

# A Primer on Parkinson's Disease

A brief guide to the recognition and treatment  
of Parkinson's Disease for patients and their  
families and friends.

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## Why this primer?

Parkinson's disease or "PD" is common.

It is actually the second most common neurodegenerative disorder after Alzheimer's Disease and about 1.5 million Americans are living with PD today. Because it begins slowly and with such subtle symptoms, it is greatly underrecognized and the diagnosis is often missed until late in the disease when it can cause considerable disability. Often it is mistaken for other common disorders such as stroke, or considered "just getting older." This is partly due to common misunderstandings about what PD is and whom it affects.

It is also important to recognize this illness because it is very treatable, and the earlier the treatment begins, the better the PD patient will do. Early treatment results in a far better prognosis for the person with PD and most live an enjoyable and productive life for many years after diagnosis.

Most patients learn about the diagnosis from their primary care physician. Some actually diagnose themselves from information they seek out about their symptoms. Unfortunately, most patients with PD may never see a neurologist, and if they do, that physician may not have the practical experience and training that comes from further specialty training in movement disorders. This primer is designed not only to give you some facts about the illness, but also to give you a way to think about this illness. People who are more knowledgeable about their medical condition have better outcomes. This primer is a distillation of what we have learned and shared with our patients over the past years.

This guide is brought to you by the Movement Disorders Program of the Medical University of South Carolina, with generous support from the Fullerton Foundation of Gaffney, South Carolina. It is meant for guidance and educational purposes only, and not meant to take the place of professional medical care or in the case of social issues, competent legal advice.

Opinions expressed here about the usefulness of medication are the authors' and may not correspond to the formal indications for their use as determined by labeling of the medication agreed upon by the drug's maker and the U.S. Food and Drug Administration which licenses the medication for use. This is a common situation in neurological practice. A physician with a scientific basis for doing so is free to make rational use of any currently marketed medication.

## What is Parkinson's disease?

Parkinson's disease is a progressive neurological disorder resulting from the death of a very specific group of brain cells, or neurons. The cells are part of brain circuits that control movement, mood and thinking, among other nervous system functions. These cells produce a chemical called **dopamine**, which is essential to smooth movement and other functions. People with PD are deficient in dopamine, just like people with diabetes are deficient in insulin. The dopamine deficiency causes the symptoms of PD.

It was **James Parkinson**, a 19th century English physician, who first recognized in modern times the physical changes that occur in people with this disease, and both the symptoms and the disease have been named in his honor.

## Who gets Parkinson's disease?

Anyone can get PD. It has been found in men and women everywhere, in every country and in every ethnic and racial population on the earth.

This is not a rare illness. One in a hundred people above the age of 55 will have PD. The average age of onset is about 55 and two thirds of people will get the disease between 45 and 65. It is not a disease of old age, but middle age, affecting people in the most productive years of their lives. Many may know that actor Michael J. Fox was only 30 years old when he was diagnosed with PD. Other “famous” people living with PD are former Attorney General Janet Reno, boxer Muhammad Ali, singer Linda Ronstadt, and basketball player Brian Grant.

There are about 36,500 people living with Parkinson's Disease throughout North and South Carolina. This number likely underestimates the true prevalence of this disorder, as many counties in our states are medically underserved, and many people with PD might therefore not be diagnosed. While African Americans develop PD somewhat less often than Americans of European or Middle Eastern origin, they nevertheless represent a sizable proportion of this number.

Why some groups of people have more illness than another may hold important clues about why and how one develops PD.

# Why do some people say Parkinsonism and others say Parkinson's disease?

The term “Parkinsonism” refers to specific symptoms of a disturbed motor system. It is a shorthand term for **stiffness, slowness** and **shaking**. Just as a cough may be caused by many different illnesses in the lungs, the symptoms of Parkinsonism can have different causes as well. Parkinson's disease is one particular brain illness that causes the symptoms of Parkinsonism. It can be confusing, but as you will see later on, the symptoms of Parkinsonism can also be caused by many other brain diseases.

Parkinsonian motor symptoms result from the breakdown of a particular circuit in the brain. Consider that the brain is a giant computer with the ability to think, to sense, and to move. Many of these subsections can be affected for different reasons.

For example, a stroke, or blockage of a blood vessel leading to the brain, may damage a particular part of the brain affecting both motor and sensation and thinking circuits, but Parkinsonism is the result of disease at the level of brain cells and of very small circuits. For this reason, it has a very precise set of symptoms. These symptoms are not dramatic at first but, as the disease process wears on over time, they can become quite disabling if untreated.

