure your estate will be divided according to your wishes.

4 Don't forget the caregiver.

In the midst of looking after another's medical, physical, emotional and financial concerns, the caregiver can get lost or be forgotten. Caregivers have to make a conscious effort to see to their own needs and speak up for themselves. Keeping up social activities and hobbies, exercising regularly, taking breaks, scheduling routine doctors' appointments to maintain your health and building a strong support system (including a caregiver support group, if that's helpful) are key. Use this opportunity to evaluate your personal finances and long-term care insurance options. It is also critical to recognize limitations and monitor for caregiver burnout, which can manifest as fatigue, irritability or depression.

"The reality is that things change; the question is, how will I perceive that change, and am I willing to change along with it?"

— MICHAEL J. FOX

5 Explore palliative care.

Palliative care is not the same as hospice. While hospice is for those with a prognosis of six months or less, palliative care services can be accessed at any time in the course of disease. Palliative care teams (usually consisting of a physician, nurse, social worker and clergy member) provide medical, emotional and spiritual care to people with Parkinson's and their loved ones. Medical support is focused primarily on lessening particularly troublesome problems, such as significant cognitive, behavioral or sleep disturbances, psychosis or disabling motor symptoms.

6 Define end-of-life care wishes and advance directives.

Every one of us, Parkinson's or not, will face the end of life. Setting intentions for that time and beyond can help mitigate fear. Thinking ahead and working through possible scenarios to determine your preferences about care in the final phases of life often are beneficial to you and your family. Palliative care clinicians can help facilitate conversations to guide current and future care.

It is natural and fair to wonder aloud in these discussions whether you will die from Parkinson's and, in fact, this is a question that is regularly asked. Of course, it's impossible to predict any one individual's outcome. On the one hand, many people with Parkinson's who are optimally treated will have a normal or nearly normal lifespan. On the other, those who have particularly advancing disease are, in general, more likely to experience and succumb to certain conditions. Significant walking and balance issues and resultant decreased mobility can lead to urinary tract infections, falls and injuries, and pneumonia. Swallowing problems can cause aspiration pneumonia. Infection, injury and other illnesses can be difficult for someone in the later years of Parkinson's to recover from fully or at all. Measures can be taken to prevent these conditions, or, if they do occur, to treat them or minimize their effect. Plenty of people will never experience any of these complications. But equipped with this knowledge, you can plan for potential — but not inevitable — situations and make informed decisions about your personal goals of care.

As you do so, completing advance directives — written legal documents that detail your wishes — is often beneficial. A living will specifies whether and which life-support measures (breathing or feeding tubes, intravenous hydration, etc.) a person wants in the event he or she is seriously ill and cannot communicate. A Do Not Resuscitate (DNR) order indicates that cardiopulmonary resuscitation (CPR) should not be done if the heart and/or breathing stop. (Of course you'd only complete this if it were consistent with your wishes.) A healthcare power of attorney — someone who ensures these advance directives are fulfilled — can be designated as well. Legal counsel isn't required to complete advance directives but can be sought if helpful. These documents should be shared with your physicians and placed in the medical record. Advance directives do not expire but can be changed at any time.

Having these plans in place can be comforting. Both family and physicians are often grateful to know they are carrying out directed plans, if that becomes necessary.

REMEMBER TENET #7:
BE PREPARED.

Hospitalization and Surgery in Parkinson's Disease

Hospitalization

Hospitalization is not inevitable in Parkinson's disease, but should you find yourself in the emergency department or hospital, some special preparations can help ensure the best possible care. The hospital doctors can discuss your care with a neurologist — either your personal movement disorder specialist or a hospital consultant — if necessary. Be ready to play an active role in this conversation and to advocate for your (or your loved one's) needs.

Deviating from your normal drug regimen or taking new medications while in the hospital could temporarily worsen Parkinson's symptoms. The following tips may be helpful during hospitalization:

- Share a list of your current medications, supplements and drug allergies with your hospital providers.
- Take all medications in their bottles with you to the hospital.
- Request that medications be administered per your home schedule rather than the hospital's standard schedule (if these are different).
- If the hospital pharmacy does not carry one of your medications, ask if you can bring your own supply.
- Avoid certain anti-nausea medications and antipsychotics (which may be used to treat hallucinations, confusion and sometimes also sleep problems) if possible, as they can temporarily worsen motor symptoms.
- Use medications for pain or sleep carefully as these can cause excessive sleepiness and confusion.

Urinary tract infections (UTIs), pneumonia and injuries from falls are common precipitants for hospitalization in people with Parkinson's. UTIs and pneumonia are typically treated with antibiotics. For aspiration pneumonia, speech therapy and dietary modifications also may be recommended to help prevent future infections.

Because falls most often result from walking and balance problems, a physical therapist is usually consulted during hospitalization. The therapist may teach exercises, evaluate the need for an ambulation aid (such as a cane or walker) and provide recommendations about when you can safely leave the hospital and whether you need additional rehabilitation. After hospitalization, some people go to a rehabilitation hospital or skilled-nursing facility for additional physical therapy. Others are able to return home and get physical therapy there or in an outpatient clinic. The selection is made based on several factors, including a person's symptoms and support system at home.

Confusion, excessive sleepiness or hallucinations can develop or worsen during hospitalization because of the unfamiliar environment, altered sleep schedule or new medications. Family can help limit confusion by making sure eyeglasses and hearing aids (if applicable) are available and, although not easy, nurses can try to maintain the person's normal sleep routine. If confusion or hallucinations lead to agitation or other behaviors that compromise safety, treatment (including antipsychotic medications) may be required.

For those with deep brain stimulators, the device may need to be temporarily turned off so that certain medical tests, such as heart EKGs or brain EEGs, can be performed. MRIs of the brain or other body parts may be permitted but this depends on the specific DBS device. Strict protocols will be followed to ensure the test is completed safely, so make sure that the hospital and radiology staff are aware you have had DBS.

Surgery

The risks and benefits of any surgical procedure should be carefully considered with your movement disorder specialist and surgeon prior to the operation.

If it's an option, local anesthesia may be preferred over general as the latter could increase the risks of temporary confusion and possibly pneumonia in the post-operative period.

Most Parkinson's medications are continued until the night before surgery, with the exception of MAO-B inhibitors, which may need to be held for up to two weeks beforehand. If possible, medications should be restarted immediately following surgery. If you can't take anything by mouth or swallowing is an issue, some drugs can be crushed and given through a tube. Others are available as dissolvable tablets or can be administered through a skin patch. Certain capsules can be opened and the contents sprinkled on applesauce or food of similar consistency for immediate use. (Read more about these and other Parkinson's drugs in the Guide to Medications on page 42.) Anti-nausea medications are commonly given post-operatively but some should be avoided as they can temporarily worsen Parkinson's motor symptoms. It's important to ask your doctor what medications are being prescribed and why while you are in the hospital.

In the post-operative period, those with PD (especially in the advancing stages), may have an increased risk of confusion and longer healing times compared to people without Parkinson's. Working with a physical therapist to ensure you maintain mobility and consulting a speech therapist with any concerns about swallowing may help you get on the road to recovery more quickly.

04. Deep Brain Stimulation

Over time, medications may become less effective than they once were at controlling symptoms or cause increasingly disabling complications, such as dyskinesia. This can happen at different points in the disease course. If it does, deep brain stimulation (DBS) — today's most common surgical treatment for PD — may be considered. As with all of the currently available Parkinson's treatments, DBS addresses symptoms but is not a cure; the underlying disease continues to progress. While stories of DBS as a "miracle treatment" are common, DBS is not for everyone.

According to the company that manufactures the vast majority of DBS devices, more than 130,000 people worldwide have undergone DBS to date. For people with Parkinson's, the surgery can improve motor function and quality of life. It also can dramatically reduce medication requirements and associated side effects or complications, for a period of time — often years. Several factors are considered when determining whether someone is a good candidate for the procedure.

Diagnosis of Parkinson's disease

People with atypical forms of parkinsonism, or "Parkinson's plus" syndromes, do not benefit from this therapy. (Learn more about atypical parkinsonism at michaeljfox.org/PD360.)

Presence of Parkinson's for at least four years

Symptoms should be established, but the disease should not be so progressed as to cause considerably decreased mobility or reliance on a wheelchair. DBS generally cannot reverse these situations.

Continued medication benefit

DBS typically treats symptoms that get better with medication; it does not improve symptoms (with the exception of tremor) that don't respond to medication. (In other words, tremor that doesn't improve with medication may respond to DBS.) It works best for motor symptoms — slowness, stiffness and tremor. It doesn't work as well for imbalance, most walking problems or freezing of gait. Non-motor symptoms often don't respond and some, such as memory, thinking or speech disturbances, may even worsen following surgery.

Intact cognition (memory/ thinking abilities)

DBS can potentially exacerbate underlying cognitive problems. People with dementia may not do well with the surgery or intricacies of DBS.

Overall medical condition conducive to surgery

Certain heart diseases or problems with the blood's ability to clot might make surgery too risky.

Some people are not ideal candidates because they don't meet the criteria above. Others cannot or do not want to undergo the surgery to implant the device, periodic programming of DBS settings or future battery replacements.

When thinking about DBS, some people with PD report a wide range of emotions. Hope and optimism for how the treatment may help are common, but so are a dawning sense of the realities around the progression of the disease, grief over the loss of ability to manage symptoms with medication alone, and a natural trepidation at the idea of undergoing brain surgery.

If you are considering DBS, it is vital that you give yourself every opportunity to thoroughly assess the potential pros and cons. Discuss the procedure with your spouse, family and friends; draw on the experiences of others with PD who have had DBS; and, if possible, attend an educational seminar where you can learn more about the procedure and talk to others who are considering it as well. Ongoing conversations with the doctor who treats your Parkinson's disease also are critical to ensure all of your questions and concerns are addressed.

If you are a good candidate and decide to pursue DBS, a team of doctors will perform an intensive evaluation, including symptom and medication review, examination while on and off Parkinson's medication, brain imaging, and, if cognitive problems are present, formal neuropsychological testing. If DBS is offered, it's important to discuss anticipated benefits and to set realistic expectations. As with so many elements of Parkinson's disease, each person's response to the therapy will be unique and certain people may respond more favorably than others.

What to expect in the operating room and beyond

In DBS surgery, thin wires called electrodes are placed into one or both sides of the brain in specific areas that control movement. The patient usually remains awake during surgery to answer questions and perform tasks that ensure the electrodes are positioned correctly. (Some centers are now placing electrodes under imaging guidance, which allows a patient to be asleep during the procedure.) Electrodes are then connected to a battery-operated device, similar to a cardiac pacemaker, which is placed under the skin in the chest. This device — the neurostimulator — delivers carefully controlled electrical pulses that interrupt abnormal brain cell signaling and decrease PD symptoms.

A few weeks after surgery, a movement disorder specialist programs settings into the neurostimulator. These parameters, which are customized to treat each individual's symptoms, are tweaked over time while medications are adjusted. Most people are able to decrease (but not completely discontinue) Parkinson's drugs. Determining the optimal combination of medications and DBS settings — that which gives the most benefit with the fewest side effects — is a process that can take up to a year. Periodic programming adjustments are a routine part of therapy and eventually the neurostimulator battery will need to be replaced. This is typically an outpatient procedure, and the timing of this varies depending on the device and a person's settings.

"I'M A RISK-TAKER."

At 44, seven years after being diagnosed with Parkinson's disease, Richie Rothenberg felt encumbered by his body. He often found himself freezing without warning while powerful dyskinesias took over his body. "It was a very difficult time," he remembers.

While deep brain stimulation (DBS) isn't right for everyone, Richie's intense response to levodopa therapy meant he was an excellent candidate. On his doctor's recommendation, Richie decided to undergo the procedure in December 2010.

Unfortunately, after surgery he came down with a staph infection — a complication experienced by a small percentage of people who undergo any surgery — and spent New Year's Eve getting the whole apparatus taken out.

"I had to wait another six weeks before I could be ready to do it again," he recounts. The good news? He had done so well in the first surgery that doctors were able to redo the operation and implant the battery in one procedure the second time.

"My endurance was proven that I could stand a six- to eight-hour procedure. It's a long procedure," he says. The results were dramatic. Richie was among the rare patients who experience an immediate benefit, even before doctors had programmed his device.

It took a couple of years to get back to that instant moment. "The body settles down, the brain, the excitement settles down," he explains. "It took about two years of going in every month or so for a different tweaking of the DBS settings." He now undergoes regular outpatient procedures to maintain the pacemaker-like DBS device.

A year and a half after his operation, he married his high school sweetheart. Today, he balances serving as a bank's managing director with parenting their twin daughters and two teenage children from a previous marriage. "Parkinson's is the best thing that ever happened to me," he says. "It changed my life in a profound way that made it much more meaningful and much more appreciative and filled with love."

WATCH MORE OF RICHIE'S STORY AT
MICHAELJFOX.ORG/PD360.

GUIDE TO PARKINSON'S MEDICATIONS

All of the medications currently available for the management of Parkinson's disease are directed at improving quality of life by easing the motor and non-motor symptoms that can arise throughout the course of the disease. At this time, no disease-modifying therapy — one that stops or slows PD progression — has been proven.

MOTOR MEDICATIONS AND ASSOCIATED COMPLICATIONS IN THE EARLY AND MIDDLE YEARS

Medications for the treatment of motor symptoms are grouped into different categories according to the ways in which they work to lessen symptoms. Levodopa, a precursor to dopamine (the brain chemical that is lacking in PD), is the most commonly prescribed. At some point in the course of disease, most people will take this drug. Levodopa is generally quite beneficial, especially for treating stiffness and slowness. It also doesn't require a long period of adjusting the dose to get symptoms under control. Long-term use of levodopa, in conjunction with prolonged duration of Parkinson's, though, may be associated with motor complications, such as dyskinesia. Other medications that target motor symptoms (and can be used in conjunction with and, in some cases, instead of, levodopa) include dopamine agonists, MAO-B inhibitors, amantadine, anticholinergics and COMT inhibitors. With the exception of the latter, any of these may be selected as the first therapy. The choice is based on many factors, including the type and severity of a person's symptoms, other medical conditions and prescriptions, age and personal preference.

Physicians and researchers have long engaged in a healthy discussion over whether it's better to start levodopa sooner to control symptoms, maximize quality of life and allow a person to remain physically, socially and occupationally active as long as possible, or to avoid levodopa as long as possible to potentially delay potential motor complications. Younger people or those with milder symptoms may choose to start with a dopamine agonist, MAO-B inhibitor, amantadine, or in the case of prominent tremor, an anticholinergic. Or, for one reason or another, they may opt to start with levodopa. Ask your physician for his or her take on this issue and consider the pros and cons of both approaches.

Decisions about if, when and which medication to take are personal. Regardless of which therapy you choose, the drug will be started at a low dose and increased slowly so that the smallest effective dose — that which controls symptoms with minimal or no side effects — can be found. Over time, as symptoms progress or complications arise, medications need to be adjusted: dosages increased or decreased, daily administration schedules changed, drugs added or substituted, or different formulations tried. The latter might include switching to an extended-release form of levodopa or a dopamine agonist from an immediate-release preparation if that's not optimally controlling symptoms (it's wearing off before the next dose is due, for example). Or, if swallowing becomes difficult, a dissolvable tablet or skin patch may be prescribed instead of an oral pill.

Finding the right formulations, dosages and combinations of medications is a process that requires time and effort on the part of the person with Parkinson's, his or her caregiver, and the medical provider.

Dopamine Replacement Therapy (levodopa combined with carbidopa)

Levodopa is a drug that is converted to dopamine in the brain; it temporarily replenishes this brain chemical, which is decreased in Parkinson's. Levodopa is combined with carbidopa, a medication that prevents levodopa from breaking down before it gets to the brain and limits levodopa's side effects. Levodopa is available in immediate, sustained and extended-release preparations as well as a variety of formulations that include pills, a dissolvable tablet and an intestinal infusion. The latter, Duopa, is typically used in the later stages of disease if other medications can't be optimized for symptom control and/or drug-related complications occur. Nausea and vomiting are the most common side effects of levodopa. These often resolve with time, but if not can usually be managed by taking levodopa with a small carbohydrate snack or extra carbidopa. Other potential side effects are drowsiness, hallucinations, dizziness, low blood pressure and impulsive behaviors — such as excessive shopping, eating or interest in sex. (These are more likely in middle or advancing stages of disease but not everyone will

experience any or all of them.) Long-term use of levodopa, in conjunction with longer duration of Parkinson's disease, may lead to changes in medication response called motor complications. These include "off" time (when drugs aren't working optimally and symptoms return) and dyskinesia (uncontrolled, involuntary movements).

Examples of dopamine replacement therapies:

- **Sinemet**: immediate-release
- **Sinemet CR**: controlled-release
- **Stalevo**: immediate-release Sinemet plus Comtan (entacapone, a COMT inhibitor)
- **Rytary**: immediate- and extended-release in one capsule
- **Duopa**: immediate-release gel for infusion
- **Parcopa**: immediate-release dissolvable-in-mouth tablet

Decarboxylase Inhibitor: Lodosyn (carbidopa)

This medication prevents the breakdown of levodopa in the body so that more levodopa can get to the brain and be converted to dopamine. It also helps prevent or minimize side effects of levodopa, such as nausea and vomiting. Carbidopa is usually combined with levodopa in the dopamine replacement therapies listed above but if bothersome side effects (namely nausea and vomiting) occur with these drugs, extra carbidopa may be prescribed.

Dopamine Agonists

These drugs mimic the effect of dopamine in the brain. They are available in immediate- and extended-release preparations, and in the form of pills, a skin patch and an injection. (The latter, Apokyn, is used, if necessary, for the treatment of unpredictable "off" periods.) Compared to levodopa, this class of drugs may be slightly less effective at reducing PD symptoms but also is much less likely to induce motor complications over time. Potential side effects of dopamine agonists include nausea, drowsiness, leg swelling, low blood pressure, hallucinations and impulse control disorders, such as compulsive gambling or eating, excessive shopping or increased interest in sexual activity. The dosages of some of these medications need to be lowered if kidney function is impaired. Some people may benefit equally from all of the currently available dopamine agonists; others might develop side effects from one and not the others. Whichever is chosen is initiated at a low dose and increased gradually over weeks or months until symptoms respond, side effects arise or a target dosage is reached.

Examples of dopamine agonists:

- **Mirapex or Mirapex ER (pramipexole):** pill; immediate- or extended-release formulations
- **Requip or Requip XL (ropinirole)**: pill; immediate- or extended-release formulations
- **Neupro (rotigotine)**: skin patch; extended-release formulation
- **Apokyn (apomorphine)**: injection; immediate-release formulation

MAO-B Inhibitors

This class of drugs prevents the breakdown of dopamine in the brain — a normal process that happens in everyone (Parkinson's or not) after dopamine does its job. MAO-B inhibitors stop this from happening as rapidly so that dopamine is present for longer periods of time. These drugs can be taken alone or coupled with levodopa or dopamine agonists to boost their actions. Potential side effects include flu-like symptoms, joint pain and blood pressure changes.

Examples of MAO-B inhibitors:

- **Azilect (rasagiline)**
- **Eldepryl (selegiline)**
- **Zelapar (selegiline)**: dissolvable-in-mouth tablet

COMT Inhibitors

COMT inhibitors work solely to prevent the breakdown of levodopa and must be prescribed in conjunction with this drug. Since they allow levodopa to work longer, they are usually added if "off" times develop. COMT inhibitors can cause harmless urine discoloration, loose stools or diarrhea. Tasmar (tolcapone) also may cause liver damage so regular laboratory monitoring is required while taking this medication.

Examples of COMT inhibitors:

- **Comtan (entacapone)**
- **Tasmar (tolcapone)**

Dopamine releaser/ Antiglutamatergic: Symmetrel (amantadine)

Amantadine may exert direct and indirect effects on dopamine cells, which might decrease mild symptoms. It also may impact the brain chemical glutamate, which can lessen dyskinesia if this occurs in middle or later years of PD. Amantadine is available in pill or liquid formulations; it can be taken alone or with other Parkinson's medications at any time in the course of disease. Common side effects are nausea, dizziness and insomnia. Others include ankle swelling, leg rash (termed "livedo reticularis"), blurred vision and hallucinations.

Anticholinergics

This category of drugs works on the body's acetylcholine chemical system and restores the balance between acetylcholine and dopamine, which is disturbed in PD. Anticholinergics can be used alone or in combination with other Parkinson's drugs. They are commonly used to target tremor, especially in younger people, who are less susceptible to the drugs' side effects. These include blurred vision, dry mouth, constipation, problems with urination, short-term memory loss and confusion.

Examples of anticholinergics:

- **Artane (trihexyphenidyl)**
- **Cogentin (benztropine)**

MOTOR MEDICATIONS AND ASSOCIATED COMPLICATIONS IN MIDDLE AND ADVANCING YEARS

Depending on which motor and non-motor symptoms are present, patients in the moderate to advancing years of the disease may be on complex and sometimes hard-to-manage medication regimens. Although treatment programs differ based on the individual, by this time nearly everyone in the later stages of Parkinson's is on levodopa (often in combination with other drugs) or has tried it at some point.

Extended use of levodopa, in conjunction with longer duration of disease, can contribute to the development of motor complications.

Motor complications are divided into two categories: motor fluctuations and dyskinesia. Motor fluctuations are "off" states when medication is not working optimally to control Parkinson's symptoms. "Off" periods can come on gradually, meaning a dose of medication wears off before the next dose is due, or they can arise suddenly and unpredictably. Dyskinesia, on the other hand, usually (but not always) occurs during "on" times when medication otherwise is managing symptoms well. (In some people, it might occur as levodopa is kicking in or wearing off.) Dyskinesia is uncontrolled, involuntary movement — often writhing or wriggling — that can involve any body part. It may look like swaying, head bobbing or fidgeting. Multiple options are available to treat motor complications and therapy is chosen based on an individual's symptoms and current medications. To determine the best course of action, clinicians take several factors into account:

» The average time it takes for a dose of levodopa to start working to decrease symptoms

» The average length of time a levodopa dose works to control symptoms, and specifically if it lasts until the next scheduled dose is due

» If any doses of levodopa take longer (or fail) to kick in

» If Parkinson's symptoms ever return suddenly and unpredictably

» If dyskinesia is present and, if so, when.

Tracking this information can be difficult, but keeping a log of your symptoms and when you take medications may help guide discussions with your doctor. Conversations and medication adjustments also may go more smoothly if you can ensure you understand what is meant by "on" and "off" time as well as which of your symptoms is which (what's tremor and what's dyskinesia, for example). Ask your doctor about your symptoms or film them with your smartphone for review at your next appointment. Clinical trials are currently investigating wearable devices and smartphone apps that could make tracking symptoms and adjusting medications much easier for you and your doctor in the near future.

Options to address motor complications include:

» **Changing the dosage and/or dosing schedule of levodopa.** The goal with levodopa is to take enough in each dose to control symptoms until the next dose is due without causing or worsening dyskinesia. It can be challenging to find this balance.

» **Using an MAO-B inhibitor.** To increase total daily "on" time, MAO-B inhibitors may be combined with levodopa and/or dopamine agonists.

» **Taking a COMT inhibitor.** When levodopa wears off before the next dose is to be taken, a COMT inhibitor may be added to prolong its effect.

» **Switching to a longer-acting formulation of levodopa.** Extended-release preparations of levodopa keep a more steady level of medication in the system and thereby limit "off" times as well as dyskinesia. In some cases, switching from immediate- or controlled-release levodopa to Rytary (which combines carbidopa with both immediate- and extended-release levodopa in one capsule) might be considered. Another option may be Duopa, a levodopa/carbidopa gel that is infused continuously by an external pump into the small intestine through a surgically-placed tube.

» **Adding amantadine.** While currently under FDA review for the treatment of dyskinesia (at the time of publication, the drug was under FDA "Fast Track" review for this purpose), amantadine is commonly used to lessen this symptom if it develops. It is usually added to a regimen consisting of levodopa and/or dopamine agonists.

» **Providing apomorphine for use as needed.** This injectable dopamine agonist treats sudden "off" periods. It typically starts to work in about 10 minutes and lasts about an hour. Given the potential side effects of low blood pressure and nausea, the first dose is administered under a doctor's supervision and anti-nausea medications are taken beforehand.

» **Considering deep brain stimulation (DBS).** DBS is a surgical treatment that may be indicated for people whose symptoms still respond to medication but who have motor complications. Not everyone is a candidate, but those who are may see a substantial benefit in terms of symptom and medication reduction following the procedure. (Read more in the Deep Brain Stimulation section, page 36.)

NON-MOTOR MEDICATIONS

Non-motor symptoms associated with Parkinson's can occur at any time but typically are more numerous and prominent in the middle and later years of disease. A number of treatments are available for management, a handful of which are specifically indicated for use in people with PD. The others, although FDA-approved, don't have this specific indication because they haven't been studied in large numbers of people with Parkinson's. Regardless, these drugs are widely prescribed in the general population of people without Parkinson's and are often used to treat non-motor symptoms in Parkinson's. Presently, the only therapies FDA-approved for non-motor symptoms in Parkinson's apply to hallucinations and delusions (psychosis), low blood pressure (orthostatic hypotension) and dementia.

Parkinson's Disease Psychosis: Nuplazid (pimavanserin)

Nuplazid received FDA approval in 2016 for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. (Read more in the section on Looking Ahead with Parkinson's Disease, page 29.) When symptoms of psychosis pose safety risks or impact a person's or their caregiver's quality of life, medication may be necessary. Nuplazid works on the brain's serotonin system to decrease symptoms of psychosis and also may improve nighttime sleep and daytime wakefulness. Because it does not block the dopamine system (as the other available antipsychotics do), it typically doesn't worsen motor symptoms. Common side effects of Nuplazid are leg swelling, nausea and confusion. Like most antipsychotics, Nuplazid carries a "black box" warning of increased risk of death when used in elderly people with dementia. As with any medication, this and other possible adverse effects need to be weighed carefully against potential benefits. In some situations, other antipsychotic medications indicated for treating mood and thought disorders (such as schizophrenia) are prescribed, including Clozaril (clozapine) or Seroquel (quetiapine). These drugs affect the dopamine and serotonin systems and may exacerbate Parkinson's motor symptoms. Before Nuplazid, these were among the only drug treatments available for PD psychosis and might still be a better option in certain individuals.

Orthostatic Hypotension: Northera (droxidopa)

Northera was approved in 2014 for management of orthostatic hypotension — a decrease in blood pressure when changing positions (such as standing from sitting) that can cause dizziness, lightheadedness, fainting and, in Parkinson's, also increased gait and balance disturbances. (See Sidebar, Non-motor Symptoms of Parkinson's disease, page 24.) When dietary and behavioral adjustments are insufficient, pharmacological management may be required. Northera is converted to norepinephrine, a body chemical that naturally raises blood pressure. Potential side effects include nausea, dizziness, headache and elevated blood pressure while sitting or lying ("supine hypertension"). If the latter occurs, raising the head of the bed and/or taking blood pressure lowering medication at bedtime may be necessary. In certain cases, medications other than Northera, such as Florinef (fludrocortisone) or ProAmatine (midodrine), may be prescribed. Although these drugs aren't specifically indicated for use in PD, they were the only options available prior to Northera and may still be the best choice for some people.

Parkinson's Disease Dementia: Exelon (rivastigmine)

Exelon was approved in 2006 for the management of mild to moderate levels of dementia (significant memory and/or thinking impairment) associated with Parkinson's. (Learn more in the Looking Ahead with Parkinson's Disease section, page 28.) Exelon is an acetylcholinesterase inhibitor; it works by blocking an enzyme that breaks down acetylcholine, a brain chemical that supports memory and thinking abilities. Exelon may improve cognition, lessen associated behavioral changes (such as agitation or aggression), and delay the need for alternative living situations (such as nursing homes). Potential side effects include nausea, vomiting, diarrhea, decreased appetite, weight loss and increased tremor. Exelon is available in the form of a pill, oral solution and skin patch. In certain situations — if Exelon causes too many side effects, for example — other acetylcholinesterase inhibitors, such as Aricept (donepezil), which is indicated for Alzheimer's dementia, may be prescribed instead.

COMPLEMENTARY AND ALTERNATIVE THERAPIES IN PARKINSON'S DISEASE

Many people with Parkinson's disease feel drawn to complementary and alternative medicine (CAM), which is an umbrella term for treatments that are not part of conventional, or Western, medicine. (Conventional medicine is defined as the usual practice of medicine by physicians with M.D. [medical doctor] or D.O. [doctor of osteopathic medicine] degrees and associated allied healthcare professionals, such as physical therapists.) "Complementary" typically refers to therapies that are used in conjunction with this mainstream medicine, whereas "alternative" indicates the use of certain therapies in place of standard medical treatments. CAM may involve "natural" therapies, which include supplements, herbs and vitamins; "mind-body practices," (acupuncture, yoga or music therapy); and "manual healing methods," such as massage or movement programs.

Few CAM therapies have been put through rigorous scientific study specific to Parkinson's and, as with all currently available pharmacological and surgical therapies, none have been shown to slow or stop disease progression. If you're interested, CAM may be worth exploring, but before taking action, it's prudent to consider any scientific evidence for or against the individual therapy, as well as potential benefits, side effects and costs. It's also important to discuss any CAM approaches you are considering with your healthcare provider to ensure they won't interact with or affect your current Parkinson's treatments.

While the list below is not comprehensive, it includes CAM therapies that may bring general benefit to people with Parkinson's disease, as well as treatments that claim effects on specific aspects of Parkinson's disease.

"Natural" Therapies of General Interest in Parkinson's Disease

"Natural" compounds, such as dietary supplements and vitamins, are regulated by the U.S. Food and Drug Administration (FDA), but under a different set of guidelines from those used for prescription drugs. The FDA does not review or endorse the safety or effectiveness of these products. "Natural" therapies aren't necessarily safe or free from adverse effects, including interactions with prescription medications.

Some of the "natural" CAM therapies aimed at treating Parkinson's claim to boost mitochondria (the cell's energy producers); others say they limit inflammation. Many act as antioxidants to clear out free radicals — toxic substances formed from stresses like air pollution, sunlight, cigarette smoke and even the normal cellular processes involved in converting food to energy.

Supplements

Caffeine

In studies involving hundreds of people, greater caffeine consumption correlated with a decreased risk of Parkinson's disease. "Correlation is not causation," though, and it's not clear if this is simply an association — people with Parkinson's disease consume less caffeine — or an indication that caffeine might protect against PD. Caffeine blocks certain brain cell receptors in the basal ganglia (the part of the brain affected by PD) and in doing so, increases dopamine and decreases glutamate (another brain chemical). In one small trial, people with Parkinson's who took 200 mg of caffeine twice daily showed a mild improvement in motor symptoms. And, a survey of people with PD found that higher intake of coffee decreased the likelihood of dyskinesia (uncontrolled, involuntary movements). Caffeine is likely safe up to 200 mg twice daily but benefits of this are unknown. It's important to note that increasing caffeine intake could potentially exacerbate tremor, anxiety, sleep disturbances and urination. Researchers are currently looking into drugs that block the same brain receptors as caffeine to determine if they might lessen "off" time (periods when medication doesn't work optimally to control symptoms) and dyskinesia.

Citicholine (CDP-choline)

This is a substance that may increase dopamine levels. It is closely related to choline, a nutrient that is also contained in acetylcholine — a body chemical that

supports normal brain and nerve function. Oral and intravenous citicholine have been studied in Parkinson's. Small studies showed it might allow for a reduction in levodopa dosage and is relatively safe, though it may cause mild side effects, such as nausea, dizziness and fatigue.

Coenzyme Q10 (CoQ10)

This supplement is an antioxidant and a key factor in basic cell functioning and energy production. It became the focus of much research and patient interest in the 1990s and early 2000s, when claims were made that it held potential to slow or stop progression of Parkinson's. However, a large Phase III clinical study of CoQ10 in people with PD, sponsored by the NIH, concluded in 2011 after it failed to demonstrate any disease-modifying effect. Dosages of up to 2400 mg per day were found to be safe and well tolerated. Side effects include mild stomach upset, fatigue and dizziness. Many people with Parkinson's take CoQ10 and feel some benefit, but as with all supplements, this should be discussed with your medical provider. CoQ10 could potentially interact with prescription medications, including some blood thinners.

Creatine

Creatine is a substance that supports energy metabolism and acts as an antioxidant. A large trial of creatine 5 g twice daily in people with Parkinson's was terminated early in 2013, due to lack of evidence of neuroprotection. Based on this trial, though, creatine was felt to be generally safe and well tolerated.

Glutathione

Glutathione is an antioxidant that also may support the function of mitochondria (the principal energy producers within brain and other cells). Brain glutathione levels are decreased in people with Parkinson's. Glutathione can be administered through several routes — oral, intravenous (IV) or intranasal (through the nose). Oral glutathione is poorly absorbed and may not reach the brain in sufficient quantities. Intravenous glutathione is expensive and has potential side effects (bleeding, infection, blood clots, etc.). Two small clinical trials of IV glutathione in PD did not prove efficacy. Studies of intranasal glutathione are currently underway.

Inosine

Inosine is an antioxidant that is converted to urate in the body. In population-based studies, higher blood levels of urate were associated with a lower risk of Parkinson's disease. In previous clinical trials of other drugs for PD, higher urate levels were associated with less severity of disease over time. (These are associations, however, and not direct causations.) Inosine is currently in Phase III trials to determine whether it has a disease-modifying effect. Potential risks of inosine include kidney stones, gout and high blood pressure.

Vitamins

Vitamin B6

This vitamin is necessary for many cellular processes, including the manufacturing of brain chemicals. It also decreases homocysteine, an amino acid that, when elevated, is thought to damage dopamine cells. One trial showed a correlation between higher intake of vitamin B6 in smokers and a lower risk of PD. Vitamin B6 can increase the rate of levodopa breakdown and therefore decrease its effectiveness.

Vitamin C (Ascorbic acid)

This is an antioxidant that can improve the production of dopamine. A small study of vitamin C in people with Parkinson's who had motor fluctuations failed to demonstrate any benefit.

Vitamin D

This nutrient is important for general health and bone integrity. Vitamin D deficiency is common in the general population and among people with Parkinson's. Many physicians recommend vitamin D supplementation for bone health, but its potential benefits in PD are unknown.

Vitamin E

Alpha-tocopherol, the active component of vitamin E, is an antioxidant. A large study of high dosages of vitamin E in people with newly-diagnosed Parkinson's failed to show benefit over placebo in delaying disability or need for levodopa therapy. Vitamin E can increase risk of bleeding, so concurrent use of blood thinners is not recommended. It may also interfere with cholesterol-lowering drugs and chemotherapy agents.

Herbs

Medical Marijuana

Marijuana is derived from the plant Cannabis sativa, which contains more than 60 different compounds referred to as cannabinoids. One is the major "psychoactive" component — Delta-9-tetrahydrocannabinol (THC) — which causes alterations in perception, mood and behavior. The ratio of THC to the other cannabinoid compounds, which do not have these psychoactive effects, varies from plant to plant and among the various formulations of medical marijuana.

The body naturally makes cannabinoids that bind to receptors throughout the brain. In doing so, they impact brain chemicals, including dopamine. Cannabinoids in marijuana may have antioxidant, anti-inflammatory and potentially neuroprotective effects. However, clinical studies into marijuana's effects on Parkinson's motor and non-motor symptoms have demonstrated inconsistent outcomes. Some trials have reported benefit on non-motor symptoms (such as pain and sleep disturbances) as well as motor symptoms. Others, including studies on levodopa-induced dyskinesia, have produced mixed or negative results. (Of course, many anecdotal reports of benefit on both

non-motor and motor symptoms exist as well.) Larger, well-designed trials using consistent formulations of marijuana are necessary to determine safety and efficacy in Parkinson's. At the time of this writing, a few states have legalized medical marijuana for use in Parkinson's. (Guidelines for use differ from state to state.) Marijuana should be used cautiously, balancing potential benefits against side effects, which could include nausea, dizziness, weakness, mood and behavioral changes, hallucinations and cognitive impairment.

Mucuna Pruriens

Mucuna Pruriens is an herbal supplement that contains levodopa — the most commonly prescribed therapy for Parkinson's disease, which is converted to dopamine in the brain. Unfortunately, the actual amount of levodopa contained in M. pruriens supplements is highly variable. The supplements are also impure, containing trace amounts of serotonin (a brain chemical best known for its role in mood regulation), nicotine and probably several other compounds as well. A study of HP-200, a formulation of M. pruriens, in people with PD led to decreased disability, claims of safety and minor gastrointestinal side effects. Another trial compared M. pruriens to standard levodopa therapy, finding no difference in motor symptoms or motor complications between the two, but a potentially faster onset of action to symptom control with Mucuna pruriens. If the supplement is combined with standard levodopa, it could cause dyskinesia, and if taken on its own, it could cause inconsistent symptom control (because of unknown and varying levodopa amounts).

Traditional Chinese Herbal Medicines

These are sometimes used to treat non-motor symptoms associated with PD, such as fatigue, or sleep or gastrointestinal disturbances. Small studies have shown potential benefit on both non-motor and motor symptoms, but neither efficacy nor safety have been proven.

"Natural" Therapies for Conditions Associated with Parkinson's Disease

DEPRESSION

Depression is a distinct condition that can be associated with Parkinson's disease, not solely a reaction to the diagnosis or life with a chronic disease. It occurs in many, but not all, people with PD. If untreated, it can aggravate both motor and non-motor symptoms of Parkinson's. Prescription drugs and/or counseling are available but, depending on the severity and an individual's preference, supplements are sometimes chosen instead. As with any therapy, these oral supplements and herbs should be reviewed with your healthcare provider before they are taken, especially since they could interact with certain prescription antidepressants and migraine medications.

5-hydroxytryptophan (5-HTP)

This is a precursor for synthesis of serotonin, a brain chemical involved in mood and behavior. Studies comparing 5-HTP to standard antidepressants in the general population found some benefits on depression. It has not been studied specifically in people with PD.

S-adenosylmethionine (SAMe)

SAMe plays a role in many processes, including the production and breakdown of dopamine. Levodopa could decrease levels of SAMe, and SAMe could increase levodopa's breakdown, making it less effective. One small study of SAMe in people with Parkinson's showed that it was safe and decreased depressive symptoms.

St. John's Wort

This herb, which impacts brain chemicals including dopamine and serotonin, is sometimes taken for depression. However, study results have been conflicting and neither safety nor efficacy has been definitively proven. Potential side effects include psychosis, stomach upset, sunlight sensitivity and increased anxiety.

MEMORY IMPAIRMENT

Varying levels of cognitive (memory/thinking) disturbances can occur throughout the course of Parkinson's. They range from insignificant (detectable only on formal testing) to mild cognitive impairment to more severe (dementia).

Ginkgo biloba

Ginkgo is an herb that has antioxidant and anti-inflammatory properties and affects several brain chemical (serotonin, dopamine and norepinephrine) pathways. Clinical trials on ginkgo have provided inconsistent results, although a large placebo-controlled trial in adults with no or mild cognitive impairment showed that it failed to prevent cognitive changes. No large trials have been done in people with Parkinson's. Ginkgo is likely safe but should be combined cautiously with other medications, especially as it could interact with antidepressants and blood thinners.

Phosphatidylserine

This is a component of cells' outer membranes (protective barriers). It is purported to help with memory and possibly mood as well but scientific support is lacking. It should be used cautiously in conjunction with blood thinners.

Mind-Body Practices

Acupuncture

Often a component of traditional Chinese medicine, acupuncture uses needle insertion at various points in the body to redistribute "qi," or energy, which is thought to be out of balance in the setting of disease. Small electrical pulses or bee venom can be applied with the needle to amplify the effects. Few randomized or controlled trials have been performed on acupuncture in Parkinson's and outcomes on motor and non-motor (pain, fatigue, anxiety, etc.) symptoms have been inconsistent. In general, acupuncture appears safe and

well tolerated. Anecdotally, many people report benefit.

Biofeedback

This technique helps a person achieve a greater awareness of the body and its natural reactions in order to gain control of any unwanted responses or symptoms. An MJFF-funded study applied biofeedback principles to successfully prevent and manage episodes of gait freezing in Parkinson's.

Music and Dance Therapy

Music can promote movement, expression and socialization and therefore impact an individual's physical, emotional and cognitive states. Studies have shown music can lead to positive brain chemical and structural changes. Several types of dance have demonstrated efficacy in the management of Parkinson's motor and non-motor symptoms.

Tai Chi and Yoga

Tai Chi is a traditional Chinese martial art that incorporates deep breathing, relaxation and slow movements. Studies in people with PD have shown that it's safe and potentially improves motor function and stability. Yoga is a mindfulness-based exercise that has, in some studies, demonstrated benefit on motor symptoms, balance and quality of life. Both tai chi and yoga could theoretically also lessen some non-motor symptoms. As with many forms of exercise, yoga styles and techniques differ and therefore, scientific study is challenging.

Manual Healing Methods

Manual therapy refers to treatments in which a practitioner uses his or her hands to provide therapy. In general, this seems safe and may positively impact mood and quality of life but objective data is limited.

Massage and Chiropractic Treatment

These practices manipulate the musculoskeletal system and realign the spine. Many people with Parkinson's report temporary improvements in stiffness and posture after massage and small observational studies have shown increases in walking speed as well. No controlled studies have been performed on chiropractic treatment for Parkinson's.

Movement Programs

These programs include the Bowen Technique, Trager Approach, Feldenkrais Method and Alexander Technique. None of these has been studied rigorously in PD. In the Bowen Technique, a practitioner subtly stimulates certain areas (muscles, tendons, ligaments or nerves), purportedly creating signals in the autonomic (involuntary) nervous system that stimulate the body to "heal itself." Trager therapists provide gentle movements, and individuals are taught complementary home exercises to increase relaxation, physical mobility and mental clarity. In the Feldenkrais Method, a practitioner uses gentle manual techniques to teach a person how to be more aware of and sense his or her movements to improve flexibility, coordination and posture. Teachers of the Alexander Technique gather details (through observation and light touch) about a person's movements and use this information to direct a person to couple thoughts and muscle activity in a purposeful manner. A relatively small study of people with Parkinson's who practiced the Alexander Technique showed improved disability and depression ratings.

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PARKINSON'S DISEASE GLOSSARY

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Alpha-synuclein

A protein normally found in neurons and the main component of protein clumps called Lewy bodies. Researchers believe that Lewy bodies are associated with neuron death. A mutation in the gene that directs the production of the alpha-synuclein protein is the basis for a rare, inherited form of Parkinson's disease.

Antioxidant

Chemical compound or substance that inhibits oxidation: damage to cells, proteins or genetic material by free radicals (the same chemical reaction that causes iron to rust). Some studies have linked oxidative damage to Parkinson's disease.

Ataxia

Loss of balance and decreased muscle coordination during voluntary movements.

Autonomic dysfunction

Problems with the functioning of the autonomic nervous system, which controls the underlying processes that keep our bodies working such as bladder and bowel movements, sweating, sexual function and blood pressure regulation.

Basal ganglia

Region deep within the brain consisting of large clusters of neurons responsible for voluntary movements such as walking and movement coordination. Many of the motor symptoms of Parkinson's disease are brought on by loss of or damage to dopamine neurons in this region, which encompasses the striatum, the subthalamic nucleus and the substantia nigra.

See also: ***neuron***

Biomarkers

Measurable, biological characteristics that can be used to determine the risk, presence or progression of disease. For example, high blood pressure is a biomarker of potential heart disease. No biomarker of Parkinson's disease has been validated, but researchers are working toward such a tool.

Bradykinesia

Slowing down and loss of spontaneous and voluntary movement. One of the cardinal symtpoms of Parkinson's disease. From the Greek brady, slow, and kinesia, movement.

Clinical trials

Organized medical studies that test the safety and efficacy of new treatments, such as drugs or surgical, in human beings. Also called interventional studies or trials.

Cognitive dysfunction

Loss of intellectual functions (such as thinking, remembering and reasoning) severe enough to interfere with daily activities. This may include executive dysfunction and/or changes in personality, mood and behavior. Cognitive dysfunction in Parkinson's disease typically does not respond to dopamine-replacement therapy and ranges from mild impairment to dementia.

Compulsive Behavior

Irresistible impulses to act, regardless of the rationality of the motivation. Some compulsive behaviors — excessive gambling or shopping, hypersexuality, and binge eating — have been associated with dopamine agonists used to treat Parkinson's disease.

Deep brain stimulation (DBS)

Treatment for the motor symptoms of Parkinson's. In a surgical procedure thin electrodes are implanted into the brain, targeting motor circuits that are not functioning properly. A small device (similar to a cardiac pacemaker) emits electrical pulses to stimulate a brain region and block signals that cause some Parkinson's symptoms. At present, DBS treats only the symptoms that respond to dopamine-replacement therapy (tremor, rigidity and slowness of movement) and is used primarily for patients with severe Parkinson's disease, such as those with significant medication-induced side effects like debilitating dyskinesias.

Dementia

Decline in memory and/or intellectual functioning severe enough to interfere with social or occupational functioning. Some Parkinson's patients experience dementia, generally at later stages of disease progression. This symptom does not respond to dopamine-replacement therapy.

Depression

Mental state, and non-dopamine-responsive symptom of Parkinson's disease, characterized by feelings of despondency and a lack of ability to initiate activity. Research has shown that some depression medications are safe for people with Parkinson's.

Dopamine
Neurotransmitter chemical produced in the brain that helps control movement, balance and walking. Lack of dopamine is the primary cause of Parkinson's motor symptoms.

Dopamine agonist
Class of drugs commonly prescribed in Parkinson's disease that stimulate dopamine receptors and produce dopamine-like effects. These drugs are sometimes associated with compulsive behaviors.

Dopamine-non-responsive
Refers to symptoms of Parkinson's disease that do not improve when treated with current dopamine-replacement therapies. These symptoms include cognitive dysfunction, postural instability and gait difficulty, sleep disorders, speech disorders, depression, and others.

Dopamine-replacement therapy
Class of drugs that are converted into dopamine in the brain. Levodopa is a dopamine-replacement therapy.

Dysarthria
Slurred speech. A common problem in Parkinson's disease.

Dysequilibrium
Unsteadiness or imbalance. A common problem in Parkinson's disease.

Dyskinesia
Involuntary, uncontrollable, excessive movements that are a common side effect of long-term levodopa treatment for Parkinson's disease. These movements can be lurching, dance-like or jerky; can involve any part of the body (e.g., extremities, head and neck); and are distinct from the rhythmic tremor commonly associated with Parkinson's disease.

Dysphagia
Difficulty swallowing that results from difficulty coordinating and controlling the muscles responsible for moving food from the mouth through the esophagus to the stomach. In later stages of disease, this can increase the risk of food or liquid "going down the wrong tube," which can cause pneumonia.

Dystonia
An abnormal, involuntary, often painful sustained posture or muscle cramping. This can involve any body part — hand, foot, head. It can exist as a separate disease or be part of Parkinson's, especially when medication wears off.

Essential tremor
Movement disorder that may be confused with Parkinson's disease. A fast tremor that is most pronounced when using the hands, as with writing or eating. This is in contrast to tremor of Parkinson's disease, which is most pronounced when the limb is at rest.

Executive dysfunction
Disturbances in "executive functions," which are brain processes that allow a person to plan and initiate activities toward a goal, regulate behaviors, exercise judgments, maintain attention and concentration, problem solve and multitask. Many people with Parkinson's experience some type of executive dysfunction. This symptom does not respond to dopamine-replacement therapy.

Facial masking
Decreased facial expression and blinking. A form of bradykinesia.
See also: ***hypomimia***

Familial Parkinson's disease
Parkinson's disease that runs in families and is thought to have a primarily genetic cause. Familial Parkinson's disease accounts for less than five percent of Parkinson's cases worldwide.
See also: ***sporadic Parkinson's disease***

Fatigue
State in which one feels tired or exhausted, and the capacity for normal work or activity is reduced. Common, poorly understood symptom of Parkinson's disease.

Festination
Involuntary quickening of steps and shuffling, which makes it difficult for a person to stop moving. Festination is a common feature of Parkinson's disease.

Freezing
Abrupt and temporary inability of Parkinson's patients to move. This symptom frequently occurs when beginning to walk, moving through doorways or turning around.

Gait difficulty or dysfunction
Refers to any abnormality of walking associated with Parkinson's — imbalance, shuffling, or freezing, for example.
See ***postural instability***

Genetic predisposition

Any inherited genetic pattern that may make some individuals more prone than others to certain health conditions, disorders or diseases.

Hypomimia

A clinical term for facial masking — an immobile face with reduced blinking. From the Greek hypo, less, and mimia, imitation or expression.

See also: ***facial masking***

Levodopa

Most commonly administered drug to treat Parkinson's motor symptoms. In the brain, levodopa is converted into dopamine — the brain chemical that is lacking in Parkinson's disease.

See also: ***Sinemet***, ***dopamine***

Lewy bodies

Abnormal protein clumps that accumulate in brain cells in Parkinson's disease. Researchers believe that Lewy bodies play a role in the degeneration and death of dopamine neurons. At autopsy, the presence of Lewy bodies is used to confirm a Parkinson's diagnosis.

LRRK2

Gene implicated in one to two percent of all Parkinson's disease cases. The LRRK2 gene directs the production of the LRRK2 protein kinase, an enzyme that modifies the function of other proteins.

Micrographia

Small, cramped handwriting that is a symptom for many Parkinson's patients.

Mild cognitive impairment

Also known as MCI, a decline in memory and/or intellectual functioning that is not as severe as dementia. MCI occurs frequently in Parkinson's disease and may progress to dementia in some patients.

Monoamine oxidase B inhibitors (MAO-B Inhibitors)

Drugs that enhance the effect of dopamine-replacement therapy by preventing enzymes from breaking the medications down. Some studies suggest that MAO-B inhibitors may slow the progression of Parkinson's disease but this has not been proven in the clinic.

Motor Fluctuations

Inconsistent and sometimes unpredictable responses to levodopa. This can include wearing "off."

See also: ***Off phenomenon***

Movement disorders

Conditions that interfere with normal movement. Some, like Parkinson's disease, are characterized by lack (or "poverty") of movement, others by excessive movement. Besides Parkinson's, conditions categorized as movement disorders include essential tremor, multiple system atrophy, progressive supranuclear palsy, Huntington's disease, Tourette's syndrome and cerebral palsy.

Movement disorders specialist

Neurologist with specific training in the subspecialty of movement disorders. Movement disorders specialists typically treat a greater number of patients with movement disorders.

Multiple System Atrophy

Movement disorder that may be confused with Parkinson's disease. MSA is a degenerative condition characterized by low blood pressure when standing. It may lead to parkinsonism, rigidity, ataxia, fainting or incontinence. Also known as Shy-Drager syndrome.

Neurodegeneration

Slow and progressive death (degeneration) of certain brain cells in conditions such as Parkinson's disease, Alzheimer's disease and Lou Gehrig's disease (ALS).

Neurologist

Physician specializing in diseases and disorders of the brain, spinal cord, nerves and muscles, including stroke, Parkinson's disease, epilepsy, Alzheimer's disease and muscular dystrophy.

See also: ***movement disorders specialist***

Neuron

Nerve cell used to transmit information within the central nervous system. Parkinson's disease involves death of and/or damage to dopamine neurons.

Neuroprotective

Providing protection to or stimulating the regrowth of any part of the body's nervous system. No currently available treatment for Parkinson's disease has been proven to provide a neuroprotective or neuroregenerative effect. Available Parkinson's disease treatments are symptomatic.

Neurotransmitter

Specialized chemical messenger (e.g., dopamine, norepinephrine, serotonin) that allows nerve cells to communicate with each other. Most neurotransmitters play different roles throughout the body, many of which are not yet known.

See also: ***dopamine***, ***serotonin***

Non-motor symptoms

Poorly understood symptoms of Parkinson's that affect capabilities and characteristics other than movement. These include cognitive impairment, sleep problems and depression and typically do not respond to dopamine-replacement therapy.

Olfactory dysfunction

Reduced or impaired ability to smell, which can be an early sign of Parkinson's disease. Researchers are studying olfactory dysfunction as a possible avenue toward a biomarker of Parkinson's disease.

Off phenomenon

Times when medication loses benefit and symptoms of Parkinson's return. As disease progresses, this can come on before the next medication dose is due. Onset can be gradual or sudden and unpredictable.

Parkin

Mutations in this gene have been associated with a familial form of Parkinson's disease. Researchers believe that the normal function of parkin is to help degrade one or more proteins that are toxic to dopamine neurons.

Parkinson's disease

Chronic, neurodegenerative disorder that affects one in 100 people over age 60. The cardinal symptoms are bradykinesia, resting tremor, rigidity and postural instability or gait dysfunction, but most patients experience non-motor symptoms, as well. While the average age at onset is 60, many people are diagnosed much younger. There is no objective test, or biomarker, for Parkinson's, so the rate of misdiagnosis can be relatively high. Estimates of the number of people living with the disease therefore vary, but research indicates that at least 1 million people in the United States, and more than 5 million worldwide, have Parkinson's disease.

Parkinsonism

Generic term referring to slowness and mobility problems that result from or look like Parkinson's disease. Several conditions that are not actually Parkinson's disease, including multiple system atrophy and progressive supranuclear palsy, as well as a number of medications, can result in parkinsonism and a misdiagnosis of Parkinson's disease.

Physical therapy

Use of exercises and physical activities to help condition muscles and restore strength and movement. Physical therapy may be useful to maintain balance and flexibility as part of an overall Parkinson's disease treatment regimen.

Pill-rolling

Description of the typical resting tremor of the hands in Parkinson's disease, so named because the alternating movements of the thumb and forefinger give the appearance of rolling a small object between the fingers.

See also: ***tremor***

Postural instability

Difficulty with standing or walking, characterized by dizziness, imbalance or incoordination, which can lead to falls. These symptoms do not respond to dopamine-replacement therapy.

See also: ***gait dysfunction***

Prognosis

Expected future course of an illness.

Progressive Supranuclear Palsy (PSP)

Movement disorder that can be mistaken for Parkinson's disease. PSP is a neurodegenerative disease characterized by problems looking up and down, frequent falls and parkinsonism. It does not consistently respond to dopamine-replacement therapy.

PWP

Abbreviation for "People with Parkinson's" or "Person with Parkinson's."

Resting tremor

An unwanted and uncontrollable movement that affects a limb (or less commonly the head or chin) when it is at rest and stops for the duration of a voluntary movement. One of the cardinal clinical features of Parkinson's disease.

See also: ***tremor***

Rigidity

Abnormal stiffness in a limb or other body part. One of the cardinal clinical features of Parkinson's disease, rigidity is often most apparent when a clinician moves a patient's limb.

Serotonin

Brain chemical that may be deficient in some cases of depression and whose potential role in Parkinson's disease is under investigation.

Sinemet

Brand name of the most commonly prescribed medication for Parkinson's. A combination of levodopa and carbidopa.

See also: ***levodopa***

Sleep disorders

Chronic troubles with amount, duration or quality of sleep. Many people with Parkinson's do not feel rested and have daytime sleepiness. Both Parkinson's disease and Parkinson's medications can contribute to sleep disturbances.

Speech disorders

Symptoms of slurring words, decreased volume and tone of speech, and hoarseness of voice that affect up to 90 percent of people with Parkinson's at some time in the course of their disease. Speech therapy is the recommended treatment as these symptoms do not respond to dopamine-replacement therapies.

See also: ***physical therapy***

Sporadic Parkinson's disease

Most common form of Parkinson's disease, accounting for upwards of 95 percent of cases, likely arising from a combination of genetic and environmental factors. Sporadic Parkinson's disease is sometimes called idiopathic, meaning that the cause is unknown. Sporadic Parkinson's disease does not run in families, unlike other (much rarer) forms of Parkinson's disease.

See also: ***familial Parkinson's Disease***

Symptomatic

1. Term used by people with Parkinson's to describe the state in which they are strongly affected by symptoms and in which their medication or treatment regimen is providing little to no relief.

2. Pertaining to treatments that affect the symptoms of a disease but not the underlying actions that cause the disease to progress. All currently available therapies for Parkinson's disease are symptomatic, meaning that they do not slow the biological disease progression.

See also: ***neuroprotective***

Tremor

Involuntary, uncontrollable, rhythmic movements (fast or slow) that may affect the hands, head, voice or other body parts. Resting tremor is one of the cardinal clinical features of Parkinson's disease.

See also: ***resting tremor***

Wearing off

"Off" periods refer to times when medication loses benefit and symptoms of Parkinson's return. As disease progresses, this can come on before the next medication dose is due. Onset can be gradual or sudden and unpredictable.

See also: ***off phenomenon***

Young-onset Parkinson's disease

A rare form of Parkinson's disease characterized by onset of symptoms before age 50.

Hallucinations/Delusions

Psychosis can be a frightening word that many people simply don't understand. But what does it really mean? In Parkinson's disease (PD), what your doctor calls psychosis usually starts with mild symptoms, but these can have a big impact on quality of life. Healthcare providers usually refer to these symptoms as "Parkinson's disease associated psychosis." Psychosis can vary from severe confusion (disordered thinking) to seeing things that aren't there (hallucinations) to believing things that are not true (delusions).

It is important to report any hallucinations or delusions to your medical team, even if they are not bothersome.

How Common is Parkinson's disease Psychosis (PDP)?

Between 20-40% of people with Parkinson's report the experience of hallucinations or delusions. When followed as the disease progresses over the years, this number increases. The increase does not mean that the hallucinations are persistent across the majority of patients. However, it is important to note that these statistics sometimes include "delirium," in which the symptoms are temporary due to medication that needs to be adjusted or infection that needs to be treated, and "isolated minor symptoms" or "minor hallucinations," including illusions, where instead of seeing things that are not there (hallucinations), people misinterpret things that are really there. These are the most common types of psychosis in people with PD, with different studies placing the occurrence between 25-70% of people with Parkinson's. Typically, if the person with PD only has these minor hallucinations, their doctor will not prescribe an antipsychotic medication, though more significant psychosis that requires medication may develop over time. In one study, 10% of those with minor hallucinations had their symptoms resolved within a few years, while 52% saw their symptoms remain the same and 38% saw their psychosis symptoms get worse.

We recommend that people with Parkinson's not use a single percentage to represent the prevalence of hallucinations and PDP. Parkinson's is a complex disease and as it progresses the percentages and risk of symptoms will change.

What Are Hallucinations?

Hallucinations are when someone sees, hears or feels something that is not actually there. They are best described as deceptions or tricks played by the brain that involve the body's senses. Hallucinations are not dreams or nightmares. They happen when the person is awake and can occur at any time of day or night.

Types of Hallucinations

- **Visual:** Hallucinations in people with PD are usually visual. Common hallucinations include seeing animals or people, such as a furry

creature running by or a deceased love one sitting in the room.

- **Auditory:** Hearing voices or sounds that are not real is less common but is reported by a small percentage of people with PD.
- **Olfactory:** Smelling an odor that is not related to an actual source is rare in PD.
- **Tactile:** Feeling something imaginary, like bugs crawling on your skin, is rare in PD.
- **Gustatory:** Sensing a bitter or abnormal taste in your mouth that has no source is rare in PD.

More about Hallucinations

- Hallucinations are most often a side effect of medication and are not necessarily a sign of a decline in cognitive abilities. Most hallucinations experienced by people with PD are fleeting and non-threatening. However, in some cases hallucinations may become threatening or bothersome.
- Although hallucinations can affect anyone taking medication to manage PD symptoms, they are more common in people who have problems with thinking or memory, or when under medical stress.
- Visual hallucinations are more likely to occur in low light or low visibility situations. To reduce risk, increase lighting in particularly dark areas, such as hallways.
- Hallucinations may occur in the peripheral vision (out of the corner of the eye), in the form of a flash of light, people or small animals such as cats or dogs. Images often disappears when the person looks more closely.
- Sometimes people with PD have presence hallucinations — the feeling that someone is in the room with them or standing behind them.
- Some people are aware that hallucinations are occurring. This is called "retaining insight." With insight, you might be able to create coping mechanisms. However, some people find them incredibly real, or may lose insight as the disease progresses.

Tips for Living with Hallucinations

It is important for people with PD to talk about hallucinations with their family and care team, because they are manageable and can be troublesome if not treated. Discuss all possible symptoms with your doctor, no matter how minor, rare or bizarre you may think they are.

- Good lighting and stimulating activities in the evening can help keep hallucinations at bay.
- While a hallucination is occurring, caregivers can help their loved one by reassuring them that they will be safe and validating their partner's experience. For example, say, "I'll take the cat outside" instead of arguing that there is no cat.

What Are Illusions?

Illusions are another sensory misperception. Instead of seeing something that isn't there, people with illusions misinterpret real things in the environment. For example, the clothes in the closet may look like a group of people.

Like visual hallucinations, illusions tend to occur in low light or low visibility situations.

What Are Delusions?

Delusions are illogical, irrational, dysfunctional views or persistent thoughts that are not based in reality. They are not deliberate and are very real to the person with PD. People with delusions who feel threatened may become argumentative, aggressive, agitated or unsafe.

- Delusions are less common in PD than visual hallucinations. They affect about eight percent of people with PD.
- Compared to hallucinations, delusions tend to be more complicated, present a greater risk for behavioral disturbances and safety concerns, are typically more difficult to treat and represent a more obvious deterioration or decline in one's condition.
- Delusions can begin as generalized confusion at night. Over time, confusion can develop into clear delusions and behavioral disturbances during the day.

- All forms of delusions can be seen with PD, although delusions of jealousy and persecution (like paranoia) are most widely reported and represent a greater challenge for treatment. These delusions can lead to aggression, which can pose a serious safety risk to the person with PD, family members and caregivers.
- Paranoia can lead to medication noncompliance — a person refusing to take medications, believing they are poisonous or deadly.
- Delusions can be associated with dementia. As a result, people with delusions are often confused and extremely difficult to manage. In these cases, many caregivers require outside assistance.

Examples of Delusions in PD

- Jealousy
    - Belief: Your partner is being unfaithful.
    - Behavior: Paranoia, agitation, suspiciousness, aggression.
- Persecutory
    - Belief: You are being attacked, harassed, cheated or conspired against.
    - Behavior: Paranoia, suspiciousness, agitation, aggression, defiance, social withdrawal.
- Somatic
    - Belief: Your body functions in an abnormal manner. You develop an unusual obsession with your body or health.
    - Behavior: Anxiety, agitation, reports of abnormal or unusual symptoms, extreme concern regarding symptoms, frequent visits with the clinician.

What Causes Hallucinations and Delusions?

Medication, dementia and delirium are the three main contributors to the development of psychosis in Parkinson's disease. Determining the cause can be difficult because these conditions can overlap and produce similar symptoms. Once a probable cause is determined, treatment can begin.

Medications

Many PD medications can lead to symptoms of psychosis:

- Classic PD medications like carbidopa-levodopa (Sinemet) and :dopamine agonists are designed to increase dopamine levels, improving motor symptoms. However, by boosting the dopamine supply, these medications can inadvertently cause serious emotional and behavioral changes.
- Other medications used to treat PD can also cause these symptoms by lowering levels of acetylcholine, shifting its balance with dopamine. These medications include amantadine and anticholinergics (Artane and Cogentin). In addition to the prescription drugs, anticholinergics are typically the main ingredient in over-the-counter sleep aids and many allergy medications.

Dementia

Dementia is a term used to describe a group of symptoms associated with a decline in memory and thinking. It is commonly associated with Alzheimer's disease, but people with PD can also develop it.

- Hallucinations and delusions can result from the basic chemical and physical changes that occur in the brain, regardless of other factors such as PD medications. This is most commonly seen in cases of PD with dementia.
- If psychosis and dementia occur early in the disease process, doctors may consider a diagnosis of Lewy body Dementia (LBD).

Delirium

Delirium is a reversible change in a person's level of attention and concentration.

- Delirium usually develops over a short period of time (hours to days) and resolves following treatment of the underlying condition.
- Signs of delirium include altered consciousness or awareness, disorganized thinking, unusual behavior and hallucinations.
- Because there are so many symptoms, delirium can be confused with other conditions, such as dementia or drug-induced psychosis.

- To diagnose delirium, a person's level of concentration or attention must go through a change.
- People with Parkinson's have a higher risk of delirium when admitted to the hospital, due to the new settings for the procedure or surgery, which may be unrelated to their PD.

Common causes of delirium include:

- Infection, such as urinary tract infection or pneumonia
- Imbalance of sodium, potassium, calcium or other electrolytes
- Stroke
- Heart disease
- Liver disease
- Fever
- Vitamin B12 deficiency
- Head injury
- Sensory changes, such as hearing loss and vision changes

In addition to medical conditions and changes, many commonly used drugs and chemicals can also cause delirium:

- Anticholinergic medications: diphenhydramine hydrochloride (Benadryl®), trihexyphenidyl (Artane®), benztropine (Cogentin®), ranitidine (Zantac®) and oxybutynin (Ditropan®)
- Narcotics containing codeine or morphine
- Antibiotics
- Nonsteroidal anti-inflammatory drugs (NSAIDS) including Aleve®, Motrin® and Advil®
- Insulin
- Sedatives
- Steroids
- Anti-seizure medications
- Alcohol
- Recreational drugs

Risk Factors for Psychosis

Not everyone with Parkinson's will develop hallucinations or delusions, but there are several things can increase your risk:

- Dementia or impaired memory
- Depression: Individuals suffering from depression and PD are at a greater risk. In addition, severe depression alone can cause psychosis.
- Sleep disorders, such as vivid dreaming. Individuals commonly report vivid dreaming prior to the onset of psychosis. Other associated sleep disturbances include REM sleep disorder and general insomnia.
- Impaired vision
- Older age
- Advanced or late-stage PD
- Use of PD medications

Treating Psychosis

Treating Parkinson's disease psychosis is a multi-step process that begins with talking to your health care team. They will follow a series of steps to figure out how best to address your symptoms.

Step 1. The first step is to perform a clinical evaluation of your symptoms considering prior history, disease stage, and available support systems. This assessment will help determine if something is medically wrong and you need treatment right away, or if you can keep an eye on the condition and wait.

Step 2. Treatment, when needed, generally begins with adjustment of your PD medications and referral to counseling. If there is nothing medically wrong with you, your doctor may reduce or eliminate medications, often in a specific order, to lessen the symptoms of psychosis. This is a balancing act as dopamine, which is used to steady your motor symptoms, can also, in high levels, increase psychological side effects.

Step 3. If further intervention is needed, your doctor may initiate antipsychotic therapy, using drugs to rebalance the chemical levels in the brain and reduce episodes of hallucinations, illusions, and delusions

Medications Used for Treating Psychosis

Antipsychotic agents are designed to balance abnormal chemical levels in the brain. Up until the 1990s, the use of antipsychotics in PD was controversial because the drugs used until that time work by reducing excess dopamine. This alleviated psychosis but caused dramatic worsening of PD motor symptoms.

Fortunately, medications that are better tolerated by people with PD are now available. Today, there are three antipsychotic medications considered relatively safe for people with PD: quetiapine (Seroquel®), clozapine (Clozaril®) and the newest agent, pimavanserin (Nuplazid®). They cause limited worsening of PD while treating hallucinations and delusions.

Pimavanserin

- Pimavanserin was approved by the U.S. Food and Drug Administration (FDA) in 2016 specifically for the treatment of Parkinson's disease psychosis.
- Unlike other antipsychotics, it does not block dopamine. It is a selective serotonin inverse agonist, meaning it targets serotonin receptors.

Clozapine

- Clozapine (Clozaril) has been studied and proven effective in improving hallucinations and delusions in PD. However, due to a rare, yet serious side effect known as agranulocytosis — a reduction in white blood cells that interferes with the body's ability to fight infection — there is a tendency use this medication only if quetiapine is not tolerated or effective.
- Anyone who takes clozapine is required to get weekly blood tests for the first six months, and every two weeks thereafter, to monitor white blood cell levels.

Quetiapine

- Quetiapine (Seroquel) has fewer side effects, but there is limited evidence for its efficacy in people with Parkinson’s.

- It is most often prescribed to be taken just before going to bed because it may be mildly sedating.

*It is important to familiarize yourself with antipsychotic medications, as many can worsen motor symptoms and should not be prescribed for people with PD. Some of these medications, such as haloperidol (Haldol), are commonly prescribed in the hospital setting for patients who are agitated or anxious. Treating clinicians should be aware that certain antipsychotic medications can make the condition of the person with PD worse.

How to Talk to Someone with Hallucinations or Delusions

- It is usually not helpful to argue with someone who is experiencing a hallucination or delusion. Avoid trying to reason. Keep calm and be reassuring.
- You can say you do not see what your loved one is seeing, but some people find it more calming to acknowledge what the person is seeing to reduce stress. For example, if the person sees a cat in the room, it may be best to say, "I will take the cat out" rather than argue that there is no cat.

Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

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Inbrija (inhaled levodopa), a new therapy for “off” time

When Parkinson’s disease (PD) symptoms re-emerge. Under-the-tongue apomorphine, also for “off” time, is currently under review with the U.S. Food and Drug Administration (FDA).

For many people, these medications may offer a different and, in some ways, easier route to manage symptoms. But it can be hard to know if and when to add a new drug and what you should ask your doctor. Here, we discuss the new and existing treatments for “off” and tips for thinking about newer medications.

What is “off” time?

“Off” time is when PD symptoms return between medication doses. Not everyone experiences “off” time, but it’s more common the longer you have Parkinson’s and the longer you take levodopa. “Off” time may involve movement problems (tremor, slowness and stiffness) as well as non-movement symptoms (anxiety, sweating, or cloudy or fuzzy thinking). Because each person’s Parkinson’s is unique, everyone’s “off” time is unique. “Off” time can happen at different times: in the morning, before the first dose of medication; between medication doses or after meals throughout the day; or suddenly and unpredictably.

What is the new “off” treatment?

Acorda’s Inbrija is an inhaled form of levodopa, which is the most commonly prescribed Parkinson’s drug. In the brain, levodopa turns into the chemical dopamine, which decreases in PD and causes abnormal and uncoordinated movement. Inbrija is absorbed through the lungs, so it is absorbed more quickly than a pill taken by mouth.

Inbrija is to be used as needed, up to five times per day, to rapidly reverse “off” symptoms. You take it in addition to regularly scheduled Parkinson’s medications. This is similar to asthma treatment, where a person may take a daily medication to control breathing and use a rescue inhaler if sudden problems arise.

In clinical trials, Inbrija started to work in as little as 10 minutes and lasted up to an hour. The most common potential side effects of Inbrija include nausea, cough, upper respiratory infection, or changes in saliva or spit color.

Should I take Inbrija?

If you have recurring or sporadic “off” times, you may want to consider Inbrija. But because this is an add-on medication, it may be helpful to first ensure your current treatment is working as well as it can. Adjustments to how and when you take your medications could lessen “off” time.

For some people, separating levodopa from high-protein meals (meat, fish, nuts or beans, for example) by 30 to 60 minutes may ease symptoms. Levodopa and dietary protein are absorbed in the same part of the gut. When you take medication and protein at the same time, less medication may be absorbed, potentially leading to "off" time.

Changing your medication's dose or timing also may help. If your symptoms start to return gradually about an hour before every levodopa dose, for example, your doctor may recommend you take it more often or increase the dose, or add a longer-acting PD drug to prevent "wearing off."

If you still have "off" time despite dietary and medication adjustments, Inbrija may be an option. Even for those whose symptoms are fairly well controlled, it may be good to have a rescue therapy on hand just in case "off" time comes on at an unpredictable or inconvenient moment.

Isn't Apokyn already available for "off" time?

Apokyn, injectable apomorphine, has been available since 2004 to use as needed for Parkinson's "off" time. Apomorphine mimics the brain chemical dopamine, which decreases in PD. When prescribing Apokyn, doctors typically add medication to prevent nausea and observe your first dose to make sure blood pressure doesn't drop too low. The main side effects are nausea, low blood pressure or dizziness, and sleepiness as well as redness and bruising from the injections. The FDA currently is reviewing a reformulation of this medication — a strip that dissolves under the tongue, similar to a Listerine breath strip.

How do my doctor and I choose the right therapy?

When thinking about a new therapy (whether it's new to the market or just new to you), consider which of your symptoms are most bothersome and how they interfere with what you want and need to do. Will the new medication treat these better than your current therapies? Always weigh the potential benefits (such as quick relief of "off" time) against the possible side effects (different for each drug) and costs. Other considerations include:

Success or difficulty with similar drugs.

Have you had a good or bad response to a drug that works in the same way? You might have a similar effect with a new drug. For example, if other dopamine agonists caused intolerable nausea or sleepiness, you may want to avoid the Apokyn injection.

Other medications.

How might the drug impact your other prescription or over-the-counter medications? Inbrija should not be taken with certain antidepressants and anti-anxiety medications called non-selective MAO-B inhibitors. (These are different than Parkinson's MAO-B

inhibitors such as Azilect and selegiline.) Always review medications with your doctor and pharmacist to avoid possible drug interactions.

Medical conditions.

How might the drug affect diseases you live with or risk factors you have? Inbrija was not tested in people with asthma or COPD (chronic obstructive pulmonary disease), so you may want to exercise caution or choose another therapy if you have one of these respiratory diseases. (Clinical trials did not find evidence of significant lung problems with the drug.) Many people also worry about dyskinesia (involuntary, uncontrolled movement), which is a potential risk with higher levodopa doses over longer periods. If you take large doses of levodopa in daily Sinemet or Rytary, for example, talk with your doctor about the benefits and risks of adding more.

Delivery method.

How do you prefer to take medication? Inbrija is like an asthma inhaler; you breathe the medication into the lungs. Apokyn is like an insulin shot; it's injected under the skin. For some, taking medication through an inhaler is challenging or uncomfortable. Others have a hard time managing injections because their hands are stiff and slow during "off" time. Think about what fits your symptoms and your lifestyle and what's most practical for you. If you can't or won't use it, no drug will do you any good at all.

What's the bottom line?

People respond differently to different medications, and treating Parkinson's can be a bit of trial and error. Talk with your doctor about your symptoms, diet and current medications, new medications, and what's on the horizon so that together you can make an informed decision about your care.

Loss of Smell

Not all people with reduced sense of smell will go on to develop Parkinson's, but most people with PD have some loss of their sense of smell.

In fact, reduced sense of smell, called hyposmia, is often an early sign of Parkinson's. Looking back, you may realize you were losing your sense of smell several years before you received a Parkinson's diagnosis.

Hyposmia is an under-recognized symptom, as it is not a common concern for doctors to ask about or for patients to report. If you or someone you know has trouble smelling foods like bananas, dill pickles or licorice, ask your doctor about Parkinson's.

Managing Loss of Smell

There are not any treatments for lost sense of smell. However, reduced ability to smell might affect your appetite, since taste is linked to smell. If you find yourself gaining or losing weight, learn more about diet and nutrition and call our Helpline for tips: 1-800-4PD-INFO (473-4636).

Medical Marijuana

With medical marijuana now legalized in 33 states and Washington, DC, it is obvious that there is strong interest in its therapeutic properties. Researchers are testing marijuana, which is also called cannabis, as a treatment for many illnesses and diseases, including neurological conditions, with Parkinson's disease (PD) high on the list. But despite several clinical studies, it has not been demonstrated that cannabis can directly benefit people with PD.

The Science Behind Marijuana

What is the science and pharmacology behind marijuana, and can it be used to treat Parkinson's symptoms?

The **endocannabinoid system** is located in the brain and made up of cannabinoid receptors (a receptor is molecular switch on the outside of a cell that makes something happen inside a cell when activated) that are linked to **neurons** (brain cells) that regulate thinking and some body functions.

Researchers began to show enthusiasm to study cannabis in relation to PD after people with PD gave anecdotal reports and posted on social media as to how cannabis allegedly reduced their tremors. Some researchers think that cannabis might be neuroprotective— saving neurons from damage caused by PD.

Cannabinoids (the drug molecules in marijuana) have also been studied for use in treating other symptoms, like bradykinesia (slowness caused by PD) and dyskinesia (excess movement caused by levodopa). Despite some promising preclinical findings, researchers have not found any meaningful or conclusive benefits of cannabis for people with PD.

Researchers issue caution for people with PD who use cannabis because of its effect on thinking. PD can impair the executive function — the ability to make plans and limit risky behavior. People with a medical condition that impairs executive function should be cautious about using any medication that can compound this effect.

The Pharmacology of Cannabis

Marijuana contains more than 100 neuroactive chemicals that work with two types of cannabinoid receptors, **type 1 (CB1)** located in the brain and **type 2 (CB2)** located in the brain and peripheral immune system. Cannabinoids have powerful, indirect effects on these receptors, but researchers are unsure how. People with PD have less CB1 receptors than people who do not have PD. A boost to the CB1 receptor through an agonist, like marijuana, can improve tremors and may alleviate dyskinesia. Similarly, the other receptor, CB2, is also being studied to determine if it can modify the disease or provide neuroprotective benefits. However, a unified hypothesis does not currently exist for either receptor because there is too much conflicting data on the effectiveness of cannabinoids and these receptors.

Cannabis can contain two different types of molecules that interact with cannabinoid receptors: agonists and antagonists. An **agonist** is a drug that attaches to the same receptor as a natural chemical and causes the same effect. A **dopamine agonist** is a drug that is not dopamine, but attaches to the dopamine receptor. An **antagonist** is different as it attaches to the receptor, but blocks the action of the natural chemical. Medical marijuana can contain both cannabinoid agonists *and* antagonists. Recreational marijuana use is derived from its effects on agonists.

The varying amounts of cannabinoid agonists and antagonists in different marijuana plants makes cannabis studies difficult to conduct. When researchers study the effects of a medication, dosages are controlled and often set to a specific number of milligrams. When testing medical marijuana, the dosage administered can vary dramatically depending on the plant and method of administration.

Delta-9-tetrahydrocannibinol (THC)

THC is a primary component of marijuana. Cannabidiol is the other primary component. THC has a long latency of onset and cannot be easily measured for a therapeutic or medicinal dose. Medical marijuana studies primarily provide participants with THC and/or cannabidiol as a capsule, nasal spray or liquid formulation.

PD-Related Medicinal Marijuana Trials

The use of cannabinoids has been suggested to help with managing neurological and non-neurological conditions. Literature on medical marijuana is incredibly varied. Studies have not clearly supported the use of marijuana for PD. The clinical studies of cannabis as a PD treatment that have been conducted did not use the clinical trial gold standard of a double blind, placebo controlled trial design. Some studies had as few as five subjects.

While some results have been positive, the effects of medical marijuana are probably not completely understood, which is why more studies, especially those with more subjects, are needed. Most doctors don't support study results because these studies do not meet minimum research standards.

Below are several PD-related medical marijuana studies that have been conducted to evaluate the use of cannabinoids:

- The Therapeutic Potential of Cannabinoids for Movement Disorders: clinical observations and trials of cannabinoid-based therapies suggest a possible benefit to tics and probably no benefit for tremor in dyskinesias or PD motor symptoms. Further preclinical and clinical research is needed to better characterize the pharmacological, physiological and therapeutic effects of this class of drugs in movement disorders.
- Cannabinoids Reduce Levodopa-induced Dyskinesia in Parkinson's Disease: A Pilot Study: the authors demonstrate that nabilone, the cannabinoid receptor agonist, significantly reduces levodopa-induced dyskinesia in PD.
- Neurokinin B, Neurotensin, and Cannabinoid Receptor Antagonists and Parkinson Disease: evaluation of the effects of three antagonists on the NK3, neurotensin and cannabinoid receptors on the severity of motor symptoms and levodopa-induced dyskinesias after administration of a single dose of levodopa in 24 patients with PD. The study concluded that the drugs tested were safe, but did not improve Parkinsonian motor disability.
- The Endocannabinoid System as an Emerging Target of Pharmacotherapy: reviews the endocannabinoid system and its regulatory functions in health and disease.

Risks and Benefits for People with PD

There are risks and benefits associated with the use of cannabis for people with PD. Benefits include a possible improvement in anxiety, pain management, sleep dysfunction, weight loss and nausea. Potential adverse effects include: impaired cognition (impairment in executive function), dizziness, blurred vision, mood and behavioral changes, loss of balance and hallucinations. Chronic use of marijuana can increase risk of mood disorders and lung cancer.

Medical Marijuana and Legislation by State

Washington, DC, and 33 states passed legislation allowing the use of marijuana-based products for medical purposes. In some states

patients must register to possess and use cannabis. Other states require patients to acquire a document from a physician stating that the patient has an approved condition. Under federal law doctors cannot prescribe cannabis, but many states authorize them to issue certifications that allow patients to obtain medical marijuana.

PD is a qualifying condition for medical marijuana in: Connecticut, Florida, Illinois, Louisiana, Massachusetts, Michigan, Missouri, New Hampshire, New Mexico, New York, Ohio, Pennsylvania and Vermont.

Medical marijuana is legal in: Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Hawaii, Illinois, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, Utah, Vermont, Washington, West Virginia and Washington, DC.

Parkinson's Foundation Centers of Excellence and Medicinal Marijuana

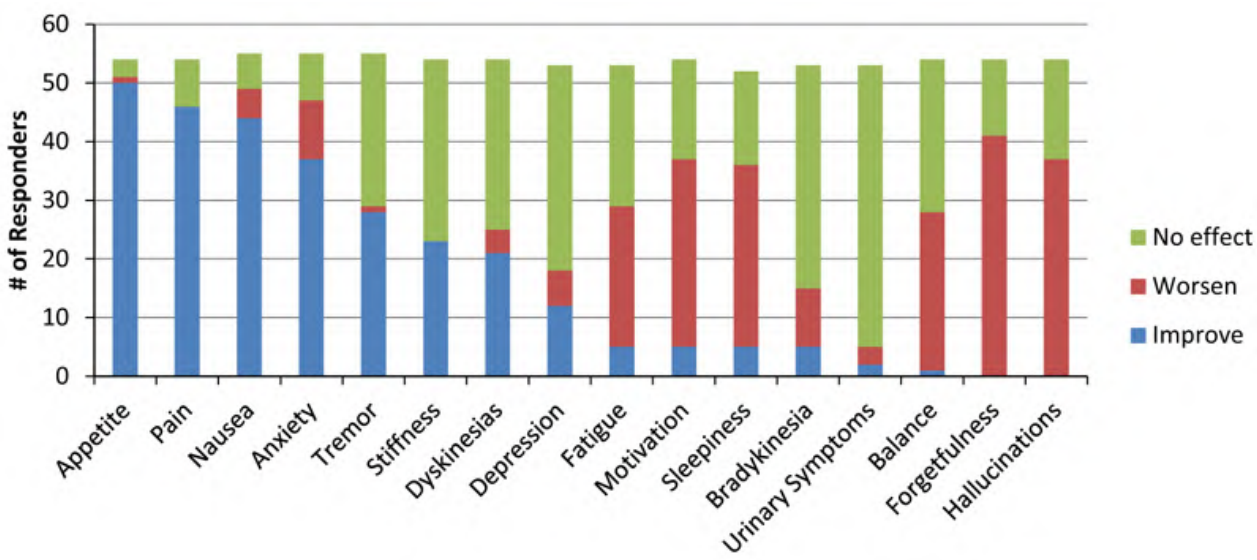
The Parkinson's Foundation, in partnership with Northwestern University researchers, studied attitudes about cannabis at 40 Centers of Excellence. To the best of our knowledge, this is the first study to provide data on the practices, beliefs and attitudes of expert PD physicians concerning cannabis use.

The results were interesting: most experts said they knew what cannabis did, but disagreed on the details. While there is no general agreement on what the benefits might be for people with PD, the survey confirmed that cannabis is a popular subject within Parkinson's Foundation centers as 95 percent of neurologists reported patients have asked them to prescribe it.

Cannabis study results also included:

- Only 23 percent of physicians had any formal education on the subject of cannabis (such as a course or lecture), thus 93 percent of physicians want cannabis taught in medical school.
- Physicians reported that 80 percent of their patients with PD have used cannabis.

- Only 10 percent of physicians have recommended the use of cannabis to patients with PD.
- In terms of memory: 75 percent of physicians felt that cannabis would have negative effects on short-term memory and 55 percent felt that cannabis could have negative effects on long-term memory
- Only 11 percent of physicians have recommended use of cannabis in the last year



This graph shows how physicians expect cannabis would improve, worsen, or show no effect to PD-related symptoms given their expertise and observations of patients with PD.

The study emphasized that physicians would be more apt to use medical marijuana as a treatment if it was approved through regulation instead of legislation. Nearly all medications are only approved after passing a science-based evaluation proving their effectiveness in a process overseen by the U.S. Food and Drug Administration. Since cannabis has been approved through legislation rather than regulation, there are no labels, dosage recommendations or timing instructions that physicians can reference.

Is Medical Marijuana an Option for Me?

What's next for a person with PD who wants to know if medical marijuana is an option? "Marijuana should never be thought of as a replacement for dopaminergic and other approved therapies for PD,"

said Dr. Michael S. Okun, the Parkinson's Foundation National Medical Director.

Research is still needed to determine how medical marijuana should be administered and how its long-term use can affect symptoms of PD. To keep patients safe, states that legalize medical marijuana will eventually need to develop training programs for doctors and medical teams that prescribe medical marijuana. Consult your doctor to see if medical marijuana is an option for you.

Page reviewed by Dr. Bhavana Patel, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

Prescription Medications

Surgical Treatment Options

Medical Marijuana

Over the Counter & Complementary Therapies

Exercise

Clinical Trials

information

MEDICAL OPTIONS FOR PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

It is primarily related to a lack of dopamine as a result of degeneration of dopamine producing neurons within the mid – brain. Dopamine is a neurotransmitter which conveys messages between neurons to ensure effective planning, initiation and maintenance of movement. Most pharmaceutical treatment options focus on restoring the balance of dopamine and other neurotransmitters by several means.

- Dopamine Replacement Therapy
- Dopamine Agonists

NB: The medications in this information sheet are listed in alphabetical order.

Dopamine Replacement Therapy (Levodopa)

The use of levodopa to replace dopamine remains the gold standard treatment for Parkinson's and a positive response to levodopa will assist in the process of diagnosis. Levodopa can have a positive effect on the symptoms of bradykinesia and muscle rigidity. Tremor is the least responsive symptom to levodopa.

Levodopa is a precursor to dopamine and crosses the blood brain barrier where it is converted to dopamine and corrects the imbalance of neurotransmitters. In order to ensure it passes the blood brain barrier and to prevent the breakdown of levodopa the addition of decarboxylase inhibitors (either Carbidopa or Benzedride) is necessary.

In Australia, levodopa is currently available as:

- Duodopa® is a gel form of levodopa which is delivered directly into the duodenum via a PEGJ tube.
- Kinson® is a generic form of levodopa and is available in one dose only (100/25)
- Levo - Carbidopa® is a generic form of levodopa and is available in one dose only (250/25)
- Madopar® is available in standard, controlled release (HBS) and a dispersible form when more rapid action is required. Several dosages are available.
- Sinemet® is available in standard and controlled release (CR) forms with several dosages available. It may also be prescribed as a liquid which must be prepared freshly every 24 hours and refrigerated.
- Stalevo® is levodopa with carbidopa and an additional ingredient (entacapone) and will be discussed under COMT inhibition.

Dopamine Agonists

These medications mimic dopamine and stimulate the dopamine receptors. They may be prescribed as initial therapy or in conjunction with levodopa.

There are two types of dopamine agonists (non ergoline derived and ergoline derived). Ergoline derived are used less commonly because of a small risk of fibrotic reactions (e.g. cardiac valve, pulmonary and pleural fibrosis) associated with long term use.

In Australia the more commonly used dopamine agonists are:

- Apomine® (apomorphine) given by subcutaneous injection or via a subcutaneous infusion using a pump.
- Movapo® (apomorphine) as above
- Neupro® (rotigotine) is a trans dermal patch which is applied to different skin areas each day. It is important to hold the patch firmly in place for 60 seconds to ensure fixation. Neupro® must not be worn during an MRI scan or cardioversion.
- Sifrol® (Pramipexole) is available in an extended release (ER) formulation which is taken once daily and normal release which is taken three times a day.

Less frequently used dopamine agonists are:

- Cabaser ® (cabergoline)
- Parlodel® (bromocriptine)

MEDICAL OPTIONS FOR PARKINSON'S

Potential Adverse Effects of Dopaminergic Medications (Levodopa and Dopamine Agonists)

When medications are first introduced there are some common effects which are usually short lived and manageable as the body adjusts. These include:

- Nausea and occasionally vomiting. It is recommended that medication is taken with food initially. Motilium® (Domperidone) may be prescribed. Other anti nausea medications such as Maxolon® and Stemetil® should be avoided as they can worsen the Parkinson's symptoms.
- Dizziness due to a drop in blood pressure on standing may occur - avoid rising quickly.

Other possible side effects are:

- Ankle swelling may occur with dopamine agonists
- Constipation - this may occur as a side effect of medication in addition to being a symptom of Parkinson's. Additional fluids and a high fibre diet are recommended.
- Hallucinations are usually related to progression of the condition and long term dopaminergic medications. They may or may not be frightening.
- Increased dreams, which may be vivid, may occur due to Parkinson's but may be exacerbated due to medications.
- Motor fluctuations – these include 'wearing off' of the benefit of the medication before the next dose is due. Dyskinesias (involuntary movements) may develop with long term use of levodopa especially with higher doses.
- Sedation or excessive sleepiness may occur and is more common with dopamine agonists.

Treatment with dopaminergic medications (especially at higher doses) can sometimes lead to behavioural changes e.g. obsessive compulsive disorder. This may take the form of gambling, excessive shopping, eating, increased libido or an interest in pornography.

If you believe that you are experiencing side effects from medications this should be discussed with your treating specialist of General Practitioner. They may consider adjusting the choice or dose of medication.

Other forms of medications used in the management of Parkinson's are:

- COMT Inhibition
- MAO Type B Inhibition
- Amantadine
- Anticholinergic Therapy

COMT Inhibition

Catechol-O-methyltransferase (COMT) is a naturally occurring enzyme which metabolizes both levodopa and dopamine. By inhibiting the action of COMT more levodopa is available – in theory, providing a more prolonged response to each dose .

Currently, in Australia, the available COMT inhibitors are:

- Comtan® (entacapone) is taken with each dose of levodopa – taken by itself Comtan® has no therapeutic action. It is available in one dose only.
- Stalevo® is a combination of levodopa, carbidopa and entacapone and is available in several doses.

COMT inhibitors may exaggerate existing levodopa side effects. Discoloration of urine is a non harmful side effect. A small percentage of people taking these medications may experience diarrhoea. This may occur after being on the medication for an extended period of time.

MAO Type B Inhibition

Monoamine oxidase (MAO) is a naturally occurring enzyme which is responsible for the breakdown of dopamine. MAO Type B inhibitors are reputed to scavenge free radicals formed by the oxidative metabolism of dopamine hence the unproven theory that they may have a neuro protective effect.

Currently, in Australia, the available MAO Type B inhibitors are:

- Azilect® (rasagiline mesylate) – taken once a day
- Eldepryl® (selegiline hydrochloride) – taken twice a day with the second dose taken no later than noon otherwise sleep may be disturbed.
- Selgene® (selegiline hydrochloride) – as above

MEDICAL OPTIONS FOR PARKINSON'S

Drug interactions may occur with these medications. Pethidine and some forms of antidepressants should be treated with caution. It is essential to discuss this with the treating specialist.

Amantadine

Amantadine is an antiviral agent and its mode of action in Parkinson's is not clear. It is reported to give some improvement to symptom control. More recently it has been used to reduce dyskinesia.

Currently, in Australia amantadine is available as:

- Symmetrel® (amantadine hydrochloride)

Possible side effects are insomnia, confusion, swollen ankles and a mottled rash on the lower limbs.

Anticholinergic Therapy

Prior to the development of dopaminergic replacement therapy, anticholinergic therapy was the only treatment option available. Anticholinergics correct the imbalance between dopamine and acetylcholine. They can be useful in addressing tremor.

Currently in Australia the available anticholinergics are:

- Akineton® (biperiden hydrochloride)
- Artane® (benzhexol hydrochloride)
- Benztrop® (benztropine mesylate)
- Cogentin ® (benztropine mesylate)

These are rarely used due to commonly occurring side effects such as dry mouth, urinary retention, blurred vision and confusion. The development of the newer forms of medications has also reduced the use of anticholinergic therapy.

MEDICATION WARNING

Some medications used in the treatment of other medical conditions have the potential to alter the dopamine system. It is important to consider the possibility that treatment for other conditions may cause or worsen Parkinson's symptoms.

The most commonly prescribed medications which are not recommended in Parkinson's are:

- Maxolon® Pramin® (metoclopramide)
- Stemetil® Stemzine® (prochlorperazine)
- Serenace® (haloperidol)

If treatment for nausea or vomiting is required Motilium® is a safe alternative.

SUMMARY

The medications described in this information sheet are used in the treatment of Parkinson's in Australia. The pharmaceutical management of Parkinson's is complex and medications should be prescribed by a specialist such as a neurologist or a geriatrician. Medications will need to be reviewed and changed as the condition progresses. It is important to have regular reviews.

As each person with Parkinson's presents differently, it is essential that the medical management be prescribed on an individual basis bearing in mind potential side effects.

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Medications Used in the Treatment of Parkinson's

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Parkinson's is a progressive neurological condition primarily related to the loss of dopamine producing cells within the brain. This brochure is intended as a guide to the medications used in the treatment of Parkinson's. Specific questions relating to your own medication should be directed to an experienced health care professional.

The management of Parkinson's can be challenging due to medication interactions and side effects. Response to medications may change over time. Timing of medications may be critical to obtain optimal benefit with minimal side effects and varies for each individual.

LEVODOPA (L-dopa)

Levodopa remains the main medication used in the treatment of Parkinson's. It is a precursor of dopamine which is reduced in Parkinson's. The addition of a decarboxylase inhibitor enables larger amounts of levodopa to pass into the brain. These medications are available in varying doses.

SINEMET® (L-dopa + carbidopa)
100/25; 250/25
200/50 CR (Controlled Release)

KINSON® (L-dopa + carbidopa)
100/25

LEVO/CARBIDOPA® (L-dopa + carbidopa)
250/25

DUODOPA® (L-dopa + carbidopa) -20/5 per ml
A gel preparation administered by a permanent tube directly into the duodenum.

MADOPAR® (L-dopa + benserazide)
50/12.5; 100/25; 200/50
100/25 HBS (Long Acting)
Madopar® Rapid – 50/12.5; 100/25
NB. Madopar® Rapid must be dissolved.

Side effects may include nausea, increased dreams, dizziness and with long term use hallucinations and dyskinesias (involuntary movements) may occur.

COMT INHIBITORS

This group of medications inhibits COMT (an enzyme which metabolises levodopa), thus making more levodopa available.

STALEVO® (L-dopa/carbidopa/entacapone)

Stalevo® 50 (50/12.5/200)
Stalevo® 75 (75/18.75/200)
Stalevo® 100 (100/25/200)
Stalevo® 125 (125/31.25/200)
Stalevo® 150 (150/37.5/200)
Stalevo® 200 (200/50/200)

COMTAN® (Entacapone) 200mg

This is a COMT inhibitor and must be taken with a dose of levodopa.

Side effects of both include an increase of levodopa effects (e.g. increased dyskinesia) and rarely diarrhoea. A harmless side effect is discolouration of urine.

AMANTADINE

Amantadine is an anti-viral agent that has anti-parkinsonian effects.

SYMMETREL® (amantadine hydrochloride)
100mg

Side effects are rare but may include insomnia, confusion, a mottled rash on the legs and swollen ankles.

ANTICHOLINERGICS

This group of medications act by balancing acetylcholine and dopamine. They are useful in the treatment of tremor particularly in the younger person with Parkinson's.

ARTANE® (benzhexol hydrochloride) 2mg; 5mg

BENZTROP® (benzhexol hydrochloride) 2mg

COGENTIN® (benztropine mesylate) 2mg

AKINETON® (biperiden hydrochloride) 2mg

Side effects (especially in the older patient) include dry mouth, urinary retention, blurred vision and confusion.

MONOAMINE OXIDASE TYPE B INHIBITORS

This group of medications inhibits the enzyme monoamine oxidase which is responsible for the break down of dopamine within the brain.

SELGENE® ELDEPRYL® (selegiline hydrochloride) 5mg - usually taken twice a day. It is important to take this medication no later than 1200 noon as it may cause sleep disturbance.

AZILECT® (rasagiline) 1mg - taken once a day. Can be taken at any time of the day.

MEDICATION INTERACTIONS WITH SELGENE® , ELDEPRYL® & AZILECT®

WARNING: Serious reactions may occur when patients taking selegiline or rasagiline are given Pethidine or certain types of antidepressants. Check with your health care professional before taking ANY medication if you have been prescribed selegiline or rasagiline.

DOPAMINE AGONISTS

This group of medications acts on the dopamine receptors and mimic dopamine. They can be used in combination with levodopa or alone.

SIFROL®(pramipexole)
0.125mg; 0.25mg; 1mg; 1.5mg

SIFROL ER®(Extended Release)(pramipexole)
0.375mg; 0.75mg; 1.5mg; 2.25mg; 3mg; 3.75mg; 4.5mg
This medication is taken once a day.

SIMIPEX® (pramipexole)
0.125mg; 0.25mg; 1mg
A generic form of Sifrol®.

Side effects may include nausea, dizziness (due to blood pressure changes), confusion and increased sleepiness. Some people may experience compulsive behaviour disorder in the form of gambling, eating or shopping. Increased libido has also been reported.

CABASER® (cabergoline) 1mg; 2mg
This medication is taken once a day.

PARLODEL® (bromocriptine mesylate)
2.5mg; 5mg; 10mg

KRIPTON® (bromocriptine mesylate)
2.5mg; 5mg; 10mg

Side effects as above and in addition but less frequently pulmonary or peritoneal fibrosis and cardiac valve changes may occur.

APOMINE®, MOVAPO® (apomorphine hydrochloride)
Used under specialist medical supervision. Given by intermittent subcutaneous injection or continuous subcutaneous infusion.

Apomorphine can cause severe nausea and vomiting and the specialist may prescribe MOTILIUM® (domperidone) to address this side effect.

DOPAMINE AGONISTS CONT.

NEUPRO® (rotigotine)
2mg; 4mg; 6mg; 8mg.

A transdermal (applied to skin) patch which is applied daily.

In addition to the side effects of other dopamine agonists a rash at site of application may occur.

This brochure provides information on the medications used in Parkinson's in layman's terms. It is designed to be used only as a guide. Please consult your doctor, pharmacist or Parkinson's Nurse Specialist with any queries.

Compiled by Janet McLeod, Senior Parkinson's Nurse Specialist, Parkinson's W.A. Inc.

Reviewed by Oksana Burford, Pharmacist, (Professional Advisory Board), Parkinson's W.A. Inc.

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October 2017

Patient Leaflets

The following patient Leaflets cover most of the Medications used in the treatment of Parkinson's Disease Motor Symptoms.

There are also a number of Medications used in the treatment of the Non-Motor Symptoms of Parkinson's Disease.

These have not been included in the selection of Patient leaflets.

Package leaflet: Information for the patient **UK**

Madopar 50 mg/12.5 mg **Roche**
Madopar 100 mg/25 mg
Dispersible Tablets
Levodopa and benserazide (as hydrochloride)

Please read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Madopar is and what it is used for

Madopar dispersible tablets contain two medicines called levodopa and benserazide. They are used to treat Parkinson's disease.

People with Parkinson's disease do not have enough dopamine in certain parts of their brains. This can result in slow movements, stiff muscles and tremor.

Madopar works like this:
- In your body the **levodopa** is changed into dopamine. Dopamine is the active medicine that is needed in your brain to help Parkinson's disease.
- The **benserazide** allows more of the levodopa you take to get into your brain, before it is changed into dopamine.

2. What you need to know before you take Madopar

Do not take Madopar if:
- You are allergic (hypersensitive) to levodopa, benserazide or any of the other ingredients of Madopar (listed in Section 6: Contents of the pack and other information).
- You have a problem with the pressure in your eyes called 'narrow-angle glaucoma'.
- You have serious problems with your kidneys, liver or heart.
- You have a serious problem with your hormones, such as an overactive thyroid gland.
- You have a severe mental problem which may make you distressed and anxious, or may make you lose contact with reality and become unable to think and judge clearly.
- You have depression and have taken a medicine called a 'non-selective monoamine oxidase inhibitor' (MAOI) in the last 14 days. These medicines include isocarboxazid and phenelzine. See the section on 'Other medicines and Madopar'.

You are pregnant or trying to become pregnant. See the section on 'Pregnancy and breast-feeding'.

- You are under 25 years of age. This is because your bones may not have finished developing.
- You have ever had skin cancer.

Do not take Madopar if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before you take Madopar.

Warnings and precautions

Talk to your doctor or pharmacist before taking Madopar if:

- You have a problem with the pressure in your eyes called 'wide-angle glaucoma'.
- You have problems with your hormones, kidneys, lungs or liver.
- You have diabetes (high blood sugar).
- You have heart problems, particularly an uneven heart beat (arrhythmia) or you have had a heart attack.
- You have any mental illness, such as depression.
- You have a 'peptic ulcer', an ulcer in your stomach, or in the tube leading from it ('duodenal ulcer').
- You have something called 'osteomalacia' which causes problems with the strength of your bones.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

If any of the above apply to you, or if you are not sure, talk to your doctor or pharmacist before you take Madopar.

Other medicines and Madopar

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Madopar can affect the way some medicines work. Also some other medicines can affect the way Madopar works.

Do not take Madopar if you have taken a medicine for depression called a 'non-selective monoamine oxidase inhibitor' (MAOI) in the last 14 days. These medicines include isocarboxazid and phenelzine. If this applies to you, do not take Madopar and ask your doctor or pharmacist for advice.

In particular, tell your doctor or pharmacist if you are taking the following medicines:

- Other medicines for Parkinson's disease, such as amantadine, selegiline, bromocriptine, 'anticholinergics' called orphenadrine and benzhexol, 'dopamine agonists' called pergolide and ropinirole and a 'COMT inhibitor' called entacapone.
- Ferrous sulfate (used to treat low levels of iron in the blood).
- Antacids (used for stomach acid if you have indigestion).
- Metoclopramide (used to treat problems with digestion).
- Phenothiazines - such as chlorpromazine, promazine and prochloroperazine (used to treat mental illness).
- Thioxanthenes - such as flupentixol and zuclopenthixol (used to treat mental illness).
- Butyrophenones - such as haloperidol and benperidol (used to treat mental illness).
- Diazepam (used to treat anxiety and insomnia).
- Tetrabenazine (used to help problems controlling your muscle movement).
- Papaverine (used to improve blood flow around the body).
- Treatment for high blood pressure (hypertension), in particular reserpine.
- 'Sympathomimetics' – such as epinephrine, norepinephrine and isoproterenol (used to treat problems with your heart or asthma).
- Amphetamines - medicines used for attention deficit disorder, feeling sleepy during the day (narcolepsy) or to help control appetite and weight gain.
- Strong painkillers – such as codeine or morphine.
- Domperidone – used to help prevent you from feeling or being sick.

Operations
If you are going to have an operation, tell the doctor that you are taking Madopar. This is because you may need to stop taking it before you have a general anaesthetic.

Tests
If you need to have tests on your blood or urine, tell the doctor or nurse that you are taking Madopar. This is because the medicine may affect the results of some tests.

Pregnancy and breast-feeding
Do not take Madopar if you are pregnant, trying to get pregnant or breast-feeding. This is because Madopar may affect your baby. It is important for women to use contraception while taking the medicine.
If you get pregnant while taking Madopar, talk to your doctor straight away.

Driving and using machines
Talk to your doctor about driving and using machines or tools, when you take Madopar. This is because one of the medicines in Madopar, levodopa, can make you feel very sleepy. This can happen very quickly, even during the day. You must not drive or use machines if this happens to you. If you are in any doubt about whether you can do a particular activity, talk to your doctor.

3. How to take Madopar

Always take Madopar exactly as your doctor has told you. You should check with your doctor if you are not sure. How much you take and when you take it is different for different people.

How to take your tablets:
- Dissolve your tablets in a quarter of a glass of water or orange squash (not fresh orange juice). When you put the tablets in water, they break up quickly and the water will turn white. Stir well and drink within half an hour.
- Take them 30 min before or one hour after meals.

Patients NOT already treated with levodopa:
- The usual starting dose is one 50 mg/12.5 mg tablet (50 mg levodopa), three or four times a day.
- Your doctor will then increase your dose every 2 to 3 days until they find the right dose for you.

Patients already treated with levodopa:
- Your starting dose of Madopar will be one less 100 mg/25 mg tablet than the number of levodopa 500 mg tablets you take each day. For example, if you take four levodopa tablets (2000 mg levodopa) each day, your doctor will start by giving you three Madopar 100 mg/25 mg tablets daily.
- After one week your doctor may then start to increase your dose every 2 to 3 days until they find the right dose for you.

Patients already treated with a combined levodopa/decarboxylase inhibitor:
- The usual starting dose is one 50 mg/12.5 mg tablet (50 mg levodopa), three or four times a day.
- Your doctor will then increase your dose every 2 to 3 days until they find the right dose for you.

If you forget to take Madopar
- If you forget to take a dose, skip the missed dose. Then take the next dose when it is due.
- Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

If you stop taking Madopar
You **must not** stop taking your tablets without talking to your doctor first. This is because if you stop taking the tablets suddenly it can cause something called 'neuroleptic malignant-like syndrome' (NMLS). Early signs include increased shaking, sudden high body temperature and muscle problems including stiffness and trouble with balance and keeping upright (postural instability) especially if seen with sweating, paleness and fast heart beat. NMLS can be life threatening.

If the above apply to you, talk to a doctor or go to a hospital straight away.

If you take more Madopar than you should
If you take more Madopar than you should, talk to a doctor or go to a hospital straight away. Take the medicine pack with you. The following effects may happen if you have taken more tablets than you should: changes in your heart beat, confusion, difficulty sleeping, feeling or being sick and unusual movements of different parts of the body that you cannot control.

If someone else takes your Madopar tablets by mistake, they should talk to a doctor or go to a hospital straight away.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines Madopar can cause side effects, although not everyone will get them.

See your doctor as soon as possible if you get the following side effects:
- Allergic reactions. The signs include a rash and feeling itchy.
- Heart beat that is uneven or is faster or slower than normal.
- Bleeding in your stomach or intestines. You may see blood in your stools (they may look black and tarry) or blood when you are sick (this may look like coffee grounds).
- Low numbers of all types of white blood cells. The signs include infections of your mouth, gums, throat and lungs.
- Reduced numbers of red blood cells, white blood cells and platelets in your blood. This may make you feel tired, get infections more easily, or bruise more easily or have nose bleeds.

Other possible side effects:
Not known (frequency cannot be estimated from the available data)
Stomach and gut:
- Loss of appetite, feeling sick or being sick or diarrhoea, particularly at the start of your treatment. To help with this, your doctor may tell you to take Madopar with a low protein snack or drink or increase your dose more slowly.
- A change in the colour of your saliva, tongue, teeth or inside of your mouth.

Heart and circulation:
- Feeling dizzy when you stand up. This usually gets better if your dose is lowered.

Blood:
- Low numbers of red blood cells (anaemia). The signs include feeling tired, pale skin, palpitations (a fluttering sensation in your heart) and being short of breath.
- Changes to your liver or blood - shown in a blood test.

Mental problems:
- Feeling excited, anxious, agitated, depressed, aggressive or disorientated (the feeling of being lost).
- Believing things which are not true, hallucinations (seeing and possibly hearing things that are not really there) or losing contact with reality.
- Feeling sleepy, sometimes during the daytime.
- Falling asleep suddenly.
- Having difficulty sleeping.

Impulse Control Disorders:
You may experience an inability to resist the impulse to perform an action that could be harmful, which may include:
- Strong impulse to gamble excessively despite serious personal or family consequences.
- Altered or increased sexual interest and behaviour of significant concern to you or to others, for example an increased sexual drive.
- Uncontrollable excessive shopping or spending
- Binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms

Others:
- Unusual movements of different parts of your body which you cannot control. This may affect your hands, feet, face or tongue. Your doctor may change your dose of Madopar to help with these effects.
- You may experience 'on-off' effects. This is where you can switch quite suddenly between being 'on' and able to move, and being 'off' and immobile.
- An irresistible urge to move the legs and sometimes the arms.
- Changes to how things taste or a loss of taste.
- Redness of the face or neck.
- Sweating.
- Your urine (water) may become slightly red. This is not a cause for concern. It is caused by your body getting rid of the medicine.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Madopar

- Store Madopar dispersible tablets in their bottle, with the lid closed to protect the tablets from moisture.
- Do not store Madopar tablets above 25°C.
- Keep out of the sight and reach of children.
- Do not use Madopar after the expiry date printed on the pack.
- Do not throw away any medicines via household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Madopar contains
There are two active substances in Madopar dispersible tablets, and there are two different strengths of tablet available

- Each Madopar 50 mg/12.5 mg Dispersible Tablet contains 50 mg levodopa and 12.5 mg benserazide as the hydrochloride.
- Each Madopar 100 mg/25 mg Dispersible Tablet contains 100 mg levodopa and 25 mg benserazide as the hydrochloride.

Other ingredients in the tablets are, citric acid anhydrous (E330), pregelatinised starch, microcrystalline cellulose (E460) and magnesium stearate (E572).

What Madopar dispersible tablets look like and contents of the pack
Madopar 50 mg/12.5 mg Dispersible Tablets are round and white in colour, have Roche 62.5 marked one side and a score line on the other. Madopar 100 mg/25 mg Dispersible Tablets are round and white in colour, have Roche 125 marked one side and a score line on the other.

Madopar dispersible tablets are supplied in amber coloured glass bottles containing 100 tablets.

Marketing Authorisation Holder and Manufacturer
Roche Products Limited
6 Falcon Way
Shire Park
Welwyn Garden City, AL7 1TW
United Kingdom

This leaflet was last revised in May 2019

PACKAGE LEAFLET: INFORMATION FOR THE USER
SINEMET® 10 mg/100 mg Tablets
SINEMET® Plus 25 mg/100 mg Tablets
SINEMET® 25 mg/250 mg Tablets
(Carbidopa/levodopa)

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1 What Sinemet is and what it is used for

Sinemet improves the signs of Parkinson's disease. Parkinson's disease is a long-term illness where:
- you become slow and unsteady
- your muscles feel stiff
- you may develop shaking or trembling (called 'tremor').

If not treated, Parkinson's disease can make it hard for you to continue your normal daily activities.

Sinemet contains two different medicines called: levodopa and carbidopa.
- levodopa turns into a material called 'dopamine' in your brain. The dopamine helps to improve the signs of your Parkinson's disease.
- carbidopa belongs to a group of medicines called 'aromatic amino acid decarboxylase inhibitors'. It helps levodopa work more effectively by slowing the speed at which levodopa is broken down in your body.

2 Before you take Sinemet

Do not take Sinemet if:
- you are allergic (hypersensitive) to carbidopa or levodopa or any of the other ingredients of Sinemet (listed in Section 6)
- you have ever had skin cancer or you have any unusual moles which have not been examined by your doctor
- you are taking certain medicines called 'MAOIs' (Monoamine Oxidase Inhibitors) used for depression. You need to stop using these medicines at least

two weeks before you start Sinemet (see also under '**Taking other medicines**' below).
- you have a condition called 'narrow-angle glaucoma' that may cause a sudden build up of pressure in the eye
- you have a severe mental disorder
- you are pregnant, might become pregnant, or are breast-feeding.

Do not take Sinemet if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Sinemet.

Take special care with Sinemet

Check with your doctor or pharmacist before taking your medicine if:
- you have a history of fits (convulsions)
- you have had an ulcer in your gut (called 'duodenal' or 'peptic ulcer') or have vomited blood
- you have had a heart attack, heart beat problems, circulation or breathing problems
- you have had kidney, liver or hormonal problems
- you have had depression or other mental problems
- you have a condition called 'chronic wide-angle glaucoma' that may cause a build up of pressure in the eye. You will need to have regular checks on the pressure in your eye.
- you sometimes have sudden sleep attacks or sometimes feel very sleepy
- you are due to have surgery.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Sinemet.

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Sinemet and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This includes herbal medicines. This is because Sinemet can affect the way some other medicines work. Also some other medicines can affect the way Sinemet works.

In particular tell your doctor or pharmacist if you are taking any of the following medicines:
- Medicines for Parkinson's disease containing levodopa:
  - If they are 'slow release', you will need to wait 24 hours after your last dose before starting Sinemet.

- If they are ‘normal release’, you will need to wait 12 hours after your last dose before starting Sinemet.
- Tell the doctor or pharmacist even if you have only taken them in the past.

Medicines for Parkinson’s disease which do not contain levodopa will usually be continued. However, your dose may be changed.

- Medicines for mental problems (including depression), tuberculosis (TB), high blood pressure, muscle spasms, epilepsy or other diseases related to involuntary movements. Your dose may need to be changed.
- Medicines to treat low iron. Your dose may need to be changed.
- Medicines called ‘MAOIs’ (see also ‘**Do not take Sinemet if’**).
- Anticholinergic medicines (such as orphenadrine, trihexyphenidyl, benzatropine and procyclidine). Your dose may need to be changed.
- Phenytoin which is used to treat fits (convulsions).
- Papaverine which is used to treat impotence in men.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking this medicine. Your doctor or pharmacist has a more complete list of medicines to avoid while taking Sinemet.

Tests while you are taking Sinemet
This medication can affect some laboratory tests that your doctor may perform on blood or urine samples. Please remind your doctor if you are taking Sinemet and are having any tests.

Taking Sinemet with food and drink
Try to avoid taking your tablets with a heavy meal. If your diet contains too much protein (meat, eggs, milk, cheese) Sinemet may not work as well as it should.

Pregnancy and breast-feeding
Do not take Sinemet if you are pregnant, might become pregnant or are breast-feeding. Levodopa, one of the substances in Sinemet, is passed into human milk. Ask your doctor or pharmacist for advice before taking any medicine, if you are pregnant or breast-feeding.

Driving and using machines
- Sinemet affects different people in different ways. Some people have side effects which affect their ability to drive or use tools or machines (see Section 4 Possible side effects). Do not drive or use tools or machines if you get these effects.
- Sinemet can also make you sleepy or cause 'sudden sleep attacks'. If this happens to you, you must not drive or use tools or machines. Your doctor will tell you if you can start driving again if these attacks stop.

3 How to take Sinemet

Always take Sinemet exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Taking this medicine
- Take this medicine by mouth.
- Although your medicine can have an effect after one day, it may take up to seven days to work.
- Take them at regular time intervals according to your doctor's instructions.

- Do not change the times at which you take your tablets or take any other medicines for Parkinson's disease without first consulting your doctor.
- Try to avoid taking your tablets with a heavy meal.

If you have not had levodopa before
The usual starting dose is:
- for Sinemet Plus 25 mg/100 mg Tablets: one tablet three times a day.
- for Sinemet 10 mg/100 mg Tablets: one tablet three or four times a day.

If you have had levodopa before
- your doctor will ask you to stop taking your medicine for Parkinson's disease before you start taking Sinemet.

The usual starting dose is:
- for Sinemet Plus 25 mg/100 mg Tablets and Sinemet 25 mg/250 mg Tablets: one tablet three or four times a day.
- for Sinemet 10 mg/100 mg Tablets it will depend on what you were taking before.

More than one Sinemet product may be prescribed by your doctor. If you have been given different Sinemet tablets to take make sure that you are taking the correct one at the right time.

Children under 18 years of age
Sinemet is not suitable for children under the age of 18 years.

If you take more Sinemet than you should
If you take too many tablets see your doctor immediately.

If you forget to take Sinemet
Do not take a double dose to make up for a forgotten dose.

If you stop taking Sinemet
Do not stop taking Sinemet or change your dose without talking to your doctor first. When you stop taking Sinemet the following can occur: stiff muscles, high temperature (fever) and mental changes.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4 Possible side effects

Like all medicines, Sinemet can cause side effects, although not everybody gets them.

Stop taking Sinemet and see your doctor straight away, if you notice any of the following side effects:
- allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulty in breathing or swallowing
- chest pain
- uneven (irregular) heart beat or palpitations
- dizziness on standing-up quickly
- bleeding from your gut which may be seen as blood in your faeces or darkened faeces (gastro-intestinal bleeding)
- blood problems, the signs may include pale skin (pallor), tiredness, fever, sore throat or mild bruising and prolonged bleeding after injury
- stiff muscles, high fever

- mental changes including delusions, hallucinations and depression
- fits (convulsions).

The most common side effects are

- abnormal movements such as twitching or spasms (which may or may not be like your Parkinson's symptoms)
- nausea.

Other side effects include

- fainting, anorexia, high blood pressure
- inflammation of the veins, being sick (vomiting) diarrhoea, discoloration of urine, sweat or saliva
- on-off phenomenon, characteristic of some people with long-standing Parkinson's disease. This is when you can have unpredictable changes from being mobile - "on" - to a sudden inability to move - "off". "Off" to "on" can occur just as suddenly.
- dizziness; sleepiness (including excessive drowsiness or sudden sleep onset episodes), pins and needles
- dream abnormalities, confusion, feeling agitated, shortness of breath, hair loss

You may experience the following side effects:

- Craving for large doses of Sinemet in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Sinemet.
- inability to resist the impulse to perform an action that could be harmful, which may include:
    - strong impulse to gamble excessively despite serious personal or family consequences
    - altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
    - uncontrollable excessive shopping or spending
    - binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; he/she will discuss ways of managing or reducing the symptoms.

Side effects that have been reported with medicines containing levodopa.
These may be experienced when taking Sinemet.

Nervous system:

- loss of control over the voluntary movements of everyday life
- numbness, increased hand tremor, muscle twitching, muscle cramp, irregular movement of jaw muscles resulting in difficulty opening the mouth
- difficulty sleeping, feeling anxious or high, falling over and abnormal walking patterns
- headache

Eyes:
- drooping eyelid and dilated pupil
- changes in vision, irregular movement of the eye

Digestive system:
- indigestion, dry mouth, bitter taste
- swelling of the salivary glands, difficulty swallowing, grinding of the teeth
- hiccups, abdominal pain and distress, constipation, wind
- burning sensation of the tongue.

Sexual:
- persistent abnormal erection of the penis

Urinary:
- difficulty passing urine or incontinence (inability to control urine flow)

Skin:
- changed patches of pigmented skin, including, irritated or irregular moles, or moles in which you have noticed changes (melanoma)

General:
- weight gain or loss, swelling in the limbs
- flushing, hot flushes, increased sweating
- feeling weak, faint or tired
- hoarseness, general feeling of being unwell
- increased energy or activity, unusual breathing pattern

If any symptoms persist or you experience any other side effects please tell your doctor or pharmacist. It will help if you make a note of what you experienced, when it started and how long it lasted.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Sinemet

- Keep out of the sight and reach of children
- Sinemet 10 mg/100 mg Tablets: Do not require any special storage conditions.
- Sinemet Plus 25 mg/100 mg Tablets and Sinemet 25 mg/250 mg Tablets: Do not store above 25°C. Store in the original package to protect from light and moisture.
- Do not use Sinemet after the expiry date which is stated on the blister and carton after 'EXP.' The expiry date refers to the last day of that month.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6 Further information

What Sinemet contains

- The active substances in Sinemet 10 mg/100 mg Tablets are carbidopa (equivalent to 10 mg anhydrous carbidopa) and levodopa (100 mg).
- The active substances in Sinemet Plus 25 mg/100 mg Tablets are carbidopa (equivalent to 25 mg anhydrous carbidopa) and levodopa (100 mg).
- The active substances in Sinemet 25 mg/250 mg Tablets are carbidopa (equivalent to 25 mg anhydrous carbidopa) and levodopa (250 mg).
- The other ingredients in Sinemet 10 mg/100 mg Tablets, Sinemet Plus 25 mg/100 mg Tablets and Sinemet 25 mg/250 mg Tablets are microcrystalline cellulose, magnesium stearate, pregelatinised starch and corn starch. Additionally Sinemet Plus 25 mg/100 mg Tablets contain quinoline yellow (E104) and Sinemet 10 mg/100 mg Tablets and Sinemet 25 mg/250 mg Tablets contain Indigotine (E-132).

What Sinemet looks like and contents of the pack

Sinemet 10 mg/100 mg Tablets:
Dark dapple blue, oval tablets, with '647' and a score line on one side and plain on the other. The score line is not intended for breaking the tablet.

Sinemet Plus 25 mg/100 mg Tablets:
Yellow, oval tablets with '650' and a score line on one side and plain on the other. The tablet can be divided into equal doses.

Sinemet 25 mg/250 mg Tablets:
Light dapple blue, oval tablets, with '654' and a score line on one side and plain on the other. The tablet can be divided into equal doses.

Sinemet 10 mg/100 mg Tablets, Sinemet Plus 25 mg/100 mg Tablets and Sinemet 25 mg/250 mg Tablets are available in blister packs of 100 tablets.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Merck Sharp & Dohme Limited, Hertford Road, Hoddesdon, Hertfordshire EN11 9BU, UK.

Manufacturer:
Merck Sharp & Dohme B.V., Waarderweg 39, 2031 BN, Haarlem, The Netherlands.

This leaflet was last revised in February 2019.

PIL.SEM.19.UK.6762.IB-022

Package leaflet: Information for the user

Stalevo 100 mg/25 mg/200 mg film-coated tablets
Levodopa/carbidopa/entacapone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Stalevo is and what it is used for

Stalevo contains three active substances (levodopa, carbidopa and entacapone) in one film-coated tablet. Stalevo is used for the treatment of Parkinson's disease.

Parkinson's disease is caused by low levels of a substance called dopamine in the brain. Levodopa increases the amount of dopamine and hence reduces the symptoms of Parkinson's disease. Carbidopa and entacapone improve the antiparkinson effects of levodopa.

2. What you need to know before you take Stalevo

Do not take Stalevo if you:

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of this medicine (listed in section 6)
- have narrow-angle glaucoma (an eye disorder)
- have a tumour of the adrenal gland
- are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had non-traumatic rhabdomyolysis (a rare muscle disorder)
- have a severe liver disease.

Warnings and precautions

Talk to your doctor or pharmacist before taking Stalevo if you have or have ever had:
- a heart attack or any other diseases of the heart including cardiac arrhythmias, or of the blood vessels
- asthma or any other disease of the lungs

- a liver problem, because your dose may need to be adjusted
- kidney or hormone-related diseases
- stomach ulcers or convulsions
- if you experience prolonged diarrhoea consult your doctor as it may be a sign of inflammation of the colon
- any form of severe mental disorder like psychosis
- chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored.

Consult your doctor if you are currently taking:
- antipsychotics (medicines used to treat psychosis)
- a medicine which may cause low blood pressure when rising from a chair or bed. You should be aware that Stalevo may make these reactions worse.

Consult your doctor if during the treatment with Stalevo you:
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. If any of this happens, **contact your doctor immediately**
- feel depressed, have suicidal thoughts, or notice unusual changes in your behaviour
- find yourself suddenly falling asleep, or if you feel very drowsy. If this happens, you should not drive or use any tools or machines (see also section 'Driving and using machines')
- notice that uncontrolled movements begin or get worse after you started to take Stalevo. If this happens, your doctor may need to change the dose of your antiparkinson medicine
- experience diarrhoea: monitoring of your weight is recommended in order to avoid potentially excessive weight loss
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, a general medical evaluation including liver function should be considered
- feel the need to stop using Stalevo, see section 'If you stop taking Stalevo'.

Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to craving for large doses of Stalevo and other medicines used to treat Parkinson's disease.

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Your doctor may take some regular laboratory tests during a long term treatment with Stalevo.

If you must undergo surgery, please tell your doctor that you are using Stalevo.

Stalevo is not recommended to be used for treatment of extrapyramidal symptoms (e.g. involuntary movements, shaking, muscle rigidity and muscle contractions) caused by other medicines.

Children and adolescents

Experience with Stalevo in patients under 18 years is limited. Therefore, the use of Stalevo in children or adolescents is not recommended.

Other medicines and Stalevo

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take Stalevo if you are taking certain medicines for treating depression (combinations of selective MAO-A and MAO-B inhibitors, or non-selective MAO inhibitors).

Stalevo may increase the effects and side effects of certain medicines. These include:
- medicines used to treat depression such as moclobemide, amitriptyline, desipramine, maprotiline, venlafaxine and paroxetine
- rimiterole and isoprenaline, used to treat respiratory diseases
- adrenaline, used for severe allergic reactions
- noradrenaline, dopamine and dobutamine, used to treat heart diseases and low blood pressure
- alpha-methyldopa, used to treat high blood pressure
- apomorphine, which is used to treat Parkinson's disease.

The effects of Stalevo may be weakened by certain medicines. These include:
- dopamine antagonists used to treat mental disorders, nausea and vomiting
- phenytoin, used to prevent convulsions
- papaverine used to relax the muscles.

Stalevo may make it harder for you to digest iron. Therefore, do not take Stalevo and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Stalevo with food and drink

Stalevo may be taken with or without food. For some patients, Stalevo may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not breast-feed during treatment with Stalevo.

Driving and using machines

Stalevo may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, wait until you feel fully awake again before driving or doing anything else that requires you to be alert. Otherwise, you may put yourself and others at risk of serious injury or death.

Stalevo contains sucrose

Stalevo contains sucrose (1.6 mg/tablet). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Stalevo

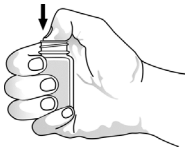
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For adults and elderly:
- Your doctor will tell you exactly how many tablets of Stalevo to take each day.
- The tablets are not intended to be split or broken into smaller pieces.
- You should take only one tablet each time.
- Depending on how you respond to treatment, your doctor may suggest a higher or lower dose.
- If you are taking Stalevo 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg or 150 mg/37.5 mg/200 mg tablets, do not take more than 10 tablets per day.

Talk to your doctor or pharmacist if you think the effect of Stalevo is too strong or too weak, or if you experience possible side effects.

To open the bottle for the first time: open the closure, and then press with your thumb on the seal until it breaks. See picture 1.

Picture 1



If you take more Stalevo than you should

If you have accidentally taken more Stalevo tablets than you should, talk to your doctor or pharmacist immediately. In case of an overdose you may feel confused or agitated, your heart rate may be slower or faster than normal or the colour of your skin, tongue, eyes or urine may change.

If you forget to take Stalevo

Do not take a double dose to make up for a forgotten tablet.

If it is more than 1 hour until your next dose:
Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose:
Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that carry on as normal.

Always leave at least an hour between Stalevo tablets, to avoid possible side effects.

If you stop taking Stalevo

Do not stop taking Stalevo unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking Stalevo and other antiparkinsonian medicines it may result in unwanted side effects.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Many of the side effects can be relieved by adjusting the dose.

If you during the treatment with Stalevo experience the following symptoms, **contact your doctor immediately**:

- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).
- Allergic reaction, the signs may include hives (nettle rash), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.

Very common (may affect more than 1 in 10 people)

- uncontrolled movements (dyskinesias)
- feeling sick (nausea)
- harmless reddish-brown discolouration of urine
- muscle pain
- diarrhoea

Common (may affect up to 1 in 10 people)

- light-headedness or fainting due to low blood pressure, high blood pressure
- worsening of Parkinson's symptoms, dizziness, drowsiness
- vomiting, abdominal pain and discomfort, heartburn, dry mouth, constipation
- inability to sleep, hallucinations, confusion abnormal dreams (including nightmares), tiredness
- mental changes – including problems with memory, anxiety and depression (possibly with thoughts of suicide)
- heart or artery disease events (e.g. chest pain), irregular heart rate or rhythm
- more frequent falling
- shortness of breath
- increased sweating, rashes
- muscle cramps, swelling of legs
- blurred vision
- anaemia
- decreased appetite, decreased weight
- headache, joint pain
- urinary tract infection

Uncommon (may affect up to 1 in 100 people)

- heart attack
- bleeding in the gut
- changes in the blood cell count which may result in bleeding, abnormal liver function tests
- convulsions
- feeling agitated
- psychotic symptoms
- colitis (inflammation of the colon)
- discolourations other than urine (e.g. skin, nail, hair, sweat)
- swallowing difficulties
- inability to urinate

Not known (cannot be estimated from the available data)

Craving for large doses of Stalevo in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Stalevo.

The following side effects have also been reported:

- hepatitis (inflammation of the liver)

- itching

You may experience the following side effects:
- Inability to resist the impulse to perform an action that could be harmful, which may include:
  - strong impulse to gamble excessively despite serious personal or family consequences
  - altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive
  - uncontrollable excessive shopping or spending
  - binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Tell your doctor if you experience any of these behaviours; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Stalevo

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away of medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Stalevo contains

- The active substances of Stalevo are levodopa, carbidopa and entacapone.
- Each Stalevo 100 mg/25 mg/200 mg tablet contains 100 mg of levodopa, 25 mg of carbidopa and 200 mg of entacapone.
- The other ingredients in the tablet core are croscarmellose sodium, magnesium stearate, maize starch, mannitol (E421) and povidone (E1201)
- The ingredients in the film-coating are glycerol (85 per cent) (E422), hypromellose, magnesium stearate, polysorbate 80, red iron oxide (E172), sucrose, titanium dioxide (E171), and yellow iron oxide (E172).

What Stalevo looks like and contents of the pack

Stalevo 100 mg/25 mg/200 mg: brownish or greyish red, oval, unscored film-coated tablets marked with ‘LCE 100’ on one side.

Stalevo comes in six different pack sizes (10, 30, 100, 130, 175 or 250 tablets). Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Eesti
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United Kingdom
Orion Pharma (UK) Ltd.
Tel: +44 1635 520 300

This leaflet was last revised in.
April 2020

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the patient

Trilasym 50mg/ 5ml Oral Solution amantadine hydrochloride

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

The full name of this medicine is Trilasym 50mg/5ml Oral Solution but is referred to as Trilasym Solution within this leaflet.

What is in this leaflet

1. What Trilasym solution is and what it is used for

Trilasym Solution contains the active substance amantadine. This is a dopaminergic drug, meaning that it can increase the levels of certain chemicals that transmit impulses in the nervous system, including the brain. It is also an antiviral medicine, which works against influenza A infections by stopping the virus from reproducing.

Trilasym Solution can be used:

- to treat Parkinson's disease by improving muscle control and reducing stiffness, shakiness and shuffling
- to prevent, or treat the signs and symptoms of, certain influenza ('flu) infections (type A)
- to reduce the pain caused by shingles (herpes zoster), a blistering skin rash caused by the same virus that causes chickenpox (the varicella zoster virus)

2. What you need to know before you take Trilasym Solution

Do not take Trilasym Solution if:

- you are allergic to amantadine hydrochloride or any of the other ingredients of this medicine (listed in section 6).
- you have epilepsy or have ever had fits (convulsions)
- you have ever had an ulcer in your stomach or small intestine

- you suffer from any serious kidney disease
- you are pregnant or trying to become pregnant (see section 2 Pregnancy and breastfeeding)
- you are breast-feeding (see section 2 Pregnancy and breast-feeding).

If any of the above applies to you, or if you are not sure, speak to your doctor or pharmacist before you take Trilasym Solution.

Warnings and precautions

Talk to your doctor before taking Trilasym Solution if you:

- suffer from any liver or kidney disease
- have a history of disease involving the heart and blood vessels
- are currently suffering from heart problems or heart failure (heart problems which cause shortness of breath or ankle swelling)
- have problems thinking clearly or quickly, feel disorientated; find it difficult to pay attention, make decisions or remember things
- sometimes see, hear, feel, smell or taste things that are not really there (have hallucinations)
- have any form of mental health problem, for example schizophrenia, dementia - have glaucoma (increased pressure in the eye)

If any of the above applies to you, or if you are not sure, speak to your doctor or pharmacist before you take Trilasym Solution.

Tell your doctor if you or your family/carer notices that you are developing urges or cravings to behave in ways that are unusual for you and you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These are called impulse control disorders and can include behaviours such as addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings.

Your doctor may need to adjust or stop your dose of Trilasym Solution.

If blurred vision or other visual problems occur please contact an eye doctor immediately.

If you have any thoughts or feelings about harming or killing yourself tell your doctor or go to a hospital straight away. There have been reports of people taking amantadine attempting to take their own life.

Children

Do not give this medicine to children under the age of 3 years old.

There have been reports of children developing hypothermia when taking amantadine. Hypothermia is a dangerous drop in body temperature below 35□C. Early signs include cold and pale skin, shivering, slurred speech, fast breathing, tiredness, confusion. If this medicine has been prescribed for a child, and he/she shows any signs of hypothermia seek immediate medical help.

Do not stop taking Trilasym Solution suddenly without discussing it with your doctor first.

Abrupt discontinuation could cause your condition to worsen or for you to have withdrawal effects which could be serious (see section 3 'If you stop taking Trilasym Solution' for further information).

Other medicines and Trilasym Solution

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because amantadine may affect the way some medicines work. Also some medicines can affect the way amantadine works.

In particular tell your doctor or pharmacist if you are taking any of the following:

- Medicines called **anti-muscarinics** or **anti-cholinergics**, which affect the way nerve cells function in order to treat certain medical conditions. They include medicines used for Parkinson's Disease e.g. procyclidine, orphenadrine; irritable bowel syndrome and diverticular disease e.g. dicycloverine, hyoscine, propantheline: asthma and chronic obstructive pulmonary disease (COPD) e.g ipratopium, tiotropium; incontinence e.g. oxybutynin, tolterodine, flavoxate
- **levodopa**, used to treat Parkinson's disease
- medicines called **anti-psychotics**, used to help people feel calmer and improve thoughts, feelings and behaviour when disturbed due to conditions such as schizophrenia, mania, delirium. Examples of anti-psychotic medicines include chlorpromazine, flupenthixol, zuclopenthixol, haloperidol, quetiapine, risperidone
- medicines called **diuretics** (water tablets), used to relieve water retention and reduce high blood pressure e.g. medicines containing hydrochlorothiazide and amiloride or triamterene.

Trilasym Solution with alcohol

Be careful when drinking alcohol whilst taking Trilasym Solution This is because it may affect you more than usual and can also increase the chances of you getting side effects from amantadine.

Pregnancy and breast-feeding

Do not take Trilasym Solution if you are pregnant or trying to become pregnant.

Do not take Trilasym Solution if you are breast-feeding because amantadine passes into breast milk and could harm your baby.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Do not drive whilst taking this medicine until you know how this medicine affects you. Trilasym Solution may cause side-effects that affect your ability to drive safely. For example, it may affect your vision or concentration make you feel dizzy or confused (see section 4). If this happens do not drive or use any tools or machines.

If you are in any doubt about whether it is safe for you to do a particular activity, talk to your doctor.

Trilasym Solution contains Sorbitol (E420), Sodium benzoate (E211), Ethanol, Propylene glycol (E1520) and Benzyl alcohol:

This medicine contains up to 6.5 g sorbitol in each 10 ml dose. Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive Trilasym Solution.

Sorbitol may cause gastrointestinal discomfort and mild laxative effect This

medicine contains 20 mg sodium benzoate in each 10 ml dose.

Sodium Benzoate may increase jaundice (yellowing of the skin and eyes) in new-born babies (up to 4 weeks old).

This medicine contains less than 1mmol sodium (23mg) per 10 ml dose, that is to say essentially 'sodium-free'.

This medicine contains small amounts of ethanol (alcohol), less than 100mg per 10ml dose.

This medicine contains up to 12 mg propylene glycol in each 10 ml dose.

If this medicine has been prescribed for a baby that is less than 4 weeks old, talk to your doctor or pharmacist before giving them this medicine, in particular if the baby is given other medicines that contain propylene glycol or alcohol.

This medicine contains 12 mg benzyl alcohol in each 10 ml dose.

Benzyl alcohol may cause allergic reactions and has been linked with the risk of severe side

effects including breathing problems (called "gasping syndrome") in young children. Do not

give to your new-born baby (up to 4 weeks old), unless recommended by your doctor.

Do not use for more than a week in young children (less than 3 years old), unless advised by your doctor or pharmacist.

Ask your doctor or pharmacist for advice if you have a liver or kidney disease or if you are pregnant or breast-feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

3. How to take Trilasym Solution

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
The box containing this medicine contains a plastic measuring cup. The cup is marked in ml (millilitres) to help you measure out the correct amount. Take your medicine using the measuring cup and rinse it out with water after each use.

Doses

The dose of Trilasym Solution depends on what it is used for. The recommended doses are as follows, although your doctor may give you a lower dose if you have kidney problems.

For the treatment and prevention of flu:

Adults

10 ml once each day.

Adults over 65 years of age may need a lower dose or a longer time between doses.

Children

10-15 years: 10 ml once each day

Under 10 years of age: the doctor will decide the dose

If you have 'flu you should take the recommended dose for 4 to 5 days.

If you have been given Trilasym Solution for the prevention of flu it should be taken for as long as protection is needed. This is usually about 6 weeks.

This medicine should not be used in children under the age of 3 years old.

For Parkinson's Disease

The starting dose is usually 10 ml once each day for the first week or longer, which is then increased to 10 ml twice a day. Your doctor will determine the best dose for you and may gradually adjust the dose during your treatment, depending upon your response. Do not take more than 40 ml a day.

Some patients may notice that this medicine loses its effect after they have taken it regularly for a few months. If you notice this, tell your doctor.

For Shingles (herpes zoster)

10 ml twice a day for 14 days.

If you are still in pain after this time your doctor may give you another 14 days treatment.

If you have kidney problems, your doctor may give you a lower dose.

If you are not sure how much Trilasym Solution to take, ask your doctor or pharmacist.

If you take more Trilasym Solution than you should

If you accidentally take too much Trilasym Solution, or someone else takes any of your medicine, contact your doctor or the nearest hospital Accident and Emergency department immediately. Show the bottle to the doctor, even if it is empty.

If you forget to take Trilasym Solution

Take it as soon as you remember, unless it is almost time for your next dose. Then. take your next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Trilasym Solution

Do not stop taking Trilasym Solution without asking your doctor first. When stopping Trilasym Solution your doctor will tell you how to reduce your dose slowly. If you stop suddenly your symptoms may get worse and you may get withdrawal effects. Withdrawal effects may include feelings of being dazed, confused, restless, distracted, withdrawn, weak, sleepy; being unable to speak, doing unusual things and seeing things that are not really there.

If you are taking anti-psychotics (used to treat mental disturbances) and you suddenly stop taking Trilasym Solution, you may develop a medical condition called Neuroleptic Malignant Syndrome which can be serious. The symptoms include:

- fever
- sweating
- a rapid heart beat
- muscle stiffness and loss of movement - confusion

- loss of bladder control (you may have a sudden urge to pass water). If you develop any of these symptoms contact your doctor immediately.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you experience any of the following serious side effects, tell your doctor immediately or go to the nearest hospital accident and emergency department

- dizziness or light-headedness
- fainting
- seizures (fits).

Other possible side effects:

Very common side effects (may affect more than 1 in 10 people):

- swollen ankles
- A blotchy, reddish-blue to purple discolouration of the skin, resembling a net or lace-like pattern.

Common side effects (may affect up to 1 in 10 people):

- loss of appetite
- anxiety
- depression
- feeling tired
- feeling overexcited
- hallucinations (seeing, hearing, feeling, smelling or tasting things that are not really there)
- difficulty in controlling movements
- blurred vision
- feeling or being sick
- difficulty concentrating
- feeling nervous
- difficulty sleeping
- muscle pain
- headache
- nightmares
- slurred speech
- feeling your heartbeat
- dry mouth

- constipation
- sweating
- postural hypotension (low blood pressure, mostly when you suddenly stand up from a lying or sitting position that makes you feel dizzy or lightheaded)

Uncommon side effects (may affect up to 1 in 100 people):

- blurred vision

Rare side effects (may affect up to 1 in 1,000 people):

- confusion
- disturbed thoughts or behaviour such as feeling paranoid
- fever, muscle stiffness, muscle pains, vomiting, sweating, dark urine - these may be symptoms of a serious condition known as neuroleptic malignant syndrome;
- unintentional passing of urine (leakage), not being able to empty the bladder completely
- disorientation (not knowing where you are)
- shaking
- diarrhoea
- skin rash
- problems with your eyes such as itchiness, redness and not being able to see clearly
- unusual uncontrollable movements
- corneal lesion, corneal oedema, reduced visual acuity

Very rare side effects (may affect up to 1 in 10,000 people):

- heart problems which can cause shortness of breath or ankle swelling
- reduction in the number of white blood cells which makes infections more likely
- changes in blood tests which show how the liver is working
- a red, itchy or burning skin rash on areas of skin exposed to sunlight

Not known side effects (frequency cannot be estimated from the available data):

- restlessness, having illusions and not making sense; a condition known as delirium
- decreased need for sleep, with heightened mood (either euphoric or irritable), feel extremely outgoing, with a great deal of energy more than normal; a condition which depending on its extent is known as hypomanic state or mania.
- Urge to behave in an usual way - strong impulse to gamble excessively, altered or increased sexual interest, uncontrollable excessive shopping or spending, binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Additional side effects in children

There have been reports of children developing hypothermia (an abnormally low body temperature, below 35ºC) but the frequency cannot be estimated from the available data:

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Trilasym Solution

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the packaging carton after EXP. The expiry date refers to the last day of that month.

Store below 25°C

Store in the original bottle, in order to protect from light.

Any unused oral solution should be discarded one month after first opening the bottle

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Trilasym Solution contains

- The active substance is amantadine hydrochloride. Each 5 ml contains 50 mg amantadine hydrochloride.
- The other ingredients are sodium benzoate (E211), sorbitol (E420), raspberry flavour containing ethanol, propylene glycol (E1520) and benzyl alcohol, citric acid monohydrate and purified water.

What Trilasym Solution looks like and contents of the pack

Trilasym Solution is a clear, colourless raspberry flavoured liquid, available in glass bottles containing 150ml of solution with a dosing cup.

Marketing Authorisation Holder and Manufacturer Marketing Authorisation Holder

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Manufacturer

Northumbria Pharma Ltd

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United Kingdom and

Purna Pharmaceuticals NV

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Belgium.

This medicinal product is authorised in the Member States of the EEA under the following names:

United Kingdom - Trilasym 50mg/ 5ml Oral Solution

Malta - Trilasym 50mg/ 5ml Oral Solution

This leaflet was last revised in 04/2019

Package leaflet: Information for the user

AZILECT® 1 mg tablets

rasagiline

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What AZILECT is and what it is used for

AZILECT contains the active substance rasagiline and it is used for the treatment of Parkinson's disease in adults. It can be used together with or without Levodopa (another medicine that is used to treat Parkinson's disease).

With Parkinson's disease, there is a loss of cells that produce dopamine in the brain. Dopamine is a chemical in the brain involved in movement control. AZILECT helps to increase and sustain levels of dopamine in the brain.

2. What you need to know before you take AZILECT

Do not take AZILECT
- If you are allergic to rasagiline or any of the other ingredients of this medicine (listed in section 6).
- If you have severe liver problems.

Do not take the following medicines while taking AZILECT:
- Monoamine oxidase (MAO) inhibitors (e.g. for treatment of depression or Parkinson's disease, or used for any other indication), including medicinal and natural products without prescription e.g. St. John's Wort.
- Pethidine (a strong pain killer).

You must wait at least 14 days after stopping AZILECT treatment and starting treatment with MAO inhibitors or pethidine.

Warnings and precautions

Talk to your doctor before taking AZILECT
- If you have any liver problems
- You should speak with your doctor about any suspicious skin changes. Treatment with AZILECT may possibly increase the risk of skin cancer.

Tell your doctor if you or your family/carer notices that you are developing unusual behaviours where you cannot resist the impulse, urges or cravings to carry out certain harmful or detrimental activities to yourself or others. These are called impulse control disorders. In patients taking AZILECT and/or other medicines used to treat Parkinson's disease, behaviours such as compulsions, obsessive thoughts, addictive gambling, excessive spending, impulsive behaviour and an abnormally high sex drive or an increase in sexual thoughts or feelings have been observed. Your doctor may need to adjust or stop your dose (see section 4).

AZILECT may cause drowsiness and may cause you to suddenly fall asleep during day time activities, especially if you are taking other dopaminergic medicinal products (used for the treatment of Parkinson's disease). For further information please refer to section driving and using machines.

Children and adolescents
There is no relevant use of AZILECT in children and adolescents. Therefore, AZILECT is not recommended for use under the age of 18.

Other medicines and AZILECT
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Especially tell your doctor if you are taking any of the following medicines:
- Certain antidepressants (selective serotonin reuptake inhibitors, selective serotonin-norepinephrine reuptake inhibitors, tricyclic or tetracyclic antidepressants)
- The antibiotic ciprofloxacin used against infections
- The cough suppressant dextromethorphan
- Sympathomimetics such as those present in eye drops, nasal and oral decongestants and cold medicine containing ephedrine or pseudoephedrine

The use of AZILECT together with the antidepressants containing fluoxetine or fluvoxamine should be avoided.
If you are starting treatment with AZILECT, you should wait at least 5 weeks after stopping fluoxetine treatment.
If you are starting treatment with fluoxetine or fluvoxamine, you should wait at least 14 days after stopping AZILECT treatment.

Tell your doctor or pharmacist if you are smoking or intend to stop smoking. Smoking could decrease the amount of AZILECT in the blood.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should avoid taking AZILECT if you are pregnant, as the effects of AZILECT on pregnancy and the unborn child are not known.

Driving and using machines
Ask your doctor for advice before you drive and operate machines, since Parkinson's disease itself as well as the treatment with AZILECT may influence your ability to do so. AZILECT can make you feel dizzy or drowsy; it can also cause episodes of sudden sleep onset.
This might be enhanced if you take other medicines to treat the symptoms of your Parkinson's disease, or if you take medicines which can make you feel drowsy, or if you drink alcohol while taking AZILECT. If you have experienced somnolence and/or episodes of sudden sleep onset before, or while taking AZILECT do not drive or operate machinery (see section 2).

3. How to take AZILECT

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose of AZILECT is 1 tablet of 1 mg taken by mouth once daily. AZILECT may be taken with or without food.

If you take more AZILECT than you should
If you think that you may have taken too many AZILECT tablets, contact your doctor or pharmacist immediately. Take the AZILECT carton/ blister or bottle with you to show the doctor or pharmacist.

Symptoms reported following overdose of AZILECT included slightly euphoric mood (light form of mania), extremely high blood pressure and serotonin syndrome (see section 4).

If you forget to take AZILECT
Do not take a double dose to make up for a forgotten dose. Take the next dose normally, when it is time to take it.

If you stop taking AZILECT
Do not stop taking AZILECT without first talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Contact your doctor right away if you notice any of the following symptoms. You may need urgent medical advice or treatment:

- If you develop unusual behaviours such as compulsions, obsessive thoughts, addictive gambling, excessive shopping or spending, impulsive behaviour and an abnormally high sex drive or an increase in sexual thoughts (impulse control disorders) (see section 2).
- If you see or hear things which are not there (hallucinations).
- Any combination of hallucinations, fever, restlessness, tremor and sweating (serotonin syndrome)

Contact your doctor if you notice any suspicious skin changes because there may be an increased risk of skin cancer (melanoma) with the use of this medicine (see section 2).

Other side effects

Very common (may affect more than 1 in 10 people)
- Involuntary movements (dyskinesia)
- Headache

Common (may affect up to 1 in 10 people)
- Abdominal pain
- Fall
- Allergy
- Fever
- Flu (influenza)
- General feeling of being unwell (malaise)
- Neck pain
- Chest pain (angina pectoris)
- Low blood pressure when rising to a standing position with symptoms like dizziness/light-headedness (orthostatic hypotension)
- Decreased appetite
- Constipation
- Dry mouth
- Nausea and vomiting
- Flatulence
- Abnormal results of blood tests (leucopenia)
- Joint pain (arthralgia)
- Musculoskeletal pain
- Joint inflammation (arthritis)
- Numbness and muscle weakness of the hand (carpal tunnel syndrome)
- Decreased weight
- Abnormal dreams
- Difficulty in muscular coordination (balance disorder)
- Depression
- Dizziness (vertigo)
- Prolonged muscle contractions (dystonia)
- Runny nose (rhinitis)
- Irritation of the skin (dermatitis)
- Rash
- Bloodshot eyes (conjunctivitis)
- Urinary urgency

Uncommon (may affect up to 1 in 100 people)
- Stroke (cerebrovascular accident)
- Heart attack (myocardial infarction)
- Blistering rash (vesiculobullous rash)

Not known: frequency cannot be estimated from the available data
- Elevated blood pressure
- Excessive drowsiness
- Sudden onset of sleep

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store AZILECT

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton, bottle or blister after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What AZILECT contains
- The active substance is rasagiline. Each tablet contains 1 mg rasagiline (as mesilate).
- The other ingredients are mannitol, colloidal anhydrous silica, maize starch, pregelatinised maize starch, stearic acid, talc.

What AZILECT looks like and contents of the pack
AZILECT tablets are presented as white to off-white, round, flat, bevelled tablets, debossed with "GIL" and "1" underneath on one side and plain on the other side.

The tablets are available in blister packs of 7, 10, 28, 30, 100 and 112 tablets or in a bottle containing 30 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

Teva B.V.
Swensweg 5
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Manufacturers

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APOMINE® Solution for Infusion

Apomorphine (a-poe-MOR-feen) hydrochloride hemihydrate

Consumer Medicine Information

What is in this leaflet

This leaflet answers some common questions about APOMINE® Solution for Infusion. It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you using APOMINE® Solution for Infusion against the benefits they expect it will have for you.

If you have any concerns about using this medicine, ask your doctor or pharmacist.

Keep this leaflet in a safe place.
You may need to read it again.

For further information on APOMINE® Solution for Infusion please contact your health care professional.

What APOMINE® Solution for Infusion is used for

APOMINE® Solution for Infusion contains apomorphine which belongs to a group of medicines called dopaminergic compounds.

Apomorphine is used in the treatment of Parkinson's disease to reduce the number and severity of bouts of freezing and stiffness (or "off" periods).

This medicine works by acting on dopamine receptors. These receptors help control movement by the body.

Ask your doctor if you have any questions about why this medicine has been prescribed for you.
Your doctor may have prescribed it for another reason.

This medicine is not addictive.

This medicine is available only with a doctor's prescription.

There is not enough information to recommend the use of this medicine in children under 18 years.

Before you use APOMINE® Solution for Infusion

When you must not use it

Do not use APOMINE® Solution for Infusion if you have an allergy to:

- apomorphine
- sodium metabisulfite
- certain types of pain killers such as morphine or other opioid analgesics.