Because Parkinsonism refers to a group of symptoms, they may come in different combinations and so the syndrome (the way the patient looks to the doctor) can come in many different patterns. You would think that motor dysfunction is all the same, but in fact there are many different types of motor functions that come together to help us move normally.

## What are the most common symptoms of Parkinsonism?

You may recognize Parkinsonism in an individual as a general slowing of their movement and their posture becomes bent over. They may have a shortened stride and have small steps. They may tilt forward because their feet cannot keep up with their center of gravity. You may find that they are slowing in general and that their arms no longer swing when they walk. You can also see that they have a tremor, or rhythmic shaking, at rest when they are not using that part of the body. While most common in the hand, shaking may also occur in the legs or the jaw.

People can often stop the shaking or move better just by thinking about it, and so, they often think that their first symptoms are not very important. It is common to wait a couple of years before seeking treatment, when earlier treatment might benefit the person greatly. While Parkinsonism can begin in many different ways, most often it begins with only one side of the body. The onset of symptoms is generally slow and mild, but there are times that it is fast enough for one to wonder if a stroke has occurred or to worry about a brain tumor.

When the illness is quite gradual in onset and people may have just slowness and stiffness without shaking, they may have symptoms for several years before a diagnosis is made. It is so gradual that it is the family that first recognizes that their loved one has slowed to the degree that they are not functioning or that their hands have lost mobility, interfering with handling everyday functions such as writing, dressing or eating.

When tremor is the first symptom, as in most patients with Parkinsonism, it is often dismissed initially.

People feel that they are nervous or they have a pinched nerve or it means nothing. In fact, shaking in one or the other hand (or, less often, the leg) at rest when you are relaxed and doing nothing in particular, is the most common presenting symptom of Parkinsonism.

While Parkinsonism early on has just a couple of ways in which it may show itself, most often either with shaking or with walking troubles, as the disease progresses it can take a number of different paths.

Parkinsonism has two different kinds of symptoms: the symptoms that you notice, and the physical signs that other people notice about you. The symptoms that you notice as a patient may be obvious such as shaking of a limb or more subtle such as a change in handwriting, difficulty getting out of a low chair, trouble rolling over in bed, or not being to be able to walk as fast as you used to. One can have a sense of not being mentally sharp. There may also be sensations of numbness or aching or tingling or a sense of heaviness to your limbs.

There are other kinds of changes that may take place, some many years in advance of the illness such as loss of sense of taste or smell or changes in bowel function such as constipation. Even seemingly restless sleep with excessive thrashing or calling out can precede the motor symptoms of PD by years. Naturally these things are quite common and not all of these symptoms will lead to Parkinson's disease. In fact, in the majority of cases, it will not lead to Parkinson's disease at all. However, these are symptoms that can be associated with Parkinsonism, but it is important to remember that what defines Parkinsonism are the motor symptoms of stiffness, slowness and shaking. Your friends and family may see these things affect you, even when you may not. Slowness can be quite subtle and it is often mistaken for normal aging.

Whether you believe in such a thing as “normal” aging, depends on how old you are. The older you get, the less you think that aging is a normal phenomenon at all. Our experience has led us to believe that if a person is not functioning well, there is something wrong and that it comes from a process of illness. So your family may tell you that you are moving more slowly, that you are not standing up straight, that you cannot keep up when going for a walk or other physical activity. That is the time to seek medical help to define whether you might have the earliest signs of Parkinsonism.

There are many different factors that will determine how a person does with Parkinsonism, but all medical authorities now recognize that the patient will have a better chance of living longer with a much better quality of life if the illness is recognized early and if treatment begins quickly under a specialist’s care. Many years ago, when treatments were not particularly effective and associated with many side effects, it was common to withhold treatment until a person was desperate for any kind of relief. This is no longer the case, and it has been very well documented in careful clinical trials that the earlier a person with Parkinson’s is treated the better they will do over the course of their illness.

## **Why do you get Parkinson’s disease?**

The short answer is, no one really knows. But we have lots of clues. There are some specific genes (inherited traits) that can result in PD in some families, but this represents a very small number of patients, and most of those patients develop the disease early in life, before age 40.