Some of the symptoms of an allergic reaction may include shortness of breath, wheezing or difficulty breathing; swelling of the face, lips, tongue or other parts of the body; rash, itching or hives on the skin.

Do not use this medicine if you have or have had any of the following medical conditions:

- certain forms of dementia eg. Alzheimer's Disease
- severe kidney or liver disease
- problems with circulation of blood in the brain (cerebrovascular disease)
- breathing problems (respiratory depression).

Do not use this medicine after the expiry date printed on the pack or if the packaging is torn or shows signs of tampering.
If it has expired or is damaged, return it to your pharmacist for disposal.

If you are not sure whether you should start using this medicine, talk to your doctor.

Before you use it

Tell your doctor or pharmacist if you have allergies to any other medicines, foods, preservatives or dyes.

Tell your doctor if you have or have had any of the following medical conditions:

- a history of severe nausea and vomiting
- heart disease
- kidney disease
- liver disease
- lung disease.
- problem gambling,
- any addictive behaviour (eg sex, shopping or eating)

Tell your doctor if you are pregnant or plan to become pregnant or are breast-feeding.
Your doctor will discuss the possible risks and benefits involved.

If you have not told your doctor or pharmacist about any of the above, tell them before you start using APOMINE® Solution for Infusion.

Taking other medicines

Tell your doctor or pharmacist if you are taking or using any other medicines, including any that you get without a prescription from your pharmacy, supermarket or health food shop.

Some medicines and APOMINE ® Solution for Infusion may interfere with each other. These include:

- tetrabenazine, a medicine used to treat movement disorders
- metoclopramide, a medicine used to treat nausea
- medicines used to treat some psychiatric (mental) conditions (eg phenothiazines, haloperidol, flupenthixol)
- papaverine, a medicine which expands blood vessels
- amphetamines.

These medicines may be affected by APOMINE ® Solution for Infusion, or may affect how well they work. You may need different amounts of your medicine, or you may need to use different medicines.

Your doctor and pharmacist have more information on medicines to be careful of or avoid while using this medicine.

How to use APOMINE ® Solution for Infusion

How much is given

Your doctor will decide what dose you will receive. This depends on your initial response to APOMINE® Solution for Infusion.

How it is given

You will usually be in hospital when you start using APOMINE® Solution for Infusion. It is recommended that you are given an anti-nausea drug (domperidone) for a few days before starting APOMINE® Solution for Infusion and that you stop all your other anti-Parkinsonian medication before you start using APOMINE® Solution for Infusion. This medicine is given as an injection under the skin (subcutaneously), usually into your lower abdomen or outer thigh. It is either injected several times a day or continuously as an infusion (ie, slow injection via a pump).

There is no need to dilute APOMINE ® Solution for Infusion prior to use.
APOMINE ® Solution for Infusion is a pre-diluted solution in a vial, intended for use as a continuous infusion with a suitable pump/syringe driver.

You and/or your carers will be trained by hospital staff to recognise when and how to give the infusions.

If you use too much (Overdose)

Immediately notify your doctor or nurse, or if you are not in hospital, telephone the Poisons Information Centre on 13 11 26 (Australia) or go to Accident and Emergency at your nearest hospital, if you think that you or anyone else may have used too much APOMINE® Solution for Infusion. Do this even if there are no signs of discomfort or poisoning.
You may need urgent medical attention.

Symptoms of an overdose may include severe nausea and vomiting, slow or troubled breathing, restlessness, hallucinations or unconsciousness.

While you are using APOMINE ® Solution for Infusion

Things you must do

If you are about to be started on any new medicine, remind your doctor and pharmacist that you are using APOMINE® Solution for Infusion.

Tell any other doctors, dentists, and pharmacists who are treating you that you are using this medicine.

If you plan to have surgery, tell the surgeon or anaesthetist that you are using this medicine.
It may affect other medicines used during surgery.

If you become pregnant while are using this medicine, tell your doctor immediately.

Keep all of your doctor's appointments so that your progress can be checked.

Things you must not do

Do not use APOMINE® Solution for Infusion to treat any other complaints unless your doctor tells you to.

Do not give this medicine to anyone else, even if they have the same condition as you.

Things to be careful of

Be careful driving or operating machinery until you know how APOMINE® Solution for Infusion affects you.
This medicine may cause drowsiness, sudden onset of sleepiness, dizziness or light-headedness in some people. If you have any of these symptoms, do not drive, operate

machinery or do anything else that could be dangerous.

Side effects

Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well while you are using APOMINE® Solution for Infusion.
APOMINE® Solution for Infusion helps most people with Parkinson's disease, but may have unwanted side effects in a few people. All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some of the side effects.

If you are over 65 years of age you may have an increased chance of experiencing side effects.

Do not be alarmed by this list of possible side effects.
You may not experience any of them.

Ask your doctor, nurse or pharmacist to answer any questions you may have.

Tell your doctor, nurse or pharmacist if you notice any of the following and they worry you:

- nausea or vomiting
- drowsiness
- sudden onset of sleepiness
- dizziness or light-headedness
- pain and sores at the injection sites
- unpleasant metallic taste
- runny nose
- watery eyes
- spontaneous penile erection
- confusion
- lack of impulse control
- decreased or increased sexual arousal
- increased need to gamble
- compulsive eating, shopping or medication use.

The above list includes the more common side effects of your medicine. They are usually mild and short-lived.

If any of the following happen tell your doctor immediately or go to Accident and Emergency at your nearest hospital:

- hallucinations
- severe nausea and vomiting.

The above list includes serious side effects which may require medical attention. These side effects are rare.

Tell your doctor, nurse or pharmacist if you notice anything that is making you feel unwell.

Other side effects not listed above may occur in some people.

After using APOMINE® Solution for Infusion

Storage

Store the APOMINE® Solution for Infusion below 25°C. Keep unused vials in the outer cardboard carton.

Store in original package in order to protect from light **and do not refrigerate or put in the freezer.**

APOMINE® Solution for Infusion is for single use only. Once opened, the contents of the vial should be used immediately. **Discard any unused solution.**

Keep it where children cannot reach it.

Disposal

If your doctor tells you to stop using this medicine or the expiry date has passed, ask your pharmacist what to do with any medicine that is left over.

Product description

What it looks like

APOMINE® Solution for Infusion is supplied as a clear and colourless to slightly yellow solution that comes in a 20 mL glass vial in packs of 1, 5 and 10.

Ingredients

APOMINE® Solution for Infusion contains:

- apomorphine hydrochloride hemihydrate
- sodium metabisulfite
- sodium chloride
- hydrochloric acid
- water for injections

APOMINE® Solution for Infusion does not contain lactose, sucrose, gluten, tartrazine or any other azo dyes.

Strength

20 mL glass vial containing apomorphine hydrochloride hemihydrate 5 mg/mL

Sponsor

Pfizer Australia Pty Ltd
Level 17, 151 Clarence Street
Sydney NSW 2000

Glass Vial
20 mL AUST R 260149

This leaflet was prepared in May 2019.

Package leaflet: Information for the user

Neupro 2 mg/24 h transdermal patch
Rotigotine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Neupro is and what it is used for

What Neupro is
Neupro contains the active substance rotigotine.

It belongs to a group of medicines called 'dopamine agonists'. Dopamine is a messenger in the brain which is important for movement.

What Neupro is used for
Neupro is used in adults to treat the signs and symptoms of:
- **Parkinson's disease** – Neupro can be used on its own or with another medicine called levodopa.
- **Restless Legs Syndrome (RLS)** – this can be associated with discomfort in your legs or arms, urge to move around, sleep disturbance and feeling tired or sleepy during the day. These symptoms are either reduced or their duration is shortened with Neupro treatment.

2. What you need to know before you use Neupro

Do not use Neupro if:
- you are **allergic** to **rotigotine** or any of the **other ingredients** of this medicine (listed in section 6)
- you need to have a **magnetic resonance imaging** (MRI) scan (diagnostic pictures of the inside of the body, created using magnetic rather than x-ray energy)
- you need '**cardioversion**' (specific treatment for abnormal heart beat).

You must take your Neupro patch off just before undergoing magnetic resonance imaging (MRI) or cardioversion to avoid skin burns because the patch contains aluminium. You can put a new patch on afterwards.

If any of the above apply to you, do not use Neupro. If you are not sure about this, talk to your doctor, pharmacist or nurse first.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Neupro. This is because:
- your **blood pressure** needs checking regularly while using Neupro, especially at the start of the treatment. Neupro may affect your blood pressure.
- your **eyes** need checking regularly while using Neupro. If you notice any problems with your eyesight between checks, talk to your doctor straight away.
- if you have serious **liver problems**, your doctor may need to change the dose. If your liver problems get worse during treatment, talk to your doctor straight away.
- you may get **skin problems** caused by the patch – see '**Skin problems caused by the patch**' in section 4.
- you may **feel very sleepy** or **fall asleep suddenly** – see '**Driving and using machines**' in section 2.
- your symptoms of **Restless Legs Syndrome** may start earlier than usual, be more intense and involve other limbs. If you experience such symptoms either before or after beginning treatment with Neupro, contact your doctor as your treatment may need to be adjusted.

Loss of consciousness can occur
Neupro can cause loss of consciousness. This can happen especially when you start using Neupro or when your dose is increased. Tell your doctor if you lose consciousness or feel dizzy.

Changes in behaviour and abnormal thinking
Neupro can cause side effects that change your behaviour (how you act). You may find it helpful to tell a member of your family or carer that you are using this medicine and ask them to read this leaflet. This is so that your family or carer can tell you, or your doctor, if they are worried about any changes in your behaviour.

These include:
- unusual urges or cravings which you cannot resist and that could harm yourself or others – the symptoms are mainly seen in patients with Parkinson's disease
- abnormal thinking or behaviour – most of the symptoms occur more frequently in patients with Parkinson's disease.

See '**Changes to your behaviour and abnormal thinking**' in section 4 for more information.

Children and adolescents
Do **not** give this medicine to **children** below 18 years of age because it is not known if it is safe or effective in this age group.

Other medicines and Neupro
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines.

If you are treated with Neupro and levodopa at the same time, some side effects may get more serious. This includes seeing or hearing things that are not real (hallucinations), movements you cannot control related to Parkinson's disease ('dyskinesia'), and swelling of legs and feet.

Do not take the following medicines while using Neupro – because they may decrease its effect:
- 'anti-psychotic' medicines – used to treat certain mental illnesses
- metoclopramide – used to treat nausea (feeling sick) and vomiting.

Talk to your doctor before using Neupro if you are taking:
- sedating medicines such as benzodiazepines or medicines used to treat mental illness or depression.
- medicines that lower blood pressure. Neupro may decrease blood pressure when you stand up – this effect may be worsened by the medicines used to lower blood pressure.

Your doctor will let you know if it is safe to keep taking these medicines while using Neupro.

Neupro with food, drink and alcohol
Because rotigotine enters your bloodstream through your skin, food or drink does not affect the way this medicine is absorbed by the body. You should discuss with your doctor if it is safe for you to drink alcohol while using Neupro.

Pregnancy and breast-feeding
Do not use Neupro if you are pregnant. This is because the effects of rotigotine on pregnancy and the unborn baby are not known.

Do not breast-feed during treatment with Neupro. This is because rotigotine may pass into your breast milk and affect your baby. It is also likely to lower the amount of milk you produce.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Driving and using machines
Neupro may make you feel very sleepy and you may fall asleep very suddenly. If this happens, do not drive. In isolated cases, people have fallen asleep while driving and this has caused accidents.

Also do not use tools or machines if you feel very sleepy – or do anything else which may put others or yourself at risk of serious injury.

Neupro contains sodium metabisulphite (E223)
Sodium metabisulphite (E223) may rarely cause severe hypersensitivity (allergic) reactions and bronchospasm (breathing distress caused by narrowing of the airways).

3. How to use Neupro

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Which strength patches to use
The dose of Neupro will depend on your illness – see below.

Neupro is available in different strength patches which release the medicine over 24 hours. The strengths are 1 mg/24 h, 2 mg/24 h, 3 mg/24 h, 4 mg/24 h, 6 mg/24 h and 8 mg/24 h. The patches of 1 mg/24 h and 3 mg/24 h are used for the treatment of Restless Leg Syndrome, while the patches of 4 mg/24 h, 6 mg/24 h and 8 mg/24 h are used for the treatment of Parkinson's disease. The patches of 2 mg/24 h are used for the treatment of Parkinson's disease and Restless Leg Syndrome.
- You may have to use more than one patch to reach your dose, as prescribed by your doctor.
- For doses higher than 8 mg/24 h (doses prescribed by your doctor above the available strengths), multiple patches must be applied to achieve the final dose. For example the daily dose of 10 mg may be reached by applying one patch of 6 mg/24 h and one patch of 4 mg/24 h.
- The patches should not be cut into pieces.

Treatment of Parkinson's disease
Patients not taking levodopa – early stage of Parkinson's disease

- Your starting daily dose will be one 2 mg/24 h patch each day.
- From the second week your daily dose may be increased by 2 mg each week – until you get to the right maintenance dose for you.
- For most patients, the right dose is between 6 mg and 8 mg each day. This is normally reached within 3 to 4 weeks.
- The maximum dose is 8 mg each day.

Patients taking levodopa – advanced stage of Parkinson's disease

- Your starting daily dose will be one 4 mg/24 h patch each day.
- From the second week your daily dose will be increased by 2 mg each week – until you get to the right maintenance dose for you.
- For most patients, the right dose is between 8 mg and 16 mg each day. This is normally reached within 3 to 7 weeks.
- The maximum dose is 16 mg each day.

Treatment of Restless Legs Syndrome

- Your starting dose will be one 1 mg/24 h patch each day.
- From the second week, your daily dose may be increased by 1 mg each week – until you get to the right maintenance dose for you. This is when you and your doctor agree that the symptoms are being controlled well enough and the side effects of the medicines are acceptable.
- The maximum dose is 3 mg per day.

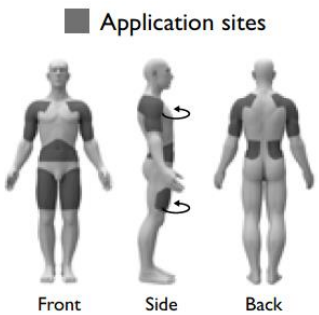
If you have to stop taking this medicine, see **'If you stop using Neupro'** in section 3.

How to use the Neupro patches:
Neupro is a patch that is put on the skin.

- Make sure that you take the old patch off before putting on a new one.
- Stick the new patch on **a different area of the skin each day**.
- Leave the patch on your skin for 24 hours, then take it off and put on a new one.
- **Change the patches** at about the **same time every day**.
- **Do not cut the Neupro patches into pieces.**

Where to stick the patch
Put the sticky side of the patch onto clean, dry, healthy skin on the following areas as shown in grey on the pictures opposite:

- Shoulder or upper arm.
- Belly.
- Flank (your side, between the ribs and hips).
- Thigh or hip.



To avoid skin irritation

- Stick the patch onto a **different area of skin each day**. For example, put it on the right side of your body one day, then on the left side of your body the next day. Or on your upper body one day, then on your lower body the day after that.
- Do **not** stick Neupro on the **same area of skin** twice **within 14 days**.
- Do **not** stick the patch on **broken or damaged skin** – or on skin that is **red or irritated**.

If you still get problems with your skin because of the patch, please see **'Skin problems caused by the patch'** in section 4 for more information.

To **prevent the patch becoming loose or falling off**

- Do **not** put the patch in an area where it can be **rubbed by tight clothing**.
- Do **not** use **creams, oils, lotions, powders** or other **skin products** where you will put the patch. Also do not use them on or near a patch you are already wearing.
- If you need to stick the patch to a hairy area of skin, you must **shave** the area at least **3 days before** sticking the patch there.
- If the edges of the patch lift, the patch may be taped down with adhesive medical tape.

If the patch falls off, put on a new patch for the rest of the day – then replace the patch at the usual time.

- Do **not** let the area of the patch **get hot** – for example too much sunlight, saunas, hot baths, heating pads or hot-water bottles. This is because the medicine may be released faster. If you think that too much heat has been applied, contact your doctor or pharmacist.
- Always check that the patch has not fallen off after activities such as **bathing, showering or exercising.**
- If the patch has **irritated your skin, keep** that area **protected from direct sunlight**. This is because it may change the colour of the skin.

How to use the patch

- Each patch is packed in a separate sachet.
- Before opening the sachet decide where you are going to stick this new patch and check you have removed any old patch.
- Stick the Neupro patch onto your skin as soon as you have opened the sachet and removed the release liner.

1.
To open the sachet, hold the sachet in both hands.

2.
Peel apart the foil.

3.
Open the sachet.

4.
Take the patch out of the sachet.

5.
The sticky side of the patch is covered by a transparent release liner.

- Hold the patch in both hands with the release liner facing you.

6.

- Bend the patch in half.

This makes the S-shaped break in the liner open up.

7.

- Peel off one side of the release liner.
- Do not touch the sticky side of the patch with your fingers.

8.

- Hold the other half of the rigid release liner.
- Then put the sticky half of the patch onto your skin.
- Press the sticky side of the patch firmly into place.

9.
Fold back the other half of the patch and remove the other side of the release liner.

10.

- Press the patch down firmly with the palm of your hand.
- Keep it pressed for about 30 seconds.

This makes sure the patch is touching the skin and the edges stick down well.

11.

Wash your hands with soap and water straight after handling the patch.

How to take off a used patch

- Slowly and carefully peel off the used patch.
- Gently wash the area with warm water and mild soap. This will remove any stickiness that stays on your skin. You can also use a little baby oil to remove any stickiness that will not wash off.
- Do not use alcohol or other dissolving liquids – such as nail polish remover. These may irritate your skin.

If you use more Neupro than you should

Using higher doses of Neupro than your doctor has prescribed may cause side effects such as feeling sick (nausea) or vomiting, low blood pressure, seeing or hearing things that are not real (hallucinations), feeling confused, very sleepy, having involuntary movements and convulsions. In such cases, contact your doctor or hospital straight away. They will tell you what to do.

If you forget to change the patch at your usual time

- If you have forgotten to change the patch at your usual time, change it as soon as you remember Take off the old patch and use a new one.
- If you have forgotten to stick on a new patch after removing the old one, use a new patch as soon as you remember.

In both cases, use a new patch at the usual time on the following day. Do not use a double dose to make up for a forgotten dose.

If you stop using Neupro

Do not stop using Neupro without talking to your doctor. A sudden stop could lead to a medical condition called 'neuroleptic malignant syndrome' which could be life-threatening. The signs include: loss of muscle movement (akinesia), rigid muscles, fever, unstable blood pressure, increased heart rate (tachycardia), confusion, low level of consciousness (such as a coma).

If your doctor says you should stop Neupro, the **daily dose** should be **lowered gradually**:

- **Parkinson's disease** – lowered by 2 mg every other day.
- **Restless Legs Syndrome** – lowered by 1 mg every other day.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor, pharmacist or nurse if you notice any side effects.

Side effects more likely at the start of treatment
You may **feel sick** (nausea) and **vomit at the start of treatment**. These effects are usually mild or moderate and only last for a short time. **Talk to your doctor** if they last for a long time or if you are worried about them.

Skin problems caused by the patch
- You may get redness and itching on the skin where the patch has been – these reactions are usually mild or moderate.
- The reactions normally go away after a few hours – once you remove the patch.
- **Talk to your doctor** if you have a skin reaction that lasts longer than a few days or is severe. Also do this if it spreads outside the area of skin that was covered by the patch.
- Avoid sunlight and solarium exposure on areas of skin showing any kind of skin reaction caused by the patch.
- To help avoid the skin reactions, you should put the patch on a different area of skin every day, and only use the same area again after 14 days.

Loss of consciousness can occur
Neupro can cause loss of consciousness. This can happen especially when you start using Neupro or when your dose is increased. Tell your doctor if you lose consciousness or feel dizzy.

Changes in behaviour and abnormal thinking
Tell your doctor if you notice any changes in behaviour, thinking or both, that are listed below. They will discuss ways of managing or reducing symptoms.

You may find it helpful to also tell a member of your family or carer that you are using this medicine and ask them to read this leaflet. This is so that your family or carer can tell you, or your doctor, if they are worried about any changes in your behaviour. Neupro can cause unusual urges or cravings which you cannot resist such as the impulse, drive or temptation to do things that could harm yourself or others – the symptoms are mainly seen in patients with Parkinson's disease.

These may include:
- strong impulse to gamble too much – even if this seriously affects you or your family
- altered or increased sexual interest and behaviour which causes significant concern to you or others – for example, an increased sex drive
- uncontrolled shopping or spending too much
- binge eating (eating large amounts of food in a short period of time) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger).

Neupro may cause other behaviours and abnormal thinking. These may include:
- abnormal thoughts about reality
- delusions and hallucinations (seeing or hearing things that are not real)
- confusion
- disorientation
- aggressive behaviour
- agitation
- delirium.

Tell your doctor if you notice any changes in behaviour, thinking or both that are listed above. They will discuss ways of managing or reducing symptoms.

Allergic reactions
Contact your doctor if you notice signs of an allergic reaction – these can include swelling of the face, tongue or lips.

Side effects when using Neupro for Parkinson's disease
Tell your doctor, pharmacist or nurse if you get any of the following side effects:

Very common: may affect more than 1 in 10 people
- headache
- feeling sleepy or dizzy
- feeling sick (nausea), vomiting
- skin reactions under the patch such as redness and itching

Common: may affect up to 1 in 10 people
- falling
- hiccups
- weight loss
- swelling of legs and feet
- feeling weak (fatigue), feeling tired
- feeling of heartbeat (palpitation)
- constipation, dry mouth, heartburn
- redness, increased sweating, itching
- vertigo (sensation of whirling motion)
- seeing or hearing things that are not real (hallucinations)
- low blood pressure when standing up, high blood pressure
- difficulty falling asleep, sleep disorder, difficulty sleeping, nightmare, unusual dreams
- movements you cannot control related to Parkinson's disease (dyskinesia)
- fainting, feeling dizzy when standing up because of fall in blood pressure
- unable to resist the impulse to perform an action that is harmful involving excessive gambling, repetitive meaningless actions, uncontrolled shopping or spending too much
- binge eating (eating large amount of food in a short period of time), compulsive eating (eating more food than normal and more than needed to satisfy hunger)

Uncommon: may affect up to 1 in 100 people
- blurred vision
- weight increase
- allergic reaction
- low blood pressure
- increased heart rate
- increased sex drive
- abnormal heart beat
- stomach discomfort and pain
- generalised itching, skin irritation
- falling asleep suddenly without warning
- unable to achieve or maintain an erection
- feeling agitated, disorientated, confused or paranoid
- increased or abnormal liver test results
- sight problems such as seeing colours or lights
- increased levels of creatine phosphokinase (CPK) (CPK is an enzyme found mainly in skeletal muscles).

Rare: may affect up to 1 in 1,000 people
- delusion
- delirium
- feeling irritable
- being aggressive

- psychotic disorders
- rash over larger parts of the body
- involuntary muscle spasms (convulsion)

Not known: it is not known how often these happen
- craving large doses of medicines like Neupro – more than needed for the illness. This is known as 'dopamine dysregulation syndrome' and can lead to use of too much Neupro.
- diarrhoea
- dropped head syndrome
- rhabdomyolysis (a rare severe muscle disorder which causes pain, tenderness and weakness of the muscles and may lead to kidney problems)

Tell your doctor, pharmacist or nurse if you notice any of the side effects listed above.

Side effects when using Neupro for Restless Legs Syndrome
Tell your doctor or pharmacist if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people
- headache
- feeling sick (nausea)
- feeling weak (fatigue)
- skin irritations under the patch such as redness and itching

Common: may affect up to 1 in 10 people
- itching
- feeling irritable
- allergic reaction
- increased sex drive
- high blood pressure
- vomiting, heartburn
- swelling of legs and feet
- feeling sleepy, falling asleep suddenly without warning, difficulty in sleeping, sleep problems, having unusual dreams
- unable to resist the impulse to perform an action that is harmful involving excessive gambling, repetitive meaningless actions, uncontrolled shopping or spending too much
- binge eating (eating large amount of food in a short period of time) or compulsive eating (eating more food than normal and more than needed to satisfy hunger)

Uncommon: may affect up to 1 in 100 people
- feeling agitated
- feeling dizzy when standing up because of a fall in blood pressure

Rare: may affect up to 1 in 1,000 people
- being aggressive
- disorientation

Not known: it is not known how often these happen
- craving large doses of medicines like Neupro – more than needed for the illness. This is known as 'dopamine dysregulation syndrome' and can lead to use of too much Neupro
- seeing or hearing things that are not real (hallucinations)
- nightmares
- paranoia
- confusion

- psychotic disorders
- delusion
- delirium
- feeling dizzy
- loss of consciousness, involuntary movements (dyskinesia)
- involuntary muscle spasms (convulsion)
- blurry vision
- visual disturbances such as seeing colours or lights
- vertigo (sensation of whirling motion)
- feeling of heartbeat (palpitation)
- abnormal heart rhythm
- low blood pressure
- hiccups
- constipation, dry mouth
- stomach discomfort and pain
- diarrhoea
- redness, increased sweating
- generalised itching, skin irritation
- generalised rash
- unable to achieve or maintain an erection
- weight loss, weight increase
- increased or abnormal liver function test results
- increased heart rate
- increased levels of creatine phosphokinase (CPK) (CPK is an enzyme found mainly in skeletal muscles)
- falling
- rhabdomyolysis (a rare severe muscle disorder which causes pain, tenderness and weakness of the muscles and may lead to kidney problems)

Talk to your doctor or pharmacist if you notice any of the side effects listed above.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Neupro

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and box.

Do not store above 30°C.

What to do with the used and unused patches
- Used patches still contain the active substance ‘rotigotine’, which may be harmful to others. Fold the used patch with the sticky side inwards. Put the patch in the original sachet and then throw it away safely, out of the reach of children.

- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Neupro contains
The active substance is rotigotine.
- Each patch releases 2 mg of rotigotine per 24 hours. Each patch of 10 cm^2 contains 4.5 mg of rotigotine.

The other ingredients are:
- Poly(dimethylsiloxane, trimethylsilyl silicate)-copolymerisate, povidoneK90, sodium metabisulphite (E223), ascorbyl palmitate (E304) and DL-α-tocopherol (E307).
- Backing layer: Polyester film, siliconized, aluminized, colour coated with a pigment (titanium dioxide (E171), pigment yellow 95, pigment red 166) layer and imprinted (pigment red 144, pigment yellow 95, pigment black 7).
- Release liner: Transparent fluoropolymer coated polyester film.

What Neupro looks like and contents of the pack
Neupro is a transdermal patch. It is thin and has three layers. It is square-shaped with rounded edges. The outside is tan-coloured and is imprinted with Neupro 2 mg/24 h.

Neupro is available in the following pack-sizes:
Boxes containing 7, 14, 28, 30 or 84 (multipack containing 3 packs of 28) patches, which are individually sealed in sachets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

UCB Pharma S.A.
Allée de la Recherche 60
B-1070 Bruxelles
Belgium

Manufacturer

UCB Pharma S.A.
Chemin du Foriest
B-1420 Braine l'Alleud
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
UCB Pharma SA/NV
Tél/Tel: +32-(0)2 559 92 00

Lietuva
UCB Pharma Oy Finland
Tel: +358-92 514 4221 (Suomija)

Sifrol®

Tablets

pramipexole dihydrochloride monohydrate

Consumer Medicine Information

What is in this leaflet

This leaflet answers some common questions about Sifrol.

It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking Sifrol against the benefits it is expected to have for you.

If you have any concerns about taking this medicine, ask your doctor or pharmacist.

This leaflet was last updated on the date at the end of this leaflet. More recent information may be available. The latest Consumer Medicine Information is available from your pharmacist, doctor, or from www.medicines.org.au and may contain important information about the medicine and its use of which you should be aware.

Keep this leaflet with your medicine.
You may need to read it again.

What Sifrol is used for

Sifrol is used to treat the symptoms of Parkinson's disease and Restless Legs Syndrome (RLS).

PARKINSON'S DISEASE

Parkinson's disease is a disease of the brain that affects body movement.

The symptoms of Parkinson's disease are caused by a lack of dopamine, a naturally occurring chemical produced by certain brain cells. Dopamine relays messages in the part of the brain that controls movement. When too little dopamine is produced, this results in Parkinson's disease.

RESTLESS LEGS SYNDROME (RLS)

RLS is a neurological disorder in which there is an overwhelming urge to move the legs to stop unpleasant sensations.

The sensations vary from person to person and range from uncomfortable to irritating to painful. The symptoms usually occur when sitting or lying down - which often leads to problems falling or staying asleep. Sometimes the arms and body may be affected. Current evidence suggests that RLS may be due to faulty dopamine signals in certain areas of the brain.

How Sifrol works

Sifrol contains the active ingredient pramipexole dihydrochloride monohydrate. It belongs to a group of medicines known as dopamine agonists, which bind to dopamine receptors. It is believed that Sifrol works by having a similar effect as dopamine in the brain.

Ask your doctor if you have any questions about why Sifrol has been prescribed for you.
Your doctor may have prescribed it for another reason.

Sifrol is not addictive.

This medicine is available only with a doctor's prescription.

Before you take Sifrol

When you must not take it

Do not take Sifrol if you have an allergy to:

- any medicine containing pramipexole dihydrochloride monohydrate (the active ingredient) or
- any of the ingredients listed at the end of this leaflet.

Some of the symptoms of an allergic reaction may include:

- rash, itching or hives on the skin
- swelling of the face, lips, tongue or other parts of the body
- shortness of breath, wheezing or difficulty breathing.

Do not give this medicine to a child or adolescent under the age of 18 years.
Safety and effectiveness in children younger than 18 years have not been established.

Do not take this medicine after the expiry date printed on the pack, or if the packaging is torn or shows signs of tampering.
If it has expired or is damaged, return it to your pharmacist for disposal.

If you are not sure whether you should start taking this medicine, talk to your doctor.

Before you start to take it

Tell your doctor if you have allergies to any other medicines, or any other substances, such as foods, preservatives or dyes.

Tell your doctor if you have, or have had, any of the following medical conditions:

- kidney problems
- mental illnesses
- low blood pressure
- trouble controlling your muscles (dyskinesia).

Tell your doctor if you are pregnant, or plan to become pregnant.
Your doctor can discuss with you the benefits and risks of taking Sifrol.

Tell your doctor if you are breastfeeding, or plan to breastfeed.
Sifrol is not recommended during breastfeeding, as it may pass into breast milk.

If you have not told your doctor or pharmacist about any of the above, tell them before you start taking Sifrol.

Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines including any that you buy without a prescription from your pharmacy, supermarket or health food shop.

Some medicines and Sifrol may interfere with each other. These include:

- levodopa, levodopa/carbidopa combination, or other medicines used to treat Parkinson's disease (e.g. amantadine)
- medicines used to treat high blood pressure or heart problems (e.g. digoxin, diltiazem, procainamide, quinidine, triamterene, verapamil, hydrochlorothiazide)
- medicines used to treat mental illness/psychoses
- metoclopramide, a medicine used to treat nausea and vomiting
- some medicines used to treat stomach or duodenal ulcers (e.g. cimetidine or ranitidine)
- quinine, a medicine used to prevent malaria
- some antibiotics (e.g. trimethoprim, cephalosporins, penicillins)
- indometacin, a medicine used to treat arthritis
- chlorpropamide, a medicine used to treat diabetes
- other medicines that can cause drowsiness or sleepiness (e.g. antihistamine or some cough and cold preparations).

These medicines may be affected by Sifrol or may affect how well it works. You may need different amounts of the medicine, or you may need to take different medicines. Your doctor or pharmacist will advise you.

Your doctor and pharmacist may have more information on medicines to be careful with or to avoid while taking Sifrol.

How to take Sifrol

Follow all directions given to you by your doctor or pharmacist carefully.
They may differ from the information contained in this leaflet.

Sifrol is available in a number of tablet strengths. Your doctor or pharmacist will tell you which strength of Sifrol tablet and how many tablets you will need to take each day. This depends on your condition and whether or not you are taking any other medicines.

If you do not understand the instructions on the label, ask your doctor or pharmacist for help.

How much to take

The dose varies from patient to patient. Your doctor may first start you on a low dose of Sifrol and slowly increase the amount of Sifrol until the right dose is reached to control your condition.

PARKINSON'S DISEASE

The usual starting dose is one Sifrol 0.125 mg tablet three times a day.

Depending on how you respond to the treatment, your doctor may increase your daily dose gradually in steps of 0.75 mg at weekly intervals until the right dose for your needs is reached. The maximum dose is 4.5 mg of Sifrol per day.

RESTLESS LEGS SYNDROME

The usual starting dose is one Sifrol 0.125 mg tablet once a day, usually 2 to 3 hours before you go to bed.

Depending on how you respond to the treatment, your doctor may increase your dose gradually every 4 to 7 days until the right dose for your needs is reached. The maximum dose is 0.75 mg of Sifrol per day.

Follow all directions given to you by your doctor or pharmacist carefully.

How to take it

Swallow the tablets with a full glass of water.

Sifrol can be taken with or without food.

When to take it

Take Sifrol at about the same time each day.

Taking it at the same time each day will have the best effect. It will also help you remember when to take it.

How long to take it

Continue taking Sifrol for as long as your doctor tells you.

This medicine helps to control your condition, but does not cure it. It is important to keep taking your medicine even if you feel well.

If you forget to take it

PARKINSON'S DISEASE

If it is almost time for your next dose, skip the dose you missed and take the next dose when you are meant to.

Otherwise, take it as soon as you remember, then go back to taking it as you would normally.

Do not take a double dose to make up for the dose that you have missed.
This may increase the chance of you getting an unwanted side effect.

RESTLESS LEGS SYNDROME

If you forget to take Sifrol before you go to bed and you wake up late in the night or early morning, do not take any Sifrol as you may have trouble waking in the morning.

Skip the dose you missed and take the next dose when you are meant to.

If you are not sure what to do, ask your doctor or pharmacist.

If you have trouble remembering to take your medicine, ask your pharmacist for some hints.

If you take too much (overdose)

Immediately telephone your doctor, pharmacist or Poisons Information Centre (telephone 13 11 26) for advice, or go to Emergency at your nearest hospital if you think that you or anyone else may have taken too much Sifrol. Do this even if there are no signs of discomfort or poisoning.
You may need urgent medical attention.

If you take too much Sifrol you may have nausea, vomiting, abnormal uncontrolled movements, hallucinations, agitation and dizziness or light-headedness.

While you are taking Sifrol

Things you must do

Tell all doctors and pharmacists who are treating you that you are taking Sifrol.

Tell your doctor or pharmacist if you feel that Sifrol is not helping your condition.

Tell your doctor if, for any reason, you have not used Sifrol exactly as prescribed.
Otherwise, your doctor may think that it was not effective and change your treatment unnecessarily.

Tell your doctor as soon as possible if there is any worsening of your condition.

If you or your family notices an increase in compulsive behaviour, seek immediate medical advice.

Tell your doctor if you experience symptoms such as depression, apathy, anxiety, fatigue, sweating or pain after stopping or reducing your Sifrol treatment. If the problems persist for more than a few weeks, your doctor may need to adjust your treatment.

Tell your doctor if you develop an inability to keep your body and neck straight and upright. For example, you may experience abnormal posture such as forward bending of the head and neck, forward bending of the lower back or sidewards bending of the back.

Things you must not do

Do not give Sifrol to anyone else, even if they have the same condition as you.

Do not stop taking Sifrol or change the dose without checking with your doctor.
It is important not to suddenly stop taking your Sifrol tablets, unless advised to do so by your doctor. If you stop taking it suddenly, your condition may worsen or you may have unwanted side effects.

If you are using Sifrol for your Parkinson's Disease and your doctor asks you to stop taking Sifrol, the dose will normally be reduced gradually over several days.

Things to be careful of

Be careful driving or operating machinery until you know how Sifrol affects you.

This medicine may cause drowsiness, hallucinations and episodes of sudden onset of sleep in some people.

Make sure you know how you react to Sifrol before you engage in any activities where impaired alertness may put yourself or others at risk of serious injury.

If you experience excessive drowsiness or an episode of sudden onset of sleep (while performing daily activities), do not drive or perform any potentially dangerous activities, and contact your doctor.

Be careful when drinking alcohol while taking Sifrol.
Combining Sifrol and alcohol can make you more drowsy or sleepy.

Be careful getting up from a sitting or lying position.
You may feel dizzy or lightheaded while taking Sifrol, especially during the first few weeks of treatment. If you wish to stand up, you should do so slowly.

You should monitor your skin and see your doctor in case of any concerns.
Patients with Parkinson's disease may have an increased risk of developing melanoma.

Side effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking Sifrol.

Sifrol helps most people with Parkinson's disease or RLS, but it may have unwanted side effects in a few people. All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some of the side effects.

Do not be alarmed by these lists of possible side effects.
You may not experience any of them.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor if you notice any of the following and they worry you:

- feeling sick (nausea)
- vomiting
- constipation
- diarrhoea
- dry mouth
- drowsiness
- tiredness
- confusion or hallucinations (seeing, feeling or hearing things that are not there)
- restlessness
- dizziness
- headache
- light-headedness on standing up, especially when getting up from a sitting or lying position (hypotension)
- blurred vision
- swelling of hands, ankles or feet
- uncontrollable twitching, jerking or writhing movements
- difficulty sleeping or unusual dreams
- weight gain or loss
- loss or gain of sexual drive
- forward bending of the head and neck.

Some of these side effects are more common at the start of treatment and lessen or disappear with time.

Tell your doctor immediately if you or your family notice any of the following side effects:

- loss of memory (amnesia)
- fainting
- signs of allergy such as rash or hives on the skin; swelling of the face, lips, tongue or other parts of the body; wheezing or difficulty breathing
- excessive sleepiness or sudden onset of sleep during normal daily activities
- compulsive behaviour such as gambling, hypersexuality, shopping, eating, medication use and repetitive purposeless activities
- mental illness causing severe suspiciousness (paranoia)
- shortness of breath or tightness in the chest
- shortness of breath, swelling of the feet or legs due to fluid build-up (heart failure).

These are serious side effects. You may need urgent medical attention or hospitalisation. These side effects are rare.

Tell your doctor if you notice anything else that is making you feel unwell.
Other side effects not listed above may also occur in some people.

After taking Sifrol

Storage

Keep Sifrol in the pack until it is time to take it.

Keep Sifrol in a cool dry place where the temperature stays below 30°C.

Pramipexole: Patient drug information

(For additional information see "Pramipexole: Drug information")

You must carefully read the "Consumer Information Use and Disclaimer" below in order to understand and correctly use this information.

Brand Names: US

Mirapex; Mirapex ER

Brand Names: Canada

ACT Pramipexole; APO-Pramipexole; Auro-Pramipexole; DOM-Pramipexole [DSC]; Mirapex; PMS-Pramipexole [DSC]; RATIO-Pramipexole; SANDOZ Pramipexole; TEVA-Pramipexole [DSC]

What is this drug used for?

- It is used to treat Parkinson's disease.
- It is used to treat restless leg syndrome.
- It may be given to you for other reasons. Talk with the doctor.

What do I need to tell my doctor BEFORE I take this drug?

- If you are allergic to this drug; any part of this drug; or any other drugs, foods, or substances. Tell your doctor about the allergy and what signs you had.
- If you have kidney disease.
- If you are taking another drug that has the same drug in it.

  This is not a list of all drugs or health problems that interact with this drug.

  Tell your doctor and pharmacist about all of your drugs (prescription or OTC, natural products, vitamins) and health problems. You must check to make sure that it is safe for you to take this drug with all of your drugs and health problems. Do not start, stop, or change the dose of any drug without checking with your doctor.

What are some things I need to know or do while I take this drug?

All products:

- Tell all of your health care providers that you take this drug. This includes your doctors, nurses, pharmacists, and dentists.
- Avoid driving and doing other tasks or actions that call for you to be alert until you see how this drug affects you.
- To lower the chance of feeling dizzy or passing out, rise slowly if you have been sitting or lying down. Be careful going up and down stairs.
- Check your blood pressure as you have been told.
- Do not stop this drug without talking to your doctor. When you stop this drug, you may have signs of withdrawal. If you need to stop this drug, follow how to stop it as your doctor has told you. Call your doctor right away if you have any of these signs when lowering the dose or stopping this drug: fever, confusion, severe muscle stiffness, not caring about things, anxiety, depression, feeling tired, trouble sleeping, sweating, or pain.
- Avoid drinking alcohol while taking this drug.
- Talk with your doctor before you use marijuana, other forms of cannabis, or prescription or OTC drugs that may slow your actions.
- Neuroleptic malignant syndrome (NMS) is a severe and sometimes deadly health problem that has happened when drugs like this one were stopped all of a sudden. NMS has also happened when the dose was lowered. Call your doctor right away if you have any fever, muscle cramps or stiffness, dizziness, severe headache, confusion, change in thinking, fast or abnormal heartbeat, or are sweating a lot.
- If you are 65 or older, use this drug with care. You could have more side effects.
- Tell your doctor if you are pregnant, plan on getting pregnant, or are breast-feeding. You will need to talk about the benefits and risks to you and the baby.

Extended-release tablets:

- You may see something that looks like the tablet in your stool. If this happens, talk with your doctor.

What are some side effects that I need to call my doctor about right away?

WARNING/CAUTION: Even though it may be rare, some people may have very bad and sometimes deadly side effects when taking a drug. Tell your doctor or get medical

help right away if you have any of the following signs or symptoms that may be related to a very bad side effect:

For all uses of this drug:

- Signs of an allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat.
- Strong urges that are hard to control (such as eating, gambling, sex, or spending money).
- Fever.
- Feeling confused.
- Muscle stiffness.
- Passing urine more often.
- Very bad dizziness or passing out.
- Sweating a lot.
- Shortness of breath, a big weight gain, or swelling in the arms or legs.
- Change in eyesight.
- Trouble controlling body movements that is new or worse.
- Trouble moving around.
- Hallucinations (seeing or hearing things that are not there).
- Memory problems or loss.
- Muscle pain or weakness.
- Mental, mood, or behavior changes that are new or worse.
- Some people have fallen asleep during activities like driving, eating, or talking. Some people did not feel sleepy and felt alert right before falling asleep. This has happened up to 1 year after this drug was started. If you fall asleep during activities, do not drive or do other tasks or actions that call for you to be alert while you take this drug. Call your doctor right away if this happens or you feel very sleepy.
- Some people have had changes in posture that cannot be controlled. These may include neck bending forward, bending forward at the waist, or tilting sideways when you sit, stand, or walk. Changes in posture may happen several months after you start this drug or after an increase in dose. Call your doctor if you have any changes in posture.

Restless leg syndrome:

- For restless leg syndrome, tell your doctor if your signs become worse or start earlier in the day.

What are some other side effects of this drug?

All drugs may cause side effects. However, many people have no side effects or only have minor side effects. Call your doctor or get medical help if any of these side effects or any other side effects bother you or do not go away:

- Headache.
- Upset stomach.
- Diarrhea or constipation.
- Not hungry.
- Trouble sleeping.
- Feeling dizzy, sleepy, tired, or weak.
- Dry mouth.
- Strange or odd dreams.
- Muscle spasm.
- Weight loss.
- Stuffy nose.
- Flu-like signs.

These are not all of the side effects that may occur. If you have questions about side effects, call your doctor. Call your doctor for medical advice about side effects.

You may report side effects to your national health agency.

How is this drug best taken?

Use this drug as ordered by your doctor. Read all information given to you. Follow all instructions closely.

All products:

- Take with or without food. Take with food if it causes an upset stomach.
- Keep taking this drug as you have been told by your doctor or other health care provider, even if you feel well.

Regular-release tablets:

- For restless leg syndrome, take this drug 2 to 3 hours before bedtime.

Extended-release tablets:

- Swallow whole. Do not chew, break, or crush.

What do I do if I miss a dose?

Regular-release tablets:

- Skip the missed dose and go back to your normal time.
- Do not take 2 doses at the same time or extra doses.
- If you miss taking this drug for a few days in a row, call your doctor before you start taking it again.

Extended-release tablets:

- Take a missed dose as soon as you think about it.
- If it has been 12 hours or more since the missed dose, skip the missed dose and go back to your normal time.
- Do not take 2 doses at the same time or extra doses.
- If you miss taking this drug for a few days in a row, call your doctor before you start taking it again.

How do I store and/or throw out this drug?

- Store at room temperature protected from light. Store in a dry place. Do not store in a bathroom.
- Keep all drugs in a safe place. Keep all drugs out of the reach of children and pets.
- Throw away unused or expired drugs. Do not flush down a toilet or pour down a drain unless you are told to do so. Check with your pharmacist if you have questions about the best way to throw out drugs. There may be drug take-back programs in your area.

General drug facts

- If your symptoms or health problems do not get better or if they become worse, call your doctor.
- Do not share your drugs with others and do not take anyone else's drugs.
- Some drugs may have another patient information leaflet. If you have any questions about this drug, please talk with your doctor, nurse, pharmacist, or other health care provider.
- If you think there has been an overdose, call your poison control center or get medical care right away. Be ready to tell or show what was taken, how much, and when it happened.

Last Reviewed Date

2021-08-05

Consumer Information Use and Disclaimer

This information should not be used to decide whether or not to take this medicine or any other medicine. Only the healthcare provider has the knowledge and training to decide which medicines are right for a specific patient. This information does not endorse any medicine as safe, effective, or approved for treating any patient or health condition. This is only a brief summary of general information about this medicine. It does NOT include all information about the possible uses, directions, warnings, precautions, interactions, adverse effects, or risks that may apply to this medicine. This information is not specific medical advice and does not replace information you receive from the healthcare provider. You must talk with the healthcare provider for complete information about the risks and benefits of using this medicine. The use of this information is governed by the Lexicomp End User License Agreement, available at https://www.wolterskluwer.com/en/solutions/lexicomp/about/eula.

Topic 10988 Version 165.0

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Do not store Sifrol or any other medicine in the bathroom or near a sink. Do not leave it in the car or on window sills.
Heat and dampness can destroy some medicines.

Keep your Sifrol where young children cannot reach it.
A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking this medicine or the expiry date has passed, ask your pharmacist what to do with any medicine that is left over.

Product Description

What it looks like

Sifrol is the brand name of your medicine.

Sifrol 0.125 mg tablets are round, white tablets with 'P6' on one side and company symbol on the other.

Sifrol 0.25 mg tablets are oval, white, scored tablets with 'P7' on one side and company symbol on the other.

Sifrol 1 mg tablets are round, white, scored tablets with 'P9' on one side and company symbol on the other.

Sifrol 0.25 mg and 1 mg tablets are available in blister packs of 10 (sample pack)* and 100 tablets.

Sifrol 0.125 mg tablets are available in blister packs of 10 (sample pack)*, 30 and 100* tablets.

* Not distributed in Australia.

Ingredients

Each Sifrol 0.125 mg tablet contains pramipexole dihydrochloride monohydrate 0.125 mg.

Each Sifrol 0.25 mg tablet contains 0.25 mg pramipexole dihydrochloride monohydrate.

Each Sifrol 1 mg tablet contains 1 mg pramipexole dihydrochloride monohydrate.

Each Sifrol tablet also contains the following ingredients:

- mannitol
- maize starch
- colloidal anhydrous silica
- povidone
- magnesium stearate.

Supplier

Sifrol tablets are supplied in Australia by:

Boehringer Ingelheim Pty Limited
ABN 52 000 452 308
Sydney, Australia

www.boehringer-ingelheim.com.au

This Consumer Medicine Information was updated in September 2018.

Australian Registration Numbers

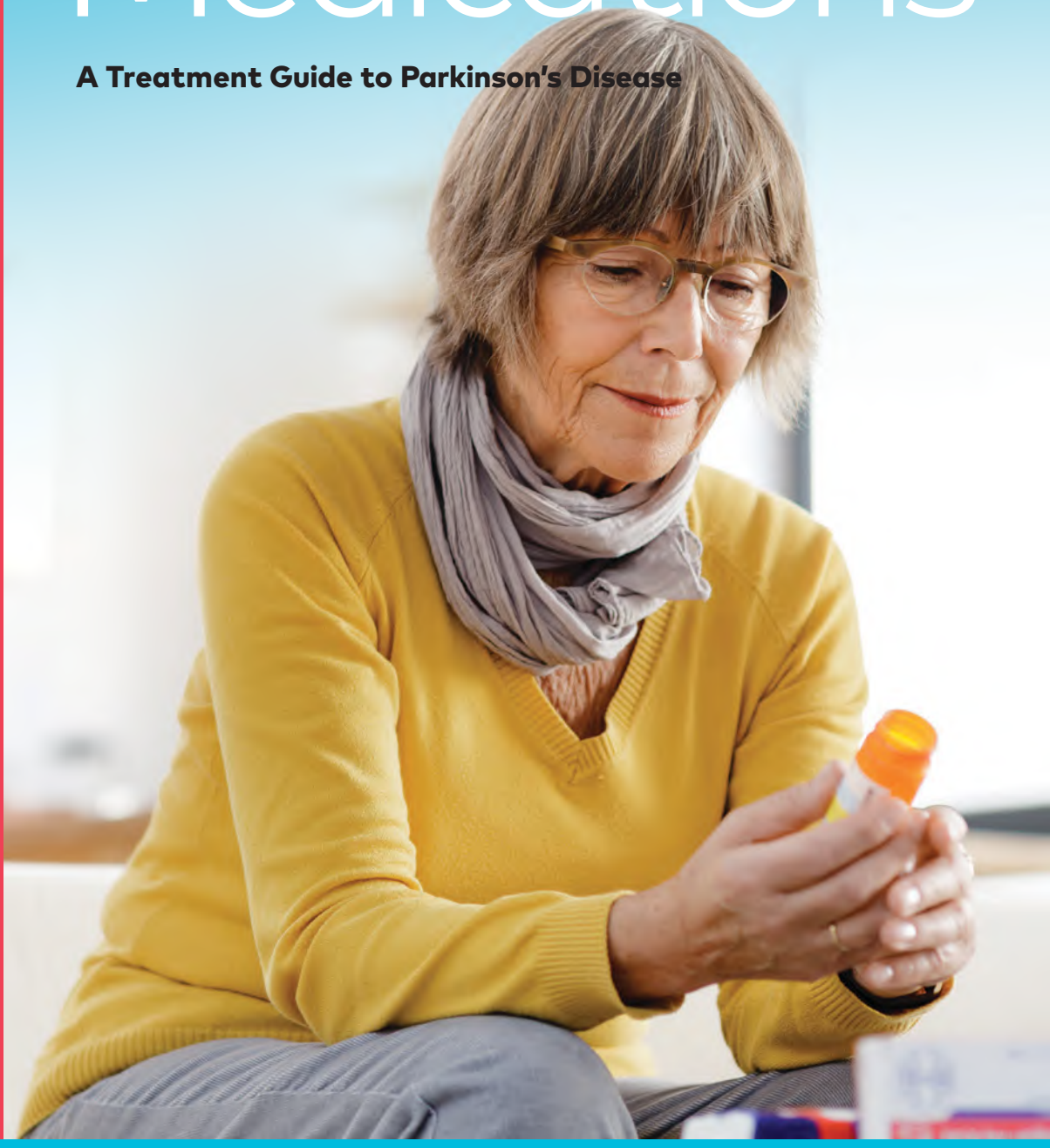
Sifrol 0.125 mg tablets
AUST R 67238

Sifrol 0.25 mg tablets
AUST R 66484

Sifrol 1 mg tablets
AUST R 66485

Medications

A Treatment Guide to Parkinson's Disease



Parkinson's Foundation

About this book

GLOSSARY

Definitions for all words underlined in blue can be found in the glossary starting on page 57. A comprehensive Parkinson's disease glossary can be found at Parkinson.org/Glossary.

INDEX

An index of key words and topics can be found on page 65.

PARKINSON'S FOUNDATION RESOURCES

Certain pages include tip sheets with practical pointers. You can find more helpful tips in the books, fact sheets, videos, webinars and podcasts in our PD library at Parkinson.org/Library.

There is no standard treatment for Parkinson's disease (PD). Treatment for each person with Parkinson's is based on his or her symptoms. There are many medications available to treat the Parkinson's symptoms, although none yet that reverse the effects of the disease.

It is common for people with PD to take a variety of these medications – all at different doses and at different times of day – to manage symptoms.

The information included here will explain the types of medications available to manage motor and non-motor symptoms in the hopes that it will help you to work with your Parkinson's specialist to find the right balance of medications to help you live well with Parkinson's.

Contents

Acknowledgements
This book was written and reviewed by:
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Steven Swank, PharmD, BCACP
University of Kansas Medical Center

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Neurocrine® BIOSCIENCES

Design: Ultravirgo

CHAPTER ONE

About Parkinson's Disease

If you're reading this book, you are probably already familiar with Parkinson's disease, but here are some basics: Parkinson's is a progressive 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, slow movements, stiffness and muscle cramping 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 a neurologist, who asks you questions about your health and medical history and observes your movement. Your doctor may want you to have some tests or imaging; some, like an MRI, can help rule out other conditions, while others, like DaTScan, may help confirm a Parkinson's diagnosis if there is uncertainty. The goal of treatment is to help you manage your symptoms. Good symptom management can help you to stay healthy, exercise, and keep yourself in the best possible shape. Although at this time there is no way to correct the brain changes that cause Parkinson's, we know that exercise can help you maintain your ability to fight the disease and that staying healthy can reduce setbacks that make PD progress faster. Great care is an important part of living your best life with Parkinson's.

Lack of dopamine in people with Parkinson's was first described in the 1960s. Dopamine is a type of neurotransmitter, or chemical messenger, one of several chemicals your brain cells use to send signals to one another. Soon after, dopamine-replacement therapy using levodopa became – and remains – the gold standard treatment. However, we know that the dopamine system is not the only one affected by Parkinson's. The disease process also disrupts other brain networks, including those linked to mood, behavior and thinking (cognition). You might also hear that Parkinson's is linked to a protein in the human brain called alpha-synuclein. 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.

You and your family may have questions or fears about Parkinson's and genetics. While there are several genetic mutations that can increase your risk, for the vast majority of people, Parkinson's is not inherited. There is no test that can accurately predict who will develop Parkinson's. Extensive gene and biomarker research is underway to uncover the possible factors involved in – not necessarily causes of – disease development.

CHAPTER TWO

Medications for Motor Symptoms

The following medications used to treat Parkinson's disease are discussed in this chapter:

- **Levodopa**
- **Dopamine Agonists**
- **MAO-B Inhibitors**
- **COMT-Inhibitors**
- **Amantadine**
- **Anticholinergics**
- **Adenosine A2a Antagonists**

The main goal of these medications is to lessen motor symptoms, or the symptoms that affect movement in people with Parkinson's disease. Since these symptoms are caused by changes in the amount of dopamine in the brain, most medications are used to replace, copy or enhance the effect of dopamine.

Sifrol®

Tablets

pramipexole dihydrochloride monohydrate

Consumer Medicine Information

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It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking Sifrol against the benefits it is expected to have for you.

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Keep this leaflet with your medicine.
You may need to read it again.

What Sifrol is used for

Sifrol is used to treat the symptoms of Parkinson's disease and Restless Legs Syndrome (RLS).

PARKINSON'S DISEASE

Parkinson's disease is a disease of the brain that affects body movement.

The symptoms of Parkinson's disease are caused by a lack of dopamine, a naturally occurring chemical produced by certain brain cells. Dopamine relays messages in the part of the brain that controls movement. When too little dopamine is produced, this results in Parkinson's disease.

RESTLESS LEGS SYNDROME (RLS)

RLS is a neurological disorder in which there is an overwhelming urge to move the legs to stop unpleasant sensations.

The sensations vary from person to person and range from uncomfortable to irritating to painful. The symptoms usually occur when sitting or lying down - which often leads to problems falling or staying asleep. Sometimes the arms and body may be affected. Current evidence suggests that RLS may be due to faulty dopamine signals in certain areas of the brain.

How Sifrol works

Sifrol contains the active ingredient pramipexole dihydrochloride monohydrate. It belongs to a group of medicines known as dopamine agonists, which bind to dopamine receptors. It is believed that Sifrol works by having a similar effect as dopamine in the brain.

Ask your doctor if you have any questions about why Sifrol has been prescribed for you.
Your doctor may have prescribed it for another reason.

Sifrol is not addictive.

This medicine is available only with a doctor's prescription.

Before you take Sifrol

When you must not take it

Do not take Sifrol if you have an allergy to:

- any medicine containing pramipexole dihydrochloride monohydrate (the active ingredient) or
- any of the ingredients listed at the end of this leaflet.

Some of the symptoms of an allergic reaction may include:

- rash, itching or hives on the skin
- swelling of the face, lips, tongue or other parts of the body
- shortness of breath, wheezing or difficulty breathing.

Do not give this medicine to a child or adolescent under the age of 18 years.
Safety and effectiveness in children younger than 18 years have not been established.

Do not take this medicine after the expiry date printed on the pack, or if the packaging is torn or shows signs of tampering.
If it has expired or is damaged, return it to your pharmacist for disposal.

If you are not sure whether you should start taking this medicine, talk to your doctor.

Before you start to take it

Tell your doctor if you have allergies to any other medicines, or any other substances, such as foods, preservatives or dyes.

Tell your doctor if you have, or have had, any of the following medical conditions:

- kidney problems
- mental illnesses
- low blood pressure
- trouble controlling your muscles (dyskinesia).

Tell your doctor if you are pregnant, or plan to become pregnant.
Your doctor can discuss with you the benefits and risks of taking Sifrol.

Tell your doctor if you are breastfeeding, or plan to breastfeed.
Sifrol is not recommended during breastfeeding, as it may pass into breast milk.

If you have not told your doctor or pharmacist about any of the above, tell them before you start taking Sifrol.

Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines including any that you buy without a prescription from your pharmacy, supermarket or health food shop.

Some medicines and Sifrol may interfere with each other. These include:

- levodopa, levodopa/carbidopa combination, or other medicines used to treat Parkinson's disease (e.g. amantadine)
- medicines used to treat high blood pressure or heart problems (e.g. digoxin, diltiazem, procainamide, quinidine, triamterene, verapamil, hydrochlorothiazide)
- medicines used to treat mental illness/psychoses
- metoclopramide, a medicine used to treat nausea and vomiting
- some medicines used to treat stomach or duodenal ulcers (e.g. cimetidine or ranitidine)
- quinine, a medicine used to prevent malaria
- some antibiotics (e.g. trimethoprim, cephalosporins, penicillins)
- indometacin, a medicine used to treat arthritis
- chlorpropamide, a medicine used to treat diabetes
- other medicines that can cause drowsiness or sleepiness (e.g. antihistamine or some cough and cold preparations).

These medicines may be affected by Sifrol or may affect how well it works. You may need different amounts of the medicine, or you may need to take different medicines. Your doctor or pharmacist will advise you.

Your doctor and pharmacist may have more information on medicines to be careful with or to avoid while taking Sifrol.

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If you do not understand the instructions on the label, ask your doctor or pharmacist for help.

How much to take

The dose varies from patient to patient. Your doctor may first start you on a low dose of Sifrol and slowly increase the amount of Sifrol until the right dose is reached to control your condition.

PARKINSON'S DISEASE

The usual starting dose is one Sifrol 0.125 mg tablet three times a day.

Depending on how you respond to the treatment, your doctor may increase your daily dose gradually in steps of 0.75 mg at weekly intervals until the right dose for your needs is reached. The maximum dose is 4.5 mg of Sifrol per day.

RESTLESS LEGS SYNDROME

The usual starting dose is one Sifrol 0.125 mg tablet once a day, usually 2 to 3 hours before you go to bed.

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Depending on how you respond to the treatment, your doctor may increase your dose gradually every 4 to 7 days until the right dose for your needs is reached. The maximum dose is 0.75 mg of Sifrol per day.

Follow all directions given to you by your doctor or pharmacist carefully.

How to take it

Swallow the tablets with a full glass of water.

Sifrol can be taken with or without food.

When to take it

Take Sifrol at about the same time each day.

Taking it at the same time each day will have the best effect. It will also help you remember when to take it.

How long to take it

Continue taking Sifrol for as long as your doctor tells you.

This medicine helps to control your condition, but does not cure it. It is important to keep taking your medicine even if you feel well.

If you forget to take it

PARKINSON'S DISEASE

If it is almost time for your next dose, skip the dose you missed and take the next dose when you are meant to.

Otherwise, take it as soon as you remember, then go back to taking it as you would normally.

Do not take a double dose to make up for the dose that you have missed.
This may increase the chance of you getting an unwanted side effect.

RESTLESS LEGS SYNDROME

If you forget to take Sifrol before you go to bed and you wake up late in the night or early morning, do not take any Sifrol as you may have trouble waking in the morning.

Skip the dose you missed and take the next dose when you are meant to.

If you are not sure what to do, ask your doctor or pharmacist.

If you have trouble remembering to take your medicine, ask your pharmacist for some hints.

If you take too much (overdose)

Immediately telephone your doctor, pharmacist or Poisons Information Centre (telephone 13 11 26) for advice, or go to Emergency at your nearest hospital if you think that you or anyone else may have taken too much Sifrol. Do this even if there are no signs of discomfort or poisoning.
You may need urgent medical attention.

If you take too much Sifrol you may have nausea, vomiting, abnormal uncontrolled movements, hallucinations, agitation and dizziness or light-headedness.

While you are taking Sifrol

Things you must do

Tell all doctors and pharmacists who are treating you that you are taking Sifrol.

Tell your doctor or pharmacist if you feel that Sifrol is not helping your condition.

Tell your doctor if, for any reason, you have not used Sifrol exactly as prescribed.
Otherwise, your doctor may think that it was not effective and change your treatment unnecessarily.

Tell your doctor as soon as possible if there is any worsening of your condition.

If you or your family notices an increase in compulsive behaviour, seek immediate medical advice.

Tell your doctor if you experience symptoms such as depression, apathy, anxiety, fatigue, sweating or pain after stopping or reducing your Sifrol treatment. If the problems persist for more than a few weeks, your doctor may need to adjust your treatment.

Tell your doctor if you develop an inability to keep your body and neck straight and upright. For example, you may experience abnormal posture such as forward bending of the head and neck, forward bending of the lower back or sidewards bending of the back.

Things you must not do

Do not give Sifrol to anyone else, even if they have the same condition as you.

Do not stop taking Sifrol or change the dose without checking with your doctor.
It is important not to suddenly stop taking your Sifrol tablets, unless advised to do so by your doctor. If you stop taking it suddenly, your condition may worsen or you may have unwanted side effects.

If you are using Sifrol for your Parkinson's Disease and your doctor asks you to stop taking Sifrol, the dose will normally be reduced gradually over several days.

Things to be careful of

Be careful driving or operating machinery until you know how Sifrol affects you.

This medicine may cause drowsiness, hallucinations and episodes of sudden onset of sleep in some people.

Make sure you know how you react to Sifrol before you engage in any activities where impaired alertness may put yourself or others at risk of serious injury.

If you experience excessive drowsiness or an episode of sudden onset of sleep (while performing daily activities), do not drive or perform any potentially dangerous activities, and contact your doctor.

Be careful when drinking alcohol while taking Sifrol.
Combining Sifrol and alcohol can make you more drowsy or sleepy.

Be careful getting up from a sitting or lying position.
You may feel dizzy or lightheaded while taking Sifrol, especially during the first few weeks of treatment. If you wish to stand up, you should do so slowly.

You should monitor your skin and see your doctor in case of any concerns.
Patients with Parkinson's disease may have an increased risk of developing melanoma.

Side effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking Sifrol.

Sifrol helps most people with Parkinson's disease or RLS, but it may have unwanted side effects in a few people. All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some of the side effects.

Do not be alarmed by these lists of possible side effects.
You may not experience any of them.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor if you notice any of the following and they worry you:

- feeling sick (nausea)
- vomiting
- constipation
- diarrhoea
- dry mouth
- drowsiness
- tiredness
- confusion or hallucinations (seeing, feeling or hearing things that are not there)
- restlessness
- dizziness
- headache
- light-headedness on standing up, especially when getting up from a sitting or lying position (hypotension)
- blurred vision
- swelling of hands, ankles or feet
- uncontrollable twitching, jerking or writhing movements
- difficulty sleeping or unusual dreams
- weight gain or loss
- loss or gain of sexual drive
- forward bending of the head and neck.

Some of these side effects are more common at the start of treatment and lessen or disappear with time.

Tell your doctor immediately if you or your family notice any of the following side effects:

- loss of memory (amnesia)
- fainting
- signs of allergy such as rash or hives on the skin; swelling of the face, lips, tongue or other parts of the body; wheezing or difficulty breathing
- excessive sleepiness or sudden onset of sleep during normal daily activities
- compulsive behaviour such as gambling, hypersexuality, shopping, eating, medication use and repetitive purposeless activities
- mental illness causing severe suspiciousness (paranoia)
- shortness of breath or tightness in the chest
- shortness of breath, swelling of the feet or legs due to fluid build-up (heart failure).

These are serious side effects. You may need urgent medical attention or hospitalisation. These side effects are rare.

Tell your doctor if you notice anything else that is making you feel unwell.
Other side effects not listed above may also occur in some people.

After taking Sifrol

Storage

Keep Sifrol in the pack until it is time to take it.

Keep Sifrol in a cool dry place where the temperature stays below 30°C.

Do not store Sifrol or any other medicine in the bathroom or near a sink. Do not leave it in the car or on window sills.
Heat and dampness can destroy some medicines.

Keep your Sifrol where young children cannot reach it.
A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking this medicine or the expiry date has passed, ask your pharmacist what to do with any medicine that is left over.

Product Description

What it looks like

Sifrol is the brand name of your medicine.

Sifrol 0.125 mg tablets are round, white tablets with 'P6' on one side and company symbol on the other.

Sifrol 0.25 mg tablets are oval, white, scored tablets with 'P7' on one side and company symbol on the other.

Sifrol 1 mg tablets are round, white, scored tablets with 'P9' on one side and company symbol on the other.

Sifrol 0.25 mg and 1 mg tablets are available in blister packs of 10 (sample pack)* and 100 tablets.

Sifrol 0.125 mg tablets are available in blister packs of 10 (sample pack)*, 30 and 100* tablets.

* Not distributed in Australia.

Ingredients

Each Sifrol 0.125 mg tablet contains pramipexole dihydrochloride monohydrate 0.125 mg.

Each Sifrol 0.25 mg tablet contains 0.25 mg pramipexole dihydrochloride monohydrate.

Each Sifrol 1 mg tablet contains 1 mg pramipexole dihydrochloride monohydrate.

Each Sifrol tablet also contains the following ingredients:

- mannitol
- maize starch
- colloidal anhydrous silica
- povidone
- magnesium stearate.

Supplier

Sifrol tablets are supplied in Australia by:

Boehringer Ingelheim Pty Limited
ABN 52 000 452 308
Sydney, Australia

www.boehringer-ingelheim.com.au

This Consumer Medicine Information was updated in September 2018.

Australian Registration Numbers

Sifrol 0.125 mg tablets
AUST R 67238

Sifrol 0.25 mg tablets
AUST R 66484

Sifrol 1 mg tablets
AUST R 66485

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How to take it

Swallow the tablets with a full glass of water.

Sifrol can be taken with or without food.

When to take it

Take Sifrol at about the same time each day.

Taking it at the same time each day will have the best effect. It will also help you remember when to take it.

How long to take it

Continue taking Sifrol for as long as your doctor tells you.

This medicine helps to control your condition, but does not cure it. It is important to keep taking your medicine even if you feel well.

If you forget to take it

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Otherwise, take it as soon as you remember, then go back to taking it as you would normally.

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Sifrol 1 mg tablets are round, white, scored tablets with 'P9' on one side and company symbol on the other.

Sifrol 0.25 mg and 1 mg tablets are available in blister packs of 10 (sample pack)* and 100 tablets.

Sifrol 0.125 mg tablets are available in blister packs of 10 (sample pack)*, 30 and 100* tablets.

* Not distributed in Australia.

Ingredients

Each Sifrol 0.125 mg tablet contains pramipexole dihydrochloride monohydrate 0.125 mg.

Each Sifrol 0.25 mg tablet contains 0.25 mg pramipexole dihydrochloride monohydrate.

Each Sifrol 1 mg tablet contains 1 mg pramipexole dihydrochloride monohydrate.

Each Sifrol tablet also contains the following ingredients:

- mannitol
- maize starch
- colloidal anhydrous silica
- povidone
- magnesium stearate.

Supplier

Sifrol tablets are supplied in Australia by:

Boehringer Ingelheim Pty Limited
ABN 52 000 452 308
Sydney, Australia

www.boehringer-ingelheim.com.au

This Consumer Medicine Information was updated in September 2018.

Australian Registration Numbers

Sifrol 0.125 mg tablets
AUST R 67238

Sifrol 0.25 mg tablets
AUST R 66484

Sifrol 1 mg tablets
AUST R 66485

You can refer to the Medications for Motor Symptoms fact sheet included with this book for a summary of the medications used to treat the primary motor symptoms of Parkinson's disease (PD) including typical dosages, side effects and indications. Detailed discussions of the medications follow. Medications listed will follow the format of "general name (brand name)."

Remember that medication usage is only a part of the whole treatment plan for effectively treating PD. Regular exercise, physical therapy, occupational therapy, speech therapy, holistic practices, nutritional consultation, support groups, education, psychological counseling, use of assistive devices and caregiver relief are all important aspects of the best treatment plan.

Pronunciation Key (accented syllable in bold)

NAME	PRONUNCIATION
Levodopa	Lee-voe-**doe**-pa
Carbidopa	Car-bee-**doe**-pa
Ropinirole	Row-**pin**-er-ole
Pramipexole	Pram-i-**pex**-ole
Rotigotine	Row-**tig**-oh-teen
Apomorphine	Ae-poe-**more**-feen
Selegiline	Sell-**edge**-ah-leen
Rasagiline	Rah-**saj**-ah-leen
Safinamide	Suh-**fin**-a-mide
Entacapone	En-**tak**-a-pone
Tolcapone	**Talk**-a-pone
Amantadine	A-man-**ta**-deen
Istradefylline	Iz-stra-da-**fi**-leen

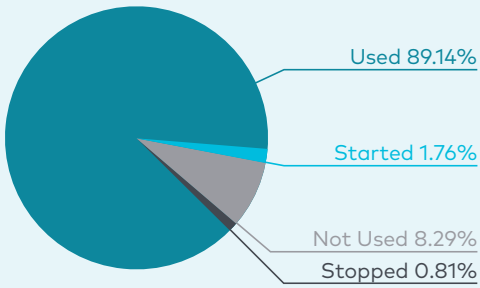
Levodopa

Through experimental trials in the 1950s, scientists discovered that depleting the dopamine in the brains of mice caused a condition that is similar to Parkinson's disease. Conversely, adding dopamine back into the brains of mice got rid of these symptoms. As they continued to experiment with these results, scientists successfully developed the medication known as levodopa in the 1960s.

Levodopa was the first medication proven effective for treating a chronic degenerative neurologic disease. When levodopa is in pill form, it is absorbed into the blood stream. It travels through the blood from the small intestine to the brain. Once it is in the brain, it is converted into dopamine. Levodopa that has not been converted into dopamine has no impact on Parkinson's symptoms. Dopamine cannot be given to treat PD because its chemical structure will not allow it to cross the "blood-brain barrier," a screen that protects the brain by keeping out drugs and other chemicals that might be harmful.

LEVODPA USE IN PEOPLE WITH PARKINSON'S

As of November 2019, more than 35,000 evaluations had taken place on more than 13,000 people with Parkinson's. This chart shows the percentage of people using levodopa before and after visit and not using levodopa at each of those 35,000+ visits.



In the early days of levodopa therapy, large doses were required to relieve symptoms. As a result, nausea and vomiting were common. The solution to this undesirable effect was the development of carbidopa, a drug that improves the effect of levodopa. Carbidopa does not enter the brain at usual dosages and prevents levodopa from being converted to dopamine outside the brain. When combined with levodopa, carbidopa allows an 80% decrease to the levodopa dose while maintaining the same benefits as a full dose.

Carbidopa/levodopa is marketed as Sinemet in the United States. In fact, the name says it all: "sin" "emet" roughly translates from "without" "vomiting" in Latin. This is a major improvement to levodopa on its own, though nausea is a common side effect of carbidopa/levodopa.
The generic product is intended to be chemically the same as the name brand, and, for most people, works just as well. The rate of use for the generic brand in the body may be anywhere from 20% more to 20% less available than the name brand drug. If you observe a difference in your response to medication immediately after switching from name brand to generic, or between two different generics, speak with your physician about ways to make full use of your medication. Carbidopa/levodopa greatly reduces PD symptoms in the majority of persons with a clinical diagnosis of PD, although its effect on tremor may vary compared to its effect on other symptoms. Facial expression, posture, speech, gait and handwriting usually improves. Levodopa's half-life – a measure of how long a drug stays in the bloodstream before being broken down by the body – is relatively short, about 60–90 minutes. In early stages of the disease, considered the "honeymoon" period, people with Parkinson's may not take their levodopa consistently and still have no worsening of their PD symptoms. However, as the disease advances, Because levodopa has a short half-life, there may be fluctuations of blood and brain levels of dopamine, which is responsible for the motor fluctuations that people who have had PD longer may experience. Motor fluctuations result in "off" periods, which are times during the day when carbidopa/levodopa is not providing the optimal control in PD symptoms.

Levodopa is safe and effective for people with PD. There is no reliable data that levodopa speeds disease progression or produces damage to brain cells. Levodopa is extremely beneficial to people with PD, and can dramatically improve quality of life. Levodopa is effective throughout the disease course, however, due to disease progression, the dose of levodopa needs to be increased over time. There are certain symptoms that do not respond to levodopa, like falling, balance difficulty, speech, swallowing, or memory issues. Expert practitioners in the Parkinson's Foundation Parkinson's Outcomes Project report utilizing levodopa more than any other drug for Parkinson's therapy, and used levodopa more as the disease progressed.

People with PD who use levodopa long-term may experience dyskinesia at some point, usually three to five years after starting the medication. The term dyskinesia describes involuntary, erratic, writhing movements of the face, arms, legs and/or trunk. These usually occur one to two hours after a dose of levodopa has been absorbed into the bloodstream and is having its peak clinical effect. Dyskinesia tends to be more severe as the dose of levodopa increases. It can be severe enough to interfere with activities of daily living and cause discomfort if they can't be controlled. In advanced PD, when motor fluctuations are common, it is often difficult to produce the "on" response.

The likelihood of developing dyskinesia is low early in the disease, and – if it occurs – is usually mild. Most people with PD prefer some dyskinesia in order to get the most out of levodopa. Sometimes, the fear of dyskinesia leads to under treatment of PD symptoms. The ideal strategies for management of dyskinesia and the associated "wearing-off" are detailed below in discussing the adjunctive therapies to levodopa (dopamine agonists, MAO-B inhibitors, COMT-inhibitors, Amantadine and DBS).

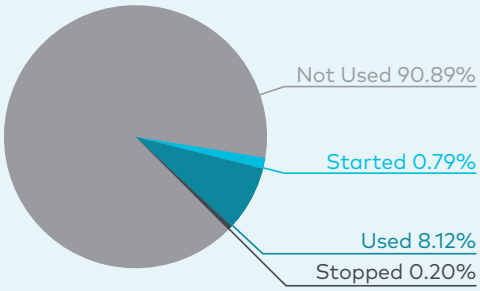
In 1988, the U.S. Food and Drug Administration (FDA) recommended that the daily dose of Sinemet should not exceed 800 mg per day, and as of 2013, this recommendation has not been revised. In 2018 the labeling of Sinemet recommends not exceeding a levodopa total daily dose of 2,000 mg per day. As movement disorder specialists, general neurologists and primary care doctors have learned, many people with Parkinson's can easily tolerate the higher doses used to minimize symptoms. Some people with PD encounter problems with insurance reimbursement of higher daily doses because of the FDA regulation. An insurance decision can be appealed if necessary.

A controlled release (CR) formulation was originally designed to enhance carbidopa/levodopa and possibly decrease "off" time and the number of pills needed per day. The CR pill is absorbed slower than regular carbidopa/levodopa. This may help people who need longer response times or overnight dosing. But, for others, this may be undesirable as there may be a delay in effect as only about 70% of the levodopa is usually absorbed before the pills pass through the intestinal tract.

Carbidopa/levodopa extended release (ER) capsules (Rytary), approved by the FDA in 2015, contain beads of carbidopa and levodopa that dissolve and are absorbed at different rates. Therapeutic levels are reached about an hour after taking it, similar to carbidopa/levodopa immediate release (IR). The levodopa levels in the blood are maintained for 4–5 hours before they decline. Clinical trials indicate that people who experience changes in motor symptoms throughout the day on other oral carbidopa/levodopa products may be able to switch to carbidopa/levodopa ER capsules and experience less "off" time while requiring fewer medication doses. **Dosages of carbidopa/levodopa ER capsules are not interchangeable with dosages of other carbidopa/levodopa products.** For prescribing and dosing information to share with your doctor, visit Parkinson.org/Rytary.

RYTARY USE IN PEOPLE WITH PARKINSON'S

This chart shows the percentage of people in the Parkinson's Outcomes Project using and not using Rytary. Out of 11,000+ visits tracked in the study (over 7,000 patients), doctors started a patient on Rytary at 88 (0.79%) of visits.



Carbidopa/levodopa ER can be taken with or without food. Interestingly, high fat meals can delay and reduce absorption, but may lengthen the benefit of the dose. People who have difficulty swallowing capsules can carefully open the Rytary capsule and sprinkle the contents on a small amount of applesauce (1 to 2 tablespoons) and consume it immediately.

Another formulation is the orally dissolving carbidopa/levodopa (Parcopa). It's also useful for people who have difficulty swallowing or who don't have a liquid to wash down a dose of medication.

In 2018 the FDA approved INBRIJA™, a levodopa inhalation powder as a treatment for "off" periods in people with PD who are treated with carbidopa/levodopa. Powder from capsules is breathed in through an inhaler. It can be used up to five times a day as needed, improving "off" symptoms as soon as 10 minutes and lasting up to 60 minutes. This can improve symptoms for people with decreased gut movement while waiting for oral carbidopa/levodopa to take effect.

The most common side effects of carbidopa/levodopa are:

- Nausea
- Vomiting
- Loss of appetite
- Lightheadedness
- Lowered blood pressure
- Confusion

Such side effects can be minimized with a low starting dose when initiating treatment with any antiparkinson drug and increasing the dose slowly to a satisfactory level. This is particularly helpful in elderly people with PD whose tolerance for medications is often less than in younger persons. Taking drugs with meals can also reduce the frequency and intensity of gastrointestinal side effects. For those patients who have persistent nausea or vomiting, adding extra carbidopa (Lodosyn) to each dose of carbidopa/levodopa can help.

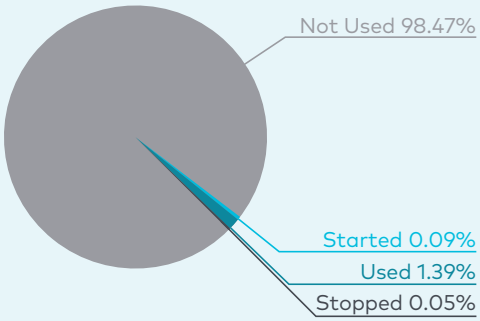
The stomach is an important route for carbidopa/levodopa, since levodopa is absorbed in the small intestine. People with Parkinson's often experience delays in the emptying of their stomach and a carbidopa/levodopa pill can sit in the stomach for a long time, causing a delay in the proper dosage. In addition, carbidopa/levodopa is absorbed into the bloodstream through a similar process that transports amino acids, the building blocks of proteins. As a result, some people experience less benefit if they take their carbidopa/levodopa with a stomach full of protein like meats, cheeses and other dairy products. For improved medication absorption, take carbidopa/levodopa one hour before a protein-rich meal or two hours afterwards. After several years of using carbidopa/levodopa, and alongside the development of motor fluctuations, many people with PD experience the benefits of a dose more quickly when the drug is taken on an empty stomach. Fortunately, most people with PD should have no problem with feeling "on" even if they take their medication with a meal.

Carbidopa/levodopa enteral suspension, known as Duopa in the United States, and Duodopa in other parts of the world, combines carbidopa/levodopa in a gel that is slowly and consistently pumped into the intestine through a surgically placed tube. This provides a smooth absorption of the medicine and can cut down on motor fluctuations and dyskinesia.

One of the major drawbacks to the pump approach is the need for surgery to implant a small tube. The tube is inserted through the abdomen into the stomach and then into the small intestine. The surgery takes about 30 minutes. As with any surgery there are risks including infections and other complications. For more information on Duopa and the pump, download our book *Surgical Options* at Parkinson.org/Books, or call our Helpline at 1-800-4PD-INFO.

DUOPA USE IN PEOPLE WITH PARKINSON'S

This chart shows the percentage of people using and not using duopa before and after each of those 11,000+ visits. At 10 (0.09%) of the visits, doctors started a patient on duopa.



What are "on" and "off" times

"On-off" fluctuations, also called motor fluctuations, are changes in your ability to move. 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.

Dopamine Agonists

A dopamine agonist (DA) is a chemical that acts like dopamine in the brain. Unlike levodopa, dopamine agonists are not converted into dopamine, they just act like it. There are multiple dopamine agonists available in the U.S. including:

- Ropinirole (Requip, Requip XL)
- Pramipexole (Mirapex, Mirapex ER)
- Rotigotine (Neupro skin patch)
- Apomorphine (Apokyn subcutaneous injection)

Bromocriptine (Parlodel) is also available but is not recommended, as it is a different type of Dopamine Agonist (ergo Dopamine Agonist) that is associated with a greater risk of heart and heart valve issues.

DAs improve the motor symptoms of PD, but they are less effective than levodopa. DAs can be used early in the course of PD as a single drug (monotherapy) or later in combination with carbidopa/levodopa (combination or adjunct therapy). Dopamine agonists have longer half-lives, or longer duration of action, than levodopa and can be helpful in reducing "off" time or to generally enhance the benefits of levodopa.

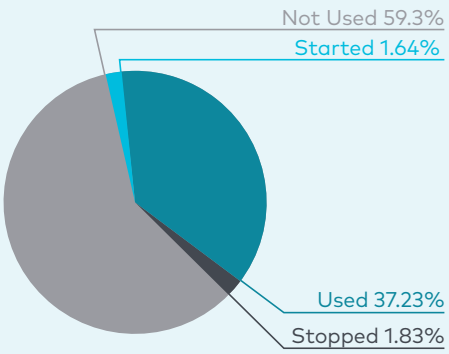
The negative effects of DAs are generally similar to those of carbidopa/levodopa. However, certain side effects, such as excessive daytime sleepiness, visual hallucinations, confusion and swelling of the legs, occur more commonly with dopamine agonists than with levodopa. Dyskinesia is rarely seen with the use of DAs when combined with levodopa.

One of the major issues with dopamine agonists are impulsive behaviors like uncontrolled gambling, sex, eating, shopping, etc. Those taking DAs may also engage in repetitive and relatively purposeless activities like organizing, sorting or collecting items. This is called punding. We collectively refer to these behaviors as impulse control disorders (ICDs). The underlying physiology is most likely related to overstimulation of dopamine receptors in the part of the brain responsible for instant gratification.

Data from the FDA and many other sources support the association of DAs and ICDs, though they can also be seen with the use of carbidopa/levodopa. Rotigotine, the DA patch, may have a lower incidence of impulse control issues, though it is unclear why. Older people with PD are more likely than younger people to have negative effects with using DAs.

DOPAMINE AGONIST

This chart shows the percentage of people using and not using dopamine agonists at each of the more than 35,000 evaluations for over 13,000 people with Parkinson's. At 1.64% of the visits, doctors started a patient on DAs. At 1.83% of visits, doctors took the patient off DAs.



People with PD should be aware of the risks before using dopamine agonists, and clinicians prescribing dopamine agonists should monitor for behavioral disorders. Remember that people suffering from impulse control issues may not have insight into the behavioral problems, and this lack of insight underscores the importance of involving care partners in monitoring plan.

Pramipexole (Mirapex) and Ropinirole (Requip) were approved by the FDA in 1997 and are currently the most commonly used DAs. They are both effective in the early treatment of motor symptoms of PD and in controlling motor fluctuations in later stages of the disease. Both these DAs are also available as once a day, long acting medications.

Rotigotine (Neupro) was approved by the FDA in 2007 and is formulated for use as a once-daily transdermal (skin) patch that is changed every 24 hours. Clinical trials have shown that it is just as effective as oral DAs, such as pramipexole and ropinirole. The side effects are similar, with the addition of skin irritation under the patch in up to 40% of people with PD. Most people with PD have been able to tolerate the patch by rotating the sites of the patch on their bodies. Fewer than 5% of those studied in the clinical trials discontinued its use due to skin irritation. The patch can be helpful for people with PD who have stomach problems because the patch bypasses the stomach.

Apomorphine (Apokyn) was first used to treat PD in 1950, but was associated with many side effects, especially nausea and vomiting. It returned in the 1990s as a self-injectable "rescue" drug for people with PD who experience "off" episodes. When a person is having an "off" episode, a self-injected dose of Apokyn can reverse the "off" period within

minutes and bridge the gap until the dose of levodopa takes effect, which can be about 90 minutes. An anti-nausea medication, usually trimethobenzamide (Tigan) may be used (but is not required) prior to the first injection but can be discontinued after the first week or two if the person with PD does not experience nausea or vomiting. Apokyn can be used as many as five times per day.

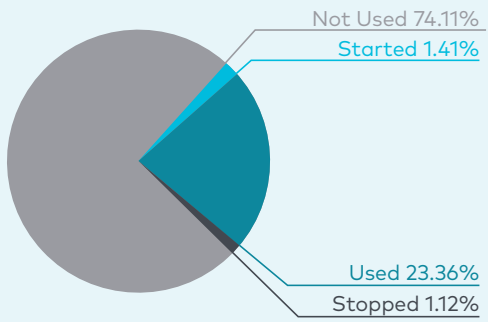
MAO-B Inhibitors

Monoamine Oxidase Type B (MAO-B) is an enzyme in our body that breaks down several chemicals in the brain, including dopamine. By giving a medication that blocks the effect of MAO-B, an MAO-B inhibitor), more dopamine is available to be used by the brain. This can modestly improve many motor symptoms of PD.

MAO-B inhibitors also provide some benefit for the motor symptoms of PD and are useful as early monotherapy or as an add-on to other medications, including levodopa. When used with other medications, MAO-B inhibitors may reduce "off" time and extend "on" time.

MAO-B INHIBITOR

This chart shows the percentage of people in the Parkinson's Outcomes Project using and not using MAO-B Inhibitors. More than 35,000 evaluations tracked in the study (over 13,000 patients), doctors started a patient on MAO-B inhibitors at 1.41% of visits.



In addition, animal studies showed that that MAO-B inhibitors might slow the progression of PD, offering neuroprotection. This was first tested in humans in the late 1980s in a clinical trial of the MAO-B inhibitor l-deprenyl, now sold under the name selegiline (Eldepryl). The goal of this study was to determine if selegiline could delay the need for levodopa as PD symptoms worsened, compared to Vitamin E and a placebo. Selegiline was shown to delay the need for levodopa by nine months, suggesting neuroprotection. However, this benefit may simply have been from the antiparkinson symptom effect of selegiline. Vitamin E had no benefit in the clinical trial.

Selegiline is available in two formulations: standard oral (Eldepryl,) and orally disintegrating, or dissolving (Zelapar). Oral selegiline is taken twice a day and orally-disintegrating selegiline is taken once daily. Standard oral selegiline is changed into a stimulant, which can contribute to side effects of jitteriness and confusion.

Rasagiline (Azilect), is another MAO-B inhibitor and is structurally different from selegiline. It does not have an stimulant-like byproduct. Taken once each day, rasagiline came to the U.S. market in late 2006. Clinical trials of Azilect as monotherapy or adjunctive therapy showed mild but definite effectiveness, and there was also an hint of slowing disease progression. A worldwide study of rasagiline's potential for neuroprotection was published in 2008, and follow-up data from the original study. These results suggest that the use of rasagiline earlier in PD may offer the greatest long-term advantage and potentially manage symptoms over time, although true disease modification remains unproven.

Safinamide (Xadago) was approved by the FDA in 2017. This medication affects the dopaminergic system by blocking MAO-B, thereby blocking the breakdown of dopamine.

The most common side effects of MAO-B inhibitors include mild nausea, dry mouth, lightheadedness and constipation. Pharmacists routinely warn patients about interactions with other drugs, especially the antidepressants, when they start taking an MAO-B inhibitor, but negative side effects are very rare.

Any person with PD taking MAO-B inhibitors should review all medications and possible adverse interactions with their physician before starting any new medications. **The following medications should always be avoided by people taking MAO-B inhibitors:**

- Meperidine (Demerol)
- Tramadol (Rybix, Ryzolt, Ultram)
- Droperidol (Inapsine)
- Methadone (Dolophine, Methadose)
- Propoxyphene (Darvon, PP-Cap)
- Cyclobenzaprine (Amrix, Fexmid, Flexeril)
- Halothane (Fluothane)

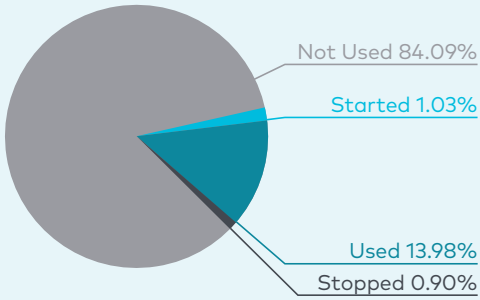
If it becomes necessary to take any of these medications for a planned surgery, consult with your Parkinson's neurologist and the anesthesiologist to decide whether to wean off of your MAO-B inhibitors ahead of the surgery.

COMT-Inhibitors

Catechol-O-methyl transferase (COMT) is an enzyme that deactivates levodopa in the body before it is absorbed in the bloodstream and taken to the brain. There are drugs that can block COMT, which makes levodopa more available to the brain, and they have been approved by the FDA for treating PD. The COMT-inhibitors increase the benefit of levodopa, reducing "off" time and lengthening "on" time. COMT-inhibitors are generally well-tolerated, though they may exaggerate some levodopa-related side effects, particularly dyskinesia. Additional side effects include confusion, hallucinations, discoloration of urine (reddish-brown or rust-colored) and diarrhea.

COMT-INHIBITORS

This chart shows the percentage of people in the Parkinson's Outcomes Project using and not using COMT-Inhibitors. Out of 35,000+ visits tracked in the study (over 13,000 patients), doctors started a patient on COMT-Inhibitors at 1.03% of visits.



Entacapone (Comtan), tolcapone (Tasmar), and newly approved opicapone (ONGENTYS®) are the three COMT-inhibitors approved by the FDA to treat PD. Opicapone is taken once daily and is only approved for those experiencing "off" episodes. Entacapone is prescribed with each dose of levodopa, and tolcapone is taken three times a day. COMT-inhibitors without levodopa have no effect on Parkinson's symptoms. There is no potential benefit from taking entacapone or tolcapone to try to extend the life of other PD medications. In fact, taking tolcapone without levodopa can lead to liver damage and can be potentially fatal. Hence, tolcapone should be used only after all other adjunct PD medications have been tried and should be discontinued if there is no benefit after three weeks. Before starting tolcapone, blood liver tests should be done and rechecked every two to four weeks for the first six months and periodically thereafter.

Carbidopa/levodopa/entacapone (Stalevo) is a combination drug which includes entacapone and levodopa in one pill. It is more convenient compared with carbidopa/levodopa + entacapone taken separately.

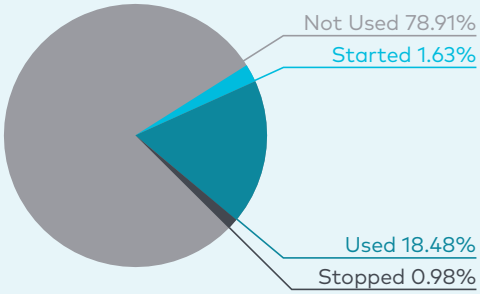
Amantadine

Amantadine (Symmetrel) was created as an anti-influenza medication in the 1960s, but its benefit in PD was first discovered in 1969, when observers noticed, by accident, that people with PD who took Amantadine to prevent influenza experienced less tremor. Amantadine often provides immediate benefit for most PD motor symptoms. It is unique in that it can also reduce levodopa-induced dyskinesia.

Amantadine has become a useful adjunctive medication in people with advanced PD and motor fluctuations. Its path through the brain is not fully known, but it is likely that it interacts with multiple receptors at various sites in the brain to achieve its positive effect. Amantadine is cleared from the body by the kidneys, so a person with kidney problems may require a lower dose.

AMANTADINE

This chart shows the percentage of people in the Parkinson's Outcomes Project using and not using Amantadine. Out of 35,000+ visits tracked in the study (over 13,000 patients), doctors started a patient on Amantadine at 1.63% of visits.



Amantadine is most commonly available as a 100 mg capsule, although liquid and tablet forms are also available. If the person with PD requires lower doses or has difficulty swallowing, the liquid or tablet formulations would be preferred.

The most frequent side effects of Amantadine are nausea, dry mouth, lightheadedness, insomnia, confusion, pedal edema and hallucinations. Urinary retention is another side effect, though it is rare. Another possible side effect is livedo reticularis, a web-like, purple discoloration of the skin, usually on the legs and with some accompanying leg swelling. This side effect is only experienced by 1% of Amantadine users. Stopping the drug will resolve this adverse effect, although if the drug is providing benefit there is no harm in continuing it. Amantadine should not be stopped suddenly, but rather slowly reduced, due to risk of a serious withdrawal syndrome.

Amantadine ER tablets (OSMOLEX ER™) is an extended release form of amantadine which is taken every day upon waking and can reduce "off" time of Parkinson's disease. The tablets should not be split, crushed, nor chewed as this could cause serious side effects by releasing all the medication at once, also known as "dose dumping."

Another amantadine-based medication, Amantadine ER capsules (GOCOVRI®) is the only medication to treat dyskinesia and "off" time in people with PD taking carbidopa/levodopa. It must be taken before bedtime and provides control of dyskinesia upon awakening and throughout the day. This medication is different from immediate-release amantadine and amantadine ER tablets (OSMOLEX ER™), which are not approved for dyskinesia or "off" time. GOCOVRI can start to reduce dyskinesia after 2 days, with most of the effect seen by 4 weeks. Some people may see additional benefit after 12 weeks. Reduced "off" time should be seen after about 2 weeks. For people with difficulty swallowing, the GOCOVRI capsules may be opened and contents sprinkled on small amount of soft food (teaspoon of applesauce) and swallowed. The capsule contents should not be crushed. Alcohol should be avoided when taking extended release amantadine (GOCOVRI or OSMOLEX ER), due to potential risk that this could break the extended release mechanism and cause "dose dumping."

Anticholinergics

The earliest medications used in PD blocked brain receptors for acetylcholine (a nervous system neurotransmitter) called anticholinergics. It is believed that acetylcholine and dopamine maintain a delicate balance in the normal brain, which is upset by the destruction of dopamine and the break down of dopamine-producing cells. Drugs that block the effect of acetylcholine have the potential for restoring the normal balance of these two chemicals, thereby reducing the symptoms of PD.

The anticholinergics can provide modest benefit mainly for tremor, but they can also cause significant mental and physical side effects. Confusion, hallucinations, decreased short-term memory, dry mouth, blurry vision and urinary retention are potential side effects, particularly in older persons with PD. As such, these medications are typically utilized in younger people.

Additionally, research from the Parkinson's Foundation Parkinson's Outcomes Project has supported the finding that cognitive slowing is a side effect of anticholinergics.

Trihexyphenidyl (formerly available as Artane) and Benztropine (Cogentin) are the two most common anticholinergics prescribed in PD. Dosing is usually two to three times a day. The common antihistamine and sleeping agent diphenhydramine (Benadryl) also has anti-tremor properties.

Adenosine A2a Antagonists

Istradefylline (NOURIANZ™) is an adenosine receptor antagonist indicated as adjunctive treatment to carbidopa/levodopa in adult patients with Parkinson's experiencing "off" episodes. Since it is not dopaminergic, it can reduce "off" time by 30–60 minutes per day without worsening dyskinesia. However, dyskinesia can still be a side effect. Reduction in "off" time should be seen by 4 weeks. People with PD who smoke the equivalent of 20 cigarettes per day or more will require a higher dose (40mg) of medication. This is because the cigarettes cause the liver to increase the breakdown of (metabolize) Nourianz, making the medication less effective. It should be taken upon wakening to reduce the chance of causing insomnia.

CHAPTER THREE

Medications for Non-Motor Symptoms

The following non-motor symptoms and their treatments are discussed in this chapter:

- **Mood Disorders: Depression and Anxiety**
- **Impaired Thinking, Daytime Sleepiness and Sleep Disorders**
- **Dementia and Hallucinations**
- **Orthostasis (Low Blood Pressure Upon Standing)**
- **Gastrointestinal Symptoms: Nausea and Vomiting, Constipation, Early Satiety**
- **Drooling**
- **Urinary Symptoms**
- **Sexual Dysfunction**
- **Seborrheic Dermatitis and Excessive Sweating**
- **Pain**

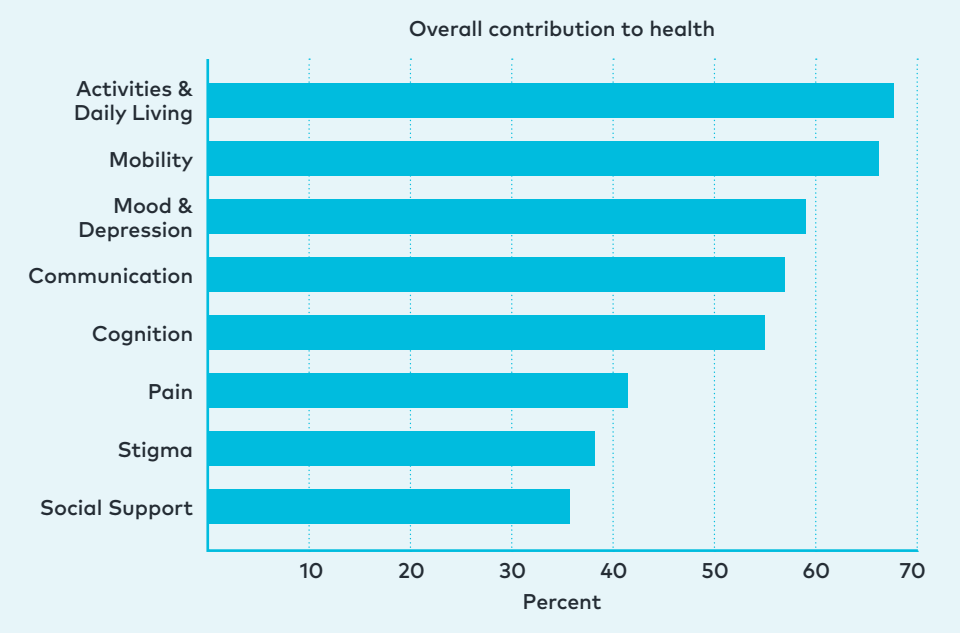
There is ever-growing recognition of the importance of "non-motor" symptoms of PD, which were identified as early as 1817 by James Parkinson. Although he didn't differentiate motor from non-motor symptoms, he observed that his patients experienced symptoms of fatigue, confusion, sleep disturbances, constipation, drooling and disturbances of speech and swallowing. Speech, swallowing and drooling are included among non-motor symptoms although the root cause is in part motor: decreased coordination of the muscles of the mouth and throat.

Non-motor symptoms are very common in PD. In one recent study, 90% of people with PD reported experiencing at least one of the non-motor symptoms listed in Table 1. Unfortunately, it has also been shown that physicians and healthcare team members do not recognize these symptoms in their patients up to 50% of the time. Just as physicians assess complaints of slowness, stiffness or tremor, they should also address issues related to sleep, memory, mood, etc. People with PD are encouraged to be proactive in discussing these issues with their doctor. Don't wait to be asked!

Mood Disorders

The Parkinson's Outcomes Project was initiated in 2009 as a large, multicenter study partnering with many of the Parkinson's Foundations Centers of Excellence. This research collaborative is helping to define the symptoms and treatments that have the greatest impact on PD patients and their quality of life. Not surprisingly, being able to move and go about one's day are very important to quality of life. However, one of the first findings of the project was that, collectively, that mood and anxiety are the two PD symptoms that can have the largest impact on health status, and has consistently found Mood & Depression to be in the top 3 factors contributing to overall health.

A Parkinson's Foundation book specifically designed to address these issues, titled *Mood: A Mind Guide to Parkinson's*, is a comprehensive resource available online or in print. To request a free print copy, call our Helpline at 1-800-4PD-INFO (473-4636); online, go to Parkinson.org/Books. What follows is a brief summary of some important features of mind and mood disorders in PD with emphasis on the medications used for treatment.



Depression

Depression is a common but under-recognized symptom, affecting up to 50% of people with PD at some point during the course of the disease, often in its earliest stages. There is no specific timeframe for depression in PD; depression can occur before motor symptoms, when the diagnosis is first made or in advanced disease. The definitive cause is not completely understood but it is likely related to an imbalance of chemicals in the brain (including dopamine, serotonin and norepinephrine). Some people who report depression related to their PD improve with adequate treatment of the most bothersome motor symptoms. However, many others require more aggressive management with psychotherapy and antidepressants.

Along with "feeling blue," symptoms of depression may include:

- Insomnia or excessive sleeping
- Loss or reduction of energy levels
- Loss of interest or pleasure in
- Diminished attention and
- Social or recreational activities concentration
- Sexual dysfunction
- Loss or gain of appetite and weight
- Feelings of guilt and self-pity
- Thoughts of death or suicide

Antidepressants

Medications used to treat depression in general are also used to treat depression in PD. There is no specific medication approved to treat depression in PD. As detailed below, several different classes of medication may be helpful.

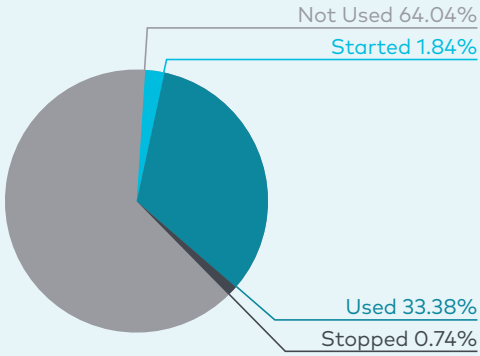
Most people with PD who are experiencing depression are treated with one of several common categories of antidepressants including the selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). A large clinical trial published in 2012 confirmed the benefits of SSRIs and SNRIs for many people with PD. Occasionally, older tricyclic antidepressants (TCAs) are used, especially in younger people with PD with sleep difficulties. However, TCAs tend to cause more side effects than the SSRIs, including confusion, forgetfulness, hallucinations, lightheadedness, blurry vision, urinary retention and dry mouth. SSRIs are generally better tolerated by people with PD, though loss of libido is a relatively common adverse effect. The antidepressants buproprion and mirtazapine are also notable for their lack of sexual side effects. There is some evidence that pramipexole, a dopamine agonists may have antidepressant properties in people with PD.

Recognizing a medication's side effects can be used to the advantage of the person with PD. For example, more sedating medications may be appropriate for nighttime dosing in the PD person with insomnia. Or a TCA that causes dry mouth may help to reduce the severity of drooling. The Medications for Non-Motor Symptoms fact sheet included with this book reviews the antidepressants commonly used in treating people with PD.

While many individuals improve with antidepressants, the person with PD and his or her physician, psychologist, social worker and other healthcare team members should also recognize the value of psychotherapy, or counseling in improving this non-motor symptom of PD. The importance of this is underscored by research from the Parkinson's Outcomes Project. Counseling plus medication was 25% more effective at resolving depression than medication alone for people with Parkinson's experiencing severe, long-term (at least two years) depression. So, while medication can be helpful, counseling is necessary to realize the full benefits of treatment. Cognitive-behavioral therapy, an approach that helps in developing the skills and actions to change patterns of thought and behavior related to depression, can be particularly helpful.

ANTIDEPRESSANT

As of May 2015, more than 35,000 evaluations had taken place on over 13,000 people with PD. This chart shows the percentage of people using and not using antidepressants at each of those 35,000+ visits. At 1.84% of the visits, doctors started a patient on antidepressants.



Counseling can be offered in an individual or a group setting. Therapeutic exercise such as physical workouts, yoga, Tai Chi, massage and meditation also may help to improve mood in PD. Electroconvulsive therapy can be a consideration of last resort for people with severe depression who do not respond to drugs. It is effective and safe when managed by experts and may also temporarily improve motor symptoms.

Mood may also change during "on-off" fluctuations. A general state of unease or dissatisfaction with life (dysphoria), irritability and anxiety are the most common mood changes in the "off" state. If you notice a relationship between mood changes and the timing of your PD medication, tell your neurologist. They might adjust your levodopa-replacement medications or dosing to reduce "off" time, which, in turn, may help your mood.

Anxiety

Often seen in combination with depression, anxiety can also appear early in the course of PD. People with PD may describe feelings of unease, jitteriness, worry and panic. Anxiety may also cause physical symptoms such as difficulty breathing or swallowing, heart fluttering, shaking and "cold sweats."

Feelings of anxiety can be related to motor symptoms. For example, the appearance of tremor or freezing during an "off" period or during social situations may cause anxiety or embarrassment. This anxiety can worsen the intensity of the symptoms, creating a vicious cycle and possibly leading to a panic attack.

Along with specific feelings of anxiety as described above, people with PD may also experience the following:

- Generalized anxiety involves features of excessive worry throughout most of the day without dramatic fluctuation.
- Obsessive-compulsive disorder refers to repetitive thoughts/ideas that cause anxiety (obsessions) and behaviors that relieve those feelings (compulsions).
- Social avoidance, which can be especially troubling to someone whose personality is normally outgoing, involves avoiding social situations and opportunities to interact with friends and others as a result of anxiety or embarrassment.

Obsessive-compulsive disorder can become worse as a result of dopaminergic agents, particularly the dopamine agonists.

There are many options for treating anxiety in PD, including medications, traditional psychotherapy and cognitive behavior therapy (CBT). It is important for people with PD to inquire about the services of a psychologist, counselor, social worker and/or other appropriate members of the healthcare treatment team.

Anxiety can be part of non-motor fluctuations associated with levodopa. In such cases, working to optimize doses of levodopa may improve anxiety, and decreasing the intervals between levodopa doses may relieve the sense of anxiety that occurs as part of the "off" phase. Of course, adjusting your medication schedule should always be discussed with your physician.

SSRIs and related medications are commonly used for depression, but some of the SSRIs (listed in Table 3) may also improve anxiety. It may take several weeks of taking an SSRI for the person with PD to realize its full benefit. Buspirone (Buspar) is also particularly effective in treating generalized anxiety.

Benzodiazepines are a popular and effective class of anti-anxiety drugs that can be potent in reducing symptoms of panic and worry. At times they can even help to control tremor in anxious patients by reversing the negative effects of anxiety that can cause tremor to worsen. Each of the approved benzodiazepines has different practical advantages, including duration of action, so the appropriate medication should be

chosen based on frequency and severity of symptoms. For example, longer-acting benefits may be achieved with clonazepam (Klonopin) than with alprazolam (Xanax) or lorazepam (Ativan). Common side effects of benzodiazepines include drowsiness, confusion, lethargy and imbalance when walking. People with PD may develop a tolerance to the benzodiazepines over time, and discontinuation must be done gradually to avoid withdrawal symptoms.

A host of effective, non-pharmacologic techniques are readily available for treating anxiety including psychotherapy, behavior modification, biofeedback, meditation, massage, yoga, exercise, acupuncture and more.

You are not alone. For more information on depression, anxiety and treatment, read the Parkinson's Foundation book, Mood: A Mind Guide to Parkinson's Disease or call the foundation's free Helpline at 1-800-4PD-INFO (473-4636) to speak with a Parkinson's specialist.

Impaired Thinking and Dementia

Cognitive impairment is when a person has trouble remembering, learning new things, concentrating, or making decisions that affect their everyday life. More than 30% of persons with PD may experience some degree of cognitive impairment at some point after a Parkinson's diagnosis. These alterations fall on a broad spectrum from mild cognitive impairment to severe dementia. Mild cognitive impairment occurring early in the course of illness may be a nuisance to the person with PD and his or her loved ones, especially if he or she is still working. However, it usually will not affect routine activities of daily living.

Progression to dementia is the greatest worry for many people with PD, as this usually implies a significant and possibly permanent compromise in lifestyle and quality of life.

People with PD may experience difficulty with:

- Speed of mental processing
- Attention/concentration – losing their train of thought in conversation
- Problem solving, decision-making, multi-tasking and planning
- Short-term memory
- Language production

In most cases, the cognitive impairment associated with PD is not Alzheimer's disease, and the severity of the cognitive deficits and the effect of those deficits on day-to-day functioning are not as disabling.

Parkinson's disease dementia (PDD) occurs when the specific deficits in attention/concentration, problem-solving and memory are severe enough to interfere with the person's ability to function appropriately at work and/or in social situations on a daily basis.

A closely related parkinsonian disorder – dementia with Lewy bodies (DLB) – is similar but different from PDD in important ways. The main difference in making the diagnosis is the timing of significant impairments in one's thinking in relation to motor symptoms. If cognitive impairment begins before or within one year of motor symptoms, the diagnosis is DLB; if cognitive impairment follows the appearance of motor parkinsonian symptoms by more than one year, the diagnosis can be classified as PDD. Additional distinguishing characteristics such as fluctuating awareness and attention span, visual hallucinations and altered spatial orientation. Fluctuating awareness refers to periods of mental clarity alternating with periods of confusion, distractibility, sleepiness and psychosis (usually visual hallucinations).

Evaluation for change in cognitive function in persons with PD should be part of a complete medical workup for other causes of cognitive impairment, some of which may be treatable. If the change in cognitive ability is sudden, severe, and accompanied by significant alteration in consciousness, an underlying cause aside from PD should be considered. This could mean infection (usually of lungs or bladder), vitamin depletion, dehydration, thyroid disease, intoxication by drugs, constipation, sleep deprivation or head injury from falls.

A similar evaluation should be done if the change is more gradual and chronic, but the likelihood of finding a reversible cause of dementia is less likely. Many of the anti-PD medications and other drugs (for example narcotic pain killers) can cause confusion mimicking dementia, particularly in elderly PD persons. A careful evaluation of current medications is always important, paying particular attention to PD medications like anticholinergics, amantadine and dopamine agonists.

Medications that are approved for people with PD dementia are rivastigmine or Exelon. Other medications approved by the FDA for the treatment of memory disorder in Alzheimer's disease are donepezil (Aricept), galantamine (Razadyne) and memantine (Namenda).

Acetylcholinesterase Inhibitors
Rivastigmine (Exelon) was approved by the FDA in 2006 for treatment of dementia in PD. Donepezil (Aricept), and galantamine (Razadyne) are the next most frequently prescribed medications to address symptoms of cognitive impairment in PD. Originally approved by the FDA for the treatment of Alzheimer's disease, donepezil and rivastigmine have been effective for some people with PD, though benefits are sporadic and modest. Most common side effects include tremor, drooling and bladder issues. Rivastigmine has been shown to help with apathy that can happen in PD Dementia.

Glutamate Antagonists
Memantine (Namenda) is approved for moderate-to-severe Alzheimer's disease in the U.S. It may help cognitive symptoms in PD by blocking the brain's receptors that are activated by the neurotransmitter glutamate. It is commonly used in combination with donepezil, although the results of treatment are often disappointing in PD dementia.

Other stimulants, such as methylphenidate (Ritalin), and medications used for excessive daytime sleepiness, such as modafinil (Provigil), are sometimes used in PD for fighting fatigue and improving alertness. They are not specifically used for cognitive issues.

PD Psychosis

People with PD psychosis (PDP) may experience visual hallucinations, illusions, or delusions. These are more commonly seen in people with PD who develop dementia in the late stages of disease.

- A hallucination occurs when a person believes they see, smell, hear or feel something that **is not** actually there.
- An illusion is a misperception or misleading view of reality – that is, a misperception of something that **is** actually there. For example, a belt may appear to be a snake.
- A delusion is a form of self-deception in which the person develops a false belief despite strong evidence that the belief is false. For example, that someone is stealing from them despite reassurance from family that no one is stealing anything.

Feeling a "sense of presence" is also fairly common, when they feel like someone else in the room with them when no one else is present.

PDP can occur in people with Parkinson's, whether or not they take medications. It can also occur with or without underlying dementia.

Visual hallucinations are the most common form of hallucination in PD psychosis. They often involve seeing little people, animals or insects. The most common delusions are paranoid delusions. This means that the person with PD may suspect that someone is plotting to do something harmful, most commonly believing that spouse is being unfaithful. Delusions are difficult to manage and should be urgently treated. Often those with PDP, especially with dementia, have hallucinations and agitation at the end of the day after sundown, when darkness can be disorienting. The term "sundowning" is named after this inopportune time of day. Fatigue after the day's activities can also cause collapse of a stable mental status.

Additionally, if the person with PD moves to an unfamiliar environment, such as a hospital, vacation site or new home, the stress of geographical disorientation can sometimes lead to the development or return of hallucinations, delusions and confusion. Fortunately, many people with PD retain insight, understanding that the hallucination is not real and that their mind is "playing tricks" on them. Others react by becoming extremely troubled and frightened.

Many people with PD also experience vivid dreams at night, which some experts believe may be "precursors" to hallucinations. Others never progress to having waking visions or delusional thoughts. Vivid dreams can be due to other sleep disorders, such as rapid eye movement (REM) behavioral disorder (discussed later in this chapter).

Your healthcare team will want to assess and treat hallucinations and psychosis using the following guidelines:

1. **Fully characterize the behavior.** How frequent and severe are your hallucinations? Do they occur day and night? Do you retain insight during hallucinations? Does the problem pose a physical, emotional or financial threat to you or your family? Has your memory, personality and/or concentration been changing?

2. **Identify any other medical problems you are experiencing.** Other medical problems could trigger a decline in cognitive ability. For example, are there any signs of infection such as fever, cough, painful urination or diarrhea? Are there symptoms of underlying depression? Are there other medical conditions that require attention (e.g., disorders of the heart, liver or kidneys; dehydration)?

3. **Review the list of all PD medications you are taking, paying special attention to any recent medication changes.** Your healthcare team can evaluate if the mental changes you are experiencing are related to PD medications. Virtually all of the anti-PD medications have the potential to cause mental clouding and hallucinations, especially at high doses or in combination with other risk factors.

   If your doctor recommends medication changes, they may decrease or stop Amantadine and anticholinergics first, because the risk of psychosis usually outweighs the modest benefit that these medications provide.

   In practice, the risk of cognitive and psychiatric complication is higher with dopamine agonists than with levodopa. Thus, when the symptoms of psychosis require action to help someone who is on a combination of levodopa and dopamine agonists, doctors will typically taper off of and eventually stop the agonist. Levodopa then becomes the only dopaminergic medication the individual is taking. The risk of psychosis usually outweighs the benefit that these medications provide. Not only is levodopa the best drug for treating PD, it also has the best "therapeutic margin," or highest ratio of benefit to side effects.

4. **Discuss medications you may be taking for other illnesses.** Your physician or healthcare team will want to assess whether any non-PD medications or other substances are impacting your mental changes. Have any new medications been started, or doses changed (e.g., sleep aids, narcotics [especially narcotic pain medications like Percocet], antibiotics, steroids, anti-anxiety or anti-depressant medications)? Consider over-the-counter medications too. Could illicit drugs, marijuana or alcohol be involved?

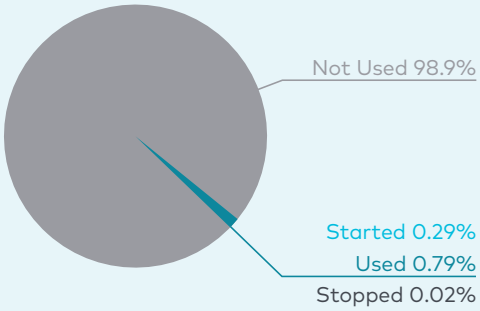
Based on the findings in the four steps above, your physician and healthcare team will be able to suggest the best course of treatment.

In 2016, the FDA approved pimavanserin (Nuplazid) as the first and only drug specifically designed to treat Parkinson's disease psychosis. Pimavanserin is not a dopamine-blocking drug like clozapine and quetiapine. In fact, it acts on serotonin receptors just like antidepressants. It is the safest choice when treating people with PD who are experiencing psychosis. There are fewer side effects with this medication than other antipsychotics because it only targets serotonin. Unlike dopamine-blocking drugs, it does not typically worsen motor symptoms, cause

excessive sleepiness, start fluctuations in blood pressure, or affect drooling and bladder function. However, common side effects are confusion, leg swelling, and worsening hallucinations. It should be noted that it can take up to three weeks for this medication to provide full benefits. It is extremely important that you find the right antipsychotic drug for you. In addition to pimavanserin, there are currently two antipsychotic medications that are suitable for use in people with PD: clozapine and quetiapine.

PIMAVANSERIN

This chart shows the percentage of people in the Parkinson's Outcomes Project using and not using Pimavanserin. Out of 11,000+ visits tracked in the study (over 7,000 patients), doctors started a patient on Pimavanserin at 32 (0.29%) of visits.

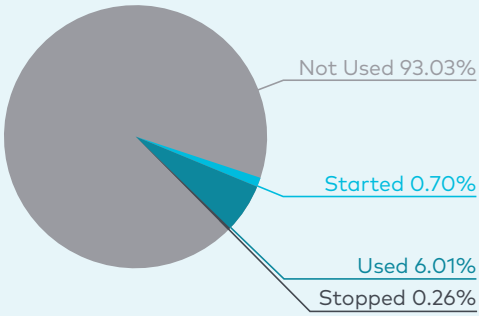


Clozapine (Clozaril) can be used effectively, especially at low doses, in people with PD without a risk of worsening Parkinson's symptoms. In 1990, the FDA approved clozapine for use in the treatment of schizophrenia as long as the patient completes weekly blood counts for the first six months (then every 2 weeks for 6 months if stable, and then monthly if stable thereafter). For those on hospice, the blood counts can be reduced to once every 6 months. This is so that your healthcare provider can monitor the low, but significant, risk that clozapine can depress your white blood count and increase the risk of serious infection. This requirement has made the use of clozapine inconvenient, but safe. Experience has shown that low dose clozapine has an important place in the management of the psychosis that can occur in persons with PD. Additional risks with clozapine include seizures, heart inflammation, low blood pressure and fainting.

Quetiapine (Seroquel) had been widely used for people with PDP before pimavanserin was approved. It has the advantage of not requiring frequent blood counts. Common side effects include dizziness, dry mouth and weight gain. Although clinical trials did not report clinical success with quitepine, physicians in general have had positive experiences with it in treating hallucinations and other symptoms of psychosis. Occasionally people with PD may require a combination of therapy with pimavanserin or quetiapine.

ANTIPSYCHOTIC

This chart shows the percentage of people in the Parkinson's Outcomes Project using and not using antipsychotics. Out of 35,000+ visits tracked in the study (over 13,000 patients), doctors started a patient on antipsychotics at 0.70% of visits.



Sleep Disorders

Disturbed sleep is so common among people with PD that it has become a major focus of therapeutic interest and research. The specific disorders include:

- Restless leg syndrome (RLS)
- Periodic limb movements of sleep (PLMS)
- Rapid eye movement (REM)-sleep behavior disorder (RBD)
- Excessive daytime sleepiness (EDS)
- Insomnia
- Co-existing obstructive sleep apnea (OSA)

Difficulty controlling tremor, stiffness and poor bed mobility can account for an inability to sleep at night. Excessive daytime sleepiness (EDS) can also account for difficulty sleeping, due to the possible reversal of the sleep cycle. For more information on medical causes of disrupted sleep, including obstructive sleep apnea and congestive heart failure, please check with your physician or healthcare provider.

To provide your physician and your healthcare team with the most accurate medical history, it is useful for the spouse, partner, housemate or professional caregiver to help describe your nighttime activities. An Epworth Sleepiness Scale (see Appendix C) can help identify daytime sleepiness and provide clues to disruption of sleep at night. This questionnaire (given in the office or completed at home) examines a person's tendencies to fall asleep during the day during daily activities, such as driving or watching television. An overnight evaluation by a trained specialist (often a neurologist) can provide even more information. This can be helpful especially **if co-existing obstructive sleep apnea (OSA) is suspected, a breathing disorder that flares up during sleep that**

affects, and can even stop, breathing. The evaluation typically will include monitoring heart rate, breathing activity, snoring, involuntary movements and quality of sleep. Treatment of OSA which can include a using a CPAP (Continuous Positive Airway Pressure) breathing machine at night can improve daytime sleepiness.

Restless leg syndrome (RLS) is a common disorder characterized by unpleasant sensations in the legs at rest and an uncontrollable urge to move the legs in order to relieve these feelings. RLS sensations are often described as burning, creeping, tugging or like "insects crawling inside the legs." Often called paresthesia (numbness and tingling) or dysesthesias (unpleasant numbness and tingling), the sensations range in severity from uncomfortable and irritating to painful. Voluntary movement of the legs, particularly walking, relieves the uncomfortable urge, at least temporarily. These symptoms occur after prolonged sitting or laying in bed. When experiencing symptoms of RLS, sleep can be significantly disrupted, which can cause daytime sleepiness or sleep deprivation. Some people with PD confuse RLS, an abnormal sensory perception, with levodopa-induced dyskinesia, an overt involuntary movement of the legs.

Periodic limb movements of sleep (PLMS) describes episodes of repetitive, jerky involuntary leg movements during sleep. Like many of the sleep disorders, the bed partner is more aware of the involuntary movements than the person with the symptom. RLS and PLMS often occur together in people with PD.

Diagnosis can be fairly simple when the symptoms are obvious, but your physician or provider may recommend an overnight sleep study. Additionally, it may be recommended that blood ferritin levels be tested. If ferritin levels are low, iron replacement therapy may be recommended. Extra nighttime doses of Parkinson's medications may bring relief. Your healthcare provider may also consider gabapentin, benzodiazepines (like clonazepam) or low-dose opiates.

REM-sleep behavior disorder (RBD) is characterized by acting out dreams during the REM sleep phase. It involves active behaviors (e.g., kicking, fighting, yelling or thrashing) during the phase of sleep when dreaming normally occurs. The person experiencing RBD may even walk or fall out of bed during REM sleep. The history provided by the person with PD, their care partner may be sufficient for a presumed diagnosis, but an overnight sleep study can confirm it. RBD is often present for months or years before the onset of the motor symptoms of PD.

Anticholinergics, selegiline and dopaminergic drugs can all worsen the RBD behaviors. For treatment of RBD, low-dose benzodiazepines (e.g., clonazepam) or melatonin at bedtime may help.

Excessive daytime sleepiness (EDS) is very common in PD. It may be a symptom of Parkinson's or can result from disruption of nighttime sleep, sleep apnea and PD medications, especially dopamine agonists. It is most problematic for the person with PD who is experiencing cognitive decline. People with PD may even suffer "sleep attacks" during the day, which are described as the sudden and irresistible urge to sleep or the sudden and unwarned onset of sleep, not preceded by sleepiness. This happens significantly more often in people with PD who take moderate to high doses of the dopamine agonists.

Insomnia is an inability to fall asleep or, more commonly, to stay asleep. Itis more complicated in PD because there are extra factors that might contribute, including normal nighttime awakening, wearing-off of anti-Parkinson medication, depression, anxiety and a change in circadian rhythm.

Treatment of EDS and insomnia can be challenging and usually requires a multi-faceted approach. Discuss with your healthcare provider whether to reduce dosage, change medication timing, or even eliminate dopamine agonists. Cognitive behavioral therapy (CBT) provided by a psychologist or other trained health care provider can help with insomnia. Medications such as melatonin, eszopiclone, or low-dose doxepin (1–3 mg) may help with staying asleep. Other options for EDS include CNS stimulant medications like Ritalin, modafinil, or Nuvigil.

Every attempt should be made to normalize the sleep-wake cycle and to improve sleep hygiene. This means:

- Establishing regular bedtimes and rising times
- Reducing caffeine and alcohol intake
- Limiting daytime naps
- Avoiding food and drink within several hours of bedtime

It is recommended that you avoid use the bed for non-sleeping tasks such as reading, doing work or watching television, as these activities can condition the body for wakefulness. Once you've improved your sleep hygiene, a helpful look to over the counter supplements, like melatonin, before prescription medications. Doses as high as 10–15mg can be used for better sleep.

Some antidepressant drugs, such as amitriptyline (Elavil), trazodone (Desyrel) or mirtazapine (Remeron), can promote sleep due to their sedative properties. Most over-the-counter preparations are not suggested for use unless recommended by a physician, although the antihistamine diphenhydramine (Benadryl) may double as a sleeping pill and an anti-tremor drug because of its anticholinergic properties. Amitriptyline and diphenhydramine should be avoided by older people with Parkinson's because they can worsen cognition, cause constipation, dry mouth and increase risk of arrhythmias. If motor symptoms such as stiffness and tremor interrupt sleep because of the gap between night and morning doses, an extra dose of carbidopa/levodopa may be taken late in the evening or during the night upon awakening. Some people with PD use controlled-release carbidopa/levodopa or carbidopa/levodopa extended capsules (Rytary) at bedtime.

Other sleeping medications can be beneficial such as hydroxyzine, Ambien, Lunesta, Sonata, Rozerem, quetiapine, clonazepam and others.If nighttime sleeping problems are controlled but excessive daytime sleepiness persists, increased coffee intake in the morning is also worth a try.

Stimulants such as methylphenidate (Ritalin) and mixed amphetamine salts (Adderall) can be tried. Indicated for narcolepsy and attention-deficit disorder, they can be used carefully to increase daytime wakefulness and alertness. They should be given in low doses and taken in the morning initially, preferably before 8 a.m. If additional amounts of the drug are needed, they should be taken before noon. Side effects include palpitations, high blood pressure, confusion, psychosis and insomnia if the dose is too high or taken too late in the day.

The non-stimulant modafinil (Provigil), approved only for treatment of narcolepsy, also is potentially useful. Its mode of action in the brain is unknown, but it has a good track record of reducing daytime sleepiness with fewer side effects because it is not a stimulant.

It should be noted that the use of methylphenidate, amphetamine and modafinil for the treatment of EDS in PD is not approved by the FDA ("off label" use), which means that most health insurance plans may not cover them.

Orthostasis

The terms orthostasis or orthostatic hypotension describes the drop of blood pressure when a person with PD rises from being seated or lying down. Normally when a person rises, blood pressure drops but is maintained in a small range by protective reflexes in the body's blood vessels that are controlled by the body's autonomic nervous system (ANS). When a person with PD stands, the normal reflexes that protect against a drop in blood pressure are impaired. The result, typically within 1–3 minutes of standing, is lightheadedness, dizziness and fainting — symptoms that reflect a lack of blood flow to the brain.

Since the ANS is often impaired in PD, autonomic functions such as blood pressure regulation, gastrointestinal motility and sweating can be affected. When orthostasis is related to a disease of the nervous system, like in PD, it is called neurogenic orthostatic hypotension (NOH).

NOH in PD can be brought on by anti-Parkinson medications, especially the dopamine agonists amantadine and carbidopa/levodopa. In addition, the drugs commonly used to treat high blood pressure can make orthostasis worse. Any person who experiences orthostatic symptoms should inform all healthcare providers involved with their care.

People with PD often assume, mistakenly, that any symptom in any organ system is caused by PD. It is good to remember that having PD doesn't protect you from getting unrelated medical problems. A good example of a frequent parallel problem is back, neck and limb pain due to degenerative arthritis of the spine. Pain caused by PD symptoms certainly occurs, but it is usually an aching discomfort and feeling of heaviness of the large muscles of the legs, which often occurs during an "off" period. The same thing can be said of light-headedness or dizziness. Orthostatic hypotension is usually the primary reason for the symptom, but general medical causes involving the heart or lungs must be explored. In addition, other medications prescribed, particularly medications for high blood pressure, should be closely examined. The overlap of multiple health issues in people with PD underscores the need for the PD specialist to communicate regularly with the primary care physician, other specialists and/or healthcare team members.

For a person with Parkinson's experiencing orthostasis and high blood pressure, their blood pressure may be high while sitting but normal when standing, so they should always have their BP checked both in a sitting and standing position even at a primary care office or a visit to the emergency

room. If you experience dizziness or lightheadedness, your doctor may also check your blood pressure in a lying position and then a standing position one hour later, preferably after breakfast or lunch.

If a person with PD experiences orthostasis, it is appropriate for the physician or healthcare provider to consider decreasing the dosages of medications that may cause this problem, such as dopamine agonists, amantadine and carbidopa/levodopa. If drugs for hypertension are being used, the doses should be reduced or even discontinued.

Drugs are not the only remedy for orthostasis. The following non-pharmacologic techniques are important:

- Change positions slowly, particularly when rising from a seated to standing position. Pause for several seconds between each move. Walking with an assisted device (cane or walker) may also be helpful.
- Increase fluids, salt and caffeine in the diet.
- Wear support stockings and elevate legs periodically during the day. If this doesn't help, ask your physician or healthcare provider if medications to raise blood pressure would be appropriate. For more information on NOH, visit nohmatters.com.

Fludrocortisone (Florinef) will increase blood pressure by increasing retention of salt and blood volume. Increased dietary salt will enhance its effect. Fludrocortisone should be started at once a day dosing of 0.1 mg. Dosing higher than three times a day should be avoided. Leg edema (swelling) and high blood pressure when lying flat are potential adverse effects. Drinking plenty of water, about 8–10 glasses per day, will also help improve this condition.

Midodrine (Proamatine) increases blood pressure by stimulating the norepinephrine receptors and is dosed three times per day. There is an higher chance of developing high blood pressure while lying flat (supine hypertension) with midodrine than fludrocortisone, so if midodrine is prescribed this should be carefully monitored.

Pyridostigmine (Mestinon) can be used either as monotherapy or as an adjunctive drug to enhance the blood pressure raising effect of fludrocortisone and midodrine. Ordinarily used to treat the neuromuscular disease myasthenia gravis, pyridostigmine might have a small, but significant, increase in diastolic blood pressure.

Droxidopa (Northera) is believed to work by increasing standing blood pressure through elevating levels of norepinephrine, a chemical in the body that helps regulate blood pressure. Northera is approved for the treatment of orthostatic dizziness, lightheadedness, or the feeling that you may pass out in adult patients NOH. Similar to midodrine and fludrocortisone, there is potential for the development of high blood pressure when lying flat, which should be monitored carefully.

Some drugs for orthostasis increase blood pressure when lying down (supine position). To avoid supine hypertension (high of blood pressure spikes), the last dose midodrine and droxidopa should be taken no later than 3–4 hours before bedtime. If you are on these medications and taking a nap during the day, use a recliner instead of lying down to avoid supine hypertension.

Gastrointestinal Symptoms

Nausea, constipation and early satiety (feeling full after eating less than a full meal) are common problems throughout the course of PD and are caused by the same system that is responsible for neurodegeneration in the brain. In this case, the disease process affects the autonomic nervous system (ANS), which controls the normal movements of the gastrointestinal tract. In PD the contractions of the stomach are slowed, and everything that is swallowed, including medications, stays in the stomach longer than it should because of delayed emptying.
Slowed gastric emptying translates into gas and bloating, nausea, loss of appetite and pain. In addition, constipation occurs early in the evolution of PD, and it often, but not always, increases in severity and frequency as PD progresses.

Nausea

The management of gastrointestinal disorders in PD can be complicated. Dopaminergic medications can worsen nausea, but the addition of extra carbidopa (Lodosyn) to the mixture of carbidopa/levodopa (Sinemet) usually helps to prevent or lessen this side effect. However, Lodosyn does not work if the nausea is caused by dopamine agonists.

Other medications, specifically metoclopramide (Reglan), prochlorperazine (Compazine) and promethazine (Phenergan), are available for treating nausea, but because they work by blocking dopamine receptors in the intestinal tract and the brain, they should be avoided because they can worsen the symptoms of PD.

Domperidone (Motilium) is a good choice for treating nausea and vomiting associated with the use of any of the dopaminergic anti-Parkinson drugs (levodopa and the dopamine agonists) because it does not cross the blood brain barrier and does not worsen PD symptoms. However, it is available only from sources outside the U.S. There is, however, a risk of cardiac issues with this medication.

Trimethobenzamide (Tigan) is another available medication to treat nausea in PD. Simple antacids (i.e., simethicone) are less effective but worth trying because they are inexpensive and do not require a prescription. Another medication that was initially approved for chemotherapy and radiation therapy-induced nausea and vomiting and has been proven useful for nausea in PD is ondansetron (Zofran). Since it does not block dopamine in the brain, ondansetron is safe for patients with PD, and it probably helps block nausea both in the brain and in the gut. Ondansetron or other antinausea medications in the same family (5HT3 Receptor blocker) should not be combined with apomorphine as it can cause lowering of blood pressure. Often times, ginger capsules (or ginger tea, a less expensive option) may be helpful.

Constipation

This is another example of the effect of PD on the ANS and is a major nuisance for many people with PD. Fortunately, good dietary management and the prudent use of stool softeners, laxatives and other bowel modulators are usually helpful. There are several steps to good dietary management and preventive maintenance:

- Drink plenty of water and fluids.
- Regular exercise
- Consume lots of dietary fiber in the form of fruits, fruit juices, vegetables and cereals.
- Use appropriate fiber additives, such as Metamucil, the stool softeners lactulose and polyethylene glycol (Miralax), or stimulant laxatives, such as senna/sennosides (Senokot) or bisacodyl (Dulcolax).

Another option for the treatment of constipation is lubiprostone (Amitiza) which increases the secretion of fluid in your intestines to help make it easier to pass stools (bowel movements). Lubiprostone is used to treat chronic constipation in adults.

Guidance from the neurologist, primary care doctor or healthcare provider on how to use and combine these agents is essential. A review of GI medications can be found in the Medications for Non-motor Symptoms Fact Sheet included with this book.

Drooling (Sialorrhea)

Drooling in PD can be defined as an inability to manage the flow of the saliva in and around the mouth as it is being produced by the salivary glands. It results not from overproduction of saliva, but from slowing of the automatic swallowing reflex that normally clears saliva from the mouth. Drooling is common in PD, and it ranges from mild wetting of the pillow during sleep to embarrassing outpourings of saliva which can cause stains on clothing, wet the floor and can even cause aspiration. For example, this can happen when the head is down and the mouth is held open involuntarily (as happens in advanced PD) or when a person is engaged in an activity and is distracted from the need to swallow. When severe, drooling is an indicator of more serious difficulty with swallowing (also known as dysphagia), which can cause the person to choke on food and liquids or can lead to aspiration pneumonia.

Treatment of drooling is not always effective, but the list of therapies includes:

- **Glycopyrrolate and other oral anticholinergic medications (trihexyphenidyl, benztropine, hycosamine).** These medications decrease the production of saliva. Usually this is perceived as a side effect (dry mouth), but in this case it is an advantage. Other anticholinergic side effects may be seen, including drowsiness, confusion, vomiting, dizziness, blurred vision, constipation, flushing, headache and urinary retention. These medications should be avoided in older people with Parkinson's.
- **Scopolamine patch.** This patch offers anticholinergic medicine that slows production of saliva as it is absorbed into the entire bloodstream, and anticholinergic side effects similar to oral agents may be seen.
- **1% atropine eye drops (an anticholinergic),** given as 1–2 drops under the tongue per day to dry the mouth. Systemic (wide spread) side effects are much less likely with this local treatment.

There are two botulinum toxins approved for drooling, botulinum toxin A (Xeomin) and botulinum toxin B (Myobloc). Botulinum toxin injections into the salivary glands of the cheek and below the jaw decreases production

of saliva, and hence helps decrease drooling. These injections are required approximately every 3 months.

Urinary Symptoms

Urinary frequency, urinary urgency and loss of bladder control (urge incontinence) are common complaints in PD. The urinary bladder loses its capacity to hold normal amounts of urine because the messages from the brain to the spinal cord tell the bladder to empty prematurely in PD. Urinary frequency and urgency can lead to incontinence. This can be an issue for those who experience motor fluctuations and who need to get to a toilet quickly when there is a sudden urge to empty the bladder. As with other nonmotor complaints, it is important to rule out other possible causes of urinary frequency, including urinary tract infection and enlarged prostate. Managing urinary problems with a urologist is important.

Medications that can help re-establish bladder control:

- Anticholinergic medications can relax the overactive muscles of the bladder, which allows the bladder to fill to greater capacity. There are several available by prescription.
- The alpha-adrenergic receptor blockers prazosin and tamsulosin (Flomax) relax the detrusor and make it easier for the bladder to empty. These drugs may also be used for men if an enlarged prostate is the reason for the symptoms.
- The tricyclic antidepressants nortriptyline and imipramine have anticholinergic properties in addition to other, healthful pharmacologic effects.

Your physician or healthcare provider can assess which is most appropriate for your situation.

Sexual Dysfunction

Sexual dysfunction in PD is common for many reasons, including dysfunction of the ANS. It affects men more often than women, though little has been published about this topic. It remains underdiagnosed as patients, partners and healthcare providers may not be comfortable with a frank discussion of sex. This topic certainly deserves attention, so you and/or your partner may need to initiate a conversation with someone on your healthcare team.

Many factors contribute to good sexual health for both women and men, and certain symptoms of PD can impact sexual functioning and response. Depression, often present in PD, can decrease sexual desire, and some antidepressants can affect sexual response. The motor symptoms of PD can impact both the fine motor skills of touch and the mobility that contributes to sexual activity. The expressiveness that can be an important part of non-verbal communication is often affected in PD, as both facial expression and volume of voice may decrease. If there are times of the day when your functioning is at its best, such as when you are rested and medications are maximized, this could be a good time to express yourself with a loved one.

In addition to the neurologist, other members of the healthcare team that might address sexual functioning include the psychologist, PD nurse, primary care physician and/or nurse practitioner, gynecologist for women and urologist for men.

In PD, sexual dysfunction may arise as a primary symptom resulting from the loss of dopamine, which is responsible for delivering reward and pleasure in the brain. As with other non-motor symptoms, the doctor or other healthcare provider should consider other causes of impotence and decreased libido. These include poor circulation to the genitals which commonly occurs in diabetes and peripheral vascular disease, enlarged prostate, depression and other medical conditions. Various medications, including antihistamines, antidepressants, benzodiazepines, and drugs for high blood pressure and excessive alcohol or tobacco use can also contribute to sexual dysfunction. Fortunately, most anti-PD drugs are not associated with impotency or loss of libido, with the exception of the anticholinergics. To the contrary, the dopamine agonists have been associated with disorders of impulse control, including uncontrolled sexual urges.

Male impotence, otherwise known as erectile dysfunction (ED), refers to difficulty with achieving and maintaining an adequate erection. Erectile dysfunction warrants a thorough evaluation so the physician or other healthcare provider can look for all possible causes, especially diabetes and other disorders listed above. A complete physical examination should be conducted by the general physician and urologist.

There are a variety of medication options to treat ED. Some can be injected into the penis and others are taken orally. Oral medications for ED include sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis).

Mechanical treatments include vacuum pumps, constriction rings and penile implants. Injectable medications include papaverine HCl (Papaverine vials for injection), phentolamine (Regitine vials for injection) and alprostadil (Caverject).

Seborrheic Dermatitis and Excessive Sweating

Many persons with PD will develop skin-related symptoms including seborrheic dermatitis (SD) and excessive sweating. SD is a disorder of the oil-producing glands of the skin, which can become infected with a particular yeast in patients with neurologic disease. It occurs mostly around the face and scalp in people with PD. In seborrheic dermatitis the skin is oily, reddened and scaly. Treatment of mild SD can be accomplished by the frequent use (two to three times a week) of a good dandruff shampoo. More severe cases require seeing a dermatologist.

Some people observe that they sweat profusely in the "off" state of motor fluctuations or when dyskinesia is severe enough to increase body heat. Many people report sudden and unexplained drenching sweat, often awakening them from sleep and creating a need to change bedclothes. Levodopa can also cause severe episodes of sweating. Sweating disorders in PD can be associated with other autonomic abnormalities, such as constipation and orthostasis.

For adults with facial and body presentation of Seborrheic dermatitis, medications are typically topical ketoconazole 1%–2% shampoo or other topical antifungals (such as ciclopriox); short term use of topical corticosteroids (hydrocortisone, betamethasone valerate, etc.); topical calcineurin inhibitors (pimecroliums 1% cream, tacroliums 0.1% ointment).

Thermoregulatory Functions

This inability to regulate body temperature can manifest as excessive sweating, or a drastic rise or drop in body temperature. Excessive sweating (hyperhidrosis), experienced by more than 50 percent of people with PD, consists of sudden, drenching sweats of the head and neck. Though it may occur in people taking no PD medications, it often occurs as prescriptions wear off or during episodes of dyskinesia. Adjusting dopaminergic therapy can help, and neurologists may consider reducing/removing patient's anticholingeric medications, especially in warmer weather, as Anticholinergics can block sweat secretion and add to overheating.

Conversely if patients are sweating excessively, consider reducing cholinergic medications (such as donepezil).

Pain

Almost half of people with Parkinson's experience pain during their PD experience, and it can become more common as the disease progresses. Other painful conditions may coexist with PD, including arthritis, peripheral neuropathy, spinal stenosis, and musculoskeletal strains and sprains. These alternative causes of discomfort should always be considered before assuming that pain is due to PD.

Pain in PD can be related to (1) dystonia, (2) muscles and joints, (3) nerves or nerve roots, (4) akathisia (restlessness) and/or (5) central "parkinsonian" pain. There may be a pattern between discomfort and PD medication schedule. For some people, being in the "off" state can increase a sensation of pain, adjusting medication dosage and timing will help.

The most common cause of pain in PD is related to dystonia, which is a sustained posture of the neck, arms, legs or feet. Camptocormia is an example of dystonia characterized by severe bending at the waist, causing back pain or spasms. Depending on the timing of dystonic pain, multiple different approaches may be helpful. Early morning dystonia often improves with movement and/or the first dose of dopaminergic medication. In some cases, the severity of morning dystonia merits an injection of apomorphine. If dystonia occurs as a wearing-off symptom, minimizing the "off" period with dopaminergic therapy can be beneficial. Botulinum toxin injections can also be helpful in treating localized dystonia.

Musculoskeletal pain may be related to rigidity and decreased movement/mobility. Adjustments of the PD medication schedule and physical therapy can help in these cases. Radicular, or nerve root, pain should be evaluated for a compressed root or nerve lesion. If these causes are eliminated and the radicular pain is thought to be related to Parkinson's disease, physical and/or occupational therapy may be helpful.

Non-motor painful sensations, such as abdominal pain, bloating or chest wall tightening may be related to PD. These symptoms should be addressed by the physician to rule out other primary causes.

Depression, which is common in PD, can heighten an individual's experience of pain. This highlights the importance of identifying and treating depression in Parkinson's disease.

Treatment of the pain in PD can be challenging. Some options include traditional anti-inflammatories, muscle relaxants, gabapentin, tricyclic antidepressants and additional PD medications. Opiates should be used

only in severe cases, and referral to a pain specialist is recommended. Several non-pharmacologic techniques include regular exercise, heating pads, ice packs and massage.

Anti-inflammatory medications include steroids and non-steroidal anti-inflammatory drugs (NSAIDs) and can help with musculoskeletal pain. NSAIDs are available both over-the-counter (OTC) and prescription. Some common NSAIDs include ibuprofen (Advil, Motrin), naproxen (Aleve), meloxicam (Mobic), and diclofenac (Voltaren). Oral NSAIDs should be taken with food. Common side effects of NSAIDs include nausea, stomach ulcers, and swelling/fluid retention. Steroids can have similar side effects to NSAIDs and long-term use can cause changes such as high blood sugar and high blood pressure.

Muscle relaxants may be used on an as needed basis for muscle spasms but are typically not long term solutions. Common muscle relaxants that have shown to be more effective for spasms include cyclobenzaprine (Flexeril), tizanidine (Zanaflex), and baclofen. Common side effects include dizziness, drowsiness, confusion and low blood pressure.

If pain is thought to be related to nerve pain or "neuropathic", medications such as gabapentin, serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), or opioid medications may be used. Gabapentin (Neurontin) and pregabalin (Lyrica) are commonly dosed two to three times a day but may be dosed at bedtime for restless leg. These medications must be increased gradually over several weeks to avoid side effects and reach an effective dose. Many people with PD may need 600–900 mg of gabapentin per dose to notice benefit. Common side effects include dizziness, sleepiness, blurry vision, and changes in gait/walking. Duloxetine (Cymbalta) is an SNRI can lessen nerve pain at 30–60 mg per day.

TCAs, such as amitriptyline and nortriptyline, can be effective for nerve pain but have many drug interactions and side effects that include confusion, forgetfulness, hallucinations, light-headedness, blurry vision, urinary retention, dry mouth. The mechanism of how acetaminophen (Tylenol) works is not completely understood, however it may also be helpful for neuropathic pain. It commonly comes in combination with other medications for pain. To prevent serious liver damage, for most people with PD, the total daily dose of acetaminophen should not exceed 3,000 mg per day from all sources. For some, it is advised not to exceed 2,000 mg per day due to liver disease or alcohol use.

Opioid medications such as tramadol (Ultram) or oxycodone (Oxycontin) may be used for nerve pain but is typically a last resort. This is due to many drug interactions and side effects of opioids that include drowsiness, decreased breathing, confusion, and constipation. Opioid medications can lose their effect over time requiring higher doses and higher risk of serious side effects. These medications can be addictive and some patients have accidently overdosed which lead to serious injury or death at doses commonly prescribed. Long-term use and high doses of opioids can cause a worsening of pain. This phenomenon is called "hyperalgesia ". Hyper meaning more and algesia meaning pain. Long-term use of opioids is typically reserved for cancer pain. If you are on long-term or high dose opioids, ask your doctor if you should receive a "rescue" medication called naloxone (Narcan) which can be administered by a bystander or caregiver in the event of an accidental overdose.

Involving Your Team

When pain lasts longer than two weeks, interferes with sleep, or intensifies, it's time to involve your team. Keep track of WHEN the pain started, WHERE it hurts, HOW long it lasts and WHAT it feels like (achy, sharp). It will be useful to also track when the pain starts in relation to when you take your medication. This information will help your healthcare team work more efficiently with you in designing a treatment plan.

CHAPTER FOUR

Development of New Drugs

Drugs and devices have to go through a process of clinical trials before the U.S. Food and Drug Administration (FDA) can consider approving a new therapy. A clinical trial, also called a clinical study or clinical research, is research conducted with people to answer scientific questions. Clinical trials determine if scientific concepts can be turned into safe and effective therapies that make life better for people with Parkinson's.

Phases of Clinical Research For Drug and Device Research

- **Phase I.** Tests potential treatment for the first time in a small group of people to evaluate safety, determine the safe dosage and identify side effects.
- **Phase II.** Further evaluates the safety of the treatment being tested and provides preliminary measures of effectiveness.
- **Phase III.** Determines if the treatment benefits participants and if its benefits outweigh its risks.
- **Phase IV.** After a drug or device is approved, this final phase of research can be conducted. Collects and looks over additional information about a treatment, including risks, benefits and optimal use, after FDA approval.

The entire process of bringing a new medication to the pharmacy can take up to 10 years from the time it is tested in a laboratory to the time that the doctor prescribes it as a treatment.

New Therapies on the Horizon

To fully appreciate where we are going with Parkinson's disease treatment, it is important to realize where we have come from. Since the approval of Sinemet (carbidopa-levodopa) in the 1970s, research has led to many life-changing treatments for Parkinson's. Looking at research breakthroughs in our understanding of medications, therapies and devices to treat Parkinson's, today's best care provides a different disease journey than a generation ago. Today's focus on non-motor symptoms is largely a consequence of how effective treatments are for motor symptoms.

Today, the biggest research challenge is slowing the disease progression. It has been demonstrated that today's best treatment plan – which involves expert medication, therapy, exercise and sometimes surgery – slows your experience of Parkinson's progression and may actually be helping your brain fight the disease.

New research is investigating opportunities in several areas:

- **Preventing Parkinson's.** Many researchers are looking at genetic and environmental causes of Parkinson's to see if they can identify targets for drugs that would help brain cells to fight the changes that cause Parkinson's. If we could do this, then our children could be tested for risk factors, and people with a high risk for Parkinson's could receive treatments to prevent it. Such a treatment might also slow Parkinson's disease in people who already had the disease, but it might not.

- **Slowing disease progression.** If we could make the diagnosis of the disease earlier and slow its progression, people may take a long time to experience troublesome symptoms. People with Parkinson's often have a combination of brain cells that die and others that get "sick" so that they don't work as well. If we could make a treatment that would slow the disease progression, some of these brain cells could potentially get better and start to work again, resulting in an improvement in symptoms. This would be the first step in curing Parkinson's – stopping the disease progression or slowing it enough that we can't tell the difference between Parkinson's and the changes people experience naturally from aging.
- **Diagnosing Parkinson's and measuring progression.** Most people with Parkinson's can be diagnosed by a neurologist using standard clinical tests. However, sometimes it can be difficult to tell the difference between Parkinson's disease and other conditions that mimic it. Some medications, essential tremor or small strokes can mimic Parkinson symptoms. Further, figuring out how far Parkinson's has progressed since the last evaluation is difficult, as it may depend on fluctuating medication effect, level of fatigue and external stress factors. A better measure for progression would help with clinical trials of treatments to slow the disease.
- **Replacing lost function.** It is a goal to create therapies that help the brain function like a healthy, normal brain. To some extent, we do this every day through interventions like exercise, physical therapy, occupational therapy and speech therapy, where clinicians help you compensate for the changes caused by Parkinson's. All of us have to compensate for changes in our bodies and brains as we age, and so good therapy does restore lost function. However, not all of these changes with Parkinson's can be corrected with therapy, so there is research into ways to restore cells that have been lost. Scientists call this neurorestoration. Unfortunately, unlike bones and skin, the brain doesn't have systems to automatically repair itself or to integrate a graft or transplant to replace cells that have been lost. So far, neurorestoration has turned out to be a hard task. There is not much evidence that this can be successful with surgical approaches, such as transplants of brain cells failing to be effective in well-designed trials.

  There are always ongoing studies, such as the current test of whether or not gene therapy in the brain will improve its ability to produce dopamine.

- **New symptomatic treatments.** Research is ongoing in many areas, including helping people who experience fluctuating medication effects ("on-off" fluctuations), reducing dyskinesia, achieving better motor control, and managing a range of symptoms, whether it be mood and psychiatric symptoms or autonomic symptoms like lightheadedness on standing (orthostatic hypotension), constipation and others.