It is more likely that you get Parkinson’s from a genetic vulnerability or predisposition if you are exposed to the right trigger in the environment. Are there other illness like that? Well, many, actually.

Take heart attack for example. Say you have the familial trait or tendency for high amounts of “bad” cholesterol. If you live your life virtuously, watching your diet, exercising and not smoking, you may not develop a heart attack until late in life. On the other hand, if you have the same trait, and are a couch potato, and eat lots of fast food, and have a cigarette for dessert, then you may well have your heart attack at an early age. PD is probably just like this, except for one thing: we don’t know what genes make you vulnerable. However, we know what some of the environmental triggers can be.

## **What are some environmental risk factors for Parkinson’s disease?**

Studies have shown that people in certain occupations such as farming and welding are at a higher risk for PD, but there are conflicting reports. Repeated traumatic loss of consciousness is associated with increased risk of PD. We also know that people who live in a rural environment, or drink well-water may be more prone to acquire PD. Likely, this heightened risk is explained by exposure to certain environmental toxins through these living conditions. Exposure to paraquat, a pesticide, for example, triples the risk of developing PD. Manganese, which is part of a gas released when welders melt welding rods, can also be harmful when inhaled and has been implicated in the early onset of Parkinsonism in some welders.

Agent Orange, a blend of herbicides that was used by the US military during the Vietnam war, has also been implicated as a possible risk factor for PD. As a result, Veterans with Parkinson’s disease who were exposed to Agent Orange or other herbicides during military service may be eligible for disability compensation and health care. However, there is still much to learn about environmental triggers, as most people with PD never welded or dealt with pesticides or herbicides and

most farmers and welders never get PD. In the end, PD is considered a multifactorial disease, resulting from the effect of environmental factors and genetic susceptibility.

## **If I have Parkinson's disease, is my family at risk?**

Most cases of PD occur in people with no apparent family history of the disorder. Having someone in the family with PD increases your risk but not very much. It is estimated that your lifetime risk for PD is four percent if you have a close relative with PD, opposed to two percent in the general population. Approximately 15 percent of people with PD have a family history of this disorder. Familial cases of Parkinson's disease can be caused by mutations in the LRRK2, PARK2, PARK7, PINK1, or SNCA gene, or by alterations in genes that have not been identified.

Regardless, the longer you live, the greater the chance of developing this disorder since age is the biggest risk factor for developing PD. By the time one is 80 years old, about three out of every ten people will have some sign of Parkinsonism. As Dr. Bergmann used to tell his patients: if you don't get heart disease, and you don't get cancer, and your spouse doesn't shoot you, you'll live long enough to have a neurological disease like PD. In fact, the first three items take care of most of us.

## Are there other symptoms associated with Parkinson's disease?

PD is more than a movement disorder. Because these affected brain cells run such critical brain circuits, there are many parts of the nervous system that are ultimately affected. While there is some pattern of orderly progression of brain symptoms in PD, this illness can have lots of different “first” symptoms. Symptoms may also begin at very different times and progress at very different rates among individuals. This can make diagnosis very tricky, indeed.

Any one of the symptoms listed on the next pages may occur occasionally in normal people and this means nothing by itself. It is when these symptoms are constantly present, grouped together and are disabling that they may represent the disease process of PD. Many of these occur late in the illness. Many may not occur at all in any given individual, but they are listed here for the sake of completeness and because we will be discussing them later. For example, only two thirds of PD patients will have significant shaking/tremor during their illness.

Three out of ten PD patients will have significant mental trouble over the course of their disease while a majority will suffer from some level of depression.

Symptoms commonly found at some time in Parkinson's disease

- ✓ Anxiety (often anticipatory anxiety) and panic
- ✓ Apathy/lack of motivation
- ✓ Bent over posture; flexed arm or hand
- ✓ Change in handwriting

- ✓ Constipation
- ✓ Delusions and false beliefs
- ✓ Depression
- ✓ Difficulty judging distance
- ✓ Double or blurred vision
- ✓ Drooling
- ✓ Erectile dysfunction; loss of orgasm
- ✓ Falls
- ✓ Fatigue and intolerance to exercise
- ✓ Feeling off balance
- ✓ Feet get stuck to the ground
- ✓ Impulsiveness and compulsiveness
- ✓ Irritability
- ✓ Lightheadedness; drops in blood pressure
- ✓ Loss of ability to perform motor tasks
- ✓ Loss of fine motor control and dexterity
- ✓ Loss of sense of smell
- ✓ Morning painful cramp of foot or hand
- ✓ Poor concentration

- ✓ Poor judgment
- ✓ Scaly, oily, reddened skin
- ✓ Sense of heaviness or ache in affected limb
- ✓ Shaking of part of the body at rest
- ✓ Shorter, slower stride while walking
- ✓ Sleep behavior: talking, laughing, shouting
- ✓ Sleep fragmentation; multiple awakenings
- ✓ Sleep movements: jerking, thrashing around
- ✓ Slower speed of movement
- ✓ Speech slurring and soft speech
- ✓ Stiffness with increased muscle tone
- ✓ Sudden attacks of sweating
- ✓ Swallowing difficulty
- ✓ Trouble keeping things in mind
- ✓ Unable to carry out complex tasks
- ✓ Urination: weak or sudden urge; increased frequency
- ✓ Visual illusions and hallucinations
- ✓ Word finding difficulty

## Patterns of illness, with shaking and without

In our experience of caring for many people with movement disorders, we have seen PD begin in many different ways.

Nevertheless, there are a few very recognizable patterns which will help anyone recognize that something is amiss. Giving you a portrait of a couple of patients may help.

By far, the most common and classic presentation of PD is called **tremor dominant** PD. This is the 55 year old man or woman who, for example, begins with a very slight occasional tremor in the index finger or thumb of their right hand. They keep it hidden at first. It stops when they go to do something or if they think about it. It comes out if they are excited or cold or just talking on the phone and distracted by some other mental activity. Over the next year it extends further, perhaps into the hand as a whole or up the forearm. Their spouse now feels the shaking in bed or when they are holding hands. It is harder to hide.

Associated with this they may find that the arm doesn't swing when they walk and that their handwriting gets small and difficult to read. A toothbrush becomes harder to use. Buttons become difficult. Their arm may feel heavy and numb, and they begin to hold it in a flexed posture at their side. They may have a painful cramp of their foot on the affected side, especially in early morning hours and they have to walk around on it to undo the painful curling of their toes.

The person has begun to move more slowly and they may not have noticed that they have less facial expression and a softer voice. Their spouse, however, may think that the loss of outward expression means they are depressed, and even take them to the doctor for this reason. Sometimes the patient does feel depressed.

Not a lot, but just irritable and not taking usual pleasure in things. In the doctor's office further questioning may reveal curious things like chronic trouble with constipation and more recently loss of the sense of smell.

PD is an asymmetric disease often beginning on just one side of the body. It is not surprising that it is sometimes mistaken for a stroke or brain tumor. But if there is any doubt, the images from a brain scan would reveal nothing abnormal, where it would easily show a mass or stroke. This is because the trouble of PD is at a microscopic level, too small for this kind of brain imaging to pick up. Traditional brain scans such as CT or MRI are used to rule out other possible causes of Parkinsonism; they are normal in PD.

Thankfully this common form of PD is often the slowest form of illness. It responds well to medication and some patients may not show symptoms on the other side of the body for a decade or more. On average, symptoms will begin on the other side of the body in about three years, although this second side is generally less affected.

The other common pattern of PD is called postural instability – gait disorder PD. It is associated with more disability but thankfully is a less common form of the illness. In this case the patient is often older.

A 75 year old person may have a minor tremor: perhaps a fine, fast shaking of outstretched hands, or a slight tremor that is present on one side. More prominent though is that the person has gradually slowed in the speed of their movement and has developed a flexed posture. Because their stride is shortened, they appear to be falling headlong as they move forward, their body ahead of their feet, with the feet racing to keep up. This can result in actual falling.

The sense of balance is generally impaired and the person has trouble making the kind of continuous postural adjustments normal people make. Uneven surfaces such as grass or sand may be very difficult to maneuver. At times the feet may act as though they are stuck to the ground and it takes active thought to get them moving. General slowness makes it difficult to get up from a low sofa, out of a car seat, or roll over in bed.

Because the changes are so gradual and because tremor is minor or absent, it is often several years before the diagnosis of Parkinson's disease is made. When this pattern occurs in older people, as it frequently does, it is often excused as old age, which it is not. This form of PD responds to medication as well.