  Parkinson's research has made amazing progress in the last two decades, and all the signs suggest that progress will continue unabated. There are clinical trials, including drugs and other therapies on the horizon that are likely to help people with PD in the near future. However, these change frequently as studies show effects of particular treatments. Please visit the Parkinson's Foundation website, Parkinson.org, to find information and resources on the newest research and treatment options. You can also contact our Helpline at 1-800-4PD-INFO (473-4636) or helpline@parkinson.org for help finding a clinical trial near you, so that you can help scientists find the next breakthrough therapy!

- **The role of exercise.** While treating the symptoms of the disease is not the same as slowing its progression, the Parkinson's Outcomes Project shows that people with PD who start exercising earlier and a minimum of 2.5 hours a week, experience a slowed decline in quality of life compared to those who start later. Establishing early exercise habits is essential to overall disease management.

APPENDIX A

Formula for Liquid Sinemet

Formula for Liquid Sinemet – 1 mg levodopa per 1 ml solution

- Sinemet 25/100 tablets 10 tablets (1,000 mg levodopa) (do not use Sinemet CR)
- Ascorbic acid (Vitamin C) crystals ½ tsp. (approx. 2 gms)
- Tap water or distilled water 1 liter or 1 quart

1. Mix the above ingredients in a liter/quart plastic container with lid (do not use metal).
2. Rotate or shake gently until tablets dissolve (no need to crush tablets). Tablets may not go completely into solution.
3. Formula will maintain full strength and purity for 24 to 48 hours in refrigerator.

Dosing Recommendations

Always establish a dosing plan with your physician or healthcare provider first!

1. Morning ("Jump Start") dose:
   - 60 ml of the formula (60 mg or a little more than ½ of a 25/100 tablet of carbidopa/levodopa), or may use amount comparable to usual tablet dose.
   - Adjust dose 5–10 ml up or down every three to five days until you achieve the best "on" response with the least dyskinesia.
2. Hourly dosing:
   - 30 ml of the formula on the hour while awake, or hourly proportion of usual tablet dose. (For instance, a person with PD taking one carbidopa/levodopa 25/100 tablet every two hours might try 50 ml per hour of the liquid.)
   - Adjust dose 5–10 ml up or down every three to five days until "on" periods are smoother.

For the best overall result, it is strongly recommended that you adjust the morning jump start dose prior to adjusting the hourly doses. Accuracy of the dose and exact hourly timing between doses is critical for optimal benefit. Optimal dosing can vary tremendously from one person to another.

APPENDIX B

Evaluating Research Reports

New drugs and other PD treatments often gain attention from the popular media. Publicly traded companies have to report their study results as soon as they are available and before they are presented at scientific meetings. This is usually done in form of a press release. While headlines may make it sound like new drugs are available, a closer look often reveals that the new drug is only in the early stages of research and years away from becoming an available treatment. Taking some time to evaluate the research behind the headlines can help determine the best way to use the new information.

Following are some questions to ask when evaluating clinical studies of new medications and treatments for PD:

- What is the source of the information? Has the information been published or presented at a trustworthy scientific meeting? Or is the information derived from unscientific, and possibly incorrect, opinion? Check with a member of your healthcare team to determine if the source is reliable.
- How many people participated in the study? The higher the number of participants, the more likely the results will achieve statistical significance and be more accurate.
- How was the study designed: (1) Were the subjects randomized to equal treatment groups? (2) Was the study double-blind? (3) Was a placebo group incorporated into the study's design? The gold standard for the most valid clinical trial is one that includes all of three of these elements.

APPENDIX C

Medication and Hospitalization

When hospitalized, your healthcare team may not recognize some of your PD symptoms, why they fluctuate so drastically and/or may not know that treating them requires careful medication management. They will naturally be focused on treating the condition that brought you to the hospital, which may be unrelated to PD. This lack of understanding can seriously affect your quality of life, both in the hospital and after you are discharged.

To avoid serious side effects, people with PD need their medication on time, every time – do not let the hospital staff skip or postpone doses. People with PD often have complex and precisely timed medication regimens, which can be difficult to maintain. Nurses are accustomed to dispensing medications on certain schedules and likely have an hour window to distribute medications within that schedule. They may not realize that even a 15-minute delay can make the difference between independent function and poor mobility. Additionally, hospital pharmacies may not keep your specific PD medications in stock.

To help your nurses understand, make sure that the drug schedule, with specific times, is written into the doctor's orders. It is important for you or your advocate to double check the drugs and schedules in your medical chart. If the hospital pharmacy does not stock your medications, ask to use your own. If you are told that you cannot take your own medications, ask your neurologist to write a letter or call the hospital to assure them your own medications are best. Keeping a set of your medications in their original bottles in your Aware in Care kit will help make this possible. Emphasize to the medical staff that delaying or stopping PD medications will not only affect your symptoms, but can also be dangerous. For example, missing the dose of a dopamine agonist may lead to withdrawal symptoms such as anxiety or pain.

The Parkinson's Foundation Aware in Care kit contains information to give to hospital providers about Parkinson's and what medications are safe for people with PD. Call our Helpline at 1-800-4PD-INFO (473-4636) to request your free Aware in Care kit, or order one online at 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 or in another in-patient setting, whether it's a planned visit or an emergency.

Glossary

Glossary terms are identified with a blue underline the first time they appear in this book.

A **Acetylcholine** A chemical messenger released by cholinergic nerves; involved in many brain functions, such as memory and control of motor activity. There appears to be an interplay between the actions of acetylcholine and dopamine.

Adjunctive Supplemental or secondary to (but not essential to) the primary agent (i.e., medications used to enhance levodopa therapy).

Antihistamine A drug normally used to control allergies or as a sleep aid; some (like Benadryl) are anticholinergic drugs, with anti-tremor properties.

Anxiolytic An agent, usually referring to a class of medications that reduces anxiety.

Autonomic neuropathy Damage to the autonomic nerves, which affect involuntary body functions, including heart rate, blood pressure, perspiration, digestion and other processes. Signals between the brain and portions of the autonomic system are disrupted.

Symptoms vary widely, depending on which parts of the autonomic nervous system are affected. They may include dizziness and fainting upon standing (orthostatic hypotension); urinary problems including difficulty starting urination, overflow incontinence and inability to empty your bladder completely; sexual difficulties including erectile dysfunction or ejaculation problems in men, and vaginal dryness and difficulties with arousal and orgasm in women; difficulty digesting food (gastroparesis); and sweating abnormalities including decreased or excessive sweating.

B **Benzodiazepines** A popular and effective class of anti-anxiety drugs.

C **Catechol-O-methyl transferase (COMT)** An enzyme that inactivates levodopa in the body before it gets to the brain. COMT inhibitors block the work of the enzyme, so more levodopa is available to the brain.

Chronic degenerative neurologic disease A disease characterized by the loss of cells of the brain or spinal cord, which over time leads to dysfunction and disability.

Clinical Trials A research study in humans that aims to test a new intervention – this could be a drug, surgery or therapy like exercise or diet guidelines – to make sure it is effective and safe.

Compulsive behaviors Performing an act persistently and repetitively without it necessarily leading to an actual reward or pleasure; in Parkinson's, this can be a side effect of dopamine agonists and usually takes the form of uncontrolled shopping, gambling, eating, or sexual urges. If you experience this symptom, tell your doctor immediately.

Confusion The state of being unclear, with lack of understanding of situation and/or surroundings; a symptom of many medications for Parkinson's motor and non-motor symptoms.

Controlled release formulation A type medication that is released or activated at predetermined intervals or gradually over a period of time.

Corticobasal degeneration (CBD) A progressive neurological disorder characterized by nerve cell loss and atrophy, or shrinkage, of multiple areas of the brain including the cerebral cortex and the basal ganglia. Initial symptoms may first appear on one side of the body, but eventually affect both sides. Symptoms are similar to those in PD, such as poor coordination, absence of movements, rigidity, impaired balance and abnormal muscle postures. Other symptoms may include cognitive and visual-spatial impairments, loss of the ability to make familiar, purposeful movements, hesitant and halting speech, muscular jerks and difficulty swallowing. An individual with corticobasal degeneration eventually becomes unable to walk.

D

Delusion False, fixed, idiosyncratic belief, not substantiated by sensory or objective evidence.

Dementia Not a diagnosis, but descriptive of a broad symptom complex that can arise from a variety of causes. Symptoms can include disorientation, confusion, memory loss, impaired judgment and alterations in mood and personality.

Dementia with Lewy bodies (DLB) A progressive degenerative disease or syndrome of the brain that shares symptoms of both Alzheimer's and Parkinson's disease and is characterized by fluctuating cognition, hallucinations and parkinsonism.

Detrusor A muscle that forms a layer of the wall of the bladder, responsible for allowing the bladder to store and release urine.

Diastolic blood pressure Part of the measure of blood pressure, which measures the time between beats and indicates the time that the coronary artery is able to supply blood to the heart.

Diminished/decreased libido Decreased sexual urges; a symptom of many medications for depression and anxiety.

DNA Deoxyribonucleic acid; the basic chemical substance that makes up a gene.

Double-blind study A study in which neither the participants nor the investigators know which drug a patient is taking; designed to prevent observer bias in evaluating the effect of a drug.

Dry mouth Usually from decreased saliva production; a side effect of many medications for motor and non-motor symptoms.

Dyskinesia Abnormal involuntary movement of muscles. Dystonia, athetosis and chorea are forms of dyskinesias.

Dystonia Involuntary spasms of muscle contraction that cause abnormal movements and postures.

E

Endogenous Originating internally; developing from within (e.g., an endogenous depression is not caused by external circumstances).

Enteral suspension A method of medication distribution through the gastrointestinal tract through the use of a liquid or gel-like mixture of liquids and solids.

Etiology The science of causes or origins of a disease; the etiology of Parkinson's disease is unknown.

Exogenous Originating externally; relating to external factors (i.e., an exogenous depression might arise following a major life crisis).

Extended benefit Unanticipated or potentially unexplained results of using a therapy or treatment.

Extended release (ER) formulation A type of medication designed to slowly release over an extended period of time, especially to reduce dosing frequency.

Extended risk Activities you are not doing or thoughts you may have because of a treatment that can be detrimental to your health.

F

Futility studies A drug trial design that tests whether a drug is ineffective rather than the traditional study of whether it is effective. Relatively short futility studies allow for multiple drugs to be tested more quickly and easily, and further efficacy trials are offered for drugs that "pass" the futility trial.

G

Gabapentin An anticonvulsant, or anti-epileptic, medication also used in adults to treat neuropathic pain and restless leg syndrome

Glutamate A salt or ester of glutamic acid related to the hydrolysis of proteins.

H

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.

Hallucinations Something you see, hear, smell, taste, or feel that is not actually there; can be a side effect of anticholinergics and some medications for depression and anxiety.

Hallucinosis A state of experiencing hallucinations. In PD, hallucinations are usually visual in nature and insight into reality may or may not be retained.

Holistic Characterized by the treatment of the whole person, taking into account social and other factors, not just symptoms of disease.

Holistic practices An approach to care that looks beyond standard medical care, as complementary therapies (use with standard medical treatments) or Alternative therapies (used instead of standard medical treatments).

Homocysteine An amino acid that occurs in the body and is produced when levodopa is metabolized; elevated levels of homocysteine can cause blood clots, heart disease, and stroke.

Hydrophilic Capable of uniting with or taking up water.

I

Idiopathic An adjective meaning unknown; the most common form of PD is idiopathic Parkinson's disease.

Immediate release (IR) A Type of medication that disintegrates or dissolves rapidly with no special rate controlling features.

Integrative medicine Involves bringing together conventional and complementary approaches in a coordinated way.

The National Center for Complementary and Integrative Health uses the term "complementary health approaches" when discussing practices and products of non-mainstream origin, and the term "integrative health" when talking about incorporating complementary approaches into mainstream health care.

L

Low blood pressure When blood pressure is below normal (normal range is usually between 90/60 mmHg and 120/80 mmHg); the medical name for low blood pressure is hypotension; common side effect of levodopa and dopamine agonists. See also "neurogenic orthostatic hypotension."

M

Mild cognitive impairment A transition stage between the cognitive changes of normal aging and the more serious problems of dementia. Mild cognitive impairment can affect many areas of cognition such as memory, language, attention, reasoning, judgment, reading and/or writing. Mild cognitive impairment may be irritating but it does not typically change how a person lives their life.

Mind-body therapies Therapies that work on the premise that the mind, body, and spirit do not exist in isolation and that disease and/or symptoms change when these are out of balance.

Monoamine oxidase type B (MAO-B) An enzyme in our body that breaks down dopamine; MAO-B inhibitors block the work of the enzyme, so there is more dopamine available in the brain.

Multiple system atrophy (MSA) A progressive neurodegenerative disorder characterized by symptoms of autonomic nervous system failure (such as lightheadedness or fainting spells, constipation, erectile failure in men and urinary retention) combined with tremor and rigidity, slurred speech or loss of muscle coordination.

Musculoskeletal The combined network or muscles, bones, ligaments, tendons and nerves

Myasthenia gravis A chronic autoimmune, neuromuscular disease that impacts the muscles responsible for functions involving breathing and movement.

N

Natural therapies Plant-derived chemicals and products, vitamins and minerals, probiotics, and nutritional supplements used to promote cell health and healing, control symptoms, and improve emotional wellbeing.

Nausea A feeling of sickness with an inclination to vomit; common side effect of many medications for Parkinson's symptoms.

Neurons The structural and functional unit of the nervous system, consisting of the nerve cell body and all its processes, including an axon and one or more dendrites.

Neurodegeneration Loss of cells of the brain or spinal cord. Over time, it leads to dysfunction and disability.

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.

Neurogenic orthostatic hypotension (NOH) Orthostatic hypotension (OH) is a drop in blood pressure that happens within a few minutes of standing up. Parkinson's disease and some other diseases can cause OH – in this case, it is called neurogenic OH, since it is related to dysfunction of the nervous system.

Neuroprotection An effect that results in recovery, repair, or regeneration of nervous system structure and function.

Neurorestoration Repair, replacement, or regeneration of brain cells.

Neurotransmitter A biochemical substance, such as dopamine, acetylcholine or norepinephrine, that transmits nerve impulses from one nerve cell to another at a synapse (connection point).

Non-pharmacologic Interventions that do not involve medications

Norepinephrine A chemical messenger (neurotransmitter) that plays a role in mood disorders and is released in response to stress.

Nutritional consultation The process of seeking professional guidance on how nutrition can benefit overall well-being.

Occupational therapy A type of therapy that helps maintain or develop daily living or occupational skills in times of physical change.

"Off-on" effect Sudden or varying changes in motor performance and other Parkinson's symptoms. It may correlate with effects of medication wearing off.

Open-label When both the researcher and the participant in a research study know the treatment that the participant is receiving. Open label is the opposite of double-blind when neither the researcher nor the participant knows what treatment the participant is receiving. Open-label studies should be interpreted with caution because of the potential for biased conclusions.

Oxidative stress A toxic byproduct of cell metabolism that is thought to cause nerve cell death when left unchecked in PD and other neurodegenerative disorders.

Pathogenesis The production or development of a disease.

Pedal edema The accumulation of fluid in the feet or lower legs

Peripheral neuropathy Conditions that result when nerves carrying messages from the brain and spinal cord to the rest of the body, including muscles, skin and internal organs, are damaged, resulting in weakness, numbness, and/or pain, usually in the hands or feet.

Pharmacodynamics The study of the relationship of drug concentration to drug effect; essentially what the drug does to the body.

Pharmacokinetics The study of the absorption, distribution, metabolism and excretion of drugs; essentially what the body does to the drug.

Physical therapy A type of therapy that maintains and strengthens parts of the body related to movement.

Placebo A substance containing no medication; an inactive substance or preparation used as a control in an experiment or test to determine the effectiveness of a medicinal drug.

Placebo effect The commonly observed phenomenon that people in drug studies tend to have improvement in their symptoms even when they are not receiving the actual study medication or therapy. This benefit above and beyond any actual biological benefit is due instead to the belief that the treatment will work.

Progressive supranuclear palsy (PSP) A Parkinson's-like, degenerative brain disorder that causes progressive problems with gait and balance. There is an inability to aim the eyes properly, and persons often show alterations of mood and behavior, including depression and apathy as well as progressive mild dementia. Because some symptoms are similar, PSP is often misdiagnosed as Parkinson's or Alzheimer's disease. The hallmark distinguishing factor of PSP is early gait instability and difficulty moving the eyes. PSP, like MSA and CBD, does not respond very well to levodopa therapy.

Psychological counseling A broad term used to refer to the many varieties of counseling or talk therapy available today. Also called Psychotherapy or "talk therapy."

S

Seborrheic Dermatitis A common skin condition that causes redness (on light skin) or light patches (on darker skin) and an itchy rash with flaky scales. Also called dandruff, cradle cap, seborrhea, sebhorrheic exzema and seborrheic psoriasis.

Sham surgery A surgery performed as a control in research; similar to the real procedure but omits the key therapeutic element ("fake" surgery).

Sialorrhea Increased amount of saliva in the mouth, either from excessive production of saliva or decreased swallowing.

Speech therapy A type of therapy that evaluates speech changes and creates solutions and improvements to help with speech issues.

Spinal stenosis A condition in which your spinal canal starts to narrow, which can punch the spinal cord or the nerves around it causing pain, tingling or numbness in your legs, arms or torso.

Substantia nigra The area deep within the brain where dopamine is produced.

Supine hypertension See Orthostatic Hypotension

T **Therapeutic levels** The range in which the amount of medication in your blood that is effective without causing serious problems

Tyramine An amine that causes elevated blood pressure and increased heart rate by displacing the chemical norepinephrine from storage in the body. Tyramine is generally produced by fermentation of food products.

U **Use of assistive devices** Using adaptive equipment to help one engage in daily activities such as a shower chair, elevated toilet seat or replacing buttons with Velcro.

V **Vivid dream** A dream that is very realistic and can be caused by awakening during the dream; common side effect of medications for depression and anxiety.

Index

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Parkinson's Disease

Medications

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Table of Contents

Introduction

This book concentrates on the medications used in Parkinson's disease (PD). Ideally, the treatment of PD would be symptomatic (control or reduction of symptoms), neuroprotective (halting or slowing of disease progression) and neuroregenerative (reversal of disease process).

At present, proven therapies only help to relieve symptoms. More than a dozen different medications are now being used routinely to combat the motor symptoms of PD. Many others target the non-motor complications of PD. Considerable research remains dedicated to uncovering neuroprotective or neuroregenerative strategies, but to date, no such definitive therapies have been discovered.

Throughout this manual, medications currently available for symptomatic treatment and future developments in the treatment of PD are discussed.

Chapter 1
Introduction to Parkinson's Disease

Classic Symptoms

The primary symptoms of Parkinson's disease (PD) were first described by James Parkinson in 1817 in his *Essay on the Shaking Palsy*. These include:

- Tremor (usually most noticeable when the limb is at rest)
- Bradykinesia (slowness of movement)
- Rigidity (stiffness of movement)
- Postural instability (imbalance when standing or walking)

A PD diagnosis is based on evidence of at least two out of three specific signs and symptoms: tremor, slowed mobility (bradykinesia) and/or stiffness (rigidity). The occurrence of symptoms on only one side of the body is typical of the disease in its earliest stage. The diagnosis of Parkinson's disease remains clinical; that is, there are no conventional or readily available laboratory tests or brain images that can "prove" PD, though dopamine transporter scanning may help with diagnostic puzzles (see discussion in Pathology section).

Other characteristic features of PD include:

- Micrographia (small handwriting)
- Hypophonic dysarthria (soft, less understandable speech)
- Stooped posture
- Shuffling steps
- Diminished facial expression
- Infrequent eye blinking

Early falling or postural instability, commonly seen later in classic PD, may suggest other parkinsonian syndromes such as:

- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration (CBD)
- Multiple system atrophy (MSA)
- Dementia with Lewy bodies (DLB)

As the above symptoms predominantly involve movement, they are called **motor symptoms**. Parkinson's disease is not only a disorder of motor symptoms. It is now well known that **non-motor symptoms** also can be prominent and even disabling in PD. Non-motor symptoms include changes in mood, memory, blood pressure, bowel and bladder function, sleep, fatigue, weight and sensation (Table 1). Some symptoms have features of both (i.e., mixed motor and non-motor symptoms).

Table 1. Symptoms in Parkinson's Disease

MOTOR SYMPTOMS

- Bradykinesia (slowness of movement)
- Rigidity (stiffness of movement)
- Tremor (involuntary shaking of the hands, feet, arms, legs, jaw or tongue; usually more prominent at rest)
- Postural instability (tendency to fall, usually when pivoting)

NON-MOTOR SYMPTOMS

- Mood changes (depression, anxiety, irritability)
- Cognitive changes (memory problems, personality changes, psychosis/hallucinations)
- Orthostatic hypotension (lightheadedness and low blood pressure when standing)
- Constipation and early satiety (a feeling of fullness after eating small amounts)
- Hyperhidrosis (excessive sweating)
- Seborrhea (oily skin)
- Urinary urgency and incontinence
- Sexual dysfunction
- Loss of sense of smell
- Sleep disorders
- Insomnia, excessive daytime sleepiness (EDS), rapid eye movement behavioral disorder (RBD) or active dreaming, dream enactment, involuntary movements and vocalizations during sleep, restless leg syndrome (RLS)/periodic limb movement disorder (PLMD)
- Fatigue
- Sensory problems (pain, tightness, tingling, burning)

MIXED MOTOR AND NON-MOTOR SYMPTOMS

- Drooling due to slowed swallowing (sialorrhea)
- Speech and swallowing problems

Much clinical research is being conducted to try to recognize early features of Parkinson's disease. Motor symptoms typically begin on one side of the body, often as a rest tremor or a reduced ability to use the hand, arm or leg on the affected side. Prior to the appearance of the motor features of PD, individuals may also recognize that they have experienced constipation, vivid dreams, depression and/or diminished sense of smell for months or even years. These "pre-motor" symptoms may provide the opportunity for earliest recognition of the PD complex, with more clinical trials and earlier treatment strategies on the horizon.

PATHOLOGY

Parkinson's disease is a result of the loss of specific types of brain cells (neurons) that produce a chemical called dopamine. The motor symptoms come from the slow and progressive degeneration and death of these neurons in an area of the brain called the substantia nigra, which is in the brain stem. One reason these brain cells begin to die may be due to genetic abnormalities. The earliest symptoms of PD usually don't appear for several years after the onset of neurodegeneration because there is plenty of dopamine left in reserve to compensate for the declining supply.

In other words, a person will lose at least 50% of the dopamine in his or her brain before noticing that something is wrong with his or her body. We now also know that the non-motor features of PD arise from the loss of neurons in areas of the brain outside of the substantia nigra and involve chemicals other than dopamine, particularly acetylcholine. In 2011, a computerized brain scan utilizing a radio-isotope that labels the molecule transporting dopamine into the cell (DaTscan) first became available in the United States. A DaTscan may be used to assist with the clinical diagnosis of PD and other parkinsonian syndromes when the patient's presenting symptoms are not straightforward.

TREATMENT

It is important for persons with PD to realize that although the underlying disease progresses slowly, the clinical course over many years varies greatly with each person. Effective management of PD symptoms requires an experienced and compassionate healthcare provider, the person with PD and his or her care partner to determine a treatment plan consisting of appropriate medications, regular exercise, a healthy diet, social engagement and cognitive activities, counseling and other therapies. As the disease progresses and problems accumulate, deep brain stimulation (DBS) surgery may be a reasonable therapeutic option for some individuals, although many people with PD do not qualify for DBS for a variety of reasons. However, the majority of people with PD can lead full and active lives with good symptom control for many years.

Chapter 2
Medications for Motor Symptoms

The following medications used to treat Parkinson's disease are discussed in this chapter:

- Levodopa
- Dopamine agonists
- MAO-B inhibitors
- COMT-inhibitors
- Amantadine
- Anticholinergics

The central objective of using any of the above medications is to control or manage motor symptoms. Since these symptoms are largely due to the diminishing supply of dopamine in the brain, most symptomatic medications are designed to replenish, mimic or enhance the effect of this chemical.

For quick reference, Table 2 provides a summary of the medications used to treat the primary motor symptoms of PD including typical dosages, side effects and indications. Detailed discussions of the medications follow.

Remember that medication usage is only a part of the whole treatment plan for effectively treating PD. Regular exercise, physical therapy, occupational therapy, speech therapy, holistic practices, nutritional consultation, support groups, education, psychological counseling, intelligent use of assistive devices and caregiver relief are all important aspects of the best treatment plan.

Pronunciation Key
(accented syllable in **bold**)

Levodopa	Lee-voe-**doe**-pa
Carbidopa	Car-bee-**doe**-pa
Ropinirole	Row-**pin**-er-ole
Pramipexole	Pram-i-**pex**-ole
Rotigotine	Row-**tig**-oh-teen
Apomorphine	Ae-poe-**more**-feen
Selegiline	Sell-**edge**-ah-leen
Rasagiline	Rah-**saj**-ah-leen

Table 2. Summary of Medications for Motor Symptoms in PD

Medication (product name in parentheses)	**Dosages in Milligrams (mg);** tablets unless other-wise noted	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Levodopa				
Carbidopa/ levodopa immediate-release (Sinemet)	10/100, 25/100, 25/250	150–1000 mg of levodopa total daily dose (divided 3-4 times)	Low blood pressure, nausea, confusion, dyskinesia	*Monotherapy or combination therapy* for slowness, stiffness and tremor
Carbidopa/ levodopa orally disintegrating (Parcopa)	10/100, 25/100, 25/250	150–1000 mg of levodopa total daily dose (divided 3-4 times)	Same as above	Same as above, plus need for dissolvable medication in mouth especially if swallowing is impaired
Carbidopa/ levodopa extended-release (Sinemet CR)	25/100, 50/200	150–1000 mg of levodopa in divided doses, depending on daily need	Same as above	*Monotherapy or combination therapy* for slowness, stiffness and tremor
Carbidopa/ levodopa/ entacapone (Stalevo) [see COMT-inhibitors below]	12.5/50/200, 18.75/75/200, 25/100/200, 31.25/125/200, 37.5/150/200, 50/200/200	150–1000 mg of levodopa total daily dose, depending on daily need	Same as above, plus diarrhea and discolored urine (due to entacapone)	*Replacement for carbidopa/ levodopa,* for motor fluctuations (benefit of entacapone)
Carbidopa/ levodopa extended-release capsules (Rytary)	23.75/95, 36.25/145, 48.75/195, 61.25/245	855-2340 mg of levodopa total daily dose	Same as above	*Monotherapy or adjunct therapy* for slowness, stiffness and tremor. **Note that dosages of Rytary are not interchangeable with other carbidopa/ levodopa products.**
Carbidopa/ levodopa enteral solution (Duopa)	*Clinician-determined*	Up to 2000 mg of levodopa over 16 hours	Same as above	For the treatment of motor fluctuations in patients with advanced Parkinson's disease
Dopamine Agonists				
Ropinirole (Requip)	0.25, 0.5, 1, 2, 3, 4, 5	9–24 mg total daily dose (divided 3–4 times)	Low blood pressure, nausea, leg swelling and discoloration, confusion, sleep attacks, compulsive behaviors	*Monotherapy or combination therapy* for slowness, stiffness and tremor
Ropinirole XL (Requip XL)	2, 4, 6, 8, 12,	8–24 mg once/day	Same as above	Same as above
Pramipexole (Mirapex)	0.125, 0.25, 0.5, 0.75, 1, 1.5	1.5–4.5 mg total daily dose (divided 3–4 times)	Same as above	Same as above
Pramipexole ER (Mirapex ER)	0.375, 0.75, 1.5, 2.25, 3, 3.75, 4.5	1.5–4.5 mg once/day	Same as above	Same as above
Rotigotine (Neupro)	1, 2, 3, 4, 6, 8 patch	4–8 mg once/day	Same as above	Same as above; patch delivery an advantage for some

Table 2, continued. Summary of Medications for Motor Symptoms in PD

Medication (product name in parentheses)	**Dosages in Milligrams (mg);** tablets unless other-wise noted	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Dopamine Agonists, cont.				
Apomorphine (Apokyn)	30 mg/3 ml vial	2–6 mg	Significant nausea; must take anti-nausea medication with dose, especially when starting therapy	*Adjunct therapy* for sudden wearing off; the only injectable, fast-acting dopaminergic drug
MAO-B Inhibitors				
Selegiline (l-deprenyl, Eldepryl)	5	5 mg once or twice a day	Nausea, dry mouth, light-headedness, constipation; may worsen dyskinesia; possible rare interaction with anti-depressants and other drug classes	*Monotherapy* for slowness, stiffness and tremor; *adjunct therapy* for motor fluctuations
Rasagiline (Azilect)	0.5, 1.0	1 mg once/day	Same as above	Same as above
Selegiline HCL orally disintegrating (Zelapar)	1.25, 2.5	1.25–2.5 mg once/day	Same as above	Same as above, plus need for dissolvable medication in mouth (absorbed in mouth)
COMT-Inhibitors				
Entacapone (Comtan)	200	200 mg 4–8 times daily (with each levodopa dose)	Diarrhea, discolored urine, plus enhancing side effects of levodopa, especially dyskinesia and confusion	*Combination therapy with levodopa* for motor fluctuations (not pharmacologically active by itself)
Tolcapone (Tasmar)	100, 200	100 mg up to 3 times daily	Same as above plus increased risk of liver inflammation	Same as above (second-line due to side effects)
Other Antiparkinson Medications				
Amantadine (Symmetrel)	100 mg capsules; 50mg/5ml syrup	100 mg 2–3 times daily	Nausea, confusion, leg discoloration (livido reticularis), mild anti-cholinergic effects (see below)	*Monotherapy* for slowness, stiffness, and tremor; *combination therapy* with levodopa for levodopa-induced motor fluctuations; especially helpful for suppressing dyskinesia
Anticholinergics				
Trihexyphenidyl (formerly Artane)	2, 5 mg tablets; 2 mg/5 ml elixir	1–2 mg 2 or 3 times daily	Confusion, memory issues, hallucinations, dry mouth, blurry vision, urinary retention	*Monotherapy or combination therapy*, predominantly for tremor in younger people; should be avoided in elderly
Benztropine (Cogentin)	0.5, 1, 2	0.5–2 mg 2 or 3 times daily	Same as above	Same as above

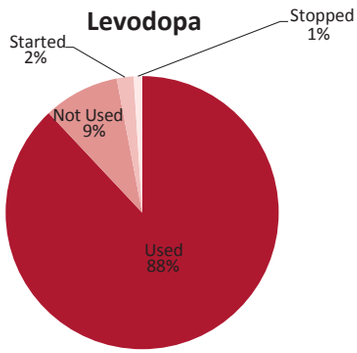
Key: *monotherapy* = medication used alone
combination or adjunct therapy = medication added to other medications

* "TYPICAL TREATMENT REGIMENS" SHOULD ACT ONLY AS A GUIDE. THE DOSAGE PRESCRIBED BY YOUR DOCTOR AND YOUR EFFECTIVE DOSE MAY VARY FROM DOSAGES LISTED.

LEVODOPA

Scientific investigators in the 1950s discovered that experimental depletion of dopamine in the brains of mice caused a condition that resembled Parkinson's disease in humans and that dopamine replacement abolished those symptoms. As they continued to explore ways to translate these observations to the human condition, their efforts led ultimately to the successful development of levodopa in the late 1960s.

Levodopa was the first medication proven effective for treating a chronic degenerative neurologic disease. Levodopa in pill form is absorbed into the blood stream from the small intestine and travels through the blood to the brain, where it is converted into the active neurotransmitter dopamine. Unconverted levodopa has no impact on Parkinson's symptoms. Dopamine cannot be given to treat PD because its chemical structure will not allow it to cross the "blood-brain barrier," a physiologic screen that protects the brain by keeping out drugs and other chemicals that might be harmful.



The *Parkinson's Outcomes Project* is the largest clinical study of Parkinson's in the world. As of May 2015, more than 19,000 evaluations had taken place on almost 8,000 people with Parkinson's. This chart shows the percentage of people using and not using levodopa at each of those 19,000+ visits. At 2% of the visits, doctors started a patient on levodopa. At 1% of visits, doctors took the patient off levodopa.

In the early days of levodopa therapy, large doses were required to relieve symptoms. As a result, nausea and vomiting were common. The solution to this inefficient delivery of the drug was the development of carbidopa, a levodopa enhancer. When added to levodopa, carbidopa enables an 80% reduction in the dose of levodopa for the same benefit and a marked reduction in the frequency of side effects.

Carbidopa/levodopa is marketed as Sinemet in the United States. In fact, the name says it all: "sin" "emet" roughly translates from "without" "vomiting" in Latin. This is a vast improvement upon levodopa alone, though nausea can be one of the more common side effects of carbidopa/levodopa. The generic product is intended to be chemically identical to the name brand and, for most people, is just as effective. The bioavailability of generic medication in the body may vary by 20% (20% more or 20% less available) compared to the original branded drug. If you observe a difference in your response to medication immediately after switching from name brand to generic, or between two different generics, speak with your physician about ways to optimize your medication.

KEY POINT: Forty years after it was first introduced, levodopa is still the most effective medication available for treatment of the motor symptoms of PD.

Carbidopa/levodopa greatly reduces PD symptoms in the majority of persons with a clinical diagnosis of PD, although the tremor response may lag behind the response of the other symptoms. Facial expression, posture, speech and handwriting may also improve. Levodopa's half-life — a measure of how long a drug stays in the bloodstream before being metabolized by the body's tissues — is relatively short, about 60-90 minutes. This results in fluctuations of blood and brain levels of dopamine and is responsible for the motor fluctuations that people with PD experience after long-term levodopa use.

A controlled release formulation (Sinemet CR) was originally designed to provide extended benefits of the same dosing of carbidopa/levodopa and possibly decrease the number of pills needed per day. The CR pill is absorbed more slowly than regular carbidopa/levodopa. Advantages may be seen for some patients needing longer responses or overnight dosing. But, for other patients, this may be less desirable as there may be a delay in effect and only about 70% of the effective levodopa is usually absorbed before the pills pass through the intestinal tract.

A new formulation of longer acting carbidopa/levodopa was approved by the FDA in January 2015. Carbidopa/levodopa extended release (ER) capsules (Rytary) contain beads of carbidopa and levodopa that dissolve and are absorbed at different rates. Therapeutic levodopa levels are reached about an hour after taking it, similar to carbidopa/levodopa immediate release (IR). These plasma levodopa concentrations are maintained for 4-5 hours before declining. Clinical trials indicate that patients with motor fluctuations on other oral carbidopa/levodopa products may be able to switch to carbidopa/levodopa ER and experience a reduction in "off" time while requiring fewer medication administrations. Dosages of carbidopa/levodopa ER are not interchangeable with dosages of other carbidopa/levodopa products. For prescribing and dosing information to share with your doctor, visit **www.parkinson.org/rytary**.

Carbidopa/levodopa ER can be taken with or without food. Interestingly, high fat meals delay absorption and reduce the amount absorbed, but can potentially lengthen the duration of benefit. People who have difficulty swallowing intact capsules can carefully open the Rytary capsule and sprinkle the entire contents on a small amount of applesauce (1 to 2 tablespoons), and consume it immediately.

Another formulation, the orally-disintegrating carbidopa/levodopa, Parcopa, is also useful for people who have difficulty swallowing or who don't have a liquid handy to wash down a dose of medication.

The most common side effects of carbidopa/levodopa are:

- Nausea
- Vomiting
- Loss of appetite
- Lightheadedness
- Lowered blood pressure
- Confusion

Such side effects can be minimized with a low starting dose when initiating treatment with any antiparkinson drug and increasing the dose slowly to a satisfactory level. This is particularly helpful in elderly people with PD whose tolerance for medications is often less than in younger persons. Taking drugs with meals can also reduce the frequency and intensity of gastrointestinal side effects. For those patients who have persistent problems, adding extra carbidopa (Lodosyn) to each dose of carbidopa/levodopa can help.

Carbidopa/levodopa is absorbed into the bloodstream through similar channels that transport amino acids, the building blocks of proteins. As a result, some patients experience less benefit if they take their carbidopa/levodopa with a stomach full of protein like meats, cheeses and other dairy products. For improved medication absorption, one can take carbidopa/levodopa one hour before a protein-rich meal or two hours afterwards. After several years of using carbidopa/levodopa and the development of motor fluctuations, many people with PD notice that the onset of benefit from a dose of levodopa is quicker when the drug is taken on an empty stomach. Fortunately, most patients should have no problem with feeling "on" even if they take their medication with a meal.

KEY POINT: After several years of a smooth response to levodopa, many people with PD notice the appearance of motor fluctuations ("wearing-off") and involuntary movements (dyskinesia). These complications can usually be managed by adjusting the amount of drug and the timing of the doses.

The chemical composition of carbidopa/levodopa prevents the drug from dissolving completely in water or other liquid, but a liquid can be prepared for use in certain unusual situations (see Appendix C).

1) If the person with PD feels full after eating small amounts and carbidopa/levodopa pills are slow to pass through the stomach to the small intestine where they are absorbed into the bloodstream, liquid Sinemet might be absorbed faster.
2) A smaller fraction of a levodopa dose can be given with the liquid formula than with the available tablet formulations, allowing for very careful adjustments in the person with PD who is experiencing dyskinesia and "wearing-off" on standard amounts of medication.

A commercially available product has been developed with this strategy in mind. Carbidopa/levodopa enteral solution, or Duopa, marketed as Duodopa outside the United States, combines carbidopa/levodopa in a gel that is slowly and consistently pumped through a tube inserted surgically through the stomach into the intestine. This provides a smooth absorption of the medicine and can cut down on motor fluctuations and dyskinesia.

One of the major drawbacks to the pump approach is the need for a percutaneous gastrojejunostomy (a small feeding tube). These types of tubes can be the starting locations for infections and other complications. Below you will find information every patient interested in the pump should be familiar with. For more information on Duopa, including information on support services, visit www.duopa.com.

- The current version of the pump requires wearing an external device.
- The pump requires changing a dopamine cassette once or twice a day. The cassettes are a little smaller than a cellular phone, and usually last about 14-16 hours.
- Even with the pump, some patients will need additional medications during the bedtime hours.
- The pump requires continuous maintenance and programming by a qualified professional.

- The tube connected to the stomach requires constant monitoring for infection and/or inflammation.
- Many patients and family members in the clinical trials for the dopamine pump commented that the pump required a lot of care and that an active caregiver may be critical for the success of the therapy.
- There is a need to compare pump effectiveness against deep brain stimulation therapy (DBS). Understanding which patients are appropriate for each technique will be important. This is currently not clearly delineated and will require a detailed discussion with the neurologist or expert clinician.
- It remains unknown if patients with dementia are viable candidates for the pump.
- Pumps are powerful symptomatic therapies, but not cures.
- The continuous infusion pump will not address the dopamine-resistant symptoms of walking, talking and thinking.
- Pumps have not been shown to delay disease progression, and they are not a cure.

Recent research underscores the safety of levodopa use for persons with PD. While there has been occasional concern about levodopa accelerating disease progression or producing toxicity, a post-mortem study of human brains, conducted in London in 2011, concluded that chronic use of levodopa did not lead to disease progression in human beings with PD. Multiple studies across many countries, including the ELLDOPA study, confirm that levodopa is extremely beneficial to the human patient, and that levodopa has had a positive effect on disease course. Expert practitioners in the Parkinson's Foundation's *Parkinson's Outcomes Project* report utilizing levodopa more than any other drug for Parkinson's therapy, and they used levodopa more (not less) as disease durations increased.

People with PD who use levodopa long-term may experience dyskinesia at some point, usually three to five years after starting the medication. The term dyskinesia describes involuntary, erratic, writhing movements of the face, arms, legs and/or trunk. These usually occur one to two hours after a dose of levodopa has been absorbed into the bloodstream and is having its peak clinical effect. Dyskinesia tends to be more severe as the dose of levodopa increases. They can be severe enough to interfere with a person's normal functioning and to cause discomfort if they can't be controlled. In advanced PD, when motor fluctuations are common, it is often difficult to produce the "on" response without dyskinesia. This makes it difficult to achieve the satisfactory benefit characteristic of the smooth "on" response that is typical of the levodopa response early in the course of the illness.

Patients should be reassured that the likelihood of developing dyskinesia remains low early in the disease, and – if it occurs – is usually quite mild. Most people with PD prefer to tolerate some dyskinesia in order to derive the benefits of levodopa. This is considered a reasonable tradeoff for getting the best "on" time. The ideal strategies for management of dyskinesia and the associated phenomenon of "wearing-off" are detailed below in discussing the adjunctive therapies to levodopa (dopamine agonists, MAO-B inhibitors, COMT-inhibitors, Amantadine and DBS).

In 1988, the FDA recommended that the daily dose of Sinemet not exceed 800 mg per day, and as of August 2013, this recommendation has not been revised. As movement disorder specialists, general neurologists and primary care doctors have learned, patients often require doses of Sinemet that exceed 800 mg/day and can easily tolerate the higher doses used to minimize symptoms. Some patients encounter problems with insurance reimbursement of higher daily doses because of the FDA regulation. An insurance decision can be appealed if necessary, and reference made to the following paper, published online in *BMJ* in 2012, which addresses the 800 mg threshold: "Carbidopa/levodopa dose elevation and safety concerns in Parkinson's patients: a cross-sectional and cohort design" by Brodell DW, Stanford NT, Jacobson CE, Schmidt P, Okun MS.

DOPAMINE AGONISTS

A dopamine agonist (DA) is a chemical that has been manufactured to act similarly to dopamine – that is, it attaches to the same cells in the brain known as receptors that dopamine activates to produce its clinical effect. Unlike levodopa, dopamine agonists are not converted into dopamine. Different dopamine agonists have been created that bind to different dopamine receptors with varying strengths. Historical and current DAs in the U.S. include:

- **Bromocriptine** (Parlodel)
- **Pergolide** (Permax)
- **Pramipexole** (Mirapex, Mirapex ER)
- **Ropinirole** (Requip, Requip XL)
- **Rotigotine** (Neupro patch)
- **Apomorphine** (Apokyn injection)

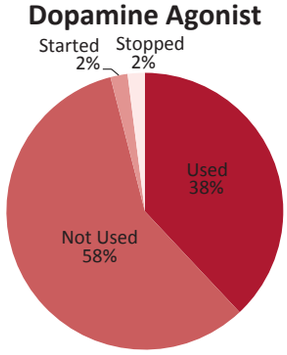
Generally DAs effectively improve the motor symptoms of PD, but they are less potent than levodopa. A DA can be used early in the course of PD as a single drug (monotherapy) or later in combination with carbidopa/levodopa (combination or adjunct therapy). Dopamine agonists have longer half-lives (longer duration of action) than levodopa and for that reason can be helpful in reducing the intensity of the "wearing-off" reaction or to generally enhance the effect of levodopa.

KEY POINT: Dopamine agonists can be used effectively as a single drug in early PD or in combination with carbidopa/levodopa later on.

The adverse effects of DAs are generally similar to those associated with the use of carbidopa/levodopa. However, certain side effects, such as excessive daytime sleepiness, visual hallucinations, confusion and swelling of the legs, occur more commonly with the use of dopamine agonists than with levodopa. Elderly people with PD are probably more likely than younger people to have troublesome adverse effects when using DAs. This may be partly due to a higher likelihood of other illnesses (also known as comorbidities) and the greater risk of undesirable interactions between Parkinson's drugs and drugs taken for other purposes. Dyskinesia can be seen with the use of DAs but less frequently than with levodopa therapy. In fact, clinical trials have shown that when combined with levodopa, treatment with a DA permits the use of a lower dose of levodopa and consequently a reduced probability that dyskinesia will occur.

One possible adverse effect of dopamine agonists is the occurrence of drug-induced compulsive behaviors, such as uncontrolled eating, shopping, gambling and sexual urges.

Patients may also engage in repetitive and relatively purposeless activities like organizing, sorting or collecting items. This is called punding. We collectively refer to these behaviors as impulse control disorders (ICDs). The underlying physiology is likely related to over-stimulation of dopamine receptors in the part of the brain responsible for instant gratification.



The *Parkinson's Outcomes Project* is the largest clinical study of Parkinson's in the world. This chart shows the percentage of people using and not using dopamine agonists at each of the more than 19,000 visits tracked in the study as of May 2015. At 2% of the visits, doctors started a patient on DAs. At 2% of visits, doctors took the patient off DAs.

Frequency surveys have shown that these abnormal behaviors are more common with dopamine agonists but can also be seen with carbidopa/levodopa. The DOMINION study published in 2010 was designed to look at the association between ICDs and dopamine replacement therapy – both dopamine agonists and levodopa. Over 3,000 patients participated in the study to quantify the four major ICDs listed above. Nearly 14% of PD patients in the study exhibited an ICD, and these were two or three times more common in patients receiving dopamine agonist therapy compared to those who were not taking agonists. Those at greatest risk include patients with a family history of gambling and those who are younger, unmarried, and/or cigarette smokers. A more recent study of baseline ICD in untreated PD patients using a newer questionnaire revealed nearly 20% of patients demonstrate some impulsivity, but this was actually no different than healthy participants without PD. Additional study will likely provide more insight into the true risk associated with the addition of these dopaminergic medications, as the newer questionnaire may be more likely to pick up such behaviors. Until more information is available to clarify this issue, people with PD should be aware of the risks before using dopamine agonists, and clinicians prescribing dopamine agonists should monitor for behavioral disorders. Remember also that the people suffering from impulse control issues may not have insight into the behavioral problems, and this lack of insight underscores the importance of involving caregivers in any proactive monitoring plan.

KEY POINT: Be aware of possible compulsive behaviors (shopping, gambling, eating, hypersexuality) related to treatment with dopamine agonists, and be sure to contact your healthcare provider if these occur.

Bromocriptine (Parlodel) and **Pergolide** (Permax) were developed in the 1970s, and both of these dopamine agonists (DAs) were derived from a plant (fungus) called ergot. When it was confirmed that pergolide can cause heart valve abnormalities in a significant minority of users, the FDA determined that the risk of using pergolide outweighed the benefit, and removed it from the U.S. market for use in PD in March 2007. Bromocriptine, the first of the DAs to become commercially successful, is still available for other medical uses; it is not used in PD.

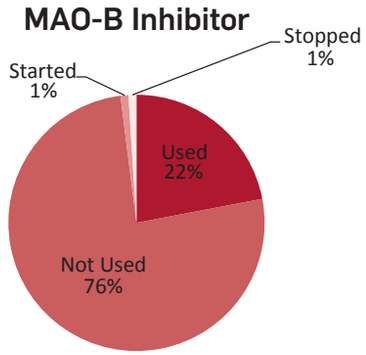
Pramipexole (Mirapex) and **Ropinirole** (Requip) were approved by the FDA in 1997 and are currently the most commonly used DAs. Neither of these dopamine agonists is ergot-derived, nor have they been associated with abnormalities of the heart valves. They are both effective in the early treatment of the motor symptoms of PD and play an important role in controlling motor fluctuations despite the greater occurrence of side effects compared with levodopa.

Rotigotine (Neupro), the newest dopamine agonist, was approved by the FDA in 2007 and is formulated for use as a once-daily transdermal (skin) patch that is changed every 24 hours. Clinical trials have shown that it is just as effective as the oral DAs pramipexole and ropinirole. The side effects are similar, with the addition of usually mild local skin irritation under the patch in up to 40% of patients. Most people with PD have been able to tolerate the patch by rotating the sites where they adhere the patch on their bodies. Fewer than 5% of those studied in the clinical trials discontinued its use due to skin irritation. The initial formulation of the patch was removed from the market worldwide in 2008 because of technical problems with the delivery system. The original patches had a tendency to show a crystallized substance on their surface after they were stored in pharmacies and in patient medicine cabinets for weeks. Neupro was redesigned and returned in 2012 with dosing available in 1, 2, 3, 4, 6 and 8 mg daily.

Apomorphine (Apokyn) was first used to treat PD in 1950, but its use was associated with many side effects, especially nausea and vomiting. It was resurrected in the 1990s in a more tolerable formulation and has found a particular niche as a self-injectable "rescue" drug for people with advanced PD and severe "off" episodes. Its short half-life (average 40 minutes) and chemical structure make it difficult, if not impossible, to take by mouth. In the person affected by severe "off" reactions, during which disabling bradykinesia and rigidity interfere with function, a self-injected dose of Apokyn can reverse the "off" period within minutes and bridge the gap of one to two hours until the next dose of levodopa takes effect. An anti-nausea medication (usually trimethobenzamide or Tigan) is required prior to injection in the early phase of treatment but can be discontinued after the first week or two. Apokyn can be used as many as five times per day as a rescue agent. Each individual's response to Apokyn is different.

MAO-B INHIBITORS

Monoamine Oxidase Type B (MAO-B) is an enzyme in our body that naturally breaks down several chemicals in the brain, including dopamine. By giving a medication that blocks the effect of MAO-B (an MAO-B inhibitor), more dopamine is available to be used by the brain. Thus, all the motor symptoms of PD can be modestly improved.



This chart shows the percentage of people in the *Parkinson's Outcomes Project* (the largest clinical study of Parkinson's in the world) using and not using MAO-B Inhibitors. Out of 19,000+ visits tracked in the study (almost 8,000 patients), doctors started a patient on MAO-B inhibitors at 1% of visits and took a patient off MAO-B inhibitors at 1% of visits.

In addition, it was suggested in animal trials that MAO-B inhibitors might actually slow the progression of PD, offering neuroprotection. This was first tested in humans in the late 1980s in a clinical trial of the MAO-B inhibitor l-deprenyl, now sold under the name selegiline (Eldepryl). The goal of the study was to determine if selegiline (compared to Vitamin E and a placebo) could delay the need for levodopa as PD symptoms worsened over time. Selegiline was shown to delay the need for levodopa by nine months, suggesting neuroprotection, but this benefit may simply have been from the antiparkinson symptom effect of selegiline. Of note, Vitamin E had no benefit in the clinical trial.

As MAO-B inhibitors do provide modest benefit for the motor features of PD, they are usually used as early monotherapy or as an adjunct (add-on) to other medications, including levodopa. When used in combination with other medications, MAO-B inhibitors may reduce "off" time and extend "on" time.

KEY POINT: MAO-B inhibitors are used by themselves for modest symptom control in early PD or in combination with other medications to reduce "off" time and extend "on" time.

Selegiline is available in two formulations: standard oral (Eldepryl, l-deprenyl) and orally-disintegrating (Zelapar). Both oral and orally-disintegrating selegiline are taken once daily. Standard oral selegiline is converted to an amphetamine like by-product which may contribute to side effects of jitteriness and confusion. Conversely, Zelapar is dissolved in the mouth and absorbed directly into the bloodstream (no byproduct) without these side effects. Because of Zelapar's absorption in the mouth, it may be preferred for convenience or out of necessity for the person who has difficulty swallowing.

Rasagiline (Azilect), the newest MAO-B inhibitor, is structurally different from selegiline and does not have an amphetamine-like byproduct that can cause jitteriness. Taken once each day, rasagiline came to the U.S. market in late 2006. Clinical trials of Azilect as monotherapy or adjunctive therapy showed mild but definite efficacy, and there was also an unproven hint of slowing disease progression. A worldwide, multi-institutional clinical trial of rasagiline's potential for neuroprotection was published in 2008 and follow-up data from the original studies has also been examined closely. These results suggest that the use of rasagiline earlier in PD may offer the greatest long-term advantage and modify the symptomatology over time, although true disease modification remains unproven. Even with this new data, the FDA indication for rasagiline remains for early monotherapy and later add-on therapy.

The most common side effects of MAO-B inhibitors include mild nausea, dry mouth, lightheadedness and constipation. It is usually well-tolerated even in the more aged patient. Special mention should be made of a unique and rare adverse effect of the MAO-B inhibitors called the "wine and cheese effect." Taking MAO-B inhibitors with the heavy consumption of aged cheeses or wines high in tyramine may theoretically raise blood pressure to dangerous levels. Also, pharmacists routinely warn patients about interactions with other drugs, especially the antidepressants, when they start an MAO-B inhibitor, but the occurrence of an adverse reaction in this setting remains very rare (this side effect is usually from MAO-A inhibitors and not MAO-B inhibitors). A study was published in 2011 that fortunately found no cases of dangerous blood pressure shifts in

over 2000 patients taking rasagiline in combination with many of the anti-depressant medications on the market today. Still, it is appropriate for any person with PD to review all medications and possible adverse interactions with their treating physician before starting anything new.

COMT-INHIBITORS

Catechol-O-methyl transferase (COMT) is an enzyme that inactivates levodopa in the body before it is transported in the bloodstream to the brain. Two drugs that block this enzyme, thereby making levodopa more available to the brain, have been approved by the FDA for treating PD. The COMT-blocking drugs or inhibitors extend the clinical benefit of levodopa, reducing "off" time and lengthening "on" time. COMT-inhibitors are generally well-tolerated, though they may exaggerate some levodopa-related side effects, particularly dyskinesia. Additional side effects include confusion, hallucinations, discoloration of urine (reddish-brown or rust-colored) and diarrhea.

KEY POINT: COMT-inhibitors extend the benefit of levodopa by reducing "off" symptoms between doses. Without levodopa, COMT-inhibitors have no effect on Parkinson's symptoms.

Entacapone (Comtan) and **Tolcapone** (Tasmar) are the two COMT-inhibitors approved by the FDA to treat PD. Entacapone is prescribed with each dose of levodopa, whereas tolcapone is taken three times a day, no matter how many doses of levodopa are prescribed. COMT-inhibitors without levodopa have no effect on Parkinson's symptoms. There is no potential benefit to be gained from taking Entacapone or Tolcapone to try to extend the life of other PD medications. Tolcapone was removed from the American market in the early 2000s because of a few instances of liver toxicity in people who used it. During clinical trials before FDA approval in 1999, transient, mild abnormalities of liver function tests were documented in 1-2% of patients and were considered to be inconsequential. Tolcapone is currently available with the condition that blood tests of liver function be conducted every two to four weeks for the first six months after beginning treatment, then periodically thereafter.

Carbidopa/levodopa/entacapone (Stalevo) is a combination drug useful in people with advanced PD who experience motor fluctuations. It works by providing relief for the motor symptoms as well as reducing "off" time. By combining the two drugs into one tablet, the manufacturer has made pill-taking a little more convenient compared with carbidopa/levodopa + entacapone taken separately. In addition, there are more dosing options (see table) to better tailor the medication needs to an individual patient. In 2012 this combination pill entered the generic market in the U.S.

AMANTADINE

Amantadine (Symmetrel) was created as an anti-influenza medication in the 1960s, but its benefit in PD was first described in 1969, when astute observers noticed, quite by accident, that people with PD who took Amantadine to prevent influenza had much better control over tremor. Amantadine often provides immediate benefit for most PD motor symptoms, but its effect frequently wanes after a few weeks or months. It is unique, however, in that it can also reduce levodopa-induced dyskinesia.

Amantadine has become a useful adjunctive medication in people with advanced PD and motor fluctuations. Its mechanisms of action are not fully known, but it is likely that it interacts with multiple receptors at various sites in the brain to achieve its positive effect. Amantadine is cleared from the body by the kidneys, so a person with kidney problems may require a lower dose.

KEY POINT: Amantadine may be particularly beneficial in people with PD who have prominent tremor or bothersome levodopa-induced dyskinesia.

Amantadine is most commonly available as a 100 mg capsule, although liquid and tablet forms can also be obtained. If the person with PD requires lower doses or has difficulty swallowing, the liquid or tablet formulations would be preferred.

The most frequent side effects of Amantadine are nausea, dry mouth, lightheadedness, insomnia, confusion and hallucinations. Urinary retention is another, rare, side effect. In less than 1% of people with PD who take this medication, another side effect is a mottled, lacey, reddish-purple discoloration of the skin, usually on the legs and with some accompanying leg swelling, known as **livedo reticularis.** Stopping the drug will resolve this adverse effect, although if the drug is providing good benefit there is no harm in continuing it.

ANTICHOLINERGICS

The earliest medications used in PD were those that blocked brain receptors for acetylcholine, called anticholinergics. It is believed that acetylcholine and dopamine maintain a delicate equilibrium in the normal brain, which is upset by the depletion of dopamine and the degeneration of dopamine-producing cells. Drugs that block the effect of acetylcholine have the potential for restoring the normal balance of these two chemicals, thereby reducing the symptoms of PD.

The anticholinergics can provide modest benefit for the motor symptoms of PD, but they can also cause significant mental and physical side effects. Confusion, hallucinations, decreased short-term memory, dry mouth, blurry vision and urinary retention are potential side effects, particularly in the older person with PD. As such, these medications are typically utilized in younger people. Experience has shown that the anticholinergics work best against tremor.

Additionally, research from the Parkinson's Foundation's *Parkinson's Outcomes Project* has supported the finding that cognitive slowing is a side effect of anticholinergics.

KEY POINT: Anticholinergics are most useful in young people with tremor-predominant PD, though side effects may limit their usefulness.

Trihexyphenidyl (formerly available as Artane) and **Benztropine** (Cogentin) are the two most common anticholinergics prescribed in PD. Dosing is usually two to three times a day. The common antihistamine and sleeping agent diphenhydramine (Benadryl) also has anti-tremor properties.

Ethopropazine, an anticholinergic and an antihistamine, may have fewer side effects but is not available in most U.S. pharmacies.

Chapter 3
Medications for Non-Motor Symptoms

The following non-motor symptoms and their treatments are discussed in this chapter:

- Disorders of mind and mood
  - Depression
  - Anxiety
  - Impaired thinking and dementia
  - Hallucinations and psychosis
- Sleep disorders
- Orthostasis (low blood pressure upon standing)
- Gastrointestinal symptoms: nausea, constipation, early satiety
- Drooling
- Urinary symptoms
- Sexual dysfunction
- Seborrheic dermatitis and excessive sweating
- Pain

There is ever-growing recognition of the importance of "non-motor" symptoms of PD, which were identified as early as 1817 by James Parkinson in his essay. Although he didn't differentiate motor from non-motor symptoms, he observed that his patients experienced symptoms of fatigue, confusion, sleep disturbances, constipation, drooling and disturbances of speech and swallowing. Speech, swallowing and drooling are included among non-motor symptoms although the root cause is in part motor: decreased coordination of the muscles of the mouth and throat.

KEY POINT: Non-motor symptoms may cause more disability for the person with PD than the classic motor features. Make sure your healthcare provider is aware of any non-motor symptoms you are experiencing!

Non-motor symptoms are very common in PD. In one recent study, 90% of people with PD reported experiencing at least one of the non-motor symptoms listed in Table 1. Unfortunately, it has also been shown that physicians and healthcare team members do not recognize these symptoms in their patients up to 50% of the time. Just as physicians assess complaints of slowness, stiffness or tremor, they should also address issues related to sleep, memory, mood, etc. People with PD are encouraged to be proactive in discussing these issues with their doctor. Don't wait to be asked!

DISORDERS OF MIND AND MOOD

The *Parkinson's Outcomes Project* was initiated in 2009 as a large, multicenter study partnering with many of the Parkinson's Foundations Centers of Excellence. This research collaborative is helping to define the symptoms and treatments that have the greatest impact on PD patients and their quality of life. One of the first findings of the project is that, collectively, mood and anxiety exact the greatest toll on health status, causing even more burden than the well-recognized motor symptoms of slowness, stiffness and tremor.

A Parkinson's Foundation book specifically designed to address these issues, titled ***Mood: A Mind Guide to Parkinson's***, is a comprehensive resource available online or in print. To request a free print copy, call our Helpline at 1-800-4PD-INFO (473-4636); online, go to **www.parkinson.org /books**. What follows is a brief summary of some important features of mind and mood disorders in PD with emphasis on the medications used for treatment.

Depression

Depression is a common but under-recognized symptom, affecting up to 50% of people with PD at some point during the course of the disease, often in its earliest stages. The definitive cause is not completely understood but it is likely related to an imbalance of chemicals in the brain (including dopamine, serotonin and norepinephrine). Some people who report depression related to their disability improve with adequate treatment of the most bothersome motor symptoms. However, many others require more aggressive management with psychotherapy and antidepressants.

KEY POINT: Depression is very common in PD, affecting up to 50% of people with PD at some point during the course of their illness. Recognition and treatment are important.

Along with "feeling blue," symptoms of depression may include:

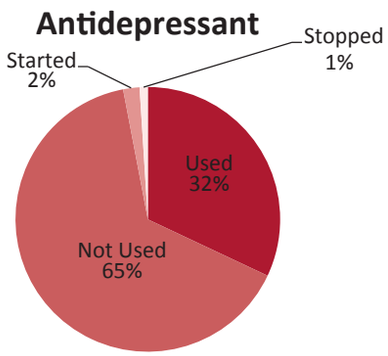
- Insomnia or excessive sleeping
- Loss of interest or pleasure in social or recreational activities
- Sexual dysfunction
- Feelings of guilt and self-pity
- Loss or reduction of energy levels
- Diminished attention and concentration
- Loss or gain of appetite and weight
- Thoughts of death or suicide

Antidepressants

Numerous medications are now available to treat depression in PD. Several trials have been published comparing one or more antidepressants to placebo. As detailed below, several different classes of medication may be helpful.

Most persons with PD who are experiencing depression are treated with one of several common categories of antidepressants including the selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and other similar neurotransmitter reuptake inhibitors. A recent large clinical trial published in 2012

confirmed the benefits of SSRIs and SNRIs for many PD patients. Occasionally, older tricyclic antidepressants (TCAs) are used, and another trial in 2009 noted the benefits of this class of medication for depression in PD. But TCAs tend to cause more side effects than the SSRIs, including confusion, forgetfulness, hallucinations, lightheadedness, blurry vision, urinary retention and dry mouth. SSRIs are generally better tolerated by people with PD, though loss of libido is a relatively common adverse effect, and recent research suggests that QTc prolongation (a potentially serious irregular heartbeat) can occur with certain SSRIs. The antidepressants buproprion and mirtazapine are notable for their lack of sexual side effects. There is preliminary evidence from a clinical trial published in 2010 that dopamine agonists have antidepressant properties in PD patients, and a controlled study of cognitive-behavioral therapy in 2011 for depression in PD was also positive.



The Parkinson's Outcomes Project is the largest clinical study of Parkinson's in the world. As of May 2015, more than 19,000 evaluations had taken place on almost 8,000 people with Parkinson's. This chart shows the percentage of people using and not using antidepressants at each of those 19,000+ visits. At 2% of the visits, doctors started a patient on antidepressants. At 1% of visits, doctors took the patient off antidepressants.

Recognizing a medication's side effects can be used to the advantage of the person with PD. For example, more sedating medications may be appropriate for nighttime dosing in the PD person with insomnia. Or a TCA that causes dry mouth may help to reduce the severity of drooling. Table 3 reviews the antidepressants commonly used in treating people with PD.

While many individuals improve with antidepressants, the person with PD and his or her physician, psychologist, social worker and other healthcare team members should also recognize the value of psychotherapy in improving non-motor symptoms of PD. Psychotherapy can be offered in an individual or a group setting. Therapeutic exercise such as physical workouts, yoga, tai chi, massage and meditation also may help to improve mood in PD. Electroconvulsive therapy can be a consideration of last resort for people with severe depression who do not respond to drugs. It is effective and safe when managed by experts, and may also temporarily improve motor symptoms.

KEY POINT: The combination of psychotherapy, antidepressants and therapeutic physical and mental exercise offers the best approach to the treatment of depression in PD.

Anxiety

Often seen in combination with depression, anxiety can also appear early in the course of PD. People with PD may describe feelings of unease, jitteriness, worry and panic. Anxiety may also cause physical symptoms such as difficulty breathing or swallowing, heart fluttering, shaking and "cold sweats."

Feelings of anxiety can be related to motor features. For example, the appearance of tremor or freezing during an "off" period or during social situations may cause anxiety or embarrassment. This anxiety can worsen the intensity of the symptoms, creating a vicious cycle and possibly leading to a panic attack.

Along with specific feelings of anxiety as described above, persons with PD may also experience the following:

- Generalized anxiety involves features of excessive worry throughout most of the day without dramatic fluctuation.
- Obsessive-compulsive disorder refers to repetitive thoughts/ideas that cause anxiety (obsessions) and behaviors that relieve those feelings (compulsions).
- Social avoidance, which can be especially troubling to someone whose personality is normally outgoing, involves avoiding social situations and opportunities to interact with friends and others as a result of anxiety or embarrassment.

Both generalized anxiety and obsessive-compulsive disorder can become worse as a result of dopaminergic agents, particularly the dopamine agonists.

KEY POINT: Anxiety in PD may manifest as panic attacks, generalized anxiety, obsessive-compulsive disorder or social avoidance.

There are many options for treating anxiety in PD, including medications, traditional psychotherapy and cognitive behavior therapy (CBT). It is important for persons with PD to inquire about the services of a psychologist, counselor, social worker and/or other appropriate members of the healthcare treatment team.

Levodopa optimization may improve anxiety in PD, and decreasing the intervals between levodopa doses may relieve the sense of anxiety that occurs as part of the "off" phase. Of course, adjusting your medication schedule should always be discussed with your physician.

SSRIs and related medications are commonly used for depression, but some of the SSRIs (listed in Table 3) may also improve anxiety. It may take several weeks of taking an SSRI for the person with PD to realize its full benefit. Buspirone (Buspar) is also particularly effective in treating generalized anxiety.

Benzodiazepines are a popular and effective class of anti-anxiety drugs that can be potent in reducing symptoms of panic and worry. At times they can even help to control tremor in anxious patients by reversing the negative effects of anxiety that can cause tremor to worsen. Each of the approved benzodiazepines has different practical advantages, including duration of action, so the appropriate medication should be chosen based on frequency and severity of symptoms. For example, longer-acting benefit may be achieved with clonazepam (Klonopin) or lorazepam (Ativan) than with alprazolam (Xanax).

Common side effects of benzodiazepines include drowsiness, confusion, lethargy and imbalance when walking. Persons with PD may develop a tolerance to the benzodiazepines over time, and discontinuation must be done gradually to avoid withdrawal symptoms.

A host of effective, non-pharmacologic techniques are readily available for treating anxiety including psychotherapy, behavior modification, biofeedback, meditation, massage, yoga, exercise, acupuncture and more.

Table 3. Summary of Medications for Depression and Anxiety in PD

Medication (product name in parenthesis)	**Dosages in Milligrams (mg);** tablets unless otherwise noted	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
REMEMBER TO DISCUSS THE RISKS OF COMBINED USAGE OF ANTI-DEPRESSANTS AND THE MAO-B INHIBITORS (SELEGILINE OR RASAGILINE) WITH YOUR DOCTOR				
Selective Serotonin Reuptake Inhibitors (SSRIs)				
Citalopram (Celexa)	10, 20, 40 mg tablets; 10 mg/2 ml solution	10–40 mg daily	Headache, nausea, insomnia, vivid dreams, sedation, jitteriness, diminished sexual libido, weight gain	*Depression*, anxiety/panic, obsessive – compulsive disorder (OCD)
Escitalopram (Lexapro)	5, 10, 20 mg tablets; 5 mg/5 ml solution	5–20 mg daily	Same as above but weight neutral	*Depression, anxiety*/panic, OCD
Fluoxetine (Prozac)	10, 20, 40, 90	10–40 mg daily	Same as above	*Depression*, anxiety/*panic*, *OCD*
Fluvoxamine (generic, Luvox CR)	25, 50, 100 CR 100, 150	25–100 mg daily/ nightly *(may be different for extended-release)*	Headache, nausea, insomnia, vivid dreams, sedation, jitteriness, diminished sexual libido, weight gain	Depression, anxiety/panic, *OCD*
Paroxetine (Paxil, Paxil CR, Pexeva)	10, 12.5, 20, 25, 30, 37.5, 40 mg tablets; 10 mg/5 ml suspension CR 12.5, 25, 37.5	10–40 mg daily *(may be different for extended-release)*	Same as above	*Depression, anxiety/panic, OCD*
Sertraline (Zoloft)	25, 50, 100 mg tablets; 20 mg/ml concentrate	25–100 mg daily	Headache, nausea, insomnia, vivid dreams, sedation, jitteriness, diminished sexual libido, weight gain	*Depression, anxiety/panic, OCD*
Vilazadone (Viibryd)	10, 20, 40	10–40 daily	Diarrhea, nausea, dizziness, dry mouth, insomnia, vomiting, vivid dreams	*Depression*, anxiety/panic, OCD

Table 3, continued. Summary of Medications for Depression and Anxiety in PD

Medication (product name in parenthesis)	**Dosages in Milligrams (mg);** tablets unless otherwise noted	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Serotonin/Norepinephrine Reputake Inhibitors (SNRIs)				
Desvenlafaxine (Pristiq)	50, 100	50 mg daily	Nausea, headache, insomnia, vivid dreams, sedation, jittery, dry mouth, constipation, diminished libido	*Depression*, anxiety
Duloxetine (Cymbalta)	20, 30, 60	10–30 mg twice a day	Same as above	*Depression, anxiety*
Milnacipran (Savella)	12.5, 25, 50, 100	50 mg twice a day	Same as above	Depression, anxiety
Nefazodone (Serzone)	50, 100, 150, 200, 250	25–100 mg twice a day	Same as above, plus requires monitoring for liver function	*Depression*, anxiety
Venlafaxine (Effexor, Effexor XR)	25, 37.5, 50, 75, 100, 150, 225 XR 37.5, 75, 150	25–75 mg twice a day *(may be different for extended-release)*	Nausea, headache, insomnia, vivid dreams, sedation, jittery, dry mouth, constipation, diminished libido	*Depression, anxiety*
Tricyclic and Related Compounds				
Amitryptiline (Elavil)	10, 25, 50, 75, 100, 150	10–50 mg nightly	Confusion, forgetfulness, hallucinations, light-headedness, blurry vision, urinary retention, dry mouth	*Depression*, anxiety
Imipramine (Tofranil, Tofranil PM)	10, 25, 50 PM 75, 100, 125, 150	10 –50 mg nightly; PM 100 mg max in elderly	Same as above	*Depression*, anxiety
Nortriptyline (Pamelor)	10, 25, 50, 75 mg capsules; 10 mg/5 ml solution	10–50 mg nightly	Same as above	*Depression*, anxiety
Trazodone (Desyrel, Oleptro) *also a serotonin modulator*	50, 150, 300	75–300 mg daily (divided)	Same as above	*Depression*, anxiety

Table 3, continued. Summary of Medications for Depression and Anxiety in PD

Medication (product name in parenthesis)	**Dosages in Milligrams (mg);** tablets unless otherwise noted	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Other Antidepressants				
Bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL, Budeprion SR, Budeprion XL, Zyban)	75, 100 SR 100, 150, 200 XL 150, 300	75–150 mg 1–2 times daily *(may be different for extended-release)*	Dry mouth, insomnia, headache, nausea, constipation, weight neutral, lack of sexual side effects, lowers seizure threshold	*Depression*
Mirtazapine (Remeron, Remeron SolTab)	7.5, 15, 30, 45 Regular or orally disintegrating tablets	15–30 mg daily	Drowsiness, increased appetite, headache, vivid dreams, lack of sexual side effects	Same as above. Also available in orally disintegrating form.
Benzodiazepines				
Alprazolam (Xanax, Xanax XR, Niravam)	0.25, 0.5, 1, 2, 3 mg tablets; 1 mg/ml solution XR 0.5, 1, 2, 3	0.25-1 mg 3–4 times daily *(may be different for extended-release)*	Drowsiness, light-headedness, depression, headache, confusion, dizziness, fatigue, constipation, blurred vision	*Anxiety/panic*. Also available in orally disintegrating form.
Clonazepam (Klonopin)	0.125, 0.25, 0.5, 1, 2	0.25–2 mg up to 3 times daily	Same as above	*Anxiety/panic*. Also available in orally disintegrating form.
Diazepam (Valium)	2, 5, 10 mg tablets; 5 mg/5 ml solution	1–5 mg up to 4 times daily	Same as above	*Anxiety/panic*
Lorazepam (Ativan)	0.5, 1, 2 mg tablets; 2 mg/ml concentrate	0.5–2 mg up to 3 times daily	Same as above	*Anxiety/panic*
Other Anti-Anxiety Medications				
Buspirone (BuSpar)	5, 7.5, 10, 15, 30	5–15 mg twice a day	Dizziness, drowsiness, dry mouth, nausea, headache	Generalized *anxiety* disorder
Propranolol (Inderal, Inderal LA, InnoPran XL)	10, 20, 40, 60, 80 mg tablets; 20 mg/5 ml & 40 mg/5 ml solution LA 60, 80, 120, 160 XL 80, 120	10–40 mg up to 3 times daily *(may be different for extended-release)*	Decreased heart rate, depression, exacerbation of pre-existing asthma	Anxiety/panic – can suppress outward signs (like racing heartbeat and shakiness)

* "Typical treatment regimens" should act only as a guide. The prescribed dosage by your doctor and your effective dose may vary from dosages listed.

Impaired Thinking and Dementia

Over time, more than 50% of persons with PD may experience some degree of impaired thinking. These alterations in thinking ability fall on a broad spectrum from mild cognitive impairment to severe dementia. Mild cognitive impairment occurring early in the course of illness may be a nuisance to the person with PD and his or her loved ones, especially if he or she is still working, but it usually will not affect routine activities of daily living. Progression to dementia is the greatest worry for many people with PD, as this usually implies a significant and perhaps permanent compromise in lifestyle and quality of life. While the majority of people with PD will develop some degree of cognitive impairment, many will not progress to severe disability.

People with PD may experience difficulty with:

- Speed of mental processing
- Attention/concentration — losing their train of thought in conversation
- Problem solving, decision-making, multi-tasking and planning
- Short-term memory
- Language production

In most cases, the impaired thinking associated with PD is not Alzheimer's disease, so the severity of the cognitive or thinking deficits and the effect of those deficits on day-to-day functioning are not as disabling.

Dementia in Parkinson's disease (PDD) occurs when the specific deficits in attention/concentration, problem-solving and memory are severe enough to interfere with the person's ability to function appropriately at work and/or in social situations. PDD is differentiated from other forms of dementia by additional distinguishing characteristics such as fluctuating awareness and attention span, visual hallucinations and altered spatial orientation. Fluctuating awareness refers to periods of mental clarity alternating with periods of confusion, distractibility, sleepiness and psychosis (usually visual hallucinations).

A closely related parkinsonian disorder — dementia with Lewy bodies (DLB) — is similar but different from PDD in important ways. The main difference in making the diagnosis is the timing of significant impairments in thinking in relation to the motor symptoms. If cognitive impairment begins before or within one year of the motor symptoms of PD, the diagnosis is DLB; if cognitive impairment follows the appearance of motor parkinsonian symptoms by more than one year, the diagnosis can be classified as PDD.

Evaluation for change in cognitive function in persons with PD should be part of a complete medical workup for other causes of impaired thinking, all of which may be treatable. If the change in thinking ability is sudden, severe, and accompanied by significant alteration in consciousness, an underlying cause separate from PD should be sought, such as infection (usually of lungs or bladder), vitamin depletion, dehydration, thyroid disease, intoxication by drugs, constipation, sleep deprivation or head injury (from tendency to fall).