## **Dementia in Parkinson's disease**

Dementia, or the progressive loss of general thinking function in clear consciousness, is found in many degenerative neurological disorders and it sometimes occurs in PD. Dementia occurs eventually in at least 30% of patients with PD. Part of the difficulty in identifying this is because PD can affect some mental processing without causing a general loss in ability that would be called dementia. (Most PD patients describe that their thinking has changed in subtle ways, though you would not be able to tell by interacting with them.) Older age and the akinetic- rigid form (non-tremor form) are associated with higher risk of dementia in PD.

This is often confused with another illness well known for dementia: Alzheimer's disease (AD). However, the dementia of PD is quite different from that of AD. In AD, the file cabinet of information empties out. The information is lost and therefore can't be found or remembered.

In PD, the file cabinet remains full; it is the retrieval system that is broken. So, in order to get the information for answering a question, the person has to go through the entire cabinet. Because answers are delayed, the person appears to think slowly. The same is true of finding words (especially formal names) as the person talks.

The dementia in PD typically includes impairment in attention, memory, executive (planning/judgment) and visuo-spatial functions, behavioral symptoms such as mood changes, hallucinations, and apathy are frequent. Patients experience a lot of tip-of-the-tongue phenomena. In some ways this is a magnification of what many of us experience with normal aging of our memory system: the more information in the cabinet, the more you have to go through to find what you are looking for.

There are also associated changes in behavior, but it would be quite rare for the PD patient to get to the place where they are paranoid or combative or can't recognize family members as is seen in AD. More often, as the illness progresses, they are placid, losing their "get up and go". They become unable to perform complex motor tasks, such as figuring out controls on appliances, or having the motor and analytical skills to be able to drive. Multi-tasking is particularly challenging.

## **Psychosis in Parkinson's disease**

Associated with the dementia of PD is the peculiar phenomenon of visual illusions or hallucinations. An illusion is seeing something that is there and misinterpreting it as something else – for example a street sign may look like a person, a face may appear in the bushes, or a robe over a chair in the bedroom or hanging in the closet may appear to be a person.

PD patients may also describe a sense of a presence of a person behind them, or see a passing shadow in the periphery. A visual hallucination is an image of something that is not there (that no one else can see). Usually hallucinations are not alarming to the patient, who commonly recognizes that the images are not real.

Eventually the hallucinations may occur more often and may occur at any time. Common hallucinations are of children or small animals. It is only rarely that people think they hear, rather than see, something.

Less often and much later in the illness these hallucinations are thought to be real but only rarely are they frightening. Delusions are fixed false beliefs. Patients with PD may sometimes feel convinced of something even though it is not true. Common themes include spousal infidelity, contamination, or that their belongings are being stolen.

Thankfully, hallucinations or delusions do not occur in most PD patients. If psychosis occurs abruptly in a patient with PD though, other causes must be investigated such as ensuring medications are being taken properly (no accidental overdose or new medication), and investigating for infection.

## **Stages of Parkinson's disease**

Patients and their families often inquire about what stage of the illness they may be in. It is important to realize though that the stages of PD are NOT like the stages of cancer and have little to no prognostic value. Instead, the stage is like a snapshot of what the patient looks like at that point in time. The first comprehensive description of how PD progresses was published over forty years ago by Margaret Hoehn and Melvin Yahr, then neurologists at Columbia University in New York.

They created a scale to use as a tool for staging PD. While it is a very general tool for describing the severity of PD, it has stood the test of time and the Hoehn and Yahr Scale is still in use today.

Because of progress in medical education, most patients are now recognized as having PD much sooner than they were in the past. As a result most patients are found in the earlier stages. It is rarer to find patients in the later stages than it was years ago before effective treatments existed.

The original 1967 Hoehn and Yahr Scale is cited below, followed by my clarification in simpler terms.

***Stage I: Unilateral involvement only, usually with minimal or no functional impairment.***

The symptoms are found only on one side of the body and the person can do just about anything they want to. This is where most tremor predominant patients begin. It is very unusual to find a patient at this stage as it is very common to have at least a subtle abnormal finding on the less affected side.

***Stage II: Bilateral or midline involvement, without impairment of balance.***

The illness is found on both sides of the body or through the center of the body involving walking, but without changing the sense of balance or causing falls. Most gait disorder – postural instability PD patients begin here.

***Stage III: First sign of impaired righting reflexes.***

This is evident by unsteadiness as the patient turns or is demonstrated when he is pushed from standing equilibrium with the feet together

and eyes closed. Functionally the patient is somewhat restricted in his activities but may have some work potential depending upon the type of employment. Patients are physically capable of leading independent lives, and their disability is mild to moderate.