A similar evaluation should be done if the change is more gradual and chronic, but the likelihood of finding a reversible cause of dementia is less than in the acute setting. Many of the anti-PD medications and other drugs (for example strong pain killers like narcotics) can cause confusion mimicking dementia, particularly as the person with PD ages. A careful

evaluation of current medications is always important, paying particular attention to the anticholinergics, amantadine and dopamine agonists.

Medications that may improve thinking ability in people with PD are available. Originally approved by the FDA for the treatment of memory disorder in Alzheimer's disease, one of these — rivastigmine or Exelon — is also approved for treating cognitive impairment in PD.

Acetylcholinesterase Inhibitors

Donepezil (Aricept), **rivastigmine** (Exelon) and **galantamine** (Razadyne) are the medications most frequently prescribed to address symptoms of cognitive impairment in PD. Originally approved by the FDA for the treatment of Alzheimer's disease, donepezil and rivastigmine have recently been shown to be well-tolerated and effective for some people with PD, though benefits are sporadic and modest. Rivastigmine was approved by the FDA in 2006 for treatment of dementia in PD. This group of drugs is usually well tolerated by persons with PD, although tremor can become more pronounced in some people.

Glutamate Antagonists

Memantine (Namenda) is approved for moderate-to-severe Alzheimer's disease in the U.S. It may help cognitive symptoms in PD by blocking the brain's receptors activated by the neurotransmitter glutamate. It is commonly used in combination with donepezil, although the results of treatment are often disappointing. Glutamate is a natural brain chemical essential for normal function but it can worsen some of the PD symptoms.

Other medications such as methylphenidate (Ritalin), a stimulant, and medications for excessive daytime sleepiness, such as modafinil (Provigil), are occasionally used for decreasing fatigue and improving alertness in PD. They are not specifically indicated for cognitive impairment.

Hallucinations and Psychosis

People with PD may experience visual hallucinations, illusions, delusions, agitation and other symptoms of psychosis. These are more commonly seen in patients who develop dementia in the late stages of disease.

- A *hallucination* occurs when a person believes he sees or hears something that isn't actually there.
- An *illusion* is a misperception or misleading view of reality – that is, a misperception of something that is actually there.
- A *delusion* is a form of self-deception in which the person develops a false belief despite strong evidence that the belief is false.

Visual hallucinations often involve scenes of people, animals or insects, while people with paranoid delusions may suspect that someone is plotting to do something harmful or that their spouse is unfaithful. Hallucinations are more common at the end of the day after sundown, when darkness can be disorienting, hence the term "sundowning." Fatigue after the day's activities can also cause collapse of a stable but fragile mental status.

Additionally, if the person with PD moves from a familiar to an unfamiliar environment, such as a hospital, vacation site or new home, the stress of geographical disorientation can sometimes lead to the emergence or reemergence of hallucinations, delusions and confusion. Fortunately, many people with PD retain insight and quickly realize that the

hallucination is not real and that their mind is "playing tricks" on them. Others react by becoming extremely troubled and frightened. The emergence of psychosis in the person with PD, in conjunction with fluctuating attention and personality, may signify the transition to Parkinson's disease with dementia (PDD).

Many people with PD also experience vivid dreams at night, which some experts believe may be "precursors" to hallucinations. Others never progress to having waking visions or delusional thoughts. Vivid dreams can be due to other sleep disorders, such as REM behavioral disorder (discussed later in this chapter).

Your healthcare team will want to assess and treat hallucinations and psychosis using the following guidelines:

1) Fully characterize the behavior. How frequent and severe are your hallucinations? Do they occur day and night? Do you retain insight during hallucinations? Does the problem pose a physical, emotional or financial threat to you or your family? Has your memory, personality and/or concentration been changing (implying worsening dementia in addition to the psychosis)?

2) Identify any other medical problems you are experiencing. Other medical problems could possibly trigger a decline in thinking ability. For example, are there any signs of infection such as fever, cough, painful urination or diarrhea? Are there symptoms of underlying depression? Are there other medical conditions (e.g., disorders of the heart, liver or kidneys; dehydration)?

3) Review the list of all PD medications you are taking. Your healthcare team can evaluate whether the mental changes you are experiencing are related to the use of exacerbating PD medications. Virtually all of the anti-PD medications have the potential to cause mental clouding and hallucinations, especially at high doses or in combination with other risk factors. Amantadine and anticholinergics should be tapered and stopped first (one at a time if you are taking both), as the risk of psychosis usually outweighs the modest benefit that these medications provide. Levodopa and the dopamine agonists are the other classic offenders, since high levels of dopamine in certain areas of the brain are associated with psychosis.

In practice, the risk of cognitive and psychiatric complications is higher with the dopamine agonists than with levodopa. Thus, when the symptoms of psychosis demand immediate action to rescue someone who is on a combination of levodopa and dopamine agonists, the first step is usually to taper and eventually stop the agonist. Levodopa becomes the only dopaminergic medication the individual is taking. Not only is levodopa the best drug for treating PD, it also has the best "therapeutic margin," or highest ratio of benefit to side effects.

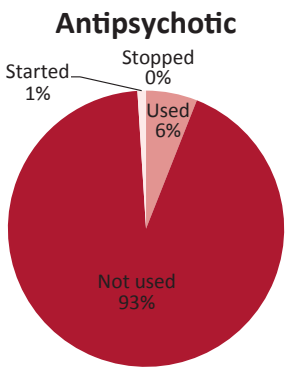
4) Discuss medications you may be taking for other illnesses. Your physician or healthcare team will want to assess whether any non-PD medications or other substances are impacting your mental changes. Have any new medications been started or doses changed (e.g., sleep aids, narcotics [especially codeine derivatives like percocet], antibiotics, steroids, anti-anxiety or anti-depressant medications)? Could illicit drugs or alcohol be involved?

Based on the findings in the four steps above, your physician and healthcare team members will be able to suggest the best course of treatment, including any appropriate antipsychotic medications. Psychosis and dopamine excess can be remedied by the use of drugs, known as neuroleptics, which block the receptors activated by dopamine. These drugs have been used for over 50 years to treat severe mental illness, particularly schizophrenia. However, most of the dopamine-blocking drugs can cause serious problems in the person with PD, leading to worsening of the motor symptoms and loss of effectiveness of the other dopaminergic medications. Therefore, it is extremely important that the right neuroleptic or antipsychotic drug be chosen. There are currently three antipsychotic medications that are suitable for use in persons with PD: pimavanserin, clozapine and quetiapine.

In 2016, the FDA approved **pimavanserin** (Nuplazid) as the first drug specifically designed to treat Parkinson's disease psychosis. Pimavanserin is not a dopamine-blocking drug like clozapine and quetiapine. It is a selective serotonin inverse agonist. This means it targets serotonin receptors. It is a safer choice when treating people with PD that are experiencing psychoses because it can reduce hallucinations without disrupting motor performance.

Clozapine (Clozaril) can be used effectively, especially at low doses, in persons with PD without a risk of worsening Parkinson's symptoms. The FDA approved clozapine for use in the treatment of schizophrenia in 1990 with the condition that weekly blood counts be completed. This is so that your healthcare provider can monitor the low but significant risk that clozapine can depress your white blood count and thereby increase the risk of serious infection. This requirement has made the use of clozapine inconvenient but safe, and experience has shown that low dose clozapine has an important place in the management of the psychosis that can sometimes occur in persons with PD. Clozapine was shown in a randomized clinical trial to be effective against psychotic behavior in PD.

Until pimavanserin was approved in 2016, **quetiapine** (Seroquel) had become the drug of choice to treat psychosis in PD; it has the advantage over clozapine of not adversely affecting blood counts. There are no major side effects and it does not require blood count monitoring. While many PD physicians have had positive individual experiences with quetiapine in treating hallucinations and other symptoms of psychosis in PD, a few small clinical trials to date have not confirmed its overall efficacy.



This chart shows the percentage of people in the *Parkinson's Outcomes Project* (the largest clinical study of Parkinson's in the world) using and not using antipsychotics. Out of 19,000+ visits tracked in the study (almost 8,000 patients), doctors started a patient on antipsychotics at 1% of visits.

Table 4. Summary of Medications for Dementia and Hallucinations in PD

Medication (product name in parenthesis)	**Dosages in Milligrams (mg);** tablets unless other-wise noted	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Acetylcholinesterase Inhibitors				
Donepezil (Aricept)	5, 10, 23	5–23 mg nightly	Nausea, headache, diarrhea, pain, insomnia, dizziness, muscle cramps, fatigue	Parkinson's disease dementia
Galantamine (Razadyne, Razadyne ER)	4, 8, 12 mg tablets; 4 mg/ml solution ER: 8, 16, 24	8–12 mg, twice a day *(may be different for extended-release)*	Nausea, vomiting, diarrhea, loss of appetite, dizziness, headache, UTI, weight loss	Parkinson's disease dementia
Rivastigmine (Exelon, Exelon Patch)	1.5, 3, 4.5, 6 mg capsules; 2 mg/ml solution Patch 4.6, 9.5 mg	1.5–6 mg, twice a day Patch 4.6–9.5 mg once/day	Nausea, vomiting, diarrhea, loss of appetite, abdominal pain, indigestion, dizziness, fatigue	*Parkinson's disease dementia*
Other Medications to Improve Thinking				
Memantine (Namenda)	5, 10 mg tablets; 2 mg/ml solution	5–20 mg/day. If more than 5 mg/day, give twice a day	Dizziness, headache, confusion, constipation, high blood pressure, cough, pain	Parkinson's disease dementia
Methylphenidate (Ritalin, Ritalin LA, Ritalin SR, Concerta, Metadate CD, Methylin, Daytrana patch)	5, 10, 20 mg tablets; 10mg/5 ml solution; LA 10, 20, 30, 40; SR 20; Concerta 18, 27, 36, 54 ER; Metadate CD 10, 20, 30, 40, 50, 60 ER; Methylin 2.5, 5, 10; Daytrana 10, 15, 20, 30	5–15 mg two or three times a day *(may be different for extended-release and patch)*	Palpitations, high blood pressure, confusion, psychosis, insomnia (if taken too late in day)	Inattentiveness, excessive daytime sleepiness, fatigue
Modafinil (Provigil)	100, 200	200 mg in the morning	Headache, nausea, nervousness, rhinitis, diarrhea, anxiety, insomnia, dizziness, dyspepsia	Inattentiveness, excessive daytime sleepiness, fatigue

For Hallucinations and Psychosis				
Pimavanserin (Nuplazid)	34	34 mg/day, taken as two 17 mg tablets once daily	Swelling of limbs, nausea, confusion, constipation, gait disturbance	*Hallucinations and psychosis*
Clozapine (Clozaril, FazaClo)	12.5, 25, 50, 100, 200	50–300 mg twice a day	**Requires weekly blood tests for low white blood cell counts.** Drowsiness, drooling, tachycardia, dizziness, constipation, low blood pressure, headache	*Hallucinations and psychosis*
Quetiapine (Seroquel, Seroquel SR)	25, 50, 100, 150, 200, 300, 400 SR 50, 150, 200, 300, 400	12.5–100 mg divided daily *(may be different for extended-release)*	Sleepiness, dry mouth, dizziness, orthostatic hypotension, tachycardia, low blood pressure, constipation, increased appetite	*Hallucinations and psychosis*

* "Typical treatment regimens" should act only as a guide. The prescribed dosage by your doctor and your effective dose may vary from dosages listed.

SLEEP DISORDERS

Disturbed sleep is so common among persons with PD that it has become a major focus of therapeutic interest and research. The specific disorders include:

- Restless leg syndrome (RLS)
- Periodic limb movements of sleep (PLMS)
- Rapid eye movement (REM)-sleep behavior disorder (RBD)
- Excessive daytime sleepiness (EDS)
- Insomnia
- Co-existing obstructive sleep apnea (OSA)

Inadequate tremor control, stiffness in the late evening and poor bed mobility can account for an inability to sleep at night as can reversal of the sleep cycle because of excessive daytime sleepiness (EDS). Each of these issues is briefly reviewed below. For more information on medical causes of disrupted sleep, including obstructive sleep apnea and congestive heart failure, please check with your physician or healthcare provider.

To provide your physician and members of your healthcare team with the most accurate history, it is useful for the spouse, partner, housemate or professional caregiver to help describe the person with PD's nighttime activities. An Epworth Sleepiness Scale (see Appendix D) can help identify the circumstances that cause daytime sleepiness and provide

clues to disruption of sleep at night. This questionnaire (given in the office or completed at home) concerns a person's tendencies to fall asleep during the day in various real life situations such as driving or watching television. A formal overnight evaluation in a sleep laboratory by a trained specialist (often a neurologist) can provide even more information, especially if OSA is suspected. The evaluation typically will include observations during sleep of heart rate, breathing activity, snoring, involuntary movements and quality of sleep.

KEY POINT: Sleep disruption related to PD may be caused by restless leg syndrome (RLS), periodic limb movements of sleep (PLMS), REM-sleep behavior disorder (RBD), excessive daytime sleepiness (EDS), insomnia or increased Parkinson's symptoms in bed.

Restless leg syndrome (RLS) is a common disorder of the general population characterized by unpleasant sensations in the legs at rest (without associated movement) and an uncontrollable urge to move the legs to relieve these feelings. RLS sensations are often described by those who experience them as burning, creeping, tugging or "like insects crawling inside the legs." Often called paresthesias (numbness and tingling) or dysesthesias (unpleasant numbness and tingling), the sensations range in severity from uncomfortable and irritating to painful. Voluntary movement of the legs, particularly walking, relieves the uncomfortable urge at least temporarily. When symptoms of RLS are unrelieved, sleep can be disrupted sufficiently to cause serious daytime fatigue from sleep deprivation. Some people with PD confuse RLS, an abnormal sensory perception, with levodopa-induced dyskinesia, an overt involuntary movement of the legs.

Periodic limb movements of sleep (PLMS) describes episodes of repetitive, jerky involuntary leg movements during sleep. Like many of the in-sleep disorders, the bed partner is more aware of the involuntary movements than the person with the symptom.

RLS and PLMS are common in persons with PD, probably because of the involvement of dopamine in causing them. Diagnostic evaluation can be fairly simple when the symptoms are obvious, but your physician or provider may prescribe an overnight sleep study to help determine a clear diagnosis. Also, the level of iron in your blood should be tested, since iron deficiency has been associated with RLS, although iron replacement therapy usually has little effect on the symptoms of RLS.

The most common medications for RLS and PLMS are the dopamine agonists and, in the person with PD, extra nighttime doses of the agonists or levodopa may bring relief. Your healthcare provider may also want to consider benzodiazepines (clonazepam), gabapentin or low-dose opiates.

REM-sleep behavior disorder (RBD) describes active behaviors (e.g., kicking, fighting, yelling or thrashing) during the phase of sleep when dreaming normally occurs (without such accompanying movements). The person experiencing RBD may even walk or fall out of bed during REM sleep. The history provided by the person with PD or their care partner or housemate may be sufficient for a presumed diagnosis, but an overnight sleep study can confirm it. RBD is often present for months or years before the onset of the motor symptoms of PD.

Anticholinergics, selegiline and dopaminergic drugs can all worsen the RBD behaviors. For treatment of RBD, low-dose benzodiazepines (e.g., clonazepam) or melatonin at bedtime may help.

Excessive daytime sleepiness (EDS) is very common in PD. It may result from disruption of nighttime sleep, and it is most problematic for the person with PD who is experiencing progressive decline in thinking ability. People with PD may even suffer "sleep attacks" during the day, which are described as the sudden, irresistible urge to sleep or the sudden, unwarned onset of sleep not preceded by sleepiness. This phenomenon is significantly increased in persons with PD who take moderate to high doses of the dopamine agonists or levodopa.

Insomnia is an inability to fall asleep or, more commonly, to stay asleep. It is more complicated in PD because of many factors that may contribute, including "normal" nighttime awakening associated with aging, wearing off of antiparkinson medication effect during sleep, depression and anxiety.

Treatment of EDS and insomnia can be challenging and usually requires a multi-pronged approach. Discuss with your healthcare provider whether to reduce, rearrange or even eliminate daytime dopamine agonists.

A contributing factor to insomnia might be drug-induced loss of impulse control. In these cases, the person with PD may develop some obsessive compulsive behaviors as a side effect of the dopamine agonists. Examples of these behaviors may include obsession with shopping, sexual activity, eating and gambling, all of which can interfere with sleep. If you experience any of these behaviors, be sure to speak with your healthcare provider.

Every attempt should be made to normalize the sleep-wake cycle and to improve sleep hygiene. This means:

- Establishing regular bedtimes and rising times
- Reducing caffeine and alcohol intake
- Limiting naps
- Avoiding food and drink within several hours of bedtime

Also, you should not use the bed as a site for non-sleeping tasks, such as reading, doing work or watching television, as these activities can condition the body for wakefulness. Sleep hygiene can be further improved by the prudent use of physician-supervised sleeping medications such as quetiapine, clonazepam and others.

Some antidepressant drugs, such as trazodone (Desyrel) or mirtazapine (Remeron), can also promote sleep due to their sedative properties. Most over-the-counter preparations are not suggested for use unless recommended by a physician, although the antihistamine diphenhydramine (Benadryl) may double as a sleeping pill and an antitremor drug because of its anticholinergic properties. If motor symptoms such as stiffness and tremor interrupt sleep because of the long gap between the last dose of antiparkinson medication in the evening and the first dose the following day, an extra dose of carbidopa/levodopa may be taken late in the evening or during the night on awakening. Some people with PD use controlled-release carbidopa/levodopa (Sinemet CR) at bedtime for this purpose, although the amount of the drug that can be absorbed by the body is limited and its half-life is not much greater than immediate-release formulations.

If nighttime sleeping problems are controlled but excessive daytime sleepiness persists, increased coffee intake in the morning is also worth a try. There has been much interest in the interplay between caffeine and PD. Increased caffeine intake in young adults may lower the risk of developing PD. A recent study highlighted the possibility of caffeine improving some of the slowness and stiffness of PD when consumed judiciously (about 1-2 cups of coffee per day).

Stimulants such as methylphenidate (Ritalin) and mixed amphetamine salts (Adderall) can be tried. Indicated for narcolepsy and attention-deficit disorder, they could be used carefully in the person with PD to increase daytime wakefulness and alertness. They should be given in low doses and taken in the morning initially, preferably before 8 a.m. If additional amounts of the drug are needed, they should be taken before noon. Side effects include palpitations, high blood pressure, confusion, psychosis and insomnia (if the dose is too high or taken too late in the day).

The non-stimulant modafinil (Provigil), approved only for treatment of narcolepsy, also is potentially useful. Its mode of action in the brain is unknown, but it has a good track record of reducing daytime sleepiness with fewer side effects because it is not a stimulant like methylphenidate and the amphetamines.

It should be noted that the use of methylphenidate, amphetamine and modafinil for the treatment of EDS in PD is not approved by the FDA ("off label" use), which means that most health insurance plans will not cover them.

ORTHOSTASIS

The terms orthostasis or orthostatic hypotension describe the tendency for blood pressure to decrease significantly when a patient rises from seated or lying to standing, causing dizziness, lightheadedness, headache, blurred or dimmed vision or fainting. Normally, blood pressure is maintained in a narrow range and is protected against major fluctuations that are too high or too low by protective reflexes in the body's blood vessels that are controlled by the body's autonomic nervous system (ANS). Since the ANS is often impaired in PD, autonomic functions such as blood pressure regulation, gastrointestinal motility, sweating, etc. can be affected. When orthostasis is related to a disease of the nervous system, like PD or multiple system atrophy, it is called neurogenic orthostatic hypotension, or nOH.

When a person with PD stands too quickly, and the normal reflexes that protect against a drop in blood pressure upon changing the body's position against gravity are impaired, the result is lightheadedness, dizziness and fainting — symptoms that reflect a lack of blood flow to the brain. This tendency in PD can be aggravated by the antiparkinson medications, especially the dopamine agonists and carbidopa/levodopa. In addition, the drugs commonly used to treat high blood pressure can make orthostasis worse. Any person who experiences orthostatic symptoms should inform all healthcare providers involved with their care.

Persons with PD often assume, mistakenly, that any symptom in any organ system is caused by PD. Therefore, it is good to remember that having PD doesn't protect you from getting other, unrelated medical problems. A good example of a frequent and straightforward parallel problem (or comorbidity) is back, neck and limb pain due almost always to degenerative arthritis of the spine. Pain attributable to PD certainly occurs, but it is usually an aching discomfort and feeling of heaviness of the large muscles of the legs, often during

an "off" period. The same thing can be said of light-headedness or dizziness. Orthostatic hypotension is usually the primary reason for the symptom, but general medical causes, especially involving the heart or lungs, must be explored. In addition, other medications prescribed by other physicians and healthcare providers, particularly medications for high blood pressure, should be thoroughly considered. The coincidence of multiple problems in many persons with PD underscores the need for the PD specialist to communicate frequently with the primary care physician, other specialists and/or healthcare team members who treat the patient as this will lead to a comprehensive treatment approach.

KEY POINT: Make certain that all healthcare providers consider causes for orthostasis and that an appropriate evaluation is completed.

If a person with PD experiences orthostasis, it is appropriate for the physician or healthcare provider to consider decreasing the dosages of potentially offending drugs such as dopamine agonists and carbidopa/levodopa to a lower level that is still compatible with control of the Parkinson's symptoms. If drugs for hypertension are being used, the doses should be adjusted. Communication between all treating physicians and members of the healthcare team is mandatory in these matters.

Drugs are not the only remedy for orthostasis. The following non-pharmacologic techniques are important:

- Change positions slowly, particularly when rising from a seated to a standing position. Pause for several seconds between each move. Walking with an assisted device (cane or walker) may also be helpful.
- Increase fluids, salt and caffeine in the diet.
- Wear support stockings and elevate legs periodically during the day.

If the foregoing measures are not effective, then ask your physician or healthcare provider if medications to raise blood pressure would be appropriate in your case. For more information on nOH, visit www.nohmatters.com.

Fludrocortisone (Florinef) will increase blood pressure by increasing retention of salt and blood volume. Increased dietary salt will enhance the effect. Florinef should be started at once a day dosing of 0.1 mg. Dosing higher than three times a day should be avoided. Leg edema (swelling) and high blood pressure when lying flat are potential adverse effects.

Midodrine (Proamatine) increases blood pressure by stimulating the autonomic nervous system directly and is dosed three times per day. The development of high blood pressure when lying flat is greater with midodrine than fludrocortisone and should be carefully monitored.

Pyridostigmine (Mestinon) can be used either as monotherapy or as an adjunctive drug to augment the blood pressure raising effect of flodrocortisone and midodrine. Ordinarily used to treat the neuromuscular disease myasthenia gravis, Mestinon has been evaluated in two single dose clinical trials (one open-label and one placebo-controlled), both of which showed a small but statistically significant elevating effect on diastolic blood pressure. Only one study, an open-label survey, has examined the long-term effect of using Mestinon for orthostatic hypotension. It, too, showed that patients were satisfied with its benefit.

Droxidopa (Northera) is believed to work by increasing standing blood pressure through elevating levels of norepinephrine, a chemical in the body that helps regulate blood pressure. Northera was approved by the FDA in 2014 for the treatment of orthostatic dizziness, lightheadedness, or the "feeling that you are about to black out" in adult patients with symptomatic neurogenic orthostatic hypotension (nOH) caused by primary autonomic failure (Parkinson's disease, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, or non-diabetic autonomic neuropathy. The studies leading to the FDA approval were short-term (10 weeks or less) and effectiveness beyond two weeks of treatment has not been demonstrated. Therefore, the continued effectiveness of Northera should be assessed periodically by your doctor. Similar to midodrine and fludrocortisone, there is potential for the development of high blood pressure when lying flat (supine hypertension) that should be monitored carefully. Northera is only available through specialty pharmacies; your doctor has to complete a treatment form and fax it to the Northera Support Center to prescribe it. For more information, visit www.northera.com.

GASTROINTESTINAL SYMPTOMS

Nausea, constipation and early satiety (feeling full after eating less than a full meal) are common problems throughout the course of PD and are attributable to the same pathology that is responsible for neurodegeneration in the brain. In this case, the disease process affects the autonomic nervous system (ANS), which controls the normal contractions of the gastrointestinal tract. In PD the contractions of the stomach are slowed, and everything that is swallowed, including medications, stays in the stomach longer than it should because of delayed emptying. Slowed gastric emptying translates into gas and bloating, nausea, loss of appetite and pain. In addition, constipation occurs early in the evolution of PD, and it often but not always increases in severity and frequency as PD progresses. All of these symptoms vary in their responses to treatment with antiparkinson drugs, but usually improve with the use of drugs that specifically speed gastrointestinal movement.

Nausea

The management of gastrointestinal disorders in PD can be complicated. Dopaminergic medications can worsen nausea, but the addition of extra carbidopa (Lodosyn) to the prefixed mixture of carbidopa/levodopa in Sinemet usually helps to prevent or lessen this side effect. However, Lodosyn does not work if the nausea is caused by dopamine agonists.

Other medications, specifically metoclopramide (Reglan), prochlorperazine (Compazine) and promethazine (Phenergan), are available for treating nausea, but because they work by blocking dopamine receptors in the intestinal tract and in the brain, they should be avoided because they can worsen the symptoms of PD.

> **KEY POINT:** Dopamine-blocking medications for GI symptoms (Reglan, Compazine and Phenergan) should be avoided in persons with PD.

Domperidone (Motilium) is a good choice for treating nausea and vomiting associated with the use of any of the dopaminergic antiparkinson drugs (levodopa and the dopamine agonists) because it does not cross the blood brain barrier and does not worsen PD symptoms. However, it is available only from sources outside the U.S. because it hasn't

been submitted to the FDA for approval by the manufacturer. Trimethobenzamide (Tigan) is another available medication to treat nausea in PD. Simple antacids (i.e., simethicone) are less effective but worth trying because they are inexpensive and do not require a prescription. Another medication that was initially approved for chemotherapy and radiation therapy-induced nausea and vomiting, and has proven useful for nausea in PD is ondansetron (Zofran). Since it does not block dopamine in the brain ondansetron is safe for patients with PD, and it probably helps block nausea both in the brain and in the gut. It should not be combined with apomorphine as it can cause lowering of blood pressure.

Constipation

This is another example of the effect of PD on the ANS and is a major nuisance for many people with PD. Fortunately, good dietary management and the prudent use of stool softeners, laxatives and other bowel modulators are usually helpful. There are several steps to good dietary management and preventive maintenance:

- Drink plenty of water and fluids.
- Consume lots of dietary fiber in the form of fruits, fruit juices, vegetables and cereals.
- Use appropriate fiber additives, such as Metamucil, the stool softeners lactulose and polyethylene glycol (Miralax), and the stimulant laxatives, such as dulcolax.

Another option for the treatment of constipation is lubiprostone (Amitiza) which increases the secretion of fluid in your intestines to help make it easier to pass stools (bowel movements). Lubiprostone is used to treat chronic constipation in adults.

Guidance from the neurologist, primary care doctor or healthcare provider on how to use and combine these agents is essential. A review of GI medications can be found in Table 5.

DROOLING (SIALORRHEA)

Drooling in PD can be defined as an inability to manage the flow of the saliva in and around the mouth as it is being produced by the salivary glands. It results not from overproduction of saliva but from slowing of the automatic swallowing reflex that normally clears saliva from the mouth. Drooling is common in PD, and it ranges from mild wetting of the pillow during sleep to embarrassing outpourings of saliva during unguarded moments. For example, this can happen when the head is down, the mouth is held open involuntarily (as happens in advanced PD) or when a person is engaged in an activity and is distracted from the need to swallow automatically. When severe, drooling is an indicator of more serious difficulty with swallowing (also known as dysphagia), which can cause the person to choke on food and liquids, or can lead to aspiration pneumonia.

Treatment of drooling is not always effective, but the list of therapies includes:

- Glycopyrrolate and other oral anticholinergic medications (trihexyphenidyl, benztropine, hycosamine). Oral anticholinergic medications, as a class, decrease the production of saliva. Usually this is perceived as a side effect (dry mouth), but in this case it is an advantage. Other anticholinergic side effects may be seen, including drowsiness, confusion, vomiting, dizziness, blurred vision, constipation, flushing, headache and urinary retention.

- Scopolamine patch. This patch offers anticholinergic medicine that slows production of saliva as it is absorbed into the entire bloodstream, and anticholinergic side effects similar to oral agents may be seen.
- 1% atropine eye drops (an anticholinergic), given as 1-2 drops under the tongue per day to dry the mouth. Systemic side effects are much less likely with this local treatment.
- Botulinum toxin A. Injection of botulinum toxin A (Botox) into the salivary glands of the cheek and jaw decreases production of saliva without side effects, except for thickening of oral mucus secretion. Botox is not always effective, but when it works the benefit can last for several months before it wears off and re-injection is necessary. Botulinum toxin should probably be avoided when secretions are deep and thick. Also, botulinum toxin B (Myobloc) causes dry mouth when used for dystonia but it is not approved by the FDA for drooling.
- Chewing gum. Gum activates the jaw and the automatic swallowing muscles reflex and can help clear saliva.

KEY POINT: Botulinum toxin A can be an effective treatment for severe drooling, although pills, the patch and mouth drops should be tried first in the interest of cost saving.

Table 5. Summary of Medications for Gastrointestinal (GI) Symptoms and Drooling in PD

Medication (product name in parentheses)	**Dosages in Milligrams (mg);** tablets unless otherwise noted)	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Medications for Nausea and Vomiting				
Carbidopa (Lodosyn)	25	Adding 25–50 mg to each dose of carbidopa/levodopa	Could worsen dyskinesia	*Reduce levodopa-induced nausea & vomiting*
Domperidone (Motilium) *NOTE: not available in the U.S. at this time*	10	10 mg up to four times daily, 15–30 minutes prior to meals	Headache, hives, hot flashes, itching of skin; itching, redness, pain, or swelling of eye;	Treat nausea, vomiting, and constipation with increasing emptying of stomach
Ondansetron (Zofran)	4, 8	4 mg up to three times daily as needed	Headache, malaise/fatigue, constipation, diarrhea	Nausea and vomiting
Trimethobenzamide (Tigan)	300 mg capsule; 200 mg suppositories	300 mg up to four times daily	Blurry vision, depression, diarrhea, confusion, dizziness, headache, drowsiness, cramps	*Treat nausea and vomiting*, premedication for Apokyn

Medication (product name in parentheses)	**Dosages in Milligrams (mg);** tablets unless otherwise noted)	**Typical Treatment Regimens***	**Potential Side Effects**	**Indications for Usage** *(italics = approved by FDA)*
Metoclopramide (Reglan)	5, 10		**Worsens PD symptoms:** dystonic reaction, confusion, dizziness, headache, drowsiness	*Treat or prevent nausea and vomiting*, and constipation with increasing emptying of stomach
Prochlorperazine (Compazine)	5, 10		Same as above	*Treat nausea and vomiting*
Promethazine (Phenergan)	12.5, 25, 50		Same as above	*Treat nausea and vomiting*
Medications for Constipation				
Lubiprostone (Amitiza)	8, 24 mcg	8–24 mcg twice daily	Bloating, gas, upset stomach, dizziness, chest pain	*Constipation*
Polyethylene glycol 3350 (MiraLax)	1 capful (17 grams) in 4–8 ozs. water or liquid	Every day if necessary, may use lower doses for maintenance	Bloating, gas, upset stomach, dizziness, increased sweating	*Constipation*
Medications for Excessive Drooling				
Atropine drops	1% opthalmic solution	Only 1–2 drops under the tongue twice a day	Dry mouth	Excessive drooling
Glycopyrrolate	1, 2	1–2 mg two or three times daily as needed	Dry mouth, drowsiness, confusion, vomiting, dizziness, blurred vision, constipation, flushing, headache, urinary retention	Excessive drooling
Scopolamine patch	1.5 mg patch	Apply patch every 3 days as needed	Same as above	Excessive drooling
Botulinum toxin A (Botox)	100 unit vials	10–100 units injected into parotid and/or submandicular glands	Dry mouth	Excessive drooling

* "Typical treatment regimens" should act only as a guide. The dosage prescribed by your doctor and your effective dose may vary from dosages listed.

URINARY SYMPTOMS

Urinary frequency, urinary urgency and loss of bladder control (urge incontinence) are common complaints in PD. The urinary bladder loses its capacity to hold normal amounts of urine because the neural impulses descending from the brain to the spinal cord tell the bladder to empty prematurely in PD. Urinary frequency and urgency can lead to urge incontinence more often in those people who are too slowed down by PD to get to a toilet quickly when the urge to empty the bladder suddenly presents itself. As with other non-motor complaints, it is important to exclude other possible causes of urinary frequency, including urinary tract infection and enlarged prostate. Co-management of urinary problems by a urologist is important.

Medications that can help re-establish bladder control:

- Anticholinergic medications can relax the overactive muscular wall of the bladder and allow the bladder to fill to greater capacity without suddenly emptying. There are several available by prescription.
- The alpha-adrenergic receptor blockers prazosin and tamsulosin (Flomax) relax the detrusor muscle at the outlet of the bladder and make it easier for the bladder to empty. These drugs may also be indicated in men if an enlarged prostate is found to be a reason for the symptom.
- The tricyclic antidepressants nortriptyline and imipramine have anticholinergic properties in addition to other, healthful pharmacologic effects.

Your physician or healthcare provider can assess which is most appropriate for your situation.

KEY POINT: Urinary frequency, urinary urgency and urge incontinence are common complaints in PD. They typically are not responsive to dopaminergic medications but can be remedied by the use of drugs that relax the bladder and allow it to fill to a greater capacity.

SEXUAL DYSFUNCTION

Sexual dysfunction in PD is common for many reasons including dysfunction of the ANS. It affects men more often than women, though little has been published in the research literature about this topic. It remains underappreciated as patients, partners and healthcare providers may not be comfortable with a frank discussion of sex. This topic certainly deserves attention, so you and/or your partner may need to initiate a conversation with someone on your healthcare team.

Many factors contribute to good sexual health for both women and men, and certain symptoms of PD can impact sexual functioning and response. Gila Bronner, a sex therapist in Israel who works with people with Parkinson's, offers the following observations. Depression, often present in the context of PD, can decrease sexual desire, and some antidepressants affect sexual response. The motor symptoms of PD can impact both the fine motor skills of touch and the mobility that contributes to satisfying sexual activity. The expressiveness that can be an important part of non-verbal communication is often affected in PD as both facial expression and volume of voice may decrease. If there are times of the day when

your functioning is optimal, such as when you are rested and medications are minimizing symptoms, this could be a good time to express yourself with a loved one.

Other members of the healthcare team that might address sexual functioning include the PD nurse, primary care physician and/or nurse practitioner, gynecologist for women and urologist for men.

In PD, sexual dysfunction may arise as a primary symptom resulting from the loss of dopamine, the principal neurochemical mediator of reward and pleasure in the brain. As with other non-motor symptoms, the doctor or other healthcare provider should consider other causes of impotence and decreased libido. These include poor circulation to the genitals that commonly occurs in diabetes and peripheral vascular disease, enlarged prostate, depression and other medical conditions. Various medications, including antihistamines, antidepressants, benzodiazepines, and drugs for high blood pressure and excessive alcohol or tobacco use can also contribute to sexual dysfunction. Fortunately, most anti-PD drugs are not associated with impotency or loss of libido, with the exception of the anticholinergics. To the contrary, the dopamine agonists have been associated with disorders of impulse control, including uncontrolled sexual urges.

Male impotence, otherwise known as erectile dysfunction (ED), refers to difficulty with achieving and maintaining an adequate erection. Erectile dysfunction warrants a thorough evaluation so the physician or other healthcare provider can look for all possible causes, especially diabetes (which can cause autonomic neuropathy) and other disorders listed above. A complete physical examination should be conducted by the general physician and urologist.

The list of treatments available to treat ED has been upgraded in the last decade from those that must be injected into the penis to oral preparations. Oral medications for ED include sildenafil (Viagra), vardenafil (Levitra), tadalafil (Cialis) and yohimbine (Yocon). Mechanical treatments include vacuum pumps, constriction rings and penile implants, while injectable medications include papaverine HCl (Papaverine vials for injection), phentolamine (Regitine vials for injection) and alprostadil (Caverject).

KEY POINT: Sexual health and sexual dysfunction should be as much a part of the conversation between the person with PD and his or her healthcare team as any other health matter.

SEBORRHEIC DERMATITIS AND EXCESSIVE SWEATING

Many persons with PD will develop skin-related symptoms including seborrheic dermatitis (SD) and excessive sweating. SD is a disorder of the oil-producing glands of the skin, which can become infected with a particular yeast in patients with neurologic disease. It occurs mostly around the face and scalp in people with PD. In seborrheic dermatitis the skin is oily, reddened and scaly. Treatment of mild SD can be accomplished by the frequent use (two to three times a week) of a good dandruff shampoo. More severe cases require consultation with a dermatologist.

Excessive sweating (hyperhidrosis) has been known to be a peculiar feature of PD for over a century. The cause is often unknown, but some individuals observe that they sweat

profusely in the "off" state of motor fluctuations or when dyskinesia is severe enough to generate significant body heat. Many people report spontaneous and unexplained drenching sweat, often awakening them from sleep and creating a need to change bedclothes. Levodopa can also cause severe, episodic sweating. A recent study showed that sweating disorders in PD are often associated with other autonomic abnormalities such as constipation and orthostasis. Botulinum toxin A can be effective in small injections for hyperhidrosis of the palms and armpits.

PAIN

Almost half of patients with Parkinson's disease experience pain or unpleasant sensations as a symptom of their PD, and it can become more common with disease progression. Other painful conditions may coexist with PD, including arthritis, peripheral neuropathy, spinal stenosis, and musculoskeletal strains and sprains. These alternative causes of discomfort should always be considered before assuming that pain is due to PD.

Pain in PD can be related to (1) dystonia, (2) muscles and joints, (3) nerves or nerve roots, (4) akathisia (restlessness) and/or (5) primary, central "parkinsonian" pain. There may be a pattern between the experience of pain or discomfort and one's PD medication schedule. For some people, being in the "off" state can increase a sensation of pain, and adjusting medication dosage and intervals will lead to improvement.

The most common cause of pain in PD is related to **dystonia**, which is a patterned posture of the neck, arms, legs or feet. Camptocormia is an example of dystonia characterized by severe bending at the waist, causing back pain or spasm. Depending on the timing of dystonic pain, several different approaches may prove helpful. Early morning dystonia often improves with movement and/or the first dose of dopaminergic medication. In some cases, the severity of morning dystonia merits a subcutaneous injection of apomorphine. If dystonia occurs as a wearing-off phenomenon, minimizing the "off" period with dopaminergic therapy is the goal of treatment. Botulinum toxin injections can also be helpful in treating focal dystonias.

Musculoskeletal pain may be related to rigidity and decreased movement/mobility. Adjustments of the PD medication schedule and physical therapy can help in these cases. **Radicular**, or nerve root, pain should be evaluated for a compressed root or nerve lesion. If these causes are eliminated and the radicular pain is thought to be related to Parkinson's disease, physical and/or occupational therapy may be helpful.

Akathitic discomfort is an inner restlessness that makes it difficult for one to sit still and is different from dyskinesias or anxiety. In about half the reported cases, additional dopaminergc therapy is helpful. **Central pain** in PD is different than dystonia, rigidity or musculoskeletal pain. It is likely caused by the PD itself, and it may feel like stabbing, burning, scalding or insects crawling on the skin.

Non-motor painful sensations, such as abdominal bloating or chest wall tightening, may be related to PD in some patients. These symptoms should be addressed by the physician to rule out other primary causes of abdominal and chest pain.

Depression, which is common in PD, can heighten an individual's experience of pain. This highlights the importance of identifying and treating depression in Parkinson's disease.

Treatment of the pain in PD can be challenging. Some options include conventional anti-inflammatories, muscle relaxants, gabapentin, tricyclic antidepressants and additional dopaminergic doses. Opiates should be used only in severe cases, and referral to a pain specialist is recommended. Several non-pharmacologic techniques include regular exercise, heating pads, ice packs and massage.

KEY POINT: Pain in PD can be related to (1) dystonia, (2) muscles and joints, (3) nerves or nerve roots, (4) akathisia (restlessness) and/or (5) primary, central "parkinsonian" pain. It also may be related to other medical conditions such as arthritis or neuropathy.

Chapter 4
Exercise Is Medicine

Content provided by Giselle Petzinger, MD, Beth Fisher, PT, PhD, Lauren Hawthorne, and Michael Jakowec, PhD

The symptoms of Parkinson's disease include more than just what doctors call the motor features – the slowness, stiffness and tremor that characterize the disease. Parkinson's impacts thinking: the disease can affect working memory, decision-making, staying attentive and concentration. Parkinson's also affects behavior; PD is linked to depression and anxiety, and it can disturb sleep.

From a biological perspective, Parkinson's results in low levels of the brain chemical dopamine, and this leads to the loss of effective communication between the higher brain structures on the surface of the brain (called the cortex) and the deep part of the brain that manages more basic functions (called the basal ganglia). The higher brain structures are where you think, and the deep structures are where those thoughts are translated into actions, particularly movement. The loss of these connections is also linked to the behavioral changes observed in Parkinson's.

In the last decade, studies and ongoing research have clearly shown us that exercise and physical therapy can help restore lost behaviors and function in people with Parkinson's. In total these studies have shown that physical therapy and exercise can improve many diverse aspects of Parkinson's by incorporating feedback, repetition, challenge, problem solving, engagement and motivation. In addition to improving symptoms, scientists are increasingly convinced that exercise may slow disease progression.

Reported benefits of exercise include:

- Improved gait and balance
- Reduced falls
- Increased flexibility and posture
- Improved endurance
- Reduced freezing of gait
- Improved working memory and decision making
- Improved attention/concentration
- Reduced depression and anxiety
- Improved quality of sleep

KEY POINT: Based on findings from the Parkinson's Foundation's *Parkinson's Outcomes Project*, the largest-ever clinical study of Parkinson's, it is recommended that people with PD engage in at least 2.5 hours of exercise a week for a better quality of life. Establishing early exercise habits is an essential part of overall disease management.

EXERCISE EFFECTS ON COGNITION

Across medicine, researchers have long linked exercise to cognitive function or thinking. More recently, researchers are finding that exercise seems to improve aspects of how you think that are frequently affected in Parkinson's. About half of people with Parkinson's experience challenges with what doctors call *executive functioning*, which involves planning activities, keeping a schedule, organizing things on your desk or in your house and similar tasks. Executive function can be impaired by problems with working memory (measured by how many things you can keep track of simultaneously), problems with keeping focused on a task and responding to changes.

The parts of the brain that perform executive function tasks are the same ones that help you to apply motor learning in changing environments. For example, you use these executive function centers when you go from walking inside the house to walking outside. You also use your executive function centers when you think about how to improve a motor skill – how to do a task you know how to do better or faster.

Today, we have ideas about how to exercise better. In the past, when scientists studied how exercise affected the brain they always studied basic aerobic training such as biking or walking on a treadmill, track or around the community. When you exercise aerobically, you make your heart healthier and you improve how your body uses oxygen. Studies of aerobic exercise have shown that it can help improve age-related changes in executive function. Scientists are now working to determine how well aerobic exercise works to slow Parkinson's disease. They are studying what is the right "dose" of exercise to get the best benefits, including looking at how to balance the benefits of exercise versus the risk that exercising too much might increase your risk of falls or injury.

Studies of Parkinson's have already shown that exercise helps. Studies of skill-based exercise have been shown to improve motor function, too. So far, we don't know which is better. In fact, the answer may be both: doing skill-based exercise *and* aerobic exercise may work best of all, in particular for targeting cognition. Your physical therapist may incorporate skills and aerobic training by having you do exercises with set goals. A goal might be to stay at a certain speed or finish a task at a certain time.

How can you try to do both skill-based exercise and aerobic exercise together?

- Learn to play tennis
- Spin training
- Walk a course (through your neighborhood) with the goal of finishing in a pre-set time

KEY POINT: Mixing up exercises that are skills-based and/or aerobic offers the opportunity to get both motor and cognitive benefits.

EXERCISE AND NEUROPLASTICITY

We've known for years that exercise improves muscle strength, flexibility, bone density and cardiovascular health. However, new research is showing us that the brain isn't just a passive beneficiary of these health benefits. When you take up a new sport, you *learn* it, and that is about your brain – not just your muscles – learning the movements. This process of teaching your brain a new pattern (whether it is a movement, being comfortable in a new place, or even learning a way to think) is called *neuroplasticity*. We have actually measured in animals that exercise leads to the following Parkinson's-fighting changes:

- Exercise changes how your brain uses the chemicals that signal from one cell to the next (*neurotransmitters*). Exercise actually made brain cells use dopamine more effectively.
- Exercise caused the animals to grow new blood vessels, helping brain cells to get the oxygen and nutrients they need to stay healthy and participate in the activities of thinking.
- Exercise changes brain circuits by changing the way the network of brain cells are connected. Exercise helps neurons grow new connections – synapses – and grow new neurons that become part of a more efficient brain network by releasing brain growth factors and other effects.
- Exercise helps the body's immune system to work more effectively, and recent research has suggested that the immune system may be a part of PD, too.

It really is amazing that by doing something enjoyable to make your body healthier, you are making your brain healthier, too.

KEY POINTS: Benefits of exercise include the following:

- Increased blood flow to the brain
- Increased expression of growth factors that strengthen brain connections
- Optimized use of energy by brain cells (improved metabolism)
- Reduced potentially harmful effects of the immune system (inflammation)
- Even better effects of the medicines you take to fight Parkinson's

Overall Key Points

- When you learn a new exercise skill (like tai chi, boxing or yoga) it helps both how you move and how you think.
- There is not just one best exercise – you should do aerobic, strength and skills exercises to get the best benefits.
- Doing a variety of different exercises, as well as pushing yourself to get better at the ones you do helps your neurons to grow new connections, resulting in learning.
- Exercise is a LIFELONG COMMITMENT.
- Exercise is medicine, and we don't see any signs that there ever will be a pill to replace it.

Chapter 5
Integrative Medicine

Written by Monique L. Giroux, MD

Thanks to advances in our ability to manage motor symptoms, our understanding of Parkinson's disease has evolved from one in which the motor symptoms were the primary focus of treatment to one where the broader effects of the disease process have become the key to successful treatment. Indeed, health is promoted and disease is best treated with a balanced, holistic approach that embraces engagement in care, positive lifestyle change, and complementary as well as conventional medicine. In this section you will expand your knowledge of available treatments to include integrative therapies. An integrative approach does not differentiate between lifestyle, complementary, and traditional medical therapies; instead, it promotes the idea that lifestyle and complementary therapies work synergistically to enhance healing, emotional wellbeing, and resilience.

Complementary therapies are increasingly popular: people in the U.S. spend over three billion dollars a year on them, and acceptance of such therapies in mainstream medicine is also growing. Exercise, once considered complementary, is now standard of care for PD. The same is true for diet and stress management. One study suggests that more than three-quarters of people with PD are turning to and embracing complementary therapies in an effort to feel better, reduce symptoms, and promote healing. Their reasons for use are varied and include the desire for control, distrust of mainstream health care, perceived safety, belief in natural products, fear of medicine side effects or toxicity, limited access to traditional treatment, cultural beliefs, marketing influences, and the belief in personal or innate healing.

There are multiple proposed mechanisms for how integrative therapies may help people with PD, including the following:

- *Cellular health:* Your body's cells, like your body itself, need to be healthy. Your cells need a healthy environment, oxygen and nutrition; they need to get rid of waste; and they even have cell-scale organs that have to work properly. For example, mitochondria are like the digestive system of the cell, turning sugars from the blood into energy the cell can use. Oxidative stress – a toxic byproduct of this cell metabolism – is like pollution in the cell's environment. Similarly, stress or injury cause inflammation, which is a warning sign, like a fire alarm, in the body. Each of these can be involved in PD and other neurodegenerative diseases. Researchers are actively studying supplements and natural therapies that can reduce or reverse these problems.
- *Neuroplasticity and neuroprotection:* Neuroplasticity refers to 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. Neuroprotection means saving neurons from damage caused by Parkinson's. This could be stopping or even reversing the course of the disease, the holy grail of Parkinson's research (there is more information about this in the next chapter). Our brains change subtly all the

time – influenced by our daily actions, activities, and thoughts. Stress causes the body to release chemicals that can harm the brain, which is why stress often leads to fatigue, inactivity and even isolation. Therefore, learning to manage stress and participating in creative and emotionally- and spiritually-rich activities can help protect the brain from harm. Even better, exercise – involving the coordinated motion of the whole body – is good for both body AND brain. Exercise can strengthen brain networks and improve the health of brain cells that have been weakened by Parkinson's.

- *Stress reduction:* Stress harms the brain, but this can be offset by activities that help you relax. Many mind-body therapies work in part by enhancing relaxation. These strategies engage the parasympathetic nervous system, the "rest and digest" response that slows many high-energy body functions, as opposed to the "fight or flight" response of the sympathetic nervous system, which increase heart rate, blood pressure, and other reflexes in response to a perceived threat.
- *Placebo and "nocebo":* Any treatment you believe will help you will give you a placebo effect – a benefit above and beyond any actual biochemical or biological benefit due to the belief that the treatment will work. Some treatments may even work entirely through this process. The strength of placebo effect depends on the expectations you have for a treatment, your prior experience with a similar treatment, and how much you value a treatment. If you fear or don't want a treatment, it can give you a "nocebo" effect – a negative effect that you experience because of fear or rejection of the treatment.

SAFE AND WISE SELECTION

Evidence-based medicine is the practice of integrating individual clinical expertise, best external evidence (research), and patient values and expectations into care decisions, and these principles are regularly applied to the safe use and promotion of traditional medical and surgical therapies. Researchers perform blinded placebo-controlled studies to insure that treatment results are due to the biological effects of the treatment rather than the psychological effects of being involved in a study. A study is blinded when neither the doctor nor the patients know who is getting the drug or treatment being studied or a dummy treatment such as a sugar pill (placebo). If a new treatment is better than the dummy treatment in the study, then health care providers can choose that treatment to help their patients. In Chapter 6, the importance of double-blind, placebo-controlled studies and their role in modern science will be briefly described. Physicians' training leads them to respect this vigorous scientific method.

Unfortunately, this level of evidence showing both safety and efficacy does not exist for many integrative therapies. With drugs, regulators monitor claims made about how effective they are. On the other hand, because they are often based on natural products, exercise, or therapies, integrative treatments tend not to be so strictly regulated. Without regulation, these treatments can be marketed based on exaggerated claims. Many products are promoted as able to treat symptoms and even cure disease, without the evidence to support these claims. Anecdotal reports and passionate personal stories are used in place of carefully conducted scientific research.

Many clinicians are skeptical of integrative therapies because there is no objective scientific research to support their use. The fact that most physicians trained in Western medicine do not have formal training in complementary therapies also makes them cautious, and perhaps uncomfortable, with the use of such products and techniques. This is understandable; however, a treatment can be helpful even if it has not been studied. Some treatments just do not lend themselves to placebo-controlled studies or are too difficult or too expensive to study. For example, supplements can be studied in a controlled manner, similar to prescription medication, but such a trial can be expensive. Massage, another example, is difficult to study, as it is difficult to find an effective placebo treatment.

How to Evaluate and Incorporate Integrative Therapies

- Discuss therapies with your medical provider. See helpful talking points in the section "How to Talk to Your Neurologist about Integrative Therapies" on page 52.
- Use the therapy or treatment to support and enhance traditional therapies treatments that have scientific proof for benefit rather than in place of these treatments.
- When possible, look for therapies with placebo-controlled research studies to support their use in people with PD.
- If there is no or limited research for the use of a desired therapy in people with PD, look for studies that evaluate the effect of these therapies in people with other chronic or neurologic conditions.
- Practice a healthy sense of skepticism when evaluating therapies based on individual stories, strong marketing campaigns, and promises.
- Don't expect vitamins and supplements to substitute for healthy nutrition or replace your medications.
- Check the label for exact contents and listed side effects. If a product does not contain a detailed label, consider not taking it.
- Analyze the risks and benefits of a treatment. If you determine that a treatment is high risk, you should not try it unless you find scientific evidence supporting its benefit.
- Broaden your definition of risk and benefit to include *extended risk* and *extended benefit*:
  - *Extended benefit* includes unanticipated or potentially unexplained results of using a therapy or treatment. For example:
    - There is no clear scientific explanation for the effects of Reiki therapy, yet there are measurable physiologic changes to suggest that Reiki can enhance the relaxation response important for health and healing.
    - You may change your behavior to focus on more positive activities or habits, such as diet and exercise, if you have less pain, more energy, and a greater focus on health.
  - *Extended risk* refers to activities you are not doing or thoughts you may have because of the treatment that can be detrimental to your health. For example:

- You choose not to go to the gym because you receive massage therapy.
- You do not improve your diet because you take vitamins.
- You do not think appropriate medicine is needed since you take supplements.

Another example of extended risk is cost. If the cost of a therapy could otherwise be used for an activity with proven benefit, such as exercise, healthy diet, or mindfulness classes, then it might not be money well spent.

- Look for products with the designation "USP Verified." The U.S. Pharmacopeial Convention (USP) is a scientific nonprofit organization that sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements. The "USP Verified" label ensures that supplements and natural therapies are produced, labelled, and stored according to accepted guidelines and Good Manufacturing Practices (GMP).
- European herbs and supplements are subject to standards and regulations. Supplements from other areas and some U.S. companies may be contaminated with harmful substances. For example, in 1998 the California Department of Health reported that 32% of Chinese patent supplements contained undeclared chemicals such as lead, mercury, and arsenic.
- Choose a balance of activities: your treatment plan could include a combination of therapies that focus on nutrition, physical and muscular health, and emotional wellbeing.
- Choose a balance of active and passive therapies. Active therapies require work and focus; examples include mindfulness meditation and maintaining a healthy diet. Passive therapies do not require such focus and include massage therapy and vitamins.
- Seek out therapists and practitioners that hold specific credentials and certification or structured training in their field.

HOW TO TALK TO YOUR NEUROLOGIST ABOUT INTEGRATIVE THERAPIES

Adapted from Optimal Health with Parkinson's Disease. A Guide to Integrating Lifestyle Alternative and Conventional Medicine *by Dr. Monique L. Giroux, page 47.*

Estimates suggest that less than half of people with PD talk to their health care provider about the complementary therapies they use. Some people do not bring it up because they don't want their providers to know, or because they don't think it's important. Other people wait for providers to ask, but many do not. This might be because they lack knowledge of these therapies or are skeptical of – and therefore hesitant to discuss or promote – them.

Fortunately, a growing number of U.S. medical schools now offer courses in complementary medicine, combining the best of Western science with other treatment modalities. The National Institutes of Health has also been instrumental in disseminating research data to practicing health care professionals through the National Center for Complementary and Integrative Health (NCCIH).

The following tips and examples can help you talk to your doctor even if he or she is skeptical of integrative therapies.

- Begin with a discussion of your goal for treatment before discussion of a specific treatment option: "I am interested in finding non-medical ways to treat my back pain. My goal is to reduce pain so that I can reduce reliance on pain medicine."
- Reinforce your self-care values and priorities: "I have always been interested in personal healing and believe that certain non-traditional therapies can be helpful. Trying these therapies also gives me a sense of hope and control, which is important to me."
- Describe the mechanism by which you believe a certain therapy may help: "Research supports the use of acupuncture for pain."
- Reinforce the fact that you would like to begin this therapy for your own self-care and not to replace appropriate traditional therapies they may prescribe: "I know this is not the only solution, so I will continue to take my medicines and see the physical therapist prescribed to help my back."
- Discuss the potential risk of the treatment and what you will measure as a sign of progress as well as reason to continue, limit, or stop treatment: "According to my research, the risk of acupuncture is low. I will be sure to find an acupuncturist that is trained and certified. There is cost associated with this treatment, so I will discuss my pain control goals with the therapist before starting and agree on a specific number of treatments before re-evaluating benefit. I will also be sure not to change any medicines without discussing with you [neurologist] first."

KEY POINT: Complementary therapies can be used to ease medication burden, but should not replace Parkinson's medications or the treatments recommended by your neurologist.

INTEGRATIVE THERAPIES

The National Center for Complementary and Integrative Health (NCCIH) categorizes integrative therapies as generally falling into one of two subgroups:

1. *Natural products* include plant-derived chemicals and products, vitamins and minerals, and probiotics. They are widely marketed and available and are often sold as nutritional supplements.
2. *Mind and body practices* include a range of procedures and techniques administered by someone who is trained in that method. The focus is on the interaction between mind, body, social, mental, and spiritual factors, and include yoga, chiropractic manipulation, meditation, massage, and acupuncture.

While not a complete list, the following section describes therapies studied for use in PD as well as some common therapies used by people with PD. The information provided should not be taken as recommendations for these substances, but should be used as discussion points when consulting with your licensed health care professional.

KEY POINTS

- Most herbs and supplements have not been rigorously studied as safe and effective treatments for Parkinson's disease.
- The FDA does not strictly regulate integrative therapies.
- There is no guarantee of safety, strength, or purity of supplements not monitored by the FDA.
- Beware of unproven treatments or websites – check everything with your health care team.

Natural Therapies

Natural therapies – plant-derived chemicals and products, vitamins, and supplements – are used by people who believe they will promote cell health and healing, control symptoms, and improve emotional wellbeing.

Vitamins and Minerals

Vitamins and minerals are not produced by the body, but they are needed in small amounts for cell growth and development. Vitamins are complex organic chemicals, meaning they can be broken down by chemical reaction; minerals are inorganic compounds, which cannot be broken down by chemical reaction. Both vitamins and minerals are found in foods and also can be taken as supplement pills. Research across many different disease states has indicated that people benefit more when they get their vitamins and minerals primarily from foods, rather than pills. This is based in part on the concept of food synergy: vitamins in their natural form are better absorbed and work together for benefits compared with the artificial ratios and chemical derivatives found in many vitamin supplements. Furthermore, there is no data to suggest that taking vitamin supplements when you are not actually deficient in those vitamins will improve health or symptoms. In other words, if you have regular levels of vitamin D, for example, you are not likely to receive benefits from taking extra vitamin D pills.

Calcium and Vitamin D

Ninety-nine percent of calcium is stored in bones. It improves bone strength and protects against osteoporosis (low bone density) and fractures from falls. Most men need 1000 to 1200mg of calcium daily, and women need about 1200mg daily. Research cautions that calcium in supplement form carries some risk not present with food sources of calcium. When researchers analyzed data from 8,000 people in 15 studies, they found that if 1,000 people were given calcium supplements for five years, they would experience 14 heart attacks, 10 strokes, and 13 deaths, in exchange for preventing just 26 fractures.

Vitamin D is the "sunshine vitamin": it is produced by the body when ultraviolet rays from sunlight hit the skin. It plays an important role in bone health by increasing how much calcium your bones can absorb. Low vitamin D levels are associated with an increased risk of developing PD, as well as depression, cognitive impairment, and falls. However, there is no data that shows treatment with vitamin D slows the progression of PD or alters symptoms after diagnosis.

Vitamin D is fat-soluble (stored in body fat), so it can be dangerous if taken in high doses. The U.S. Institute of Medicine recommends that a vitamin D level of 20 ng/mL (50 nmol/liter) or above is adequate for bone health. A simple blood test can determine if your vitamin D level is low or if you've had too much.

Food sources

- Calcium is found in many foods.
  - Milk, yogurt, and cheese are the main sources of calcium for most people in the U.S.
  - Kale and broccoli are vegetable sources of calcium.
- Few foods in nature contain vitamin D.
  - Fatty fish like tuna, mackerel, and salmon are some of the best sources of vitamin D.
  - Most milk sold in the U.S. is fortified with vitamin D.

B Vitamins

Diets low in B vitamins are linked with various negative effects, while diets high in B vitamins can lower risk for some conditions. For example:

- Low vitamin B12 is linked to cognitive difficulties and peripheral neuropathy (loss of sensation in feet that can worsen balance).
- Folate deficiency is linked to depression.
- People with diets high in B6 have lower risk of PD.

Furthermore, vitamins B6, B12, and folate can reduce excessive levels of homocysteine produced when levodopa is metabolized. This is beneficial, as elevated levels of homocysteine can cause blood clots, heart disease, and stroke.

Repeated studies show strongest benefits when B vitamins are ingested from foods and fail to show a consistent benefit of taking vitamin B pills in the absence of vitamin B deficiency. Vitamin B6 dose should be less than 100mg daily, as higher levels can cause nerve toxicity, interact with the PD medicines MAO inhibitors (rasagiline and selegiline), and block the absorption of levodopa.

Food sources

- Vitamin B6 is found in poultry, fish, and organ meats, as well as potatoes and other starchy vegetables.
- Beef liver and clams are the best sources of vitamin B12. It is also found in fish, meat, poultry, eggs, milk, and other dairy products.
- Plant foods have no B12.

Vitamins A and E

Vitamins A and E have strong antioxidant properties (see below). Diets high in carotenoids (natural vitamin A) and vitamin E are associated with lower risk of PD, though there is no evidence that taking these vitamins treats PD once diagnosed. In fact, taking high-dose vitamin E is linked to premature death, underscoring that it is preferable to consume vitamins from food rather than in pill form.

Food sources

- Vitamin A is found in beef liver and organ meats, but these are high in cholesterol, so limit their intake.
- Green leafy vegetables and colorful vegetables such as broccoli, carrots, and squash are good sources of vitamin A.
- Nuts, seeds, and vegetable oils are among the best sources of vitamin E.

Antioxidants

Antioxidants are compounds that reduce the cell-damaging effect of oxidative stress, a toxic byproduct of cell metabolism that is thought to cause nerve cell death when left unchecked in PD and other neurodegenerative disorders. Similar to vitamins and minerals, antioxidants from foods display stronger disease-fighting capacity than pill-based antioxidants. Colorful fruits and vegetables, legumes, green tea, coffee, whole grains, and many seeds and nuts are food sources of antioxidants.

Glutathione and N-Acetyl Cysteine

Glutathione is a powerful antioxidant, but its levels decline as we age. It decreases in the substantia nigra of people with PD long before symptoms are significant. Glutathione is composed of three amino acids (building blocks of protein), so it is digested in the gastrointestinal tract (similar to proteins). This means it is not effective if taken in pill form, as most pills are digested in the stomach. Despite this fact, glutathione is sometimes advertised in pill form, reminding us that supplements and their marketing are not strictly regulated. N-acetyl cysteine is an alternative pill option, since it is converted to glutathione in the body.

Intravenous (IV) glutathione has been studied but has failed to show a benefit over placebo. In addition, IV therapy is expensive and comes with risk, such as pain and infection at the IV insertion site. Current studies using a glutathione nasal spray are showing some promise.

Inosine and Uric Acid

Inosine and uric acid are powerful antioxidant and anti-inflammatory agents. Inosine is metabolized to uric acid in the body. People with PD tend to have lower uric acid levels, while higher levels of uric acid correlate with a slower decline in PD motor symptoms. At the same time, high uric acid levels can cause a painful form of arthritis called gout, as well as kidney stones and high blood pressure. A phase 3 clinical trial is underway to test whether inosine is an effective therapy in PD (see Chapter 6 for more information on the research process).

Anti-inflammatory Agents

Anti-inflammatory agents reduce cellular inflammation, which is a proposed cause of ongoing nerve cell death in PD.

Omega-3 Fatty Acids (Fish and Krill Oil)

Diets high in omega-3 are associated with a lower risk of arthritis, stroke, depression, cognitive decline, and Alzheimer's disease. There is no direct connection between PD and omega-3 fatty acids, but studies remain limited.

Fish oil is derived from the tissues of oily fish, while krill oil is obtained from small sea-living crustaceans. Fish oil pills are the most commonly used omega-3 supplement. Typical doses of fish oil are 1000 to 1500mg daily combined DHA and EPA (two types of fish-derived omega-3 fatty acids). In a placebo-controlled study, fish oil with and without antidepressants improved PD depression.

Food sources

- Cold water oily fish such as salmon, mackerel, sardines, herring, halibut, and tuna are natural sources of omega-3 fatty acids.
- Vegetarian sources include flax seed, purslane, pumpkin, and walnuts, but these are less potent.

Curcumin

Curcumin is a polyphenol with strong anti-inflammatory and antioxidant properties. It is found in the turmeric root, which is an important ingredient in Indian cooking (responsible for the yellow color of curries). Turmeric is under study for its use in PD, dementia, cancer, and brain injury.

Bioenergetics

This category includes compounds that enhance cell energy production or serve as a brain or muscle energy source.

Coenzyme Q10

Coenzyme Q10 (CoQ10) is an antioxidant that assists in the mitochondrial energy production that is necessary for cell life. (Mitochondria are small, energy-producing structures inside cells – the "power plants" of cells.) Interest in CoQ10 stems from the finding that PD is associated with mitochondrial dysfunction and impaired energy production. People with a specific mitochondrial disease can be treated with CoQ10, however a large, multicenter study using large doses of CoQ10 failed to show any benefit and was halted early.

Furthermore, CoQ10 can be expensive, and what you get differs from one commercial product to the next. This supplement is fat-soluble, so absorption can vary based on foods eaten, time of day taken, other supplements taken at the same time, and the type of CoQ10 used.

Coconut Oil and Medium Chain Fatty Acids

Coconut oil contains an abundance of medium-chain fatty acids (defined by the number of carbon molecules in the chemical structure), which are a good energy source. Medium-chain fatty acids are metabolized to ketone bodies, and the brain actually uses ketones preferentially and more efficiently than glucose. There is longstanding interest in diets high in medium-chain fatty acids for Alzheimer's disease, and there have been some reports of improvement in measures of cognitive function. However, there are no published studies of coconut oil in people with PD.

Hydroxybutyrate is a ketone body under study for potential neuroprotective effects in PD.

Creatine

Creatine is a naturally occurring amino acid found in foods (especially meat); in the human body, its greatest concentration is in our muscles. Interest in creatine for use in PD is based on its role in improving mitochondrial energy production, muscle mass, and strength. A large, multicenter trial on the effects of creatine on people with PD was stopped early when analysis showed no difference between supplement and placebo.

Neurochemicals and Neuromodulators

Some practitioners are attempting to help their patients by using drugs or supplements that are classified as either neuromodulators – which they believe will interact with our brain's immune health and circadian body rhythms or neurochemicals – which activate or inhibit nerve cell activity.

Melatonin

Melatonin is a powerful antioxidant that is responsible for regulation of circadian rhythms, sleep, and wakefulness, so it is sometimes used to help people sleep. In a small study in people with PD who were carefully monitored, modest improvements in sleep quality were experienced with 5mg and 50mg, with the 50mg showing more favorable results. Melatonin 3 to 12mg can also reduce REM sleep behavior disorder. However, the safety of doses higher than 3mg is not established, so use with caution. Early morning sedation, depression, and vivid dreaming are experienced by some people who take melatonin; it can also alter blood sugar levels in people with diabetes and influence the immune system.

Naltrexone

Naltrexone is traditionally used to treat alcohol and narcotic (opioid) addiction or overdose, as it blocks opioid receptors in the brain and spinal cord (this system plays an important role in regulating pain). Naltrexone at lower doses (4.5mg) is used in multiple neurologic conditions including PD, multiple sclerosis, and impulse control disorders, but reports of benefit in PD are based on anecdotal or individual experiences that do not control for diagnosis, symptoms studied, or placebo effect, and overall research suggests that naltrexone does not improve motor symptoms. Despite this lack of evidence, this supplement continues to gain a significant following based on individual reports and strong marketing.

Botanicals

These are herbs or chemical derivatives of plants or plant-based agents used for their medicinal properties.

Marijuana

Marijuana refers to the dried leaves, flowers, stems, and seeds from the hemp plant Cannabis sativa. Although there are many chemicals with biologic activity in the plant, tetrahydrocannabinol (THC) and cannabidiol (CBD) carry the greatest medicinal interest. THC is the chemical known for its mood-altering effects, and CBD is a powerful antioxidant that has shown neuroprotective effects in research models of head injury and neurodegenerative disease. The latter holds promise for medical use since it does not have the psychoactive effects described with the marijuana plant or THC compound. People with PD have self-reported that use of marijuana helps manage nausea, loss of appetite, muscle spasm and spasticity, pain, and anxiety. A recent study showed improved sleep, pain, tremor and bradykinesia (motor slowness) 30 minutes after smoking marijuana in clinic.

However, it is not clear whether these benefits are from a direct effect of marijuana on PD brain chemistry or physiology. Marijuana has psychoactive, behavioral, and motor effects, which can all impact tremor and movement. For example, tremor will increase with stress and improve with treatments known to enhance relaxation. Marijuana's behavioral effects may lead to greater relaxation or euphoric mood, or may mitigate the stress response, and this alone could reduce tremor. As with any drug, there are pros and cons to using marijuana, and it is important to review these with your healthcare provider. In particular, the lack of regulation and the potential addictive and psychoactive consequences (including psychosis and apathy) are potential concerns. For more information on marijuana and PD, visit **www.parkinson.org/marijuana**.

Mucuna Pruriens

Mucuna pruriens, or cowhage seeds, have been used in India and Ayurvedic medicine for the treatment of PD for thousands of years because they contain 3-4% levodopa. Because of this, mucuna pruriens is often referred to as natural dopamine.

A small, controlled study comparing the effect of carbidopa/levodopa and mucuna pruriens in patients with motor fluctuations and dyskinesia showed faster and longer "on" time, without dyskinesia, after mucuna treatment. The authors propose that benefits from mucuna pruriens may be due to more than just levodopa.

Mucuna pruriens contains levodopa and therefore carries the same potential risks and side effects of levodopa. A greater concern is the lack of information about purity, strength, contamination, and toxins such as pesticides when purchased as a supplement.

Mind-Body Therapies

Mind-body therapies work on the premise that the mind, body, and spirit do not exist in isolation and that disease and/or symptoms change when these are out of balance. Many people feel these therapies make a difference for them. Practitioners believe that these therapies help by:

- Improving emotional wellbeing
- Enhancing cellular healing
- Improving physical or cognitive performance and symptom control
- Enhancing resiliency
- Promoting inner peace, acceptance, and relaxation
- Increasing positivity

Body Therapies

The following therapies use movement of the physical body for benefit.

Feldenkrais Method and Alexander Technique

The Feldenkrais Method and Alexander Technique are ways of learning how to reduce tension in the body through exercises that improve coordination, agility, and balance. These methods help participants learn and habituate new movements that studies have indicated may help reduce falls. The focus is on mind-body awareness, rather than exertion and fitness like traditional exercise, and they also offer benefits to individual feelings of comfort and body image.

The Alexander Technique and Feldenkrais Method have many similarities and some subtle differences. Alexander Technique uses a structured hands-on approach for awareness of alignment and body position, while the Feldenkrais Method focuses on practitioner guidance and spontaneous and self-generated expression to increase ease and range of motion. Feldenkrais improved PD-associated balance problems, and the Alexander Technique improved measures of disability, depression, and attitudes toward self-care compared to a group getting massage or no treatment, and this effect seemed to persist after active training ended. In addition, the focus of the Alexander Technique on upper body postures and voice suggest that this may be of help for speech problems associated with PD, but no studies have yet tested this hypothesis.

Massage

There are many different types of massage and massage techniques. Some, such as medical massage, focus on relaxation, while others focus on muscle and deep tissue relaxation/release. Clinical studies investigating the benefits of massage in PD have shown improvement in self-reported daily activities and self-confidence. Avoid massage over DBS batteries, wires and scalp. Aggressive massage can exacerbate spasm associated with dystonia.

Music Therapy

Music therapy uses components of sound such as beat, melody, tone, and lyrics to promote healing. Research suggests that music therapy can reduce bradykinesia (slow movement)

and rhythmic sound can help freezing of gait. Music and sound can be used to improve many symptoms, including speech, apathy, low energy, and mood. A music therapist is certified by the Certification Board for Music Therapists (www.cbmt.org).

Tai Chi and Qigong

Tai chi is both an ancient martial art and an exercise. Characterized by gentle, flowing movement couple with breathing, it is becoming increasing popular due to its low impact on joints. Qigong combines the breath with subtle, flowing movement along with focused attention to release life energy (chi) and reach a calm state of mind. Both tai chi and qigong have been shown to improve in people with PD.

Yoga and Therapeutic Yoga

Yoga unites the mind and body through physical postures, use of the breath, and meditation to bring awareness to sensations of the body, thoughts, and emotions. Hatha yoga uses physical postures (poses) to join the mind and body. Therapeutic yoga blends traditional yoga with gentle postures, breathwork, meditation, and guided imagery to promote physical health, relaxation, and emotional healing. Therapeutic yoga programs are often designed to promote relaxation, reduce pain, enhance mood and relaxation, and support healing in the setting of chronic illness. It is best to look for a teacher who has experience working with people with Parkinson's.

Mindful Therapies

These therapies use the mind to influence thoughts, stress, emotional responses, and physical and sensory awareness. Examples of mindful therapies include biofeedback, guided imagery, hypnosis, guided breathwork, and meditation. Mindfulness meditation is reviewed below.

Mindfulness Meditation

Meditation is a broad term defining many practices designed to focus the mind to enhance relaxation, gain insight and control over emotional and physical responses to daily experiences, and improve compassion as well as mental or physical performance. Meditation can be performed both informally and formally. There are many formal meditation practices, including concentrative, heart-centered, mindfulness-based, reflective, creative, and visualization-based practices, but it can also be done informally. There are many apps for that!

Mindfulness-based meditation involves bringing attention or awareness to the moment without judgment. Focus is on observation, insight, and letting go. Mindfulness is particularly helpful for living with chronic illness: it increases resiliency by encouraging living life to the fullest despite, in response to, or as a result of difficulties. This is done through understanding that each moment is impermanent, change is part of life, and you have control of your thoughts, all of which helps prevent the downward spiral that can accompany distress.

Numerous studies across multiple conditions show that mindfulness meditation improves quality of life, sleep, and mental function and decreases depression, anxiety, fatigue, and pain. Studies examining the effect of this therapy on PD are underway. Brain MRI studies in people with PD practicing mindfulness meditation showed changes in brain activity and size in the amygdala, hippocampus, thalamus, and caudate nucleus, all important brain structures for control of movement, learning, and stress.

Energy Therapy

Energy medicine is a unique form of mind-body therapy based on the premise that energy is an important part of health and balance. Practitioners believe that systems of energy exist within our body, between individuals, and in the environment. They believe that balance of these energy systems affects health, and blockage or disequilibrium impacts disease. Practitioners of energy therapies use sound and heat as well as visual, electromagnetic, tactile, and emotional energy to heal.

Acupuncture

Acupuncture is an ancient treatment originating over 2500 years ago. Different forms or styles of acupuncture are performed in the U.S., influenced by Chinese, Japanese, or Korean medicine. An acupuncturist inserts tiny needles into specific body areas that they believe will change the flow of energy or Qi. According to these practices, health is associated with unobstructed energy flow, and disease is associated with blocked Qi. They believe that energy flows through the body along channels or meridians. Acupuncture points are locations where they believe these meridians are close to the skin's surface. While some studies have found a benefit from acupuncture, other studies have found that "sham acupuncture" (where a practitioner applies the acupuncture needles into places on the body that are not acupuncture points) is as good as true acupuncture.

Reiki

Reiki is a Japanese technique for healing and stress reduction that adherents believe works on the premise that an unseen energy or life force flows within our bodies and between individuals. Through placement of hands on or over different areas of the body, the Reiki practitioner is believed to transfer, guide, and direct flow of energy. Like many mind-body therapies, there are no objective controlled studies evaluating the effect of Reiki on PD, and benefits rely on personal stories and experiences. Nonetheless, there is much interest in Reiki therapy in the PD community. Meta-analysis of multiple studies suggests that Reiki may have positive effects on pain and anxiety.