Loss of balance occurs at this more advanced stage of PD, when the disease has affected both sides of the body. Many patients take several years to reach this stage, especially if they are on effective medication. If loss of balance occurs early in the disease process, it makes one think about causes of Parkinsonism other than PD. Nevertheless, when this occurs in PD patients, they can remain active despite their disability.

***Stage IV: Fully developed, severely disabling disease; the patient is still able to walk and stand unassisted but is markedly incapacitated.***

Later stages of disability are much less often seen in PD these days. It should be noted that when quality of life suffers in PD it is often due to problems other than the motor disability. Depression, medication related confusion, and dementia contribute greatly to the deteriorated state in the stage IV or V patient.

***Stage V: Confinement to bed or wheelchair unless aided.***

Very often this occurs when other illness is also present. PD is a “magnifier” of disability. For example, recovery from a broken hip is difficult in the elderly, but with PD in addition, the rehabilitation process is that much more difficult. Motivation is also affected by the disease and maintaining independence through exercise is a vital part of remaining healthy in this and any other disease.

## Other causes of Parkinsonism

As we talked about before, Parkinsonism refers to the specific symptoms produced by a disturbed motor system. It is a shorthand term for **stiffness, slowness and shaking**.

The disturbance that occurs in the motor system is the premature death of a very specific group of cells called dopamine cells. They are so named because dopamine is the chemical that they make and use to signal the next brain cell in this motor circuit. As a result, anything that harms this dopamine cell or blocks how it works will produce the symptoms of Parkinsonism.

It used to be that the most common reason by far for Parkinsonism was **medication that blocks the effect of dopamine to signal the next brain cell**. This occurred most commonly in patients who received neuroleptics, a powerful group of medication that is used in psychotic illness such as schizophrenia. Neuroleptic-induced Parkinsonism still occurs a great deal, but newer medications in this field have greatly reduced this problem.

However some neuroleptics are used for other conditions, and because physicians may not think of them as being in the neuroleptic class, their side effects are less commonly recognized. For example, **metoclopramide** (brand name: Reglan) which is used to help empty the stomach in conditions like diabetes mellitus often produces Parkinsonian symptoms when used at higher doses on a chronic basis.

Of every hundred patients that walk through our door with Parkinsonism, seventy of them will have Parkinson's disease, that very specific illness we have been talking about up until now. However, thirty of them won't have PD.

These people will have one of a number of illnesses that produce the symptoms of Parkinsonism by harming the dopamine cells in a different way. They will have additional symptoms and signs of illness because these other disorders almost always produce damage in other parts of the nervous system outside the dopamine cell circuits.

Therefore, these illnesses are often called atypical Parkinsonism or “Parkinson plus” syndromes because they have Parkinsonism plus other losses in brain function. There is a long list of these diseases, but thankfully most are rare. A few of the more important ones are listed below, together with some of the features that may separate them from true Parkinson’s disease. One thing that they all have in common is that their response to usual Parkinson medication is poor or partial at best. For this reason, these diseases often have a poorer prognosis than Parkinson’s disease.

**Progressive Supranuclear Palsy (PSP)** is a movement disorder with two forms, one of which looks a great deal like Parkinson’s disease. One of the early signs suggesting that it is not PD is the early occurrence of unexplained falls and imbalance without severe enough Parkinsonism to explain the presence of these symptoms. The other form is associated with the loss of ability to move the eyes, and loss of balance with falling, more easily recognized as an atypical syndrome. Both of these are associated with impulsiveness and changes in personality. One typical feature is the development of an “amazed” or “deer in the headlights” facial expression. The Parkinsonism of this syndrome may respond well to medication, but over time the disability caused by other parts of the nervous system dwarfs the troubles caused by the Parkinsonism.

**Multiple System Atrophy (MSA)** gets its name from the fact that a number of different brain systems deteriorate to produce the symptoms for which this illness is known. There are different patterns of progression in this syndrome, defined by the symptoms present when the illness begins. The most common form is often mistaken in its early stages as postural instability gait disorder PD. Previously known as Shy-Drager Syndrome, it is often first suspected when it only partially responds to anti-parkinson medication and, as time passes, this partial response is lost.