USE TECHNIQUES THAT WORK FOR YOU

Many people enjoy benefits from these techniques even though some have no scientific foundations and some have been tested scientifically and have failed. If integrating one or more of these alternative techniques into your care helps you feel better and more in control of your life and symptoms, there is no reason to wait for science to validate your choices. While scientists may have found no evidence that Qi exists and that acupuncture changes it, several studies have found that, for example, acupuncture does help patients who have chronic pain. If something helps you to live your best life, you don't need scientists to figure out how it works before you take advantage of that benefit!

Chapter 6
Research and Future Developments

The discussion in this chapter addresses:

- The development of new drugs
- Evaluating research reports
- Symptomatic treatment
- Neuroprotective treatment
- Neurorestorative treatment

Drugs for Parkinson's disease that are currently being investigated in clinical trials will be reviewed in this chapter. Most of these compounds are not yet available for prescription use. You may wish to periodically check with your healthcare providers to see if certain agents are close to release by the FDA or to inquire about participating in a clinical trial. You can also visit www.clinicaltrials.gov, a website sponsored by the National Institutes of Health (NIH), which offers information on clinical trials.

DEVELOPMENT OF NEW DRUGS

Here is a brief tutorial on the multi-year process by which pharmaceutical research brings new drugs to your local pharmacy. Most drugs are studied in animals before they are tested in humans. Each drug must then progress through the following series of research studies in humans before it can be approved for use by the FDA.

Phase I studies are typically conducted with healthy volunteers. The drug is tested in a small group of 20-80 people while researchers observe side effects, judge the safety of the drug and determine safe dosage ranges.

Phase II studies are conducted in a larger group of people who have the symptoms or illness that the drug is designed to treat, such as Parkinson's disease. The goal of Phase II research is to evaluate the drug's effectiveness as well as to gather more information about safety and tolerability.

Phase III studies are conducted with a much larger group of at least 1,000 people with a particular disease. In addition to testing the drug's effectiveness and cataloging possible adverse effects, Phase III testing seeks to compare the drug to other similar approved drugs or to placebo (also known as a sugar pill or dummy pill).

The two most important characteristics of a Phase III trial are:

1) **Randomization** of subjects to receive the experimental drug or placebo, which means that study participants are assigned to a treatment group using a method based on chance; it is meant to minimize the differences between groups so that study results will be unbiased and reliable. If more than one dose of a drug is being evaluated, more subjects are needed to give the study enough statistical power to reach a valid conclusion about the drug's effect on the disease being observed.

2) **Double-blind**, meaning that neither patient nor investigator knows which drug a patient is taking. This is another way to prevent observer bias in evaluating the effect of the drug.

Once a drug has successfully completed Phase I, II and III testing, it may be submitted to the FDA for approval. Once approved, the medication can be prescribed by physicians and other licensed healthcare providers.

Phase IV studies test the new, approved drug for additional benefits that may not have been studied in earlier phases. Phase IV studies also gather information regarding long term use and safety of the drug.

The entire process of bringing a new medication to the pharmacy can take up to ten years from the time that it is tested in a laboratory to the time that the doctor prescribes the drug for a person with disease.

EVALUATING RESEARCH REPORTS

New drugs and other PD treatments often garner attention from the popular media, especially televised advertisements. While headlines may make it sound like new drugs are available, a closer look often reveals that the new drug is only in the early stages of research and years away from becoming an available treatment. Taking some time to evaluate the research behind the headlines can help determine the best way to use the new information.

Following are some questions to ask when evaluating clinical studies of new medications and treatments for PD:

- **What is the source of the information?** Has the information been published or presented at a reputable scientific meeting? Or is the information derived from unscientific opinion? Check with a member of your healthcare team to determine if the source is reliable.
- **How many people participated in the study?** The higher the number of participants, the more likely the results will achieve statistical significance.
- **How was the study designed?** Were the subjects randomized to equal treatment groups? Was the study double-blind? Was a placebo group incorporated into the study's design? The gold standard for the most valid clinical trial is one that includes all of these elements.

NEW THERAPIES ON THE HORIZON

To fully appreciate where we are going with Parkinson's disease treatment, it is important to realize where we have been. Since the approval of Sinemet (carbidopa-levodopa) in the 1970s, research has yielded many life-changing treatments for Parkinson's. Taking together research breakthroughs in our understanding of medications, therapies and devices to treat Parkinson's, today's best care yields a very different disease journey than was experienced a generation ago. Today's focus on non-motor symptoms is largely a consequence of how effective treatments for motor symptoms are.

Today, the biggest research challenge is slowing progression. It has been demonstrated that today's best treatment plan – which involves expert medication, therapy, exercise and sometimes surgery – slows your experience of Parkinson's progression and may actually be helping your brain fight the disease.

New research is investigating opportunities in several areas:

- **Slowing disease progression.** The holy grail of Parkinson's research is to slow the progression of the disease. If we could diagnosis the disease earlier and slow its progression, people might never actually experience troublesome symptoms, effectively getting a "vaccination" effect. Also, people with Parkinson's often have a combination of brain cells that die and others that get "sick" so that they don't work as well. If we could make a treatment that would slow the disease progression, some of these brain cells could get better and start to work again, resulting in a moderate improvement in status.
- **Replacing lost function.** For people who have Parkinson's, it would be great if we could come up with therapies that would help the brain to function more like it does in people without Parkinson's. To date, there is not much evidence that this can be successful, with surgical approaches like transplants of brain cells failing to be effective in well-designed trials. However, there are scientists who are still working on studying therapies to replace lost cells in the brain, and there have been some promising developments.
- **Preventing Parkinson's.** Many researchers are looking at genetic and environmental causes of Parkinson's to see if they can identify targets for drugs that would help brain cells to fight the changes that cause Parkinson's. If we could do this, then our children could be tested for risk factors, and people with a high risk for Parkinson's could receive treatments to prevent it. Such a treatment might also slow Parkinson's disease in people who already had the disease, but it might not.
- **Diagnosing Parkinson's and measuring progression.** Most people with Parkinson's can be easily diagnosed by a neurologist using standard clinical tests. However, sometimes it can be difficult to tell the difference between Parkinson's disease and other conditions that mimic it, like when you experience Parkinson's-like symptoms because of other medications, essential tremor or a small stroke. Further, figuring out how far Parkinson's has progressed or your progression since your last evaluation is also difficult, as it may depend on where you are in terms of fluctuating medication effect, your level of fatigue and whether or not you got stuck in traffic on your way to the clinic. A better measure for progression would help with clinical trials of treatments to slow the disease.
- **New symptomatic treatments.** While treating the symptoms of the disease is not the same as slowing its progression, we are quite confident that exercising at least 2.5 hours a week does slow your experience of disease progression. In order to exercise, you need to have your symptoms optimally in control. Research is ongoing in many areas, including helping people who experience fluctuating medication effects (i.e., "on-off fluctuations"); reducing dyskinesia; achieving better motor control; and managing a range of symptoms, from mood and psychiatric symptoms to autonomic symptoms like lightheadedness on standing (orthostatic hypotension), constipation and others.

Parkinson's research has made amazing progress in the last two decades, and all the signs suggest that progress will continue unabated. There are trials, drugs and therapies on the horizon that are likely to help people with PD in the next few years, but these change frequently as studies show effects or no effects of a particular treatment. Please visit the Parkinson's Foundation website, **www.parkinson.org**, to find information and resources on the newest research and treatment options. You can also contact our Helpline at 1-800-4PD-INFO (473-4636) or **helpline@parkinson.org** for help finding a clinical trial near you, so that you can help scientists find the next breakthrough therapy!

WHAT DO WE MEAN BY CURE?

People often talk about how we need a *cure* for Parkinson's disease. What does that really mean?

- The first step in curing Parkinson's would be **stopping the disease progression**, or slowing it enough that we can't tell the difference between Parkinson's and the changes people experience naturally from aging. There are a number of ways in which scientists are working to help brain cells fight the effects of Parkinson's. Most of this work is looking at drugs that people with PD could take or have administered at a hospital or clinic. Scientists have some good leads that they are following with the hope of slowing the disease.
- The second step would be **restoring lost function**. To some extent, we do this every day through interventions like exercise, physical therapy, occupational therapy and speech therapy, where clinicians help you compensate for the changes caused by Parkinson's. All of us have to compensate for changes in our bodies and brains as we age, and so good therapy really does restore lost function. However, we would like to gain this benefit faster, and some of the changes with Parkinson's can't be corrected with therapy, so there is research into ways to restore cells that have been lost. Scientists call this neurorestoration. Unfortunately, unlike bones and skin, the brain doesn't have systems to automatically repair itself or to integrate a graft or transplant to replace cells that have been lost. So far, neurorestoration has turned out to be a very hard task.

A **cure for Parkinson's** would ideally offer both of these benefits. However, if we had a treatment that could dramatically slow or stop disease progression, with early diagnosis we could hold people in the earliest stages of Parkinson's for a long time.

Appendix A
Glossary

Acetylcholine – A chemical messenger released by cholinergic nerves; involved in many brain functions, such as memory and control of motor activity. There appears to be an interplay between the actions of acetylcholine and dopamine.

Adjunctive – Supplemental or secondary to (but not essential to) the primary agent (i.e., medications used to enhance levodopa therapy).

Antihistamine – A drug normally used to control allergies or as a sleep aid; some (like Benadryl) are anticholinergic drugs, with anti-tremor properties.

Anxiolytic – An agent, usually referring to a class of medications that reduces anxiety.

Autonomic neuropathy – Damage to the autonomic nerves, which affect involuntary body functions, including heart rate, blood pressure, perspiration, digestion and other processes. Signals between the brain and portions of the autonomic system are disrupted. Symptoms vary widely, depending on which parts of the autonomic nervous system are affected. They may include dizziness and fainting upon standing (orthostatic hypotension); urinary problems including difficulty starting urination, overflow incontinence and inability to empty your bladder completely; sexual difficulties including erectile dysfunction or ejaculation problems in men, and vaginal dryness and difficulties with arousal and orgasm in women; difficulty digesting food (gastroparesis); and sweating abnormalities including decreased or excessive sweating.

Benzodiazepines – A popular and effective class of anti-anxiety drugs.

Catechol-o-methyl transferase (COMT) – An enzyme that inactivates levodopa in the body before it gets to the brain. COMT inhibitors block the work of the enzyme, so more levodopa is available to the brain.

Compulsive behaviors – Performing an act persistently and repetitively without it necessarily leading to an actual reward or pleasure; in Parkinson's, this can be a side effect of dopamine agonists and usually takes the form of uncontrolled shopping, gambling, eating, or sexual urges. If you experience this symptom, tell your doctor immediately.

Confusion – The state of being unclear, with lack of understanding of situation and/or surroundings; a symptom of many medications for Parkinson's motor and non-motor symptoms.

Corticobasal degeneration (CBD) – A progressive neurological disorder characterized by nerve cell loss and atrophy, or shrinkage, of multiple areas of the brain including the cerebral cortex and the basal ganglia. Initial symptoms may first appear on one side of the body, but eventually affect both sides. Symptoms are similar to those in PD, such as poor coordination, absence of movements, rigidity, impaired balance and abnormal muscle postures. Other symptoms may include cognitive and visual-spatial impairments, loss of the ability to make familiar, purposeful movements, hesitant and halting speech, muscular jerks and difficulty swallowing. An individual with corticobasal degeneration eventually becomes unable to walk.

Delusion – False, fixed, idiosyncratic belief, not substantiated by sensory or objective evidence.

Dementia – Not a diagnosis, but descriptive of a broad symptom complex that can arise from a variety of causes. Symptoms can include disorientation, confusion, memory loss, impaired judgment and alterations in mood and personality.

Dementia with Lewy bodies (DLB) – A progressive degenerative disease or syndrome of the brain that shares symptoms of both Alzheimer's and Parkinson's disease and is characterized by fluctuating cognition, hallucinations and parkinsonism.

Diminished/decreased libido – Decreased sexual urges; a symptom of many medications for depression and anxiety.

DNA – Deoxyribonucleic acid; the basic chemical substance that makes up a gene.

Double-blind study – A study in which neither the participants nor the investigators know which drug a patient is taking; designed to prevent observer bias in evaluating the effect of a drug.

Dry mouth – Usually from decreased saliva production; a side effect of many medications for motor and non-motor symptoms.

Dyskinesia – Abnormal involuntary movement of muscles. Dystonia, athetosis and chorea are forms of dyskinesias.

Dystonia – Involuntary spasms of muscle contraction that cause abnormal movements and postures.

Endogenous – Originating internally; developing from within (e.g., an endogenous depression is not caused by external circumstances).

Etiology – The science of causes or origins of a disease; the etiology of Parkinson's disease is unknown.

Exogenous – Originating externally; relating to external factors (i.e., an exogenous depression might arise following a major life crisis).

Extended benefit – Unanticipated or potentially unexplained results of using a therapy or treatment.

Extended risk – Activities you are not doing or thoughts you may have because of a treatment that can be detrimental to your health.

Futility studies – a drug trial design that tests whether a drug is ineffective rather than the traditional study of whether it is effective. Relatively short futility studies allow for multiple drugs to be tested more quickly and easily, and further efficacy trials are offered for drugs that "pass" the futility trial.

Glutamate – A salt or ester of glutamic acid related to the hydrolysis of proteins.

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.

Hallucinations – Something you see, hear, smell, taste, or feel that is not actually there; can be a side effect of anticholinergics and some medications for depression and anxiety.

Hallucinosis – A state of experiencing hallucinations. In PD, hallucinations are usually visual in nature and insight into reality may or may not be retained.

Holistic – Characterized by the treatment of the whole person, taking into account social and other factors, not just symptoms of disease.

Homocysteine – An amino acid that occurs in the body and is produced when levodopa is metabolized; elevated levels of homocysteine can cause blood clots, heart disease, and stroke.

Hydrophilic – Capable of uniting with or taking up water.

Idiopathic – An adjective meaning unknown; the most common form of PD is idiopathic Parkinson's disease.

Integrative medicine – Involves bringing together conventional and complementary approaches in a coordinated way. The National Center for Complementary and Integrative Health uses the term "complementary health approaches" when discussing practices and products of non-mainstream origin, and the term "integrative health" when talking about incorporating complementary appoaches into mainstream health care.

Low blood pressure – When blood pressure is below normal (normal range is usually between 90/60 mmHg and 120/80 mmHg); the medical name for low blood pressure is hypotension; common side effect of levodopa and dopamine agonists. *See also "neurogenic orthostatic hypotension."*

Mild cognitive impairment – A transition stage between the cognitive changes of normal aging and the more serious problems of dementia. Mild cognitive impairment can affect many areas of cognition such as memory, language, attention, reasoning, judgment, reading and/or writing. Mild cognitive impairment may be irritating but it does not typically change how a person lives their life.

Mind-body therapies – Therapies that work on the premise that the mind, body, and spirit do not exist in isolation and that disease and/or symptoms change when these are out of balance.

Monoamine oxidase type B (MAO-B) – An enzyme in our body that breaks fown dopamine; MAO-B inhibitors block the work of the enzyme, so there is more dopamine available in the brain.

Multiple system atrophy (MSA) – A progressive neurodegenerative disorder characterized by symptoms of autonomic nervous system failure (such as lightheadedness or fainting spells, constipation, erectile failure in men and urinary retention) combined with tremor and rigidity, slurred speech or loss of muscle coordination.

Natural therapies – Plant-derived chemicals and products, vitamins and minerals, probiotics, and nutritional supplements used to promote cell health and healing, control symptoms, and improve emotional wellbeing.

Nausea – A feeling of sickness with an inclination to vomit; common side effect of many medications for Parkinson's symptoms.

Neurons – The structural and functional unit of the nervous system, consisting of the nerve cell body and all its processes, including an axon and one or more dendrites.

Neurodegeneration – Loss of cells of the brain or spinal cord. Over time, it leads to dysfunction and disability.

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.

Neurogenic orthostatic hypotension (nOH) – Orthostatic hypotension (OH) is a drop in blood pressure that happens within a few minutes of standing up. Parkinson's disease and some other diseases can cause OH – in this case, it is called neurogenic OH, since it is related to dysfunction of the nervous system.

Neuroprotection – An effect that results in recovery, repair, or regeneration of nervous system structure and function.

Neurorestoration – Repair, replacement, or regeneration of brain cells.

Neurotransmitter – A biochemical substance, such as dopamine, acetylcholine or norepinephrine, that transmits nerve impulses from one nerve cell to another at a synapse (connection point).

"Off-on" effect – Sudden or varying changes in motor performance and other Parkinson's symptoms. It may correlate with effects of medication wearing off.

Open-label – When both the researcher and the participant in a research study know the treatment that the participant is receiving. Open-label is the opposite of double-blind when neither the researcher nor the participant knows what treatment the participant is receiving. Open-label studies should be interpreted with caution because of the potential for biased conclusions.

Oxidative stress – A toxic byproduct of cell metabolism that is thought to cause nerve cell death when left unchecked in PD and other neurodegenerative disorders.

Pathogenesis – The production or development of a disease.

Pharmacodynamics – The study of the relationship of drug concentration to drug effect; essentially what the drug does to the body.

Pharmacokinetics – The study of the absorption, distribution, metabolism and excretion of drugs; essentially what the body does to the drug.

Placebo – A substance containing no medication; an inactive substance or preparation used as a control in an experiment or test to determine the effectiveness of a medicinal drug.

Placebo effect – The commonly observed phenomenon that people in drug studies tend to have improvement in their symptoms even when they are not receiving the actual study medication or therapy. This benefit above and beyond any actual biological benefit is due instead to the belief that the treatment will work.

Progressive supranuclear palsy (PSP) – A Parkinson's-like, degenerative brain disorder that causes progressive problems with gait and balance. There is an inability to aim the eyes properly, and persons often show alterations of mood and behavior, including depression and apathy as well as progressive mild dementia. Because some symptoms are similar, PSP is often misdiagnosed as Parkinson's or Alzheimer's disease. The hallmark distinguishing factor of PSP is early gait instability and difficulty moving the eyes. PSP, like MSA and CBD, does not respond very well to levodopa therapy.

Sham surgery – A surgery performed as a control in research; similar to the real procedure but omits the key therapeutic element ("fake" surgery).

Sialorrhea – Increased amount of saliva in the mouth, either from excessive production of saliva or decreased swallowing.

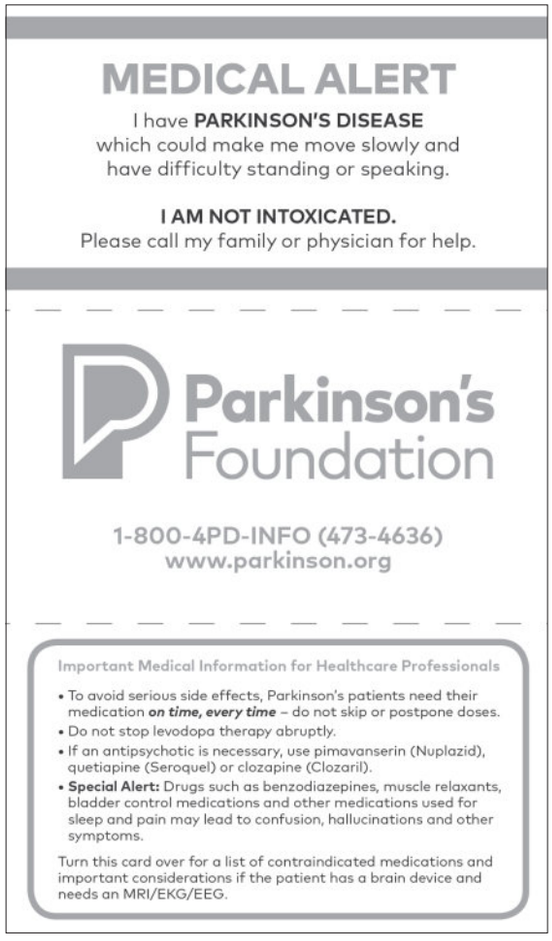
Substantia nigra – The area deep within the brain where dopamine is produced.

Tyramine – An amine that causes elevated blood pressure and increased heart rate by displacing the chemical norepinephrine from storage in the body. Tyramine is generally produced by fermentation of food products.

Vivid dream – A dream that is very realistic and can be caused by awakening during the dream; common side effect of medications for depression and anxiety.

Appendix B
Medical Alert Card

To order your free Medical Alert Card, call our Helpline at 1-800-4PD-INFO (473-4636). You can also download the card at **www.parkinson.org/books**.



MEDICAL ALERT

I have **PARKINSON'S DISEASE** which could make me move slowly and have difficulty standing or speaking.

I AM NOT INTOXICATED.
Please call my family or physician for help.

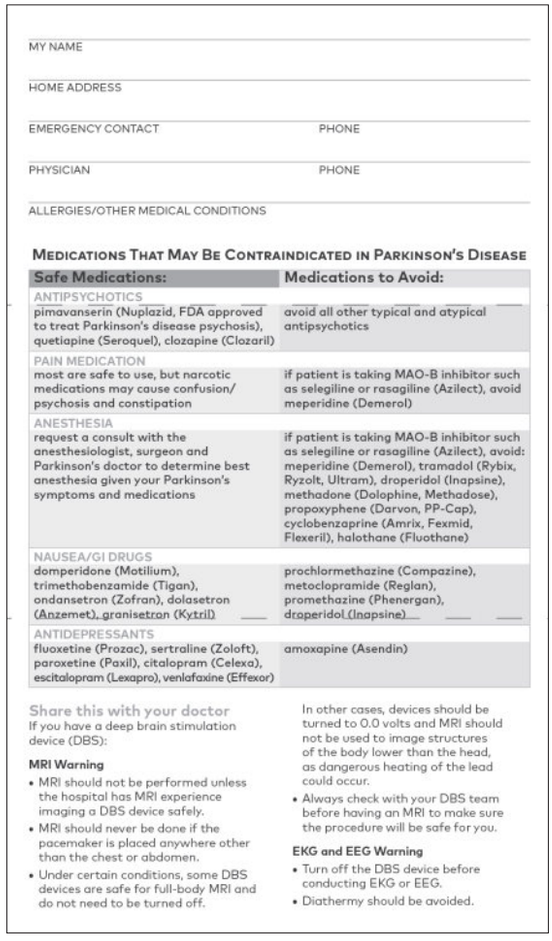
Parkinson's Foundation

1-800-4PD-INFO (473-4636)
www.parkinson.org

Important Medical Information for Healthcare Professionals

- To avoid serious side effects, Parkinson's patients need their medication ***on time, every time*** – do not skip or postpone doses.
- Do not stop levodopa therapy abruptly.
- If an antipsychotic is necessary, use pimavanserin (Nuplazid), quetiapine (Seroquel) or clozapine (Clozaril).
- **Special Alert:** Drugs such as benzodiazepines, muscle relaxants, bladder control medications and other medications used for sleep and pain may lead to confusion, hallucinations and other symptoms.

Turn this card over for a list of contraindicated medications and important considerations if the patient has a brain device and needs an MRI/EKG/EEG.



MY NAME

HOME ADDRESS

EMERGENCY CONTACT PHONE

PHYSICIAN PHONE

ALLERGIES/OTHER MEDICAL CONDITIONS

MEDICATIONS THAT MAY BE CONTRAINDICATED IN PARKINSON'S DISEASE

Safe Medications:	Medications to Avoid:
ANTIPSYCHOTICS	
pimavanserin (Nuplazid, FDA approved to treat Parkinson's disease psychosis), quetiapine (Seroquel), clozapine (Clozaril)	avoid all other typical and atypical antipsychotics
PAIN MEDICATION	
most are safe to use, but narcotic medications may cause confusion/ psychosis and constipation	if patient is taking MAO-B inhibitor such as selegiline or rasagiline (Azilect), avoid meperidine (Demerol)
ANESTHESIA	
request a consult with the anesthesiologist, surgeon and Parkinson's doctor to determine best anesthesia given your Parkinson's symptoms and medications	if patient is taking MAO-B inhibitor such as selegiline or rasagiline (Azilect), avoid: meperidine (Demerol), tramadol (Rybix, Ryzolt, Ultram), droperidol (Inapsine), methadone (Dolophine, Methadose), propoxyphene (Darvon, PP-Cap), cyclobenzaprine (Amrix, Fexmid, Flexeril), halothane (Fluothane)
NAUSEA/GI DRUGS	
domperidone (Motilium), trimethobenzamide (Tigan), ondansetron (Zofran), dolasetron (Anzemet), granisetron (Kytril)	prochlormethazine (Compazine), metoclopramide (Reglan), promethazine (Phenergan), droperidol (Inapsine)
ANTIDEPRESSANTS	
fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa), escitalopram (Lexapro), venlafaxine (Effexor)	amoxapine (Asendin)

Share this with your doctor
If you have a deep brain stimulation device (DBS):

MRI Warning

- MRI should not be performed unless the hospital has MRI experience imaging a DBS device safely.
- MRI should never be done if the pacemaker is placed anywhere other than the chest or abdomen.
- Under certain conditions, some DBS devices are safe for full-body MRI and do not need to be turned off. In other cases, devices should be turned to 0.0 volts and MRI should not be used to image structures of the body lower than the head, as dangerous heating of the lead could occur.
- Always check with your DBS team before having an MRI to make sure the procedure will be safe for you.

EKG and EEG Warning

- Turn off the DBS device before conducting EKG or EEG.
- Diathermy should be avoided.

Appendix C
Formula for Liquid Sinemet

Formula for Liquid Sinemet - 1 mg levodopa per 1 ml solution

- Sinemet 25/100 tablets 10 tablets (1,000 mg levodopa) (do not use Sinemet CR)
- Ascorbic acid (Vitamin C) crystals ½ tsp. (approx. 2 gms)
- Tap water or distilled water 1 liter or 1 quart

1) Mix the above ingredients in a liter/quart plastic container with lid (do not use metal).
2) Rotate or shake gently until tablets dissolve (no need to crush tablets). Tablets may not go completely into solution.
3) Formula will maintain full strength and purity for 24 to 48 hours in refrigerator.

Dosing Recommendations

(Always establish a dosing plan with your physician or healthcare provider first!)

1) Morning ("Jump Start") dose:
   - 60 ml of the formula (60 mg or a little more than ½ of a 25/100 tablet of carbidopa/levodopa), or may use amount comparable to usual tablet dose.
   - Adjust dose 5-10 ml up or down every three to five days until you achieve the best "on" response with the least dyskinesia.

2) Hourly dosing:
   - 30 ml of the formula on the hour while awake, or hourly proportion of usual tablet dose. (For instance, a person with PD taking one carbidopa/levodopa 25/100 tablet every two hours might try 50 ml per hour of the liquid.)
   - Adjust dose 5-10 ml up or down every three to five days until "on" periods are smoother.

For the best overall result, it is strongly recommended that you adjust the morning jump start dose prior to adjusting the hourly doses. Accuracy of the dose and exact hourly timing between doses is critical for optimal benefit. Optimal dosing can vary tremendously from one person to another.

Appendix D
Epworth Sleepiness Scale

The Epworth Sleepiness Scale is used to determine the level of daytime sleepiness. A score of 10 or more is considered sleepy. A score of 18 or more is very sleepy. If you score 10 or more on this test, you should consider whether you are obtaining adequate sleep, need to improve your sleep hygiene and/or need to see a sleep specialist. These issues should be discussed with your personal physician.

Use the following scale to choose the most appropriate number for each situation:

0 = would *never* doze or sleep.
1 = *slight* chance of dozing or sleeping
2 = *moderate* chance of dozing or sleeping
3 = *high* chance of dozing or sleeping

Fill in your answers and see where you stand.

Situation	**Chance of Dozing or Sleeping**
Sitting and reading	
Watching TV	
Sitting inactive in a public place	
Being a passenger in a motor vehicle for an hour or more	
Lying down in the afternoon	
Sitting and talking to someone	
Sitting quietly after lunch (no alcohol)	
Stopped for a few minutes in traffic while driving	
Total score (add the scores up) (This is your Epworth score)	

Appendix E
Selected Readings

Listed below is a brief selection of books currently available as general resources for Parkinson's disease.

The New Parkinson's Disease Treatment Book: Partnering with Your Doctor to Get the Most from Your Medications
J. Eric Ahlskog, PhD, MD, 2015.

Parkinson's Disease for Dummies
Michele Tagliati, MD, Gary Guten and Jo Horne, 2007.

Parkinson's Treatment: 10 Secrets to a Happier Life
Michael S. Okun, MD, 2013.

The First Year – Parkinson's Disease: An Essential Guide for the Newly Diagnosed
Jackie Hunt Christensen, 2005.

Living Well with Parkinson's Disease: What Your Doctor Doesn't Tell You... That You Need to Know
Gretchen Garie and Michael Church with Winifred Conkling, 2007.

10 Breakthrough Therapies for Parkinson's Disease
Michael S. Okun, MD, 2015.

About the Authors

David Houghton, MD, MPH, received his medical degree from the Medical College of Georgia in Augusta, Georgia and his master's in public health in epidemiology at the Rollins School of Public Health at Emory University in Atlanta. He completed his internship and residency in neurology at the Hospital of the University of Pennsylvania, followed by fellowship training in movement disorders at Pennsylvania Hospital in Philadelphia. Dr. Houghton began his clinical and academic pursuits at the University of Louisville as an assistant professor and clinical director of the Movement Disorder Surgical Program. He joined the Ochsner Health System in New Orleans, Louisiana, in 2012 as Chief of the Division of Movement and Memory Disorders.

Howard Hurtig, MD, graduated from Tulane University (BA '62, MD '66) and received training in internal medicine at Cornell-New York Hospital Medical Center ('66-'68) and neurology at the Hospital of the University of Pennsylvania ('70-'73). In 1982, he and Matthew Stern, MD, founded the Parkinson's Disease and Movement Disorders Center at the University of Pennsylvania, a Parkinson's Foundation Center of Excellence, where he is the Frank Gladys Elliott Professor of Neurology. In addition to his interest in patient care, Dr. Hurtig has conducted clinical research in experimental therapeutics, clinical-pathological correlations of Parkinson's disease and other parkinsonian syndromes and neuroimaging.

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Jill Marjama-Lyons, MD, and Gale Kittle, RN, MPH, updated the second and third editions.

David Houghton, MD, MPH, Howard Hurtig, MD, Sharon Metz, RN, MPH, and guest author Melanie Brandabur, MD, updated the fourth edition.

This 2016 edition includes contributions from Monique Giroux, MD (chapter 5, "Integrative Medicine"), as well as Giselle Petzinger, MD, Beth Fisher, PT, PhD, Lauren Hawthorne, BS, and Michael Jakowec, PhD (chapter 4, "Exercise Is Medicine").

Parkinson's Foundation Educational Books

This book is part of the Parkinson's Foundation's Educational Book Series, which addresses important topics for people with Parkinson's disease. To request a free copy of any book(s) in the series, contact our Helpline at 1-800-4PD-INFO (800-473-4636) or visit **www.parkinson.org/books**.

Your generosity makes this publication possible.

The Parkinson's Foundation is proud to provide these educational materials at no cost to individuals around the globe. If you find these materials helpful, please consider a gift so that we may continue to fight Parkinson's on all fronts: funding innovative research, providing support services and offering educational materials such as this publication. Thank you for your support.

Donate online:	www.parkinson.org/donate
Donate by mail:	Parkinson's Foundation Attn: Donor Services 200 SE 1st St, Suite 800 Miami, FL 33131
Donate by phone:	1-800-4PD-INFO (473-4636)
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Index

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2017

Medications to be Used with Caution for People with Parkinson's

12th Edition October 2017

Parkinson's is a progressive neurological condition characterised by tremor, stiffness, slowness of movement and postural instability. The symptoms are primarily due to depletion, in the brain, of the neurotransmitter dopamine. This leads to an imbalance with other neurotransmitters. The majority of medications used to treat Parkinson's aim to replace or increase the levels of dopamine within the brain.

Many medications used in the treatment of other medical conditions have the potential to alter or interfere with the brain's dopamine system and may be overlooked as having a detrimental effect on Parkinson's.

It is important to consider the possibility that treatment of other medical conditions may cause or exacerbate existing Parkinson's symptoms.

YOUR DOCTOR MAY DECIDE THE USE OF THESE MEDICATIONS IS JUSTIFIED

This leaflet provides information on those medications that most commonly cause problems for people with Parkinson's. It is not an exhaustive list and therefore a doctor or pharmacist must be consulted before any medications are taken by people with Parkinson's. This includes complementary medicines or medicines available 'over the counter' at pharmacies, health food stores and supermarkets.

This leaflet focuses on medication interactions and medications that are known to worsen the symptoms of Parkinson's. This brochure refers to medications available in Australia. Please note that overseas these medications may be known by different trade names.

Throughout the leaflet, brand names are in ***bold italics***.

Medications Associated with Interactions or Worsening of Parkinson's Symptoms

Antiemetics (Used for nausea and vomiting)

Maxolon, Pramin	Metoclopramide
Stemetil, Stemzine, Nausetil	Prochlorperazine

Antihistamines (Used for colds and hayfever)

Phenergan, Avomine, Fenezal	Promethazine
Vallergan, Vallergan Forte	Trimeprazine

Antidepressants (Used for depression)

Monoamine oxidase inhibitors (MAOIs)

Nardil	Phenelzine
Parnate	Tranylcypromine
Amira, Aurorix, Clobemix Mohexal	Moclobemide

Tricyclic and Tetracyclic anti-depressants

Anafranil, Placil	Clomipramine
Dothep, Prothiaden	Dothiepin
Deptran, Sinequan	Doxepin
Tofranil, Tolerade	Imipramine
Allegron	Nortriptyline
Lumin, Tolvon	Mianserin
Surmontil	Trimipramine

Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Noradrenaline Reuptake Inhibitors (SNRIs)

Cipramil, Ciazil, Citalobell, Talam, Celapram	Citalopram
Lexapro, Esitalo, Lexam, Esipram, Loxalate	Escitalopram
Luvox, Faverin, Movox, Voxam	Fluvoxamine
Lovan, Prozac, Fluohexal	Fluoxetine
Zactin, Auscap, Fluoxebell	Fluoxetine
Edronax	Reboxetine

THE FOLLOWING MEDICATIONS FROM THE ABOVE GROUP ARE COMMONLY UTILISED UNDER SPECIALIST SUPERVISION IN PARKINSON'S

Aropax, Paxtine, Extine	Paroxetine
Avanza, Axit, Mirtazon, Avanza SolTab	Mirtazapine
Efexor - XR, Efexor	Venlafaxine
Zoloft, Xydep, Eleva, Concorz Sertra, Setrona	Sertraline

Antipsychotics
(Used for sedation and treatment of hallucinations)

Serenace	Haloperidol
Neulactil	Pericyazine
Largactil	Chlorpromazine
Fluanxol	Flupenthixol
Modecate	Fluphenazine
Orap	Pimozide
Navane	Thiothixene
Stelazine	Trifluoperazine
Clopixol	Zuclopenthixol
Risperdal, Rispa, Ozidal, Rixadone	Risperidone

THE FOLLOWING MEDICATIONS ARE COMMONLY UTILISED UNDER SPECIALIST SUPERVISION IN PARKINSON'S

Clozaril, Clopine	Clozapine
Seroquel	Quetiapine
Zyprexa, Zyprexa Zydis	Olanzapine

Cardiovascular
(Used for heart conditions and blood pressure)

THE MEDICATIONS IN THIS GROUP ARE UNDER CONSTANT DEVELOPMENT THEREFORE IT IS VITAL THAT THE PRESCRIBING DOCTOR IS AWARE OF PARKINSON'S AS A DIAGNOSIS AND THAT THERE IS A RISK OF LOW BLOOD PRESSURE DUE TO PARKINSON'S. THE MEDICATIONS USED IN THE TREATMENT OF PARKINSON'S CAN OFTEN CAUSE A LOWERING OF BLOOD PRESSURE UPON STANDING.

AVOID: METHYLDOPA. CAUTION WITH CALCIUM CHANNEL ANTAGONISTS, ACE INHIBITORS, ANGIOTENSION II BLOCKERS AND IMDUR.

Other medications to be used with caution include

Buspar	Buspirone
Dilantin	Phenytoin
Lithicarb, Quilonum SR	Lithium
Tetrabenazine	Tetrabenazine
Clorprax, Prexaton, Zyban SR	Bupropion

Special Considerations if Apomorphine (Apomine, Movapo) is Used to Manage Parkinson's

Nausea and vomiting are side effects of **Apomorphine.**
Ondansetron (antiemetic) should not be used with **Apomorphine.**

Special Considerations if Taking Azilect, Eldepryl, Selegiline or Selgene

These medications must not be taken in combination

Medication	Interaction
Pethidine	Risk of serotonin syndrome# and other potentially life-threatening reactions
Tramadol	Risk of serotonin syndrome# and other potentially life-threatening reactions
SSRIs	Risk of serotonin syndrome# and other potentially life-threatening reactions
Dextromethorphan (cough suppressant)	Risk of serotonin syndrome#
Moclobemide	Increased risk of raised blood pressure
Tricyclic anti-depressants	Risk of serotonin syndrome# and other potentially life-threatening reactions
Clozapine	Risk of serotonin syndrome# and other potentially life-threatening reactions
St John's Wort	Risk of serotonin syndrome#
Ciprofloxacin (antibiotic)	Risk of increased levels of Azilect
Norfloxacin (antibiotic)	Risk of increased levels of Azilect

#Serotonin syndrome is a potentially fatal condition which can present as increased temperature, shivering, changes in mental status, raised blood pressure, restlessness and muscle twitching (myoclonus).

If you are contemplating surgery

- Talk to your doctor and anaesthetist before surgery and give them a current list of your medications;
- If admitted to hospital give staff a copy of your medication list and this leaflet.

This edition was reviewed by Dr B I Vieira, Consultant Physician and Janet McLeod, Senior Parkinson's Nurse Specialist, Parkinson's W.A. Inc.

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Prepared in collaboration with:

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Nutrition and PD

A balanced diet is a foundation of good health. For people with Parkinson's disease (PD), a balanced diet is even more important. In PD, there are some foods that may help to ease symptoms and help brain health, while others can affect the way medications work. While there are many things about PD that cannot be changed, the informed choice of diet can help people to live better with the disease.

Foods That Promote Brain Health

In the science of brain health, we often use the word neuroprotection: the process by which we can support the health of brain cells and their ability to communicate with one another. Over the years, various food groups have been studied, in animals and in large epidemiological studies of human populations, for their potential to promote brain health. Initial research has provided some evidence about possible benefits of certain foods. Although there isn't yet evidence about the specific benefits for Parkinson's disease, what we do know is that these foods are part of a healthy diet.

Neuroprotection

Of all the foods that have been studied for their potential to promote brain health, research into nuts and herbs has shown promise. Here is what we know.

Walnuts. Walnuts contain an essential fatty acid called omega 3 and a variety of minerals, which early studies associate with a decreased risk for dementia. Try eating five to 10 each day.

Pistachios. Emerging evidence shows these nuts (the vitamin K and antioxidants in them) may have potential for helping to reestablish lost connections between neurons. They also contain a small amount of lithium, which may help to improve mood. You can eat a few of them two or three times a week.

Macadamia nuts. Oils in these nuts may increase the production of neurotransmitters. They are high in calories, but a few a day is good for you.

Cashews. Iron, zinc and magnesium in cashews may boost serotonin — a neurotransmitter linked to good mood — and may reduce memory loss.

Almonds. Although they have scant effect on brain health, almonds contain fiber, which helps relieve constipation (a common symptom in PD).

Brazil nuts. These nuts contain selenium, a mineral that may have the potential to counteract environmental toxins like pesticides and herbicides. Eat no more than one or two a day.

Turmeric. This spice turns Indian food orange, and its active ingredient is curcumin. Eat Indian food occasionally, but don't take turmeric as a supplement.

Ceylon cinnamon. In animal studies, this spice has shown potential for normalizing neurotransmitter levels and other PD brain changes. Look for Ceylon cinnamon, which is grown in Sri Lanka and labeled as such. Organic cinnamon is also preferable.

Rosemary. Add rosemary to soups, quiches or grilled chicken. It contains antioxidants and has anti-inflammatory properties, which early animal research shows may be beneficial for brain health.

Anti-Inflammatory Foods

Fighting inflammation can be another important strategy for keeping the brain healthy. The types of fats you consume may play a role in reducing inflammation in the body, and those known as "medium-chain triglycerides" may be particularly helpful. Coconut oil contains this fat. You can cook with it just as you would with olive oil. Other anti-

inflammatory foods include oily fishes like salmon, tuna and mackerel; dark leafy green vegetables like kale, collard greens and spinach; and soy products.

Benefits of Purple and Red

Foods that contain antioxidants may also protect brain health. Antioxidants neutralize molecules known as "free radicals," which can damage healthy cells including neurons. Fruits that are purple and red, like blueberries and raspberries, contain pigments called anthocyanins, which are well-known antioxidants. Some studies suggest that drinking green tea (three cups a day) is neuroprotective, because EGCG, found in green tea, is both an anti-inflammatory agent and an antioxidant.

Foods for PD Symptoms

Nutrition adjustments can help ease some of PD's most common symptoms, both of a motor and a non-motor nature. If you experience digestive difficulties, especially constipation (which is very common in PD), try to drink more fluids, and increase your fiber intake with fruits and vegetables such as kiwi, apples, prunes, dates, figs, radishes, berries, nuts and beans. Probiotic supplements like Bifidobacterium (B. breve, B. adolentis and B. infantis), that add healthy bacteria to the gut, may also be helpful.

If drinking more water leads to urinary incontinence or urgency, increase your fluid intake by eating foods with a high water content such as tomato, cucumber, radish, celery, broccoli and grapefruit. If you struggle with weight loss or loss of appetite, try increasing your calorie intake by eating nuts and foods that contain healthy fats, like coconut and avocado. To stimulate your appetite, try bitter greens like collard and beet greens, or spicy foods. Exercise can increase muscle mass and hunger.

Fatigue and sleep difficulties are also common symptoms of PD. The culprit of these problems may be sugar. When eaten during the day, sweets briefly boost energy, but make you sleepy later. When eaten in the evening, they may keep you awake.

Another reason to limit sugar is that it causes a spike in blood glucose, which contributes to inflammation. When reaching for a snack, try foods that offer a balance of protein and fat, like nuts or avocado, or whole-grain complex carbohydrates.

How Foods Affect PD Medication

Another benefit of dietary changes can be improvement in the effectiveness of PD medications. Taking medications at mealtime can affect how quickly they are absorbed into your body, and the rate at which your body uses, or metabolizes them. If you take carbidopa-levodopa (Sinemet®), for PD symptoms, you may find that protein-rich foods such as meat, fish or eggs or high-fat foods, lengthen the time it takes for the medicine to kick in, or make the medication less effective. The latter result can also be triggered by foods that contain vitamin B6 (e.g., meats, bananas, egg yolks or lima beans).

The solution? Talk to your doctor about taking levodopa 30 to 60 minutes before meals, to give it a head start. Your doctor or a nutritionist can also give advice on how to distribute the protein you eat, to avoid having it interfere with levodopa.

Conclusion

People with PD need to eat a balanced diet in order to feel their best and maintain energy. Eating more nuts and berries, cutting back on fried food and sweets, and cooking with herbs are all elements of sound nutrition and they may also help you manage your PD.

Dr. Zwickey is Dean of Research and Graduate Studies at the National College of Natural Medicine in Portland, OR. She first presented this topic as an ExpertBriefing, which is available to view at www.parkinson.org/ExpertBriefings.

information

MOBILITY AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Parkinson's was originally classified as a movement disorder as all aspects of movement and mobility may be affected. The cause is multi-factorial:

- Basal ganglia changes
- Bradykinesia (slowness of movement)
- Motor fluctuations
- Muscle rigidity
- Postural instability

Basal Ganglia Changes

The ability to produce movement is dependent on the complex motor circuit of the basal ganglia and other parts of the mid-brain. Learned complex actions such as walking, turning in bed, sitting and standing depend on the basal ganglia. Parkinson's reduces the amount of dopamine available, resulting in disruption of the functions of the basal ganglia. Subsequently stride length and height become reduced and difficulty initiating movement and controlling movement size occurs.

Bradykinesia

Slowness of movement, a cardinal sign of Parkinson's, also includes decreased spontaneous movement and decreased amplitude of movement. Bradykinesia is a major factor in mobility and function, impacting on such tasks as eating, showering and dressing.

Parkinson's medications often initially reduce bradykinesia and re-emergence is frequently seen at end of dose and with progression of the condition.

Motor Fluctuations

Motor fluctuations are a sign of progression of the condition and also a complication of Parkinson's medications. It is estimated that 40% of people living with Parkinson's experience motor fluctuations approximately four to six years after commencing levodopa therapy. End of dose failure is a form of motor fluctuation which occurs when the benefit from the medication wears off before the next dose is due. This may result in increased bradykinesia or other mobility changes.

Muscle Rigidity

This is a cardinal sign of Parkinson's and is obvious to the clinician when a limb is passively moved rather than being reported by the person with Parkinson's. It is described as 'cogwheel' or 'lead-pipe' rigidity. 'Cogwheel' refers to the presence of tremor superimposed on rigidity and 'lead-pipe' describes the rigidity in the absence of tremor. Rigidity contributes to the classical flexed posture of Parkinson's and impacts on mobility and activities of daily living. It may also cause pain or discomfort.

Postural Instability

This usually occurs later in the progression of the condition, resulting in impaired balance and falls. The treating medical specialist will assess balance using the 'pull' test. In Parkinson's the ability to correct balance is compromised. In addition to falls caused by postural instability, there is a risk associated with Parkinson's medication.

MOBILITY AND PARKINSON'S

The aim of the medication is to improve symptoms such as bradykinesia and muscle rigidity. However, a common side effect is hypotension (low blood pressure). This often occurs on standing, when it is referred to as 'postural hypotension'. This may result in dizziness, unsteadiness and an increased risk of falling.

Movement changes related to Parkinson's include:

- Falls
- Freezing of gait and start hesitation
- Multitasking issues
- Postural changes
- Shuffling/festinating gait
- Turning changes

Falls

Falls associated with Parkinson's may occur for the reasons already outlined. The tendency to fall backwards or move backwards without warning is called retropulsion.

The fear of falling and the associated loss of confidence may be as disabling as actual falling. Avoiding falls is essential because of the risk of serious injuries.

Freezing of Gait and Start Hesitation

Freezing of gait refers to the sudden inability to walk in mid-stride, while turning or going through a confined space such as a doorway. This may occur with the progression of Parkinson's. While stressful it may only last for a few seconds. Stress and anxiety may increase the risk of freezing.

Start hesitation refers to momentary difficulty in walking especially after rising from a sitting or lying position.

Multitasking Issues

In Parkinson's the ability to carry out two or more automatic skills simultaneously may be affected. This is due to the changes in the basal ganglia.

Walking and talking simultaneously can lead to increased slowness, shuffling or even an inability to walk while talking. Walking and carrying objects may result in similar problems and can increase the risk of falling. Conscious attention to task by avoiding multitasking will ensure safer mobility.

Postural Changes

Parkinson's may result in forward flexed posture or stooping with reduced arm swing. When the trunk is stooped forwards the stride length and height becomes shorter.

Shuffling/Festinating Gait

This occurs due to postural changes, is part of the typical Parkinson's gait pattern and is a risk factor for falls due to tripping.

Turning Changes

Turning is a complex skill and when changing direction mobility may be affected as the number of steps required increases due to the shortened stride length. A quickly executed turn may result in poor balance and falls may occur. Falls associated with turning often happen without warning.

Aids and Equipment

It is recommended that mobility is reviewed by a physiotherapist with expertise in Parkinson's if a walking aid is required or if mobility is compromised. This will ensure that the appropriate aid is recommended and strategies are introduced.

MOBILITY AND PARKINSON'S

An occupational therapist can assess the safety of the home and offer advice as required. Appropriate chairs, equipment and the provision of grab rails in bathrooms will maintain independence and safety.

Accessing the above health professionals may require a GP referral. In most cases these services are available through Aged Care Assessment Teams (ACAT). For younger people there are various options available – your GP will be aware of the services available in your area.

Practical Advice for Maintenance of Safe Mobility

- Maintain an enjoyable exercise routine
- Maintain good posture by daily stretching and conscious attention to standing tall
- Wear appropriate footwear (closed shoes with flat or low heels)
- Remove unnecessary mats
- Maintain an uncluttered environment
- Be cautious when stepping backwards
- Concentrate on taking large steps
- Concentrate on placing the heel to the ground first
- Avoid multitasking
- If freezing of gait occurs use strategies such as
  - counting 1, 2, 3...
  - clapping to maintain a rhythm
  - swaying to initiate movement
  - tape applied to floor in doorways
- Turn in a wide arc or U-turn rather than a sharp change of direction
- Be aware of any changes in vision and report any difficulty with going down steps or stairs to the treating specialist
- Rise from a lying or sitting position slowly and remain by the bed or chair for a short period of time
- For bed mobility changes see Fact Sheet 2.7 - Sleep and Parkinson's
- Report dizziness on standing to the treating specialist or GP as this may be related to low blood pressure
- Report falls to the treating specialist and GP
- Consider a personal alarm device
- Arrange a referral to a physiotherapist with expertise in Parkinson's

Exercise has been proven to be essential in maintaining mobility and quality of life. Recent research suggests that tai chi, walking, movement to music and yoga are most beneficial.

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AUSTRALIA

Pain

As Parkinson's disease (PD) progresses, it is common to experience changes in the spine, hands and feet.

Pain

Parkinson's disease pain is divided into five categories:

1. **Musculoskeletal:** pain that affects the bones, muscles, ligaments, tendons and nerves. It can occur suddenly or be long-lasting and can occur in one area or several.
2. **Neuropathic/radicular:** chronic pain condition there the body sends pain signals to the brain, not caused by an injury.
3. **Dystonic:** sustained or repetitive muscle twisting, spasm or cramp that can occur at different times of day and in different stages of

Parkinson's.

4. **Akathisia**: causes the feeling of restlessness or inability to be still
5. **Central pain**: neurological condition caused by a dysfunction that affects the central nervous system and is resistant to treatment.

Nearly every person who lives with PD will experience some degree of muscle rigidity. Muscle rigidity associated with PD is most noticeable in the muscles that flex the limbs and trunk. Common experiences include bending of the neck, curling of the trunk with slumping of the shoulders and bending at the wrists, fingers, elbows, hips and knees. These changes progress over time.

A third or more people with PD eventually experience changes in posture, although this occurs most often in advanced PD. Some people experience severe postural changes with extreme leaning forward or to one side.

Other common changes include dystonia, muscle spasms and cramps that are particularly common in the feet; and osteoporosis, where weakened bones which can increase risk of falls and fractures. Lastly, it is important to look at the impact of orthopedic surgeries for non-PD related spine deformities, hip and knee replacement and other bone problems, which may present unique challenges for people with PD. Although people with PD can benefit from such surgeries, they may have a longer and more complicated recovery than people without PD.

Rigidity, weakened muscles and involuntary muscle contractions (dystonia) can cause painful deformities for people with PD. A tilted or twisted spine also can throw a person off balance and increase the risk of falling. These common changes in the skeleton and bones can occur with PD:

- Frozen shoulder: stiffness, pain and loss of range of movement in the shoulder, many people experience this symptom before a PD diagnosis.
- Flexed fingers or toes (striatal hand and foot): one finger may extend, the thumb may fold inwards, fingers may clamp down onto the palm and on the foot, the big toe may flex upward while other toes curl under.
- Stooped posture (camptocormia): the spine bends forward when walking, in the most severe cases as much as 90 degrees. This posture

arises because the hips and knees are flexed and will go away when lying down.
- Leaning sideways (Pisa syndrome): involuntarily tilting of the trunk to one side when sitting, standing or walking; always to the same side
- Scoliosis: sideways twisting, or curvature, of the spine.
- Dropped head (anterocollis): the head and neck flex forward; the chin may drop all the way down to the sternum, or breastbone (more common in multiple system atrophy than PD).
- Bone fractures: people with PD are at risk of broken bones from falling, especially from landing on the hip; and kneecap fractures also are common, painful and sometimes not diagnosed.
- Low bone density: bones may become weak and at risk for osteoporosis from lack of weight-bearing exercise, like walking, and from too little calcium and vitamin D. Other risk factors for osteoporosis include older age, gender (females > males), low body weight, and smoking. A person with PD who has osteoporosis is more likely to break a bone if they fall.

Other Symptoms: Aging or PD?

Because the biggest risk factor for developing PD is age (the average age of diagnosis is 60), skeletal problems associated with aging are often experienced by people with PD. While it is not clear that PD increases the risk or even the severity of these other skeletal conditions, the problems of PD can make the symptoms of these conditions more prominent.

- Osteoarthritis, the joint damage associated with general wear and tear on the joints, is nearly universal in aging. Osteoarthritis tends to affect larger joints such as the hip and knee.
- Arthritis of the spine is also very common. This may contribute to the development of spinal stenosis, narrowing of the canal in the spine that houses the spinal cord. In severe cases, spinal stenosis causes damage to the nerves as they exit the spine or even to the spinal cord itself.
- Disorders of the fibrous discs between the bones of the spine can also cause pain, or limb numbness or weakness.

Therapies

Medical therapies can help relieve the rigidity and muscle contractions that contribute to changes in posture. The approach to therapy very much depends on a person's unique symptoms and overall health. Your doctor may advise:

- Dopamine: the gold-standard medication for PD movement symptoms, carbidopa/levodopa (most often prescribed as Sinemet®). If you do not already take dopamine, starting on this drug may improve symptoms like stooped posture and help prevent them from becoming permanent. If you already take dopamine, review your dose and medication schedule with your doctor to be sure it is working well.
- Botulinum injections (Botox®): these injections relax muscles that are flexed or having spasms. They are typically used in specific areas that are affected, such as the hands, feet and neck, but not in larger muscles involved in postural abnormalities of the trunk.
- Deep brain stimulation (DBS): this is a surgical procedure which may offer benefit for certain types of muscle contractions
- Surgery: Surgical therapies (joint replacements, spinal surgery) may be required to treat significant osteoarthritis, disc disease or spinal stenosis. As with any surgical treatment, the risks and benefits should be weighed carefully.

Tips for Maintaining Healthy Bones

- Talk to your doctor about your PD medication regimen — medication changes that may ease skeletal/spine issues and strategies for optimizing medications to ensure they are most effective for PD.
- Ask your primary care doctor about having your bone-mineral density tested. If it is low, medications are available to help maintain or increase it.
- Discuss testing your blood level of vitamin D with your physician. If it is low, follow your doctor's advice on taking supplements.
- Reduce the risk of falls by making the home safer with the advice of an occupational therapist and using the correct assistive devices (including different types of walkers or canes) when needed as instructed by a physical therapist
- Get active and keep moving. Exercise helps maintain strong bones and can ease dystonia among other symptoms. There is no gold standard

exercise — whatever you enjoy and can do is the right exercise. Try to be active at least 30-45 minutes daily. Walking, swimming, yoga, Tai Chi, dancing, etc. are all good choices.

- See a physical therapist for advice on how to stretch, strengthen and relax your muscles and for a program of exercises tailored to your own PD symptoms.
- Ask your doctor about detecting changes in posture early, when they can be treated and before they become permanent.
- Visit your doctor for regular physicals to rule out causes of pain unrelated to PD or changes in the spine unrelated to PD.
- Alternative or complementary therapies may be helpful in some cases. For example, acupuncture or massage can help some people with pain and may be considered.

Page reviewed by Dr. Bhavana Patel, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

information

ORAL HEALTH AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Understanding the Issues

Oral health significantly impacts overall health and wellbeing but can be easily overlooked when addressing the symptoms of Parkinson's. Evidence-informed guidelines for optimal oral and dental health specific to Parkinson's are limited.

Oral and dental health challenges commonly experienced in Parkinson's may include the following:

Oral Hygiene

Oral hygiene difficulties associated with fine hand movement control, oral and facial movement control, tremor, dyskinesia, sensation, motivation, posture, fatigue and concentration can all impact on the ability to carry out effective oral hygiene. Regardless of having dentures or natural teeth, thorough and regular cleaning to remove food & fluid residue and bacteria are critical for optimal oral health. Bacteria from the mouth can travel to other parts of the body such as the lungs.

Tooth Decay and Damage

Tooth decay and damage can result from a complex combination of factors, including poor oral hygiene, dry mouth, swallowing related difficulties, inadequate nutrition, irregular dental visits and reduced awareness of oral health needs. Plaque, a sticky film of bacteria and sugars coating the teeth, leads to erosion of teeth. Consultations with a dentist help to disrupt this damaging process, protect teeth and gums and provide education for self-care. Teeth-grinding, clenching of teeth and dyskinesia in the mouth and face can damage teeth.

Gum Disease

Gum disease or gingivitis is inflammation of the gums, which if left untreated, can lead to periodontitis, a gum infection that damages soft tissues and destroys bone that support teeth. Bacteria in gum pockets can enter the bloodstream and travel to other areas of the body, increasing risk of infection.

Sialorrhea

Sialorrhea refers to reduced control of saliva, which pools in the mouth and spills out past the lips. Saliva can be very watery or thick and ropey. Sialorrhea usually results from swallowing changes. Reduced lip closure, altered sensation in the mouth, poor coordination of swallowing movements and altered head and trunk posture can all contribute to the problem of sialorrhea. It can affect social confidence and hygiene. Saliva left accumulating in the mouth and throat can threaten to leak into the airway and increase risk of aspiration pneumonia. Speak to a Parkinson's nurse specialist, general practitioner or medical specialist about this problem and request referral to a speech pathologist.

Xerostomia

Xerostomia or dry mouth, results from reduced saliva production and flow. This is a common problem in Parkinson's. This can stem from 1) the Parkinson's condition itself, 2) be an adverse side effect of some medications, 3) mouth breathing due to reduced lip closure, 4) reduced swallowing frequency, 5) stress/anxiety and/or 6) inadequate fluid intake. Saliva has various important functions, helps wash particles from the mouth and reduces the harmful effect of acids produced by plaque bacteria. Dry mouth makes it more difficult to chew, swallow and enjoy food. It interferes with speech and can contribute to problems in swallowing medication, bad breath, burning mouth, tongue ulcers, cracked lips, gum disease, increased dental cavities and mouth infections.

ORAL HEALTH AND PARKINSON'S

Nutrition and Swallowing

Good nutrition and eating habits play a key role in maintaining good oral health. The development of 'sweet tooth' tendencies in some people with Parkinson's is documented but has limited evidence base and underlying explanation. Compulsive eating has been linked with potential side effects from specific medications and should therefore be reported to the Parkinson's nurse specialist or treating medical specialist, should adjustment of medications be required.

Chewing and swallowing difficulties can result from slow, small, poorly coordinated oral and facial movements, involuntary movements of the mouth and face, reduced sensation in the mouth and throat and damaged or missing teeth.

These factors can interfere with the chewing process, swallowing efficiency and safety, the clearing of food particles from the mouth and with maintaining adequate nutrition.

Halitosis

Halitosis or bad breath can result from dry mouth, inadequate cleaning between teeth, gum disease, inadequate fluid intake, activity of bacteria in the mouth and throat, post nasal discharge and a range of medical issues. A dentist can assess and make recommendations according to the specific cause.

Pain and Burning of the Mouth

Oral pain without observable cause can present as a non-motor 'off' symptom for which the medical specialist may suggest a medication adjustment. Burning mouth (involving tongue, cheeks and palate) without an overt cause is rare but more common in people with Parkinson's than in the general population. There is some empirical evidence that this problem can be medication-related or can result from dry mouth. Dopamine has been documented to be both potential 'cause and cure'. The role of psychological factors such as stress, anxiety and depression in burning mouth also remains unclear.

Practical Tips to Maintain Optimal Oral Health

Dental Visits:

- Short and frequent dental reviews are recommended
- Consider taking a companion
- Time the appointments to coincide with 'on' times or optimal movement control

As the dentist may not be aware of the challenges associated with Parkinson's it may be necessary to mention:

- Specific teeth cleaning problems experienced
- Hypotension (blood pressure drop). Slow dental chair adjustment may help
- That reducing stress during the visit may assist movement control
- That due to slowness of movement, following instructions may take longer
- Swallowing problems (suctioning and water flow adjustments may assist with treatment procedure)
- Posture and seating requirements may require adjustments
- Involuntary movements of the mouth and face
- Possible need for fast setting materials to be used during dental treatment

If possible medication side-effects are a concern or are causing oral health problems this should be discussed with the medical specialist.

- Some medications, for example, anti-cholinergic drugs for conditions such as depression, anxiety, bladder control and tremor, can cause dry mouth
- If significant tremor or dyskinesia (involuntary writhing movements) are experienced speak with the medical specialist as medication adjustment may be of benefit.

ORAL HEALTH AND PARKINSON'S

Dry Mouth

- Chew naturally sweetened gum if chewing and swallowing abilities permit, this encourages lip closure, secretion of saliva and more frequent swallowing
- Try products for dry mouth, available in the form of gel or spray
- Be mindful of drinking adequate fluids
- Try a humidifier, nebulised saline or steam vapour inhaler
- Practice consciously maintaining lip closure whilst breathing

Saliva Control

- Ask for a speech pathologist referral if difficulty controlling saliva is experienced. Whether excessive saliva or dry mouth is experienced strategies to improve saliva control can be taught
- Saliva control difficulties are predominantly due to swallowing changes
- For persistent excess saliva the medical specialist may recommend a trial of Botulinum Toxin injection into the salivary glands or cautious use of atropine drops under the tongue or diluted in water
- For thick saliva, try nebulised saline, chew naturally sweetened gum and ensure that adequate fluids are taken

Swallowing

It is very common for people with Parkinson's to experience swallowing difficulties.

- Request referral to a speech pathologist

This can provide: a comprehensive swallowing assessment, training of conscious attention strategies to improve chewing and swallowing management and safety, advice on food textures and fluid consistency and techniques for swallowing medication effectively and safely. (See information - Swallowing and Parkinson's)

Oral Care Routine

- Request written recommendations for a personalised oral care routine from the dentist
- Adhere to recommended regular oral care schedules and allow extra time to be thorough
- If a carer/partner is available consider allowing him or her to help with oral hygiene routines if needed
- Ensure removal of food particles trapped in mouth, particularly between the teeth
- Multi-disciplinary team support can also assist in addressing the obstacles to optimal oral hygiene care. In addition to the dentist, occupational therapists, speech pathologists, Parkinson's nurse specialists can help with strategies to make oral care routine easier

Mouthwash, Toothpaste and more

- Consider using fluoridated toothpaste
- Drink tap water rather than bottled water as the fluoride will help protect against tooth decay (providing there are no swallowing changes)
- Mouthwash should ideally be Chlorhexidine-based and without alcohol. If a swallowing problem has been identified consult with a speech pathologist about the safe use of mouthwash
- Using Jumbo Swabs with excess liquid squeezed out may be a suitable option
- Use an electric toothbrush with a large handle
- Ask the dentist about using interdental brushes called 'piksters'
- Floss regularly

ORAL HEALTH AND PARKINSON'S

Maintaining Dentures

- It is very common for people with Parkinson's to have poorly-fitting dentures. Pooling of saliva, dry mouth, weight loss or involuntary mouth movements can interfere with a firm and stable fit
- A good fit is important for chewing, swallowing, speaking and comfort. Consult a dental mechanic, dentist or speech pathologist
- Ask the dentist or pharmacist about suitable denture adhesive products
- Ensure dentures are cleaned each day with a denture brush and mild liquid soap. Rinse them well with water, removing food residue, plaque and any adhesive
- Remove dentures overnight and soak them in fresh cold water. This also rests the gums.

Nutrition

- A dietician can assess nutritional status and advise on how to best meet dietary needs
- Calcium, Casein and Phosphorus are considered teeth strengthening materials, helping to repair teeth after acid attacks
- Fresh fruit, vegetable sticks, yoghurt and cheese make teeth friendly snacks
- Limit intake of sugary and/or acidy drinks such as fruit juices, energy drinks, cordials, soft drinks or "vitamin waters"
- Naturally sweetened Xylitol gum, available via pharmacies or online, has anti-bacterial properties. It encourages frequent swallowing, promotes saliva production and can help remove particles from the teeth and gum line

Postural Instability (Trouble with Balance & Falls)

Postural Instability

Postural instability is the least treatable of the major movement symptoms of PD, but there are things you can do to reduce the risk of falls.

The best approach is to start exercising early and do your best to maintain good posture. Exercise is proven to improve gait and balance and reduce falls.

In addition to exercise, early physical therapy is a good idea. You don't need to wait until you are having trouble moving to start! A physical therapist can help you develop a general exercise plan and teach you specific exercises to maintain and improve balance and posture.

Tips for Preventing Falls

Here are some basic tips to ensure that your home is safe and accessible:

- Remove throw rugs.
- Keep areas well lit; use nightlights where necessary.
- Install grab bars in the bathroom.
- Install handrails on all stairs.
- Clear clutter.
- Avoid rolling chairs.

It is helpful to go **room by room** through your home to make any needed adjustments that will create a safer home environment.

For a complete safety review of your home, ask for your doctor for an in-home occupational therapist safety assessment or find a certified aging-in-place specialist (CAPS). You can locate a CAPS on the website of the **National Association of Home Builders** or by calling 1-800-368-5242.

Tips for Preventing Backward Falls

- Avoid stepping backward.
  - Step sideways.
  - Make a safe turn, then walk forward.
- Do not stand directly in front of the oven door, refrigerator door, microwave or other appliance you are trying to open. Instead stand slightly to the side and use a "Power Stance," with one hand on a stable surface.

If a Fall Occurs

1. Remain calm. Feel and look for any pain or possible injuries before you try to get up. Plan your strategy carefully.
2. Use a heavy piece of furniture to assist you in getting up. If you doubt your ability to safely get up alone, crawl or scoot to a phone and call for help.

If you are someone who frequently falls, it is recommended that you enroll in a home emergency response system. A physical therapist can also help you prepare a system in case a fall occurs.

Care partners should also know how to **help someone get up after a fall**. A transfer belt can provide you with a firm grip to aid the person as he or she rises.

Detailed instructions for how to get up from a fall, along with more posture and balance information and tips, can be found in the Parkinson's Foundation publication *Fitness Counts.* Call our Helpline at 1-800-4PD-INFO (473-4636) to get your free copy.

information

RELATIONSHIPS AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Partners and family members may be aware of subtle changes even before formal medical diagnosis. These may include lack of motivation and spontaneity in addition to the more recognised symptoms of Parkinson's.

Relationships may be affected because of the commonly encountered changes related to the condition. These include:

- Communication
- Physical changes
- Role changes
- Depression
- Erectile dysfunction
- Loss of libido
- Hypersexuality

Communication

Effective communication is vital in relationships and Parkinson's may affect all aspects of communication (for more information refer to **Communication and Parkinson's**).

At the time of diagnosis, when a couple is coming to terms with their future with a progressive condition, honest communication is essential. The ability to maintain communication will have a positive effect on the long-term effects of living with Parkinson's.

Physical Changes

Parkinson's can affect mobility, posture and facial expression and these physical changes may impact on relationships and intimacy. These changes can result in self-esteem issues for the person living with Parkinson's and may also have implications for the partner.

Role Changes

A diagnosis of Parkinson's will affect both the person living with Parkinson's and their partner. As the condition progresses there may be a shift in role from partner to carer and at times these roles may overlap. This may result in grief, confusion and frustration.

Health professionals may add to this role confusion by labeling partners as 'carers' before the role has changed or before the couple have acknowledged the change.

Ideally, the transition from partner to carer is a natural progression eased by the love and companionship enjoyed in a long-term relationship. If required, counselling will assist in this transition.

Depression

Many people living with Parkinson's will experience depression at some time. In some cases depression may precede the diagnosis. Depression can impact greatly on relationships.

In Parkinson's there is often an associated anxiety, apathy and lack of motivation. It is recommended that any change in mood be discussed with the treating specialist who will advise on an appropriate choice of antidepressant or non-medication intervention.

Some Parkinson's medications may interact with some forms of antidepressants therefore specialist medical management is essential.

RELATIONSHIPS AND PARKINSON'S

Erectile Dysfunction

Erectile dysfunction (difficulties in achieving or maintaining an erection) may precede the diagnosis of Parkinson's and is related to the involvement of the autonomic nervous system. Difficulty in getting or maintaining an erection may be more difficult when medications are wearing off or low. In addition, there may be other health factors involved.

Communication about erectile dysfunction will assist in coming to terms with this problem. It is recommended that this be discussed with a medical practitioner as treatment options are available.

In order for medications prescribed for erectile dysfunction to be absorbed and have maximum effect, it may be necessary to take them earlier than normally prescribed due to a slowing of gastric emptying in Parkinson's.

Be aware that some erectile dysfunction medications may affect blood pressure which may already be altered due to Parkinson's.

Loss of Libido

A decrease of libido is commonly associated with aging and may also occur with both depression and Parkinson's. Open communication between partners will identify if this is an issue. A medical review of medications may reveal a reversible cause.

Hypersexuality

Hypersexuality (an increased sexual drive) occurs in Parkinson's and is frequently reported in males.

This may also occur in females but is less openly discussed. Hypersexuality may occur late in the disease progression and can affect people of all ages. It may also be associated with impulsive and uninhibited behaviours such as viewing pornography.

A common trigger for hypersexuality is medication used in the treatment of Parkinson's, of which dopamine agonists are the most commonly implicated. A specialist medical review of these medications may result in changes which will address this problem, therefore it is essential that this side effect is discussed openly and honestly.

All of these topics may not be routinely discussed by health professionals. Therefore, if they are impacting on relationships it is essential that they are highlighted. Addressing these issues in a sensitive and supportive manner will assist in maintaining a healthy relationship in the face of Parkinson's.

For further information contact
your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

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Rigidity (Stiffness)

Rigidity, while seldom the main symptom early in Parkinson's, is experienced as a stiffness of the arms or legs beyond what would result from normal aging or arthritis. Some people call it "tightness" in their limbs. Stiffness can occur on one or both sides of the body and contribute to a decreased range of motion. This can lead to problems with achiness or pain in the muscles or joints affected.

Many people with PD will have a reduced arm swing when walking, more so on the most affected side. Rigidity of the trunk is also possible, as is stiffness of the facial muscles, which contributes to facial masking.

Rigidity can also negatively impact sleep quality. Stiffness in the late evening and poor mobility in bed can make it hard to fall and stay asleep at night.

Rigidity is one of three telltale symptoms that help doctors make a Parkinson's diagnosis. The other two are slowness of movement (bradykinesia) and tremor.

Recommended for You:

Freezing or Sweating Falls When Walking with Parkinson's Disease

Gait, Balance and Falls in Parkinson's Disease

Skin Changes

Changes in the skin are common symptoms of Parkinson's disease (PD). Many people with PD develop oily or flaky skin, especially on the face and scalp. Others have trouble with dry skin or excessive sweating. Recent studies have shown an increased prevalence of skin cancer among people with PD.

Oily, Flaky or Inflamed Skin

There are tiny glands called sebaceous glands below the surface of the skin. These glands secrete an oily substance into the hair follicles. This oil normally helps protect the skin, but too much can cause problems referred to as seborrheic dermatitis. Signs of sebaceous dermatitis include:

- Oily skin, especially on the forehead, sides of the nose, scalp and eyebrows
- Skin scales that are white and flaky or yellowish and oily
- Itching
- Redness
- Chronically inflamed areas

What You Can Do

- Wash skin twice a day with warm water and rinse with cold water
- Use a neutral soap like unscented glycerin soap
- For dandruff, try a shampoo (over-the-counter) containing selenium, selenium sulfide, salicylic acid, zinc or coal tar
- In severe cases, doctors can prescribe shampoos or lotions containing selenium, ketoconazole or corticosteroids

Dry Skin

Extreme dryness of the skin also can be a problem for people with PD.

What You Can Do

- Use skin moisturizers and hair conditioners
- Consult a dermatologist

Excessive Sweating

Many people with PD experience trouble with too much sweating. Sometimes this occurs on the palms of the hands and soles of the feet. Drenching sweats, particularly at night, can also be troublesome. Excessive sweating is often a "wearing off" symptom for people who experience fluctuations in the effectiveness of their carbidopa-levodopa (Sinemet®).

What You Can Do

- Ask your doctor about adjusting your carbidopa-levodopa (Sinemet®) dose.
- Take lukewarm showers
- Wear lightweight cotton clothes in warm weather

- Drink lots of water and other liquids
- In severe cases, for drenching sweats, your doctor may prescribe a medication such as propranolol (Inderal®)
- For the palms and the feet, your doctor can prescribe topical medications including:
    - Aluminum chloride hexahydrate
    - Anticholinergics (e.g., glycopyrrolate)
    - Iontophoresis (a therapy that uses electric current)

Too Little Perspiration

Some people with PD perspire too little. This can be a side effect of anticholinergic medications (i.e. trihexyphenidyl, benztropine mesylate and procyclidine).

What You Can Do

- Decreasing the dose of anticholinergic medications — always under the supervision of your doctor — may help.

Skin Cancer

Skin cancer is relatively common in the general population and in people with PD. Of all skin cancers, people with Parkinson's should be extra-careful regarding melanoma. Melanomas are more likely to spread from the skin to internal organs than any other skin cancers.

Recent studies have suggested the likelihood of developing malignant melanoma is two to seven times higher in people with PD than the general population. While melanomas are relatively rare (even in people with PD), early diagnosis and treatment is important. People with Parkinson's should get screened by a dermatologist annually.

Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

A Practical Guide on

SLEEP AND PARKINSON'S DISEASE

THE
MICHAEL J. FOX
FOUNDATION

MICHAELJFOX.ORG

Introduction

Many people with Parkinson's disease (PD) have trouble falling asleep or staying asleep at night. Some sleep problems are caused by Parkinson's symptoms, while others may be the result of the medications used to treat those symptoms. Factors unrelated to Parkinson's can also impact sleep, including other medical conditions, normal aging or poor "sleep hygiene" (habits that prevent or interrupt a regular sleep schedule).

This guide outlines the sleep difficulties that people with Parkinson's experience most often and the treatments that may be prescribed for each. You'll also find a list of sleep hygiene tips and answers to frequently asked questions about PD and sleep.

This content was reviewed by **Rachel Dolhun**, **MD**, a movement disorder specialist and vice president of medical communications at The Michael J. Fox Foundation.

Sleep Disorders and Parkinson's

SEVERAL SLEEP DISORDERS ARE ASSOCIATED WITH PARKINSON'S DISEASE, INCLUDING:

Insomnia: Difficulty initiating or maintaining sleep. Parkinson's symptoms, such as stiffness or slowness, may make it difficult to turn over or get comfortable in bed. Or, tremor may interfere with falling or staying asleep. Insomnia may also be worsened by some PD meds, such as amantadine or selegiline. It can also be a condition in and of itself.

Treatment: Improving sleep hygiene may help. (See pointers on page 4.) If Parkinson's symptoms are contributing, medication adjustments may be beneficial. In some cases, drugs are prescribed specifically for insomnia.

Daytime sleepiness/hypersomnia: Excessive tiredness during the day. Trouble sleeping at night and some PD medications, including dopamine agonists, can contribute to this disorder.

Treatment: If you find yourself falling asleep easily during the day (i.e., you doze off while watching television or sitting quietly), talk with your doctor who will review your medications and your sleep schedule and habits. If you snore loudly, stop breathing during the night and/or have morning headaches, your doctor may also order a sleep study to exclude obstructive sleep apnea, another common treatable sleep disorder.

Ensuring good sleep hygiene is key. (Look for advice on page 4.) If Parkinson's medications are contributing to sleepiness, they may need to be adjusted. In some situations, stimulant-type medications are prescribed specifically for this symptom.

REM sleep behavior disorder (RBD): Acting out one's dreams, which occurs when normal suppression of muscle activity is impaired. Someone with RBD may kick, punch or yell during sleep. RBD often precedes the motor symptoms and diagnosis of PD by several years.

Treatment: If RBD interferes with a person's (or his or her partner's) sleep, or if it poses a safety issue, it may require treatment. Clonazepam is the most commonly prescribed medication for RBD but melatonin is an option for some people.

Restless legs syndrome (RLS): An uncomfortable sensation in the legs, particularly when sitting or relaxing in the evening, which improves with moving the legs. Because of the time of day that it occurs, RLS can interfere with falling asleep at night. It may be part of Parkinson's disease itself, a side effect of Parkinson's medications or a separate medical condition (sometimes associated with iron deficiency).

Treatment: Treatment may include adjustment of Parkinson's medications, iron supplementation (if levels are low) or prescription of an additional drug specifically to treat RLS symptoms. Note that many Parkinson's medications are indicated for treatment of RLS, even for people who don't have PD.

Obstructive sleep apnea (OSA): Fragmented or interrupted sleep caused by paused or shallow breathing; often associated with snoring. A person is often unaware of these breathing patterns but may experience excessive daytime sleepiness or fatigue, morning headaches, or memory and thinking problems as a result. OSA can be diagnosed with an overnight sleep study.

Treatment: The most common treatment for OSA is a breathing mask or oral appliance worn at night to keep the airway open during sleep. Weight loss is also recommended for overweight individuals.

Other Non-motor and Motor Symptoms That Can Affect Sleep

Stiffness (rigidity) or slowness (bradykinesia): Motor symptoms of Parkinson's that can cause pain, discomfort or difficulty turning over in bed at night.

Treatment: If motor symptoms are interfering with sleep, Parkinson's medication adjustments (such as adding a long-acting medication at bedtime or an as-needed dosage if you awaken with symptoms, for example) may help. Satin sheets or silk pajamas may make it easier to move in bed and regular exercise or physical therapy may help by improving general mobility.

Nighttime urination: The slowness and stiffness of Parkinson's may make using the bathroom at night more difficult. If walking or balance problems are present, this can be particularly challenging. Parkinson's also affects the autonomic nervous system — the part that works automatically to control bladder (and other) functions without our having to think about it — which can lead to increased urination. Other medical problems, such as prostate enlargement in men, may worsen urinary disturbances.

Treatment: Try decreasing fluid intake in the afternoon and evenings (but make sure you drink enough during the day to meet any requirements for low blood pressure and/or constipation). If this isn't enough, medications are sometimes prescribed to decrease nighttime urination. A bedside urinal or commode might lessen bathroom trips and prevent falls for those with significant walking and balance issues. A consultation with a urologist may be considered to evaluate for issues other than Parkinson's that may be playing a role as well.

Depression and anxiety: Common non-motor symptoms associated with PD, which can interfere with sleep. These mood disturbances can prevent you from falling asleep, or wake you up in the middle of the night or early in the morning.

Treatment: Many medications are available to manage depression and anxiety. Talk therapy or counseling is also beneficial for many people.

Sleep Hygiene Tips

As you work with your doctor to pinpoint and treat the cause of your sleep problem, practicing good sleep hygiene may help you get a better night's sleep. See if you find one or more of these tips helpful:

- **Keep a sleep diary.** Important notes to record include the time you go to bed and get up, how many times you awaken during the night and why, and how many hours you sleep. Keep track of the caffeinated beverages you drink (both how many and at what time of day), if you nap and your exercise routine. These notes will help you to have a productive conversation with your doctor about your sleep.
- **Limit daytime naps.** Sleeping too much during the day, especially late in the day, will likely prevent you from sleeping well at night.
- **Avoid caffeine, alcohol and exercise later in the day.** Caffeine consumed in the afternoon can keep you awake at night. Although alcohol may seem to help you fall asleep more easily, it may interrupt your sleep later in the night. Working out regularly earlier in the day can improve sleep overall but exercising too close to bedtime might make it harder to fall asleep.
- **Don't drink too much fluid before bed.** This is especially important if you experience frequent nighttime urination.
- **Use the bedroom only for sleep and intimacy.** Don't watch television, read, use your telephone or do anything other than sleep in bed. When you use your bed only for sleep, your body and mind will automatically know what's supposed to happen when you get into bed.
- **Create a bedtime routine.** An hour before bed, start to prepare for sleep. Turn off the television, computer and other electronics that emit stimulating light. Take a warm bath, drink a cup of decaffeinated tea or read something for fun. Get your body and mind in the habit of winding down and preparing for sleep.
- **Keep a regular schedule.** Go to sleep and get up at around the same time every day, even on the weekends.

Parkinson's and Sleep: Frequently Asked Questions

Should I take melatonin to help me sleep better?

Melatonin is a hormone made by the brain that helps control the sleep cycle; levels are typically low during the day and higher at night. Melatonin is available over the counter in a variety of dosages and many people use it to help manage insomnia. Before you take it, though, talk with your doctor. This and all other supplements do have potential side effects and drug interactions. Also make sure that the root cause of your sleep problems is addressed before you start taking medication or supplements just to treat them. Melatonin is sometimes recommended as a treatment for REM sleep behavior disorder, a sleep disorder in which people act out their dreams, which is commonly associated with Parkinson's.

Is it safe for people with Parkinson's to take sleep aids?

In general, it's important to be careful about combining medications or adding to complex medication regimens, particularly when it comes to medications that induce sleep. These drugs might temporarily worsen balance or memory disturbances, so they should be used cautiously in people with these problems. When dealing with a sleep problem, the first step is to determine the underlying cause, whether it's depression, motor symptoms or bladder dysfunction. Before prescribing a sleep aid, your doctor will review your current medications and investigate for an underlying cause of the sleep problem. Depending on the problem, doctors will sometimes prescribe medications that are meant to help a person fall asleep or stay asleep. Sometimes, when a person is depressed and has trouble sleeping, they will recommend anti-depressant medications that also help with sleep. Sleep aids can be used safely in PD, but this depends on the individual and his or her symptoms and other medications.

Can deep brain stimulation (DBS) help sleep?

Following DBS, some people with Parkinson's are able to sleep better at night, especially if sleep problems were related to medication wearing off. Most people also reduce their medication after DBS, so if sleep problems were due to medication side effects, DBS might make a difference there as well. DBS is otherwise not specifically a treatment for sleep disturbances and is not performed specifically for that; it's a surgical treatment that is most beneficial for the motor symptoms of Parkinson's. Not everyone is a candidate for the procedure.

Should I nap during the day?

Some people with PD who experience fatigue find that napping, particularly in the afternoon, can be energizing. If this is the case, aim for a 10- to 30-minute nap in the early afternoon (around 2 or 3 p.m.). Longer naps later in the day can interfere with your ability to fall asleep.

information

SLEEP AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Sleep changes are commonly reported in Parkinson's and often precede the diagnosis. Disturbed sleep pattern with rapid eye movement behaviour disorder is included in the Parkinson's Associated Risk Syndrome. In addition, medications used in the management of Parkinson's may affect sleep pattern.

Sleep changes are challenging both for the person living with Parkinson's and their sleep partner. This can lead to fatigue and impact on quality of life. It is widely accepted that disturbed sleep will have an impact on cognition.

Sleep disturbances associated with Parkinson's include:

- Bed mobility changes
- Rapid Eye Movement Behaviour Disorder (RBD)
- Restless Legs Syndrome
- Sleep apnoea
- Sleep fragmentation (broken sleep)
- Vivid dreams and nightmares

Bed Mobility Changes

Automatic skills such as rolling over in bed are difficult with Parkinson's. Muscle rigidity, especially of the trunk, adds to this problem and results in impaired bed mobility overnight. The use of satin nightwear or satin sheets is helpful. A self-help rail for the bed will also assist. The input of an occupational therapist and introduction of strategies is recommended. A review of medications to address overnight mobility may be discussed with the treating medical specialist.

Rapid Eye Movement Behaviour Disorder

This is reported in 25% to 50% of people living with Parkinson's. Excessive motor (movement) during the dream phase of sleep is a common feature of Parkinson's. This leads to acting out of dreams and can result in sleeptalking, shouting and intense, sometimes violent movements. These features contrast with the restricted speech pattern and movement during the day. These night time occurrences can often lead to partners sleeping separately. Discussion with the treating medical specialist is recommended.

Restless Legs Syndrome

This occurs in approximately 20% of people living with Parkinson's and involves uncomfortable sensations and the urge to move the legs, particularly overnight. Medical management includes dopamine agonists. Discussion with the treating medical specialist is recommended.

Sleep Apnoea

Reduced or intermittently absent airflow during sleep can lead to snoring with resulting disturbed sleep pattern and daytime fatigue for both bed partners. Assessment at a sleep clinic and the introduction of a continuous positive airway pressure (C-PAP) machine may be of benefit.

Sleep Fragmentation

Night time awakenings occur for a variety of reasons in Parkinson's and it is essential to assess for a regular pattern or cause.

SLEEP AND PARKINSON'S

The breakthrough of motor symptoms (tremor, stiffness and rigidity) may occur as a result of medication wearing off. Discussion with the treating medical specialist is recommended and a review of medications may be necessary.

Early morning dystonia or cramping of the lower limbs is a common occurrence and should be reported. Discussion with the treating medical specialist is recommended and a review of medications may be necessary.

Nocturia (passing urine overnight) may become more frequent and resettling to sleep may become more difficult. Fluids should not be restricted throughout the day. For males, regular prostate examination and blood tests are recommended.

Depression may result in a broken sleep pattern and should be discussed with the general practitioner or specialist.

Improving sleep habits involves a regular sleep schedule, a regular exercise program and reduction of daytime napping. Alcohol and caffeine and other stimulants should be avoided in the evenings.

Vivid Dreams and Nightmares

These occur frequently and may be increased by the medications used in the management of Parkinson's. If the nightmares are disturbing, the treating medical specialist may adjust the timing of medications.

Less commonly these dreams or nightmares may be carried over into the waking period and may be confused with hallucinations.

In addition to sleep disturbances other changes may be experienced. These include:

- Daytime fatigue
- Excessive daytime sleepiness
- Sleep attacks

Daytime Fatigue

Fatigue is a disabling, poorly understood and under-diagnosed symptom of Parkinson's. There is no clear association between the severity of fatigue and the progression of the condition. Fatigue may precede the motor symptoms. If depression is present it should be treated and the associated fatigue may improve. Otherwise, little is known about how to improve fatigue in Parkinson's.

Excessive Daytime Sleepiness

Approximately 50% of people living with Parkinson's experience excessive daytime sleepiness. This may be related to medications and sleep disruption. Monitoring and review of medications may assist.

As the condition progresses, periods of sleep are extended and it is thought that this is due to changes in the mid-brain.

Sleep Attacks

Sudden onset sleep has been described as occurring while eating or driving. It is generally accepted that all Parkinson's medications may be responsible but the dopamine agonists are a more common cause. Reporting the occurrence of sleep attacks to the treating medical specialist is essential.

Adopting a regular routine before bed will be of benefit. Night time sedation (sleeping tablets) must be assessed on an individual basis as they may cause increased daytime drowsiness and increase the risk of falls.

For further information contact
your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

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Small Handwriting

Handwriting can change as you age, especially if you have stiff hands or fingers, from arthritis or another condition, or if you have poor vision. However, small, cramped handwriting – called micrographia – is characteristic of Parkinson's and is frequently one of the early symptoms. In addition to words being generally small and crowded together, the size of handwriting might get smaller as you continue to write.

Micrographia is caused by the same processes in the brain that lead to other movement symptoms of the disease. In addition, those symptoms – slowness of movement, tremor, rigidity – can all make it harder to write.

Managing Micrographia

Medications to control movement symptoms may slightly improve micrographia. There are also some strategies that can make writing more comfortable for you and legible for your readers.

- Practice! Write one page every day.
- Use a weighted pen or a pen with a thick grip.
- Use lined paper.
- Sit upright in a comfortable chair, and write on a table.
- Write during "on" time when medication is working best.
- Take breaks as needed.

If writing becomes too difficult for you or too hard to read, try typing. If motor control makes that too hard, also, try dictation software. There are programs for your phone and computer that can help.

Updating Your Signature

Over time, your handwriting may change, as may your signature. If you or a loved one notices a change in your signature, it is a good idea to document your changes in signature over time.

When it comes to legal documents — from financial documents to advanced directives and planned giving — have your lawyer prepare several formal witnessed and notarized affidavits which you sign at different points during the day to document the changes in your signature.

This can be helpful when trying to convince a bank teller, for example, that your signature is real even though it differs from the signature card on file.

What are the Stages of Parkinson's Disease?

Written by: Emily Downward | Last reviewed: March 2017

Although Parkinson's disease (PD) is progressive and worsens over time, it is highly individual and affects people differently. Not all people who have PD will experience all the symptoms, and symptoms may vary in their severity between patients. Different people experience progression at different speeds, as well. However, physicians have established stages that describe how the disease progresses. These five stages of Parkinson's are known as the Hoehn and Yahr Scale used by physicians throughout the world to classify patients in research studies.[1,2]

Stage one of Parkinson's disease

In stage one, the earliest stage, the symptoms of PD are mild and only seen on one side of the body (unilateral involvement), and there is usually minimal or no functional impairment.

The symptoms of PD at stage one may be so mild that the person doesn't seek medical attention or the physician is unable to make a diagnosis. Symptoms at stage one may include tremor, such as intermittent tremor of one hand, rigidity, or one hand or leg may feel more clumsy than another, or one side of the face may be affected, impacting the expression.

This stage is very difficult to diagnose and a physician may wait to see if the symptoms get worse over time before making a formal diagnosis.

Stage two of Parkinson's disease

Stage two is still considered early disease in PD, and it is characterized by symptoms on both sides of the body (bilateral involvement) or at the midline without impairment to balance. Stage two may develop months or years after stage one.

Symptoms of PD in stage two may include the loss of facial expression on both sides of the face, decreased blinking, speech abnormalities, soft voice, monotone voice, fading volume after starting to speak loudly, slurring speech, stiffness or rigidity of the muscles in the trunk that may result in neck or back pain, stooped posture, and general slowness in all activities of daily living. However, at this stage the individual is still able to perform tasks of daily living.

Diagnosis may be easy at this stage if the patient has a tremor; however, if stage one was missed and the only symptoms of stage two are slowness or lack of spontaneous movement, PD could be misinterpreted as only advancing age.

Stage three of Parkinson's disease

Stage three is considered mid-stage and is characterized by loss of balance and slowness of movement. Balance is compromised by the inability to make the rapid, automatic and involuntary adjustments necessary to prevent falling, and falls are common at this stage. All other symptoms of PD are also present at this stage, and generally diagnosis is not in doubt at stage three.

Often a physician will diagnose impairments in reflexes at this stage by standing behind the patient and gently pulling the shoulders to determine if the patient has trouble maintaining balance and falls backward (the physician, of course, will not let the patient fall). An important clarifying factor of stage three is that the patient is still fully independent in their daily living activities, such as dressing, hygiene, and eating.

Stage four of Parkinson's disease

In stage four, PD has progressed to a severely disabling disease. Patients with stage four PD may be able to walk and stand unassisted, but they are noticeably incapacitated. Many use a walker to help them.

At this stage, the patient is unable to live an independent life and needs assistance with some activities of daily living. The necessity for help with daily living defines this stage. If the patient is still able to live alone, it is still defined as stage three.

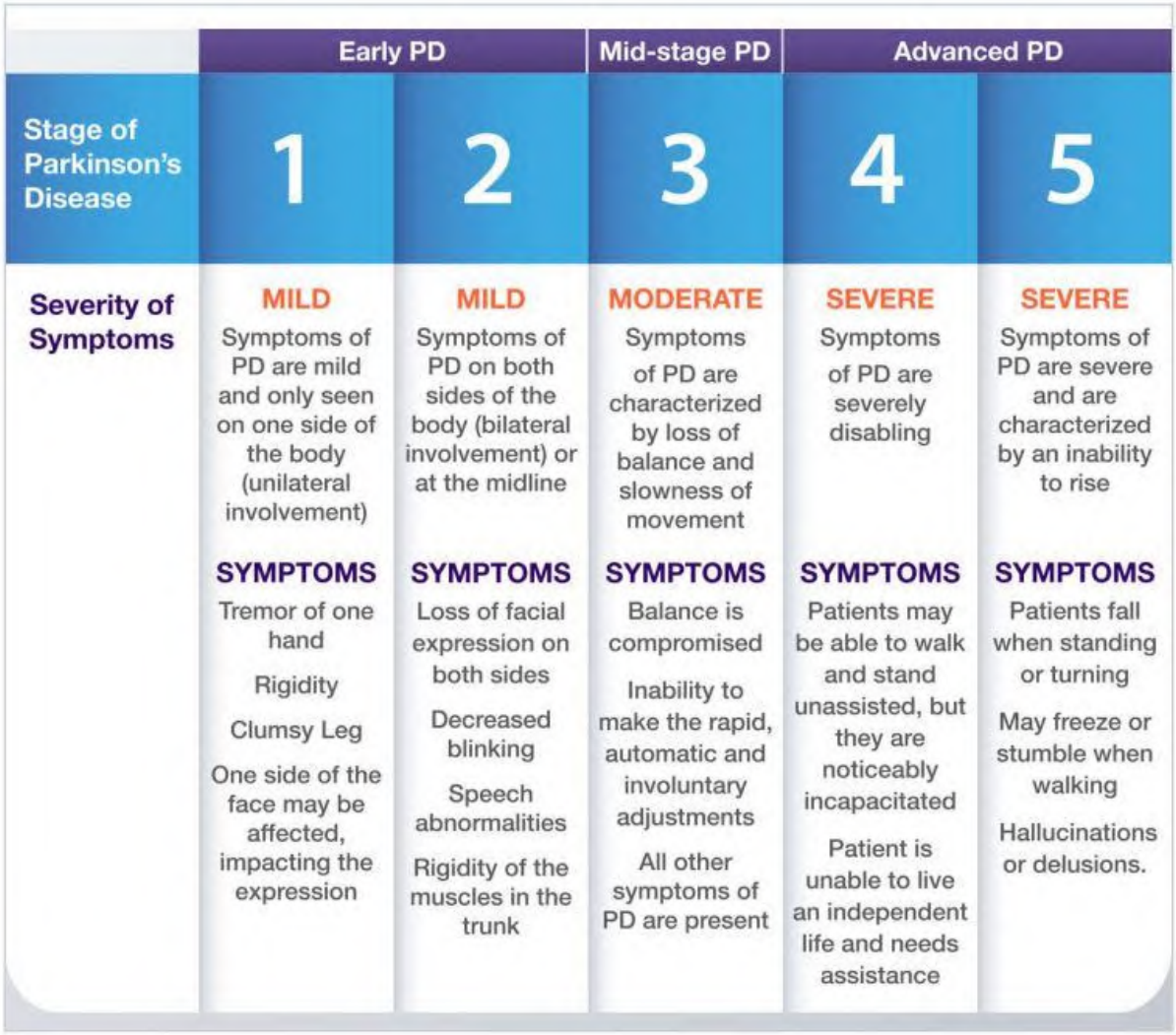
Stage five of Parkinson's disease

Stage five is the most advanced and is characterized by an inability to rise from a chair or get out of bed without help, they may have a tendency to fall when standing or turning, and they may freeze or stumble when walking.

Around-the-clock assistance is required at this stage to reduce the risk of falling and help the patient with all daily activities. At stage five, the patient may also experience hallucinations or delusions.

While the symptoms worsen over time, it is worth noting that some patients with PD never reach stage five. Also, the length of time to progress through the different stages varies from individual to individual. Not all the symptoms may occur in one individual either. For example, one person may have a tremor but balance remains intact. In addition, there are treatments available that can help at every stage of the disease. However, the earlier the diagnosis, and the earlier the stage at which the disease is diagnosed, the more effective the treatment is at alleviating symptoms.

Figure 1. Stages of Parkinson's Disease



	Early PD		Mid-stage PD	Advanced PD	
Stage of Parkinson's Disease	1	2	3	4	5
Severity of Symptoms	MILD	MILD	MODERATE	SEVERE	SEVERE
	Symptoms of PD are mild and only seen on one side of the body (unilateral involvement)	Symptoms of PD on both sides of the body (bilateral involvement) or at the midline	Symptoms of PD are characterized by loss of balance and slowness of movement	Symptoms of PD are severely disabling	Symptoms of PD are severe and are characterized by an inability to rise
	SYMPTOMS	SYMPTOMS	SYMPTOMS	SYMPTOMS	SYMPTOMS
	Tremor of one hand Rigidity Clumsy Leg One side of the face may be affected, impacting the expression	Loss of facial expression on both sides Decreased blinking Speech abnormalities Rigidity of the muscles in the trunk	Balance is compromised Inability to make the rapid, automatic and involuntary adjustments All other symptoms of PD are present	Patients may be able to walk and stand unassisted, but they are noticeably incapacitated Patient is unable to live an independent life and needs assistance	Patients fall when standing or turning May freeze or stumble when walking Hallucinations or delusions.

What Parkinson's Isn't: 6 Myths Debunked

By Allison Smith · August 21, 2017

What is Parkinson's disease?

This is a question many of us have asked our neurologists, but the answers can be confusing. This is because we are still learning about this disorder and it's impact on our lives.

However, we do know what Parkinson's isn't.

Myths about Parkinson's

Parkinson's is curable

First and foremost, as many of you know, there is no cure for Parkinson's disease. But before you get too discouraged, if you're going to get it, now is a great time to be diagnosed with Parkinson's. We have made such huge medical advances in the last decade alone, that now we have an arsenal of weapons to use against PD. Imagine being diagnosed with Parkinson's in the early 1900's… I shudder.

Parkinson's only affects movement

Since its discovery in 1817, Parkinson's disease was believed to only affect posture, mobility, gait, and balance. But now we realize just how PD can impact a person in a multitude of ways, including non-motor symptoms. Top offenders include: constipation, bladder control, drooling, swallowing, memory, depression, anxiety, sleep issues, cognition, and impaired executive functioning. Our Neurologists have their work cut out for them.

Parkinson's will kill you

Although you won't die from having Parkinson's disease, you can die from its complications. This can include aspiration of food, traumatic falls, infection, or sepsis. Just remember, you don't die from Parkinson's disease, you die with it.

Parkinson's is an old person's disease

Although PD is more common in the elderly population, there is a subset of Parkies who are under the age of 40. Like yours truly…

Parkinson's is gender-specific

Even though there are more men diagnosed with Parkinson's disease than women, PD doesn't discriminate. Some of the major differences between the sexes of Parkies is hormone levels, coping skills, lifestyle choices and careers (men could possibly be more exposed to chemicals, such as pesticides).

Parkinson's is a walk in the park

When I was first diagnosed with Parkinson's disease, I was naïve to believe that I would only be inconvenienced by a slower pace or struggle with a slight tremor. That was based on the only person I knew who had Parkinson's… Michael J. Fox. He didn't look that bad. Maybe I will get a mild case of PD… kind of like the watered-down version. Ignorance is bliss, eh?

Oh man, was I wrong. I learned quickly that Parkinson's would negatively impact many facets of my life and that each day will present a challenge of some sort. Parkinson's isn't a walk in the park. It is emotionally, physically, and mentally exhausting.

But the one thing that you can count on is your Wolfpack (people who support you). They will take that stroll with you through the botanical garden of life.

Stooped Posture

Parkinson's affects control of automatic activities, so posture changes may occur without the brain's automatic reminders to stand up straight. These changes may include stooped or rounded shoulders, decreased low back curve or forward lean of the head or whole body, making you look hunched over.

There are several factors that can lead to changes in posture:

- Muscle stiffness or rigidity
- "Off" time, when your medications aren't working as well
- When you have been in one position for too long
- If you are concentrating on another activity (like walking or working at the computer)

It is important to try to maintain an upright posture because stooped posture can have other negative effects:

- Neck or back pain can occur when natural spine curves are out of alignment.
- Stooped posture reduces your ability to take deep breaths, which impacts your ability to speak clearly and loudly. Stooped posture also reduces eye contact. Combined with other Parkinson's symptoms like low voice volume and facial masking, this can have a big impact on your ability to communicate.
- Loss of flexibility from changing posture can make it hard to do many small movements in your day, like raising arms overhead

while getting dressed or getting up out of a chair.
- Poor posture can put you off balance and lead to falls.

Managing Posture Changes

Try these strategies to maintain good posture:

- Use a mirror to check posture (both front and side views) throughout the day.
- Be aware of posture changes. Try to catch yourself stooping or leaning and take action to make corrections. Ask people to tell you if they notice you stooping.
- Change position often. Take movement breaks!
- Get back (lumbar) or neck (cervical) rolls or cushions for better postural alignment when sitting.
- Consider yoga or Tai Chi classes.
- Ask your doctor or call the Parkinson's Foundation Helpline (1-800-473-4636) for a physical therapy referral. A therapist can give you specific posture recommendations and exercises.

Stooped posture makes the muscles in the front of your body less flexible and the muscles in the back of your body weaker. Perform simple **posture exercises and stretches** throughout the day.

information

SURGERY FOR PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Levodopa (a medication taken orally or directly into the small intestine) remains the gold standard treatment for Parkinson's.

Deep brain stimulation (DBS) uses mild electric impulses to stimulate a chosen area of the basal ganglia within the midbrain. This may be the subthalamic nucleus or another target site depending on the symptoms.

Neurosurgery such as DBS may be considered as a treatment (not a cure) for suitable candidates and is available in most states in Australia. The procedure may vary from centre to centre and in most cases the patient is awake during the procedure. Your treating physician will discuss the methods practiced in the various states.

Recent research suggests that DBS should be considered earlier than was previously done. Candidates for surgery are usually selected by a panel of movement disorder experts, as not all patients are suitable and not all Parkinson's symptoms will respond to DBS.

As a result of DBS, the patient may be able to reduce the amount of medication previously required or tolerate more medication.

As with any surgery, there are risks involved. In the case of DBS these include death, stroke, speech changes or infection. In addition some people may experience increased depression and anxiety which may or may not be reversible.

Anecdotal evidence suggests there may be unexpected problems with co-ordination during some sequences of movements e.g. swimming – caution should be used.

The criteria for selection for DBS are:

- A good response to levodopa – exceptions to this rule are people with severe tremor which has not responded well to levodopa. In addition, people who are intolerant of medication may also be suitable for DBS.
- Age - while there is no definite age limitation, general fitness and ability to undergo the surgical procedure is essential.
- Intact cognition - research shows that cognitive decline does not respond well to DBS.
- Emotionally stable with no evidence of psychosis.

The main symptoms which respond to DBS are:

- Dyskinesia - involuntary movements which can affect any part of the body and vary in intensity. These are a side effect of Parkinson's medication.
- Motor fluctuations - response to medication may become unpredictable and vary between being 'on' when medication is working and 'off' when the patient experiences stiffness, rigidity and slowness.
- Tremor - an involuntary regular motion which occurs mostly at rest and may affect any limb and the lips and less frequently the head.

Research indicates that 10-15 years after surgery some patients are still demonstrating good results. However, it is important to remember that Parkinson's is a progressive condition and having DBS does not stop the progression. Ongoing monitoring and review of medication is required.

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parkinson's
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SURGERY FOR PARKINSON'S

The first stage of the surgery is the insertion of DBS leads into the area of the brain which has been targeted. Current preference is to insert the leads bilaterally following mapping of the brain by CT scan or MRI. This stage involves the wearing of a 'halo' to assist with mapping, measuring and monitoring of wire insertion. This stage can take several hours.

In some centres, surgery is carried out in two stages. Following the initial surgery, the patient may experience a transient positive response. This is due to the swelling of the target area affecting the nerve cells in the same way the stimulator will do when inserted and turned on. It is necessary for this swelling to subside before the stimulator is activated (turned on) and programmed.

The second stage of the procedure is carried out under general anesthetic and the stimulator is placed under the skin of the chest. The DBS leads sit under the scalp and run down behind the ear into the stimulator which resembles a cardiac pacemaker.

Programming of the stimulator may take several weeks to reach an optimum effect. The stimulator is a sealed unit which is run by batteries lasting approximately four to five years at which time the stimulator is changed. Some more recent stimulators are rechargeable and this is self managed at home on a regular basis as instructed by the neurologist depending on the type of stimulator implanted. It is essential that the battery life of the stimulator is checked regularly as instructed.

In the past it was not possible to undergo an MRI if a stimulator was in place. Since 2016, some DBS devices can now undergo full body MRI under specific conditions. Please refer to your neurologist if an MRI is required (to confirm eligibility). All forms of diathermy treatments (shortwave, microwave and ultrasound) are contraindicated for people who have a Deep Brain Stimulator in place

IN THIS TOGETHER
parkinson's
AUSTRALIA

information

SWALLOWING AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Dysphagia is the technical term for chewing and swallowing difficulties. Systematic review of evidence estimates that dysphagia occurs in up to 80% of people with Parkinson's. It is often unrecognised unless objectively assessed by the appropriate professionals.

The ability to chew and swallow impacts on ensuring a balanced diet and meeting specific nutritional needs.

Swallowing difficulties can interfere with taking medications, which is vital for treating the symptoms of Parkinson's.

Dysphagia can present a number of health and safety risks.

The airway is closed off automatically when we swallow in order to avoid aspiration (penetration into the airway) of food particles, fluid, saliva or medication. Dysphagia can interfere with this safety process leading to risk of chest infections or pneumonia as well as blocking the airway. Choking is rare in Parkinson's but may occur, particularly if swallowing problems are not addressed.

Swallowing difficulties can reduce enjoyment of meals; discourage appetite, cause embarrassment and increase stress and anxiety.

Weight loss is a common problem in Parkinson's and can result from a variety of factors, including dysphagia.

Inadequate fluid intake can impact kidney, bladder and bowel functions, skin, saliva control, energy levels and general health.

Fibre rich foods such a green leafy vegetables or grains can be difficult to chew and swallow and are sometimes avoided when there is dysphagia therefore increase the risk of constipation.

Why does dysphagia occur in Parkinson's?

Slowness of movement, difficulty with initiation of movement, reduced sensation, poor coordination and diminished movement size associated with Parkinson's can affect the mechanism involved in chewing and swallowing.

These can be more pronounced when in an 'off' state (when movements are diminished) or when experiencing involuntary movements such as dyskinesia.

Parkinson's affects automatic movement control. Eating, drinking and swallowing are automatic skills and when attention is focused on conversation, other thoughts, reading or television these skills may be compromised.

How can dysphagia present?

Warning sings and symptoms of dysphagia can include:

- Coughing when eating or drinking
- Difficulty swallowing medication
- Sensation that food is 'stuck' at throat level
- Difficulty shifting food from mouth to throat
- Problems effectively breaking food down when chewing
- Food residue in mouth after meals
- Sialorrhea (poor control of saliva)
- Coughing on saliva or phlegm
- Difficulty initiating a swallow
- Slow, effortful eating and drinking
- Difficulty breathing or chest discomfort during meals
- Recurring chest infections

Dysphagia can also be a 'hidden' problem. 'Silent aspiration' refers to penetration of food, fluid, saliva or medication into the airway without a cough response.

Who can help? The health professional team including a general practitioner, medical specialist, speech pathologist, Parkinson's nurse specialist, dietician, occupational therapist and physiotherapist can assess and address Dysphagia.

SWALLOWING AND PARKINSON'S

What Can Be Done?

Request a general practitioner or medical specialist referral to a speech pathologist whose role is to assess swallowing function and to plan and deliver a swallowing management program.

A speech pathologist's assessment includes an examination of the structures involved in swallowing (lips, tongue, soft palate, and voice box), an observation of eating, drinking and swallowing medication and a detailed interview.

Instrumental assessment commonly includes Video-Fluoroscopy (modified barium swallow). This is an imaging technique which provides an x-ray view of chewing and swallowing in action. This helps identify strengths and weaknesses so as to guide therapy intervention. It is particularly useful for showing 'hidden' difficulties such as 'silent aspiration'. This assessment also enables the therapist to test the efficacy of recommended strategies.

Another beneficial swallowing test is Fibreoptic Endoscopic Evaluation of Swallowing (FEES). The speech pathologist and/or ear nose and throat specialist use a fine flexible tube with a camera and light on the end of it. It is inserted via the nose and provides a computer screen view of throat function during a swallow.

A speech pathologist can provide recommendations for swallowing management and may teach exercises, strategies and techniques for safe and optimal chewing and swallowing, specific to individual needs.

The speech pathologist and dietician work as a team to advise on food and fluid choices, dietary regimes and food or fluid modification if required.

An occupational therapist can assist with seating recommendations for mealtime, aids and equipment and techniques for using cutlery.

A physiotherapist can assist with finding solutions for postural issues. Maintaining optimal posture during mealtime is critical for swallowing management. Chest physiotherapy can assist with maintaining clear airways through various techniques to shift mucous up and out of the lungs.

Expiratory strength training for both speech and swallowing is a growing area or interest for speech pathology research and clinical practice.

Ear, nose and throat specialist and gastroenterologists are consulted if required.

information

PARKINSON'S SYMPTOMS

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

The provisional medical diagnosis is based on symptoms because there is no definitive medical test or radiological procedure which diagnoses Parkinson's. The diagnostic criteria is composed of four cardinal symptoms which are:

· Tremor
· Bradykinesia
· Muscle rigidity
· Postural instability

Tremor

Although tremor is the most commonly recognised symptom, it is not present in all cases of Parkinson's (30% of those with the condition will not experience tremor) and tremor is common to other conditions.

Tremor is related to an imbalance of neurotransmitters, dopamine and acetylcholine, for this reason, tremor may be the least responsive symptom to dopamine replacement therapy.

The classic Parkinson's tremor, if present, is described as a 'resting' tremor in that it is present when the affected limb is at rest. The tremor is regular and rhythmic and occurs at the rate of 4-6 times per second.

Initially tremor may be unilateral. However, with the natural progression of the condition it can be experienced on the other side. A classic tremor presentation of Parkinson's involves the thumb and first finger and is referred to as 'pill rolling'.

Tremor may be exacerbated by stress, anxiety, fatigue and lack of sleep. It diminishes with voluntary action and is absent during sleep. Cognitive testing and motor tasks in a different body part increase the resting tremor. Unlike Essential Tremor the resting tremor of Parkinson's is less likely to be increased by caffeine or improved with alcohol.

Tremor, if unresponsive to Parkinson's medication, may be managed surgically by Deep Brain Stimulation in the appropriate patient.

Bradykinesia

Bradykinesia can be the most disabling symptom of the condition and refers to slowness of voluntary movements and a lack of normal associated movements. Initially it may be misinterpreted as slowing due to aging – however, it is out of proportion to normal aging.

Bradykinesia affects critical aspects of daily living – walking, talking, swallowing and speaking. In the eyes and face it presents as a decreased blink rate and a lack of facial expression.

PARKINSON'S SYMPTOMS

Bradykinesia is usually unilateral and initially may be confined to the distal muscles of the hand resulting in slow finger tapping and problems with fine motor tasks such as keyboard skills and fastening buttons. These difficulties are increased when dual tasking is involved.

Generalized bradykinesia is assessed by the overall slowing of all body parts – typically how easily the person rises from the sitting position and their speed of walking.

Muscle Rigidity

Muscle rigidity may not be apparent to the person with Parkinson's but is felt by the medical practitioner in limb muscles when they are passively moved. It is described as 'lead pipe' or 'cogwheel' rigidity. Muscle rigidity as with most Parkinson's symptoms first present as unilateral. However, with progression they become bilateral.

Muscle rigidity is commonly present in the wrist, shoulder and neck. It may also manifest as a slightly flexed elbow on the affected side. Early reports of a painful shoulder are associated with increased muscle rigidity and tone. The pain associated with Parkinson's is often underestimated and reported, and is usually associated with muscle rigidity.

As the condition progresses muscle rigidity can lead to the characteristic forward flexed posture.

Postural Instability

Postural instability and gait disturbances often develop later in the progression of the condition. If a loss of postural reflexes and resulting falls occur early, it is not suggestive of typical Parkinson's.

In early Parkinson's the posture may show a slight flexion of the neck or trunk with a slight lean to one side. Gait changes include reduced arm swing (unilateral) and shortened stride height and length which may lead to shuffling.

In addition to these four cardinal motor symptoms there are many others which are also considered in the diagnostic process. Often the non-motor symptoms are more challenging for the person living with Parkinson's.

Other Symptoms

Anosmia refers to a decrease or loss of sense of smell. This often precedes the diagnosis.

Anxiety is a common phenomenon in Parkinson's and can exacerbate the motor symptoms.

Constipation is a common early symptom and is due to reduced motility of the intestines and may be exacerbated by a reduction in physical activity and the introduction of Parkinson's medication.

Bradyphrenia is the term used to describe slowness of thought experienced by people with Parkinson's.

Depression is commonly experienced prior to the diagnosis and is due to a chemical imbalance. A reactive depression may occur with the diagnosis and support and information is essential at this time. Frequently apathy and lack of motivation are evident and are mistaken for depression.

Fatigue, which is not relieved by resting, is a common early symptom. This can be related to a variety of causes including disturbed sleep pattern due to changes in bed mobility, restless legs symptoms, urinary frequency and/or leg cramping.

Festination of speech describes the change in verbal fluency. This can be mistaken for a stuttering speech pattern.

Impotence (long-term) is frequently reported.

PARKINSON'S SYMPTOMS

Micrographia refers to the changes in hand writing (especially cursive). This becomes smaller in height and the written words may be unclear by the end of the sentence.

Microphonia describes decreased volume of speech often not obvious to the person with the condition.

Postural hypotension refers to a drop in blood pressure especially on rising from a lying or sitting position. This can result in unsteadiness, dizziness and falls. In addition the medications used in the treatment of Parkinson's may cause a drop in blood pressure.

Sialorrhea describes excessive saliva and is often due to decreased frequency of swallowing and poor mouth closure. In addition dry mouth can be experienced due to the medications used for the management of Parkinson's.

Sleep disturbances – a common early symptom is the tendency to 'act out' one's dreams and call out while dreaming. This can often lead to an unintentional injury to the person experiencing the dream or their bed partner.

Swallowing changes may occur in relation to liquids or solids.

Sweating and increased sensitivity to temperatures is often reported. Cold weather may exacerbate tremor. Hot weather may lead to increased sweating and postural hypotension.

The symptoms listed above reflect changes some people may experience. Not everyone will experience all symptoms. For this reason a review by a medical specialist with an interest in Parkinson's is recommended.

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parkinson's
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Tremor

The typical Parkinson's tremor occurs mostly at rest ("resting tremor") and lessens during sleep and when the body part is actively in use. For example, your hand might shake while you're sitting, or even while you're walking, but when you reach out to shake hands with someone, the tremor is less noticeable or goes away entirely.

Tremor tends to occur in the hands and is often described as "pill-rolling": imagine holding a pill between your thumb and forefinger and continuously rolling it around. But it can also appear in other parts of the body, including the lower lip, jaw or leg. These tremors can interfere with routine activities such as shaving, dressing, writing and many other tasks that require fine motor coordination.

Some people report an internal tremor, a shaking sensation inside the chest, abdomen or limbs that cannot be seen.

Tremor usually affects only one side of the body, especially during early stages of the disease. With disease progression both sides may become affected. Fatigue, stress or intense emotions can temporarily make tremors worse.

Who Is Affected by Tremor?

About 70% of people with Parkinson's experience a tremor at some point in the disease. Tremor appears to be slightly less common in younger people with PD, though it is still one of the most troublesome

symptoms. People with resting tremor usually have a more slowly progressing course of illness than people without tremor.

Tremor in Other Conditions

While tremor is a common symptom of Parkinson's, it can also be a symptom of other conditions, most notably essential tremor. The main difference between Parkinson's tremor and most other types of tremor is that in Parkinson's resting tremor is most common. Other conditions are usually characterized by "action tremor," which tends to lessen at rest and increase when you're doing something, like trying to make a phone call or take a drink.

Tremors of the head and voice are also common in essential tremor but rare in Parkinson's.

Managing Tremor

Levodopa is the medication most commonly given to control the movement symptoms of Parkinson's, and tremor usually – though not always – responds to levodopa treatment.

If dopaminergic medications do not work to control tremor, other medications are sometimes used. For example, anticholinergics can be helpful for tremor. However, they can cause significant mental and physical side effects, so their use should be carefully considered. Anticholinergics are most useful in young people with tremor-predominant PD (when tremor is the main symptom that needs managing).

If medications are not effective, deep brain stimulation (DBS) is generally successful in controlling tremor, even medication-unresponsive tremor.

The treatment for internal tremor is the same as for visible tremor.

For more information on medications and deep brain stimulation for tremor, read our books Parkinson's Disease: Medications and A Guide to Deep Brain Stimulation.

In addition to medication and surgical treatment, there are assistive devices that can help with various activities of daily living. One of these is Liftware, a utensil with a stabilizing handle to counteract PD-related tremor. It is available with spoon and fork attachments and helps steady the hand, so it can make it easier to scoop up food and bring it to the mouth.

The Parkinson's Foundation is part of the Liftware donation program for people who cannot otherwise afford the device. If you think you could benefit from the device, call our Helpline at 1-800-4PD-INFO (473-4636) to talk to one of our PD Information Specialists about whether the device is right for you.

Last but certainly not least, **exercise** is as important as medication and other therapies for managing Parkinson's symptoms and leading your best possible life.

Trouble Moving or Walking

People without PD do not think about their walking. Their arms naturally swing, and their feet naturally land on the heels with each step. They can walk and talk and carry bags, purses and plates of food without difficulty.

Individuals with PD tend to lose their automatic movements. Especially 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). Feet begin to shuffle, and performing two tasks at once becomes more difficult. Turning becomes challenging, often leading to a freezing episode and sometimes a fall.

Parkinson's Disease Is a Movement and Sensory Disorder

People with PD have trouble regulating the speed and/or size of their movements. Movements are bradykinetic (too slow) or hypokinetic (too small).

Changes in the movement system lead to challenges controlling movements, including the following:

- Starting and stopping movements
- Automatically controlling muscles
- Linking different movements to accomplish one task (e.g., moving from sitting to standing)

- Finishing one movement before beginning the next (e.g., not completely turning around before sitting down)

Changes in the sensory system also lead to challenges, particularly noticing and correcting movement and voice issues, including the following:

- Slowness or smallness of movements (e.g., when told to make the movement bigger, a person with PD may feel the movement is now "too big")
- Lack of movement (e.g., an arm that does not swing during walking)
- Changes in posture
- Changes in voice volume (e.g., when told to speak louder, a person with PD may feel they are shouting)

Walking Changes

There are many PD-related walking changes:

- Smaller steps
- Slower speed
- Less trunk movement (especially rotation)
- A narrow base of support (feet too close together)
- Less or absent arm swing (on one side of the body or both)
- Trouble turning
- The feet land flat on the floor with each step instead of on the heel (can lead to shuffling and falls)
- Festination or shuffling (quick, small, involuntary steps forward; often accompanied by stooped posture)
- Retropulsion (quick, small, involuntary steps backward)

Managing Walking Changes

- Exercise is as important as medication and other therapies for managing Parkinson's symptoms and leading your best possible life. Exercise Reported benefits of exercise include:
- Improved gait and balance

- Reduced falls
- Increased flexibility and posture
- Improved endurance
- Reduced freezing of gait

Walking Tips

- Tell yourself to land with heel first. You can do this by thinking of each step as a big kick. By thinking about what you are doing, you use a different part of your brain than the part affected by PD. You re-route the message from the brain to the feet.
- Focus on the size of your steps rather the speed of your steps.
- Avoid carrying many things while walking. People with PD have difficulty performing more than one task at a time.
- The moment you begin to shuffle or freeze, try to come to a complete stop. Take a breath, stand tall and start again, focusing on making that first step a big step.
- Stand tall and look out in front of you. Do not look directly down at your feet.
- Use a cane or walker/rollator if recommended by your therapist or doctor.

Turning Tips

- When beginning a turn from a stopped position, be sure to lead with your foot, not your upper body. Planting your feet and turning your upper body frequently leads to a freezing episode.
- If you want to turn right, shift your weight to the left foot and step out with the right foot. To turn left, shift your weight to the right and step out with the left foot.
- Try not to pivot when you turn. Instead, focus on how you lift your feet.

Freezing

Some people experience "freezing," the temporary, involuntary inability to move. This can occur at any time, though it tends to occur when

initiating a step, turning or navigating through doorways. It can be a serious problem, as it may increase risk of falling.

Managing Freezing

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

Tips for Care Partners

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."

Urinary Dysfunction and Parkinson's

Parkinson's disease (PD) has many features that have little or nothing to do with movement. Among these non-motor symptoms are problems with the autonomic nervous system — the part of the nervous system that controls "automatic" bodily functions, such as heart rate, blood pressure, sweating, sexual function and both gastrointestinal and urinary function. These symptoms are often among the most serious and complex issues faced by people with PD.

Unlike bowel dysfunction (e.g., constipation), which often occurs before Parkinson's movement symptoms, urinary dysfunction is not typically a problem until the later stages of the disease.

Bladder Problems in Parkinson's

The primary function of the bladder is twofold — to store urine as it is made and then to empty the urine. With Parkinson's, problems can emerge in both areas.

Recent studies suggest that 30-40% of people with Parkinson's have urinary difficulties. Despite the frequency of urinary dysfunction, actual urinary incontinence is relatively uncommon. Troublesome incontinence develops in only about 15% of people with Parkinson's.

The most common urinary symptoms experienced by people with Parkinson's are:

- The need to urinate frequently
- Trouble delaying urination once the need is perceived, creating a sense of urinary urgency

These symptoms usually mean you have an irritable or overactive bladder. Your bladder is signaling the brain that it is full and needs to empty when, in fact, it is not. This can happen at any time, so you might have to get up multiple times during the night to go to the bathroom.

Impairment of bladder emptying is a less frequent but still troublesome feature of urinary dysfunction in Parkinson's. This may be caused by delay or difficulty in relaxation of the urethral sphincter muscles. These muscles must relax for the bladder to empty. This can result in hesitancy in initiating urination, difficulty in generating a stream and incomplete emptying of the bladder. Dystonia – involuntary muscle contractions – of the urethral sphincter has also been described.

Treatment

Medications that work to block or reduce bladder overactivity can be useful in treating urinary frequency and urgency. These include oxybutynin, tolterodine, solifenacin and darifenacin.

These medications are not helpful for problems emptying the bladder and may actually aggravate the difficulty. Medications such as bethanechol can help, but intermittent self-catheterization is sometimes necessary. Before initiating these, a doctor must make sure that some unrelated process, such as an enlarged prostate, is not responsible for the problem.

You may benefit from seeing a bladder specialist (urologist) for help with medication and lifestyle adjustments.

Conclusion

Being aware that urinary problems, such as urinary tract infections, can be a symptom of Parkinson's is the first step toward management. Do not hesitate to bring these problems to the attention of your healthcare team. Effective treatment is often available. To learn more, visit www.parkinson.org.

information

BLADDER CONTROL AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

The most common ways that Parkinson's can affect bladder control are:

Urgency - having little warning that you need to pass urine

Frequency - having the desire to pass urine on frequent occasions, and often only passing a small amount at a time

Retention - not being able to completely empty the bladder

Nocturia - the desire to empty your bladder frequently once you have gone to bed.

Why do Urgency and Frequency Occur?

Bladder difficulties in Parkinson's are related to fluctuations in the level of dopamine affecting the function of the bladder muscle. Parkinson's is also thought to affect the nerve pathway between the bladder and the part of the brain controlling bladder function. Some of the symptoms that affect bladder control are related to the level of dopamine in your body so may fluctuate depending on your medication level.

Underlying conditions such as weak pelvic floor muscles or an enlarged prostate will contribute to bladder symptoms. Constipation can also worsen bladder symptoms by putting pressure on the bladder, making the symptoms more apparent.

What can help?

Discuss bladder problems with your General Practitioner or Neurologist, who may perform some tests to rule out urinary tract infection, or other problems that may impact on normal bladder function.

Speak with your General Practitioner or Neurologist about a referral to an Urologist, a doctor who specialises in bladder function. The Urologist will be able to look into any bladder symptoms and provide treatment plans for these.

Beware that bladder difficulties can be a sign of "wearing off". Wearing off is where some of the symptoms of Parkinson's occur or worsen between doses of medication, and are related to the level of medication becoming too low. This sensation most often occurs not long before your next medication is due. Taking your medication on time every time will help in reducing fluctuations in medication and will therefore help reduce bladder difficulties.

Managing constipation and making sure that you have regular bowel movements will also assist in minimising bladder problems.

Can exercise help?

Bladder problems in Parkinson's are related to changes in muscle function and the way the brain interprets signals from the bladder. Pelvic floor exercises will help to improve bladder tone and potentially increase the control that you have in the muscles surrounding the bladder neck. Speaking to a physiotherapist or continence nurse can help in developing some pelvic floor exercises specifically for your needs.

BLADDER CONTROL AND PARKINSON'S

Medication

There are some medications available that can assist with bladder control; these medications may have an anti muscarinic or anti cholinergic effect that appears to improve bladder control. While these medications may prove effective in improving bladder control, they can have some adverse side effects including a worsening of Parkinson's symptoms, confusion and developing a dry mouth, so caution may need to be taken when considering these medications.

Frequency

Frequency is the sensation that you need to pass urine frequently, and is often accompanied by a feeling of urgency. It is common that when you do pass urine frequently it is only a small amount. This symptom can occur day or night and many people living with Parkinson's associate it with "wearing off". Developing good medication habits will help, and trying some pelvic floor exercises may help reduce this symptom. As frequency in Parkinsons is commonly linked with "wearing off" the symptom may be more marked in the evening or at night.

Nocturia

Nocturia is the sensation that you need to pass urine often at frequent intervals during the night. In Parkinson's this commonly occurs in the first few hours after you have gone to bed, often affecting a person's sleep. The reason this occurs is related to "wearing off" and blood pressure fluctuations causing fluid retention during the day. This retained fluid is reabsorbed by the body when we lie down with our feet elevated and is then passed as urine, causing the need to pass urine on several occasions throughout the night.

You should discuss this symptom with your doctor. A simple way that nocturia can be managed is by having a rest in the afternoon with your feet elevated, allowing some of the excess fluid to be reabsorbed and passed. Anti cholinergic or anti muscarinic medications work to increase bladder control, however these medications are used with caution as they may worsen Parkinson's symptoms or cause confusion. Other practical ways of managing this symptom include reducing the volume of fluid that you drink in the hours before you go to bed, e.g. have most of your drinks between waking and 5pm. Avoid caffeinated drinks after 5pm, as they can contribute to bladder irritability. Having a bedroom which is close to the toilet, or using a commode or bottle in the bedroom can also be helpful.

Retention

Developing urinary retention can occur in Parkinson's but is uncommon. It is diagnosed through having a post urination bladder ultrasound. Sometimes medications used to assist in managing urgency can cause retention. If you are affected by urinary retention your doctor will advise you on management or refer you to a specialist.

Devices and Aids

There are a number of products that can assist with managing continence. Some people find it reassuring to wear an incontinence product, particularly if they are away from their homes and are worried they may not be able to get to a toilet in time. Products include continence pads and condom drainage for males. Funding assistance may be available to support the cost of incontinence aids and your continence nurse or GP Practice nurse can help with this.

The best person to speak with in regard to obtaining the correct continence product is a Continence Nurse (available through your local GP, Community Health Centre or Hospital).

BLADDER CONTROL AND PARKINSON'S

The National Continence Helpline 1800 33 00 66 can assist by providing you with details of the nearest services to your place of residence.

For More Information

Speak to your doctor or contact the National Continence Helpline 1800 33 00 66. The Helpline provides free information about bladder and bowel control problems as well as advice about continence products and clinics, and has a wide range of free information and resources available.

The National Continence Helpline is an Australian Government initiative managed by the Continence Foundation of Australia. For further information visit continence.org.au

Where to get help and further advice

National Continence Helpline 1800 33 00 66

Continence Foundation of Australia: continence.org.au

Parkinson's Australia: parkinsons.org.au

Bladder and Bowel website: bladderbowel.gov.au

Public Toilet Map: toiletmap.gov.au

Continence Foundation of Australia

National Office

Level 1, 30 – 32 Sydney Road, Brunswick VIC 3056

T: 03 9347 2522 F: 03 9380 1233

E: info@continence.org.au

W: continence.org.au

The Continence Foundation is the Australian peak body for awareness, education and advocacy for those with incontinence and their carers and partners.

Continence Foundation of Australia

For further information contact your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

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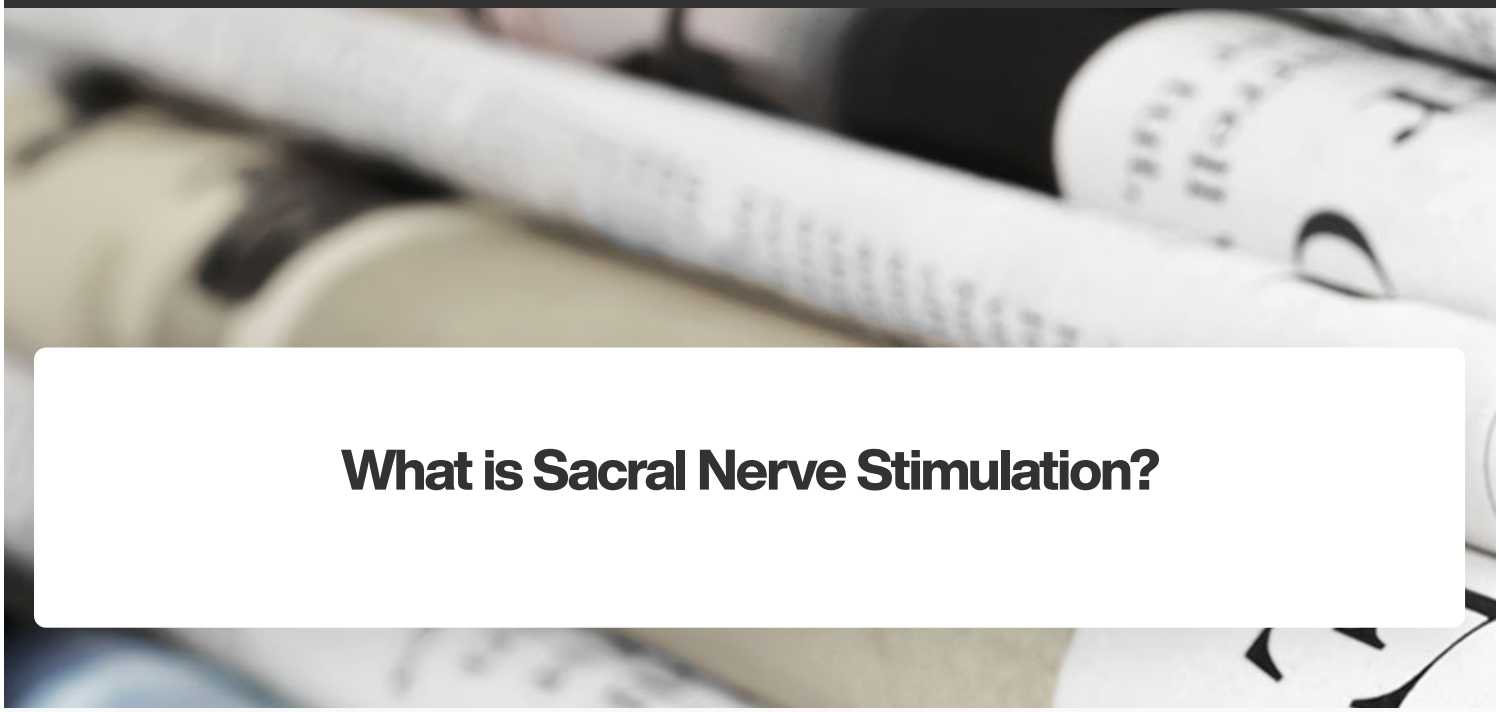

What is Sacral Nerve Stimulation?

Wed 29, May 2019

For many people living with incontinence, Sacral Nerve Stimulation (SNS) has delivered life-changing results where all other treatments failed. Urogynaecologist and Continence Foundation Board Vice-President, Dr Ian Tucker explains.

The treatment has given sufferers genuine hope for the improvement of these debilitating conditions.

Neuromodulation is a treatment that delivers either electricity, drugs or magnetic impulses to nerves in an effort to change their activity.

Sacral nerve stimulation is a means of directly stimulating the third sacral nerve with an electrical current to alter/improve bladder and bowel function, and modulate pelvic pain.

Over the past 23 years, there have been many improvements with the technique of SNS. Symptoms SNS can treat:

• Refractory urgency, urge incontinence

• Voiding difficulty

• Pelvic pain [surprisingly not covered directly by Medicare]

• Faecal incontinence

• Constipation

Urinary urgency, urge incontinence, enuresis and the closely related problem of faecal urgency and incontinence are the two most common reasons for considering SNS.

The cause of these conditions may be undetermined, familial, associated with various neurological injuries or disease states while bladder tumours, polyps or stones must be excluded before considering this treatment.

Almost all patients considering SNS will have had, and for various reasons failed, standard medical therapy such as attention to pelvic floor function and various medications, and as these conditions are often life-long, no treatment can guarantee a cure, but the improvements gained are often life-changing.

Both women and men can be candidates for SNS, however at this stage the SNS system is more commonly used to treat women. Clearly all patients must be medically fit for surgery and anticoagulants/blood thinning agents must be ceased well prior to surgery.

Since its inception, approximately 4500 patients have received this treatment in Australia with the number expected to increase as awareness and confidence in the procedure grows.

How is it performed?

SNS is carried out in two stages.

• Stage 1: insertion of the SNS lead through a 1cm incision in the buttock and with x-ray assistance Electrical stimulation through a small hole in the sacrum called the 'third sacral foramen' along the path of the third sacral nerve. This is the nerve that mediates the control of bladder and bowel function from the brain and spinal cord. Oncepositioned, the lead is then tunneled to the flank or buttock, and connected to an external lead passing through the skin to a temporary nerve stimulator.

• Stage 2: If the patient experiences a significant improvement in the first 1-2 weeks after surgery, stage 2 involves removal of the external lead and insertion of the pulse generator.

Success rates

The recently published INSITE* trial has confirmed an overall success rate of 70 per cent. When successful, the procedure is usually life changing with patients reporting a 3-5 times improvement in quality of life over standard medical treatments, with 45% reporting complete continence.

How long does SNS last?

The INSITE trial has confirmed what those of us with very long experience (more than 20 years) with SNS have observed, a long-term success rate of more than 80% at 5 years.

Current pulse generators have a battery life of up to 5 years and soon rechargeable IPG's will be available with projected battery life of more than 10 years.

Cost of SNS

The SNS system costs around $18,000. Although this may seem substantial, it is considerably less than the cost of a knee joint replacement and the procedure is Pharmaceutical Benefits Scheme (PBS) funded.

What is the recovery time following SNS?

An important factor in recovery is to minimise the risk of the lead moving. Because the greatest risk for this is in the first few weeks after surgery, patients are advised to avoid strenuous exercise, especially twisting and bending movements for at least two weeks after surgery. The surgery itself is relatively minor and often not associated with much pain.

Risks and complications of SNS

Every surgical procedure and medical treatment has potential issues and adverse events. The INSITE trial reported no unanticipated adverse events, with typical adverse experiences including, lead movement, infection - 3% [mostly in diabetics], lead fracture – 1%, high impedance in the lead, electrical 'shorting' of the lead and pain at IPG site – 5%. These adverse events are easily corrected.

Where is SNS available?

In most major Australian cities there are urogynaecologists, urologists and colorectal surgeons with the appropriate training in the procedure of SNS

Do you think you may benefit from SNS?

There is so much that can be done to help patients with the debilitating problems associated with incontinence.

Firstly, thorough investigation to accurately assess the problem[s] is fundamental and conservative treatment is always recommended as a first step. Only after conservative options have failed, should SNS be considered.

There are many patients whose lives have been transformed with SNS and all specialists will be able to put you in touch with patients who are willing to talk about their SNS experience to ensure you are fully aware of the every aspect of this treatment.

For clinicians such as myself, SNS is arguably the most exciting and satisfying treatment of any. It is immensely gratifying to see the successes but we are always trying to make progress to further improve the results and primarily the quality of life for the patient.

*INSITE trial results reproduced with permission from Medtronic

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Back

CATEGORIES

Health Articles

Bridge Magazine

Personal Stories

National Conference on Incontinence

World Continence Week

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November 2020

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September 2020

June 2020

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Men

Women

Teenagers and young adults

Children

Medical conditions

Life With Incontinence

Management

Caring for someone

Sexuality

Personal stories

Professionals

Continence learning

Academic resources

Continence journals

Scholarships and grants

Aged care resources

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Who can help?

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Financial assistance

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BACK TO TOP

Vertigo and Dizziness

Dizziness and vertigo are commonly reported symptoms in people with Parkinson's disease (PD). Most experts agree that dizziness and vertigo can be broadly defined as the sensation of spinning or whirling, and the sensation can be associated with balance problems.

In general, both symptoms are less notable in people in the early stages of Parkinson's. It is more common for older people with Parkinson's to experience dizziness or vertigo. Many people with PD experience vestibular dysfunction (balance issues related to the inner ear) even without vertigo or dizziness symptoms.

While these non-movement symptoms are common, doctors often miss the diagnosis. To optimize your treatment, know how to identify vertigo and dizziness, so you can address the issue with your care team.

Common Causes of Dizziness and Vertigo in Parkinson's and How to Treat Them:

- Orthostatic hypotension (OH): a persistent drop in blood pressure that occurs upon moving from sitting to standing or from lying down to sitting up or standing. It can result in the temporary loss of consciousness. It is the most commonly overlooked cause of dizziness in people with Parkinson's. OH can be treated with: hydration (drinking 6-8 glasses of water a day), compression stockings, increasing salt in your diet and sometimes by medications (such as Florinef, Midodrine, Droxidopa, or Mestinon). Moving the legs before standing can pump blood into the body, potentially lessening the symptoms.

- Medication-induced dizziness or vertigo: dopamine agonists are the most common drugs associated with dizziness or vertigo in PD. With the help of your doctor, this medication related issue can be treated by weaning the dosage and slowly discontinuing the drug or drugs causing the side effect. Common drugs associated with dizziness include anticonvulsants, antihypertensives, antibiotics, antidepressants, antipsychotics, pain medications and anti-inflammatory drugs.

- Deep Brain Stimulation (DBS): The surgical procedure can be associated with dizziness or vertigo. Either symptom can emerge soon after surgery. A health professional determines if the dizziness is caused by the device by simply powering it on and off. Once the device is turned off, you should be observed by your caregiver or medical team to confirm if the dizziness or vertigo resolves. If it does resolve, your healthcare team may need to check the location of the electrodes (usually by brain imaging) and possibly re-program the device. Turning the device on and off may not be enough and a full ENT evaluation may be necessary.

- Benign Paroxysmal Positional Vertigo (BPPV): sudden dizziness when turning in bed or dizziness lasting only a few seconds. It can be diagnosed using the Dix-Hallpike maneuver. It can be treated by seeing a physical therapist who is an expert in vestibular rehabilitation or by learning a series of simple movements you can self administer at home, such as the Semont maneuvers. Recent research has revealed that BPPV may occur in 11% of people with PD and who experience dizziness (Bloem, 2013).

- Migraine headaches: pain in the head can be a potential cause of dizziness or vertigo. Some experts refer to this as migraine-induced vertigo. In most cases, treating the headache or migraine can resolve the dizziness.

- Transient ischemic attack or stroke: sudden onset of dizziness, usually in the presence of other neurological signs, could possibly be a transient ischemic attack (a brief stroke-like attack) or stroke. *If a stroke is suspected, you should seek medical attention immediately and undergo appropriate imaging and potentially stroke-related therapies.*

In people with early Parkinson's disease (diagnosed for only a few years), the dizziness has in many cases linked to a lower Montreal Cognitive Assessment score (a thinking test) raising the possibility that dizziness may be a non-movement symptom associated with cognitive decline (Kwon, 2020).

Dizziness or vertigo can be tied to many causes and is not unique to Parkinson's. Symptoms can be caused by medications, low blood pressure, anxiety, cold, flu, dehydration, heart conditions and more. Tell your doctor immediately if you regularly experience dizziness or vertigo.

Page reviewed by Dr. Michael S. Okun, Parkinson's Foundation Medical Director, Professor and Chair, Department of Neurology, Executive Director of the Fixel Institute for Neurological Diseases; a Parkinson's Foundation Center of Excellence.

Recommended for You:

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VISION AND PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

Parkinson's does not cause vision loss but visual changes may occur due to impairment of eye movement. These may develop with progression of the condition. All of the Parkinson's related vision changes will impact on driving.

A neurologist will assess for vision changes as part of a routine neurological examination.

Bradykinesia (slowness of movement) is a major symptom of Parkinson's and may result in the following visual changes:

- Reduced eye blink rate
- Dry eyes
- Double vision
- Blurred vision
- Blepharospasm (involuntary closure of the eyelids)

Reduced Eye Blink Rate

Bradykinesia results in reduced eye blink rate which may be misinterpreted as staring. This adds to the facial masking or reduced facial expression. Conscious attention to blinking will assist.

Dry Eyes

Blinking cleanses the eyes by removing dust and impurities. When blink rate is reduced impurities build up leading to irritated and dry eyes. In addition reduced eye blink rate can result in excessive watering of the eyes as the tears are not distributed across the eye.

Conscious attention to blinking will assist and artificial tears in the form of eye drops can relieve dry irritated eyes.

Double Vision

Parkinson's may cause double vision due to problems moving the eyes or tracking. Tracking refers to side to side eye movements and is necessary while reading. Impaired coordination and fatigue of the muscles that move the eyes can result in non-alignment of movement. Resting the eyes when this occurs should provide relief.

Examination by an optician or ophthalmologist with an interest in Parkinson's is recommended.

Blurred Vision

Blurred vision or problems focusing may be caused by tracking problems but it may also be a side effect of some Parkinson's medications. Modifying reading glasses may improve blurred vision.

VISION AND PARKINSON'S

Blepharospasm

Blepharospasm occurs when the muscles that close the eyelids contract or go into spasm. This may result in repeated twitching of the eyelid, difficulty in maintaining eye opening and sometimes complete closure of the eyelid will occur. The latter may require treatment and botox injection may be suggested and will be required ongoing.

Parkinson's causes impaired electrical signals and feedback in the brain which may result in the following visual changes:

- Colour and contrast vision changes
- Perceptions of movement
- Visuo-spatial orientation
- Illusions (visual misinterpretations) and hallucinations

Colour and Contrast Vision Changes

People living with Parkinson's may find it difficult to discriminate between slight variations in colour. This may be worse for shades of blue or blue/green.

Contrast vision changes are associated with low light levels. For example, the person may be unable to clearly see a light coloured object on a light background.

Perception of Movement

Parkinson's may result in inaccurate perception of movements and underestimation of the speed of moving objects. This is a potential problem when driving or as a pedestrian.

Visuo-spatial Orientation

Parkinson's related problems with visuo-spatial orientation leads to difficulty assessing accurately the distance between objects. This can be evident when negotiating narrow spaces or when walking past objects. A helpful strategy may be to reach out and touch the side of the doorway or the object. An occupational therapist will give advice about everyday activities and adaption of the environment. Changes in visuo-spatial orientation may be associated with freezing or motor blocking. Use of visual or auditory cues can overcome these temporary difficulties. Problems with visuo-spatial orientation will impact on driving.

Illusions and Hallucinations

Illusions and hallucinations are associated both with Parkinson's and Parkinson's medications. Older people and those with cognitive changes are more sensitive to this side effect. It is also more common in those who have had Parkinson's for a long time.

Sudden onset illusions or hallucinations may be related to an infection or another illness (delirium).

Glaucoma and Parkinson's

Anticholinergic Parkinson's medications (for example Artane®) commonly used in the past are contraindicated with cases of glaucoma. These medications are now rarely used. Some eye drops used in the treatment of glaucoma may cause a lowering of blood pressure. Low blood pressure occurs naturally in Parkinson's and care should be taken due to the risk of falls.

Impact and Ongoing Monitoring

Changes to vision may impair mobility and increase the risk of falls. It is important to remember that many problems with vision will not be related to Parkinson's.

Eyesight changes should be discussed with a GP, and consulting an optician with expertise in neurological conditions is recommended.

For further information contact
your state Parkinson's organisation:
Freecall 1800 644 189 www.parkinsons.org.au

IN THIS TOGETHER
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Weight Management

Have you experienced changes in weight since being diagnosed with Parkinson's disease (PD)? It is common for people with PD to lose weight, yet others may gain. Changes in weight can affect overall health. Being underweight means you can lose muscle mass and strength, cause you to be prone to osteoporosis and infection. Being overweight raises risk of heart disease and high blood pressure and puts stress on your joints. Maintaining a healthy weight is key to living well with PD.

Common Causes of Weight Changes

Weight Loss

There are many reasons people with PD lose weight. Some people lose

weight even if they are eating exactly the same meals. Others find certain PD symptoms affect appetite or the ability to eat.

- Gradual loss of the sense of smell and taste is a non-motor PD symptom that makes eating less enjoyable.
- Weight loss usually levels off once PD therapy begins and people return to normal eating habits.
- Some PD medications cause nausea, which suppresses appetite.
- Motor symptoms like tremor, slowness and stiffness and complications of treatment such as dyskinesia (involuntary extra movements) can make eating difficult.
- Swallowing difficulties are common in PD and can interfere with eating.
- People who experience depression or apathy — common non-motor PD symptoms — may lose their appetite.
- Embarrassed by their slow eating, some people stop eating before they have had enough.
- People taking levodopa may have been advised to avoid taking medications with protein, making it difficult to get adequate nutrition throughout the day.

PD does not cause ongoing, unexplained weight loss. Tell your doctor if you experience this symptom — it may be a sign of a serious medical issue unrelated to PD.

Weight Gain

Weight gain is sometimes a side effect of PD therapies.

- Deep brain stimulation (DBS) is a surgical therapy that helps relieve movement symptoms in many people. Weight gain is a potential side effect.
- Dopamine agonists are medications occasionally given alone or in combination with formulations of levodopa to manage PD motor symptoms. They have been linked with compulsive behaviors, including binge eating, which leads to weight gain. Commonly prescribed dopamine agonists are Pramipexole (Mirapex®), Ropinirole (Requip®) and rotigotine transdermal system (Neupro® patch). Under the

supervision of a doctor, adjusting medications can stop a person's compulsive eating.
- Other medications, especially those used to treat psychiatric complications of the disease or its treatment, can contribute to weight gain.

Therapies

It is important that PD motor symptoms be optimally controlled. See your neurologist or movement disorders specialist to see whether he or she recommends a medication adjustment. Also, visit your primary care provider to exclude other medical reasons for weight change.

Tips for Achieving a Healthy Weight

- Whether you wish to gain weight or lose it, diet and exercise are key.
- Eat a balanced diet, with a variety of foods from all the food groups: whole grains, vegetables, fruits, dairy products and sources of protein like meat, fish and beans.
- Exercise helps keep people mobile and strong and can improve mood. Being active stimulates appetite and burns calories.

Talk to your doctor:

- Do you need to gain or lose weight?
- Get a referral for nutritional counseling — learning about nutrition and PD can help you maintain a healthy weight.
- Get advice on starting an exercise routine from a physical therapist who is experienced in PD.

To gain weight:

- Eat small, frequent meals, every two to three hours or eat a nutritious snack between meals.
- Eat foods you enjoy.
- Save your energy for eating by keeping easy-to-prepare foods on hand.
- Stimulate your appetite by seasoning food with herbs, spices and sauces.

- Include some high-calorie foods like cream and butter (if recommended by your primary care provider) in your diet.
- Consider drinking a nutritional supplement, such as Ensure® or Carnation® Breakfast Essentials™.
- Avoid filling up on coffee, tea and clear soups.
- Limit fatigue by choosing foods that are easy to chew (like smoothies, ground meats or other soft proteins)
- Ask for help cutting proteins into smaller pieces.
- Increase consumption of whole grains (whole grain rice, breads).

To lose weight:

- Consult a nutritionist or registered dietitian to plan a healthy, gradual weight loss program.
- Eat three nutritious meals a day, but limit portion sizes.
- Be mindful that a diet too strict or low in calories may decrease your energy.

    - Be as active as possible. Go for a walk every day if you can.
    - Enroll in an individual/group exercise program near your home.

Tell your doctor if you eat compulsively or binge eat —this may be a side effect of PD medications.

Page reviewed by Dr. Chauncey Spears, Movement Disorders Fellow at the University of Florida, a Parkinson's Foundation Center of Excellence.

ParkinsonsDisease.net

What Parkinson's Isn't: 6 Myths Debunked

By Allison Smith • August 21, 2017

What is Parkinson's disease? This is a question many of us have asked our neurologists, but the answers can be confusing. This is because we are still learning about this disorder and it's impact on our lives. However, we do know what Parkinson's isn't.

Myths about Parkinson's

Parkinson's is curable

First and foremost, as many of you know, there is no cure for Parkinson's disease. But before you get too discouraged, if you're going to get it, now is a great time to be diagnosed with Parkinson's. We have made such huge medical advances in the last decade alone, that now we have an arsenal of weapons to use against PD. Imagine being diagnosed with Parkinson's in the early 1900's... I shudder.

Parkinson's only affects movement

Since its discovery in 1817, Parkinson's disease was believed to only affect posture, mobility, gait, and balance. But now we realize just how PD can impact a person in a multitude of ways, including non-motor symptoms. Top offenders include: constipation, bladder control, drooling, swallowing, memory, depression, anxiety, sleep issues, cognition, and impaired executive functioning. Our Neurologists have their work cut out for them.

Parkinson's will kill you

Although you won't die from having Parkinson's disease, you can die from its complications. This can include aspiration of food, traumatic falls, infection, or sepsis. Just remember, you don't die from Parkinson's disease, you die with it.

Parkinson's is an old person's disease

Although PD is more common in the elderly population, there is a subset of Parkies who are under the age of 40. Like yours truly...

Parkinson's is gender-specific

Even though there are more men diagnosed with Parkinson's disease than women, PD doesn't discriminate. Some of the major differences between the sexes of Parkies is hormone levels, coping skills, lifestyle choices and careers (men could possibly be more exposed to chemicals, such as pesticides).

Parkinson's is a walk in the park

When I was first diagnosed with Parkinson's disease, I was naïve to believe that I would only be inconvenienced by a slower pace or struggle with a slight tremor. That was based on the only person I knew who had Parkinson's... Michael J. Fox. He didn't look that bad. Maybe I will get a mild case of PD... kind of like the watered-down version. Ignorance is bliss, eh?

Oh man, was I wrong. I learned quickly that Parkinson's would negatively impact many facets of my life and that each day will present a challenge of some sort. Parkinson's isn't a walk in the park. It is emotionally, physically, and mentally exhausting. But the one thing that you can count on is your Wolfpack (people who support you). They will take that stroll with you through the botanical garden of life.