Because this syndrome is a deterioration of systems not affected in usual PD, there are a number of findings, in addition to poor response to medication, that help separate the two syndromes. The early appearance of autonomic problems (low blood pressure, passing out, loss of bladder or bowel control, dusky or purplish feet, erectile failure, and so forth) is a strong indicator of this disorder. In addition, incoordination and imbalance, known as ataxia, is present. The early appearance of falls and speech and swallowing difficulty are suggestive of this disorders as are the absence of dementia and medication related confusion. (If dementia or confusion is present, then Lewy Body Dementia should be considered first.)

**Lewy Body Dementia (LBD)**, as mentioned earlier, is a combination of dementia and Parkinsonism presenting at roughly the same time. When the dementia begins before the appearance of Parkinsonism, it may be mistaken for Alzheimer's disease. Nevertheless, the dementia is quite distinct and is accompanied by hallucinations and fluctuations in consciousness. Sensitivity to the side effects of medication is common, for example, the patient who is delirious for a few days after taking pain medication for a simple surgical procedure.

The family will notice that the patient often acts quite normally and then has periods of confusion and this cycle may occur quite regularly. Autonomic dysfunction may be prominent as well. Some patients have such low blood pressure that fainting occurs.

Finally, there are disturbances in sleep and during periods of deep sleep the person may talk and move, at times quite vigorously. This is known as parasomnia, or REM Behavior Disorder (RBD).

**Vascular Parkinsonism**, also called **Multi-infarct Parkinsonism**, is Parkinsonism caused by multiple small or even microscopic strokes. The circulation of the brain is like a tree, with large vessels, medium sized branches, and finally, thousands of tiny twigs. While most of us are familiar with the devastating results of large blood vessels becoming clogged and blocking the blood supply to the brain, resulting in a major paralysis or loss of speech, we are less aware of the effects of progressive loss of the little twigs. As these become blocked over a lifetime, there may be a gradual loss of function that resembles Parkinson's disease. It may come on quite suddenly when some small but vital center in the brain is damaged.

As you might expect, because these microscopic strokes may occur anywhere in the brain, there is no single clinical pattern of motor troubles in multi- infarct Parkinsonism. In some, the symptoms may come on after a clearly identified stroke where a patient suffered a paralysis on one side of the body, which improves to what looks like a Parkinsonian state. Alternatively, it may be the development of gait failure, with loss of the ability to move the feet and walk, while showing few other symptoms. For this reason, the term “**lower body Parkinsonism**” has sometimes been used to describe the Parkinsonism due to vascular disease.

Because this results from destruction of brain pathways due to loss of their blood supply, there is limited benefit from anti-Parkinson medications. Careful examination of the patient often reveals that there are other brain systems affected: thinking, eye movements, emotional control, bladder and bowel control, balance and coordination may all be affected.

Risk factors for this syndrome are the same as for stroke: high blood cholesterol and triglycerides, high blood pressure, diabetes mellitus, smoking, and family history of stroke. The MRI scan shows the scarring of the brain from the underlying vascular disease. It may be surprisingly extensive or it may show only a single stroke in a critical area of the brain where motor pathways run down to control the spinal cord.

Because most of us develop atherosclerosis as we age, the occurrence of vascular Parkinsonism greatly increases as we get older. It is why a significant number of elderly above the age of eighty have the slowness and tremulousness that we associate with PD without having the full blown syndrome of Parkinsonism.

**Normal Pressure Hydrocephalus (NPH)** is a very particular syndrome that results from a disturbance of cerebrospinal fluid absorption in the brain. The brain is constantly creating a fluid that provides shock absorption protection around the brain. If the drainage system for this fluid should become blocked for any reason, it begins to slowly squeeze the brain within the tight confines of the skull. This begins to produce a specific pattern of symptoms.

First the person develops trouble with walking, sometimes described as magnetic gait, where the feet don't respond to commands to walk. Balance suffers and falls result. Thereafter the person begins to develop trouble with memory, motivation and the thinking process.

Somewhere in between these two events control of the bladder is lost. This all develops over a six to twelve month period, and the most common cause is a previous event that caused bleeding around the brain: aneurysm, head trauma, brain hemorrhage or infection, and so forth. However, in many persons, no clear cause is found.

It is important to recognize this pattern of dementia, incontinence, and walking difficulty that develops over a year's time. If performed early enough in the course of the syndrome, there is an effective neurosurgical procedure to relieve the abnormal brain fluid circulation using a shunt. This is a tube and valve system which runs out from the brain under the skin and is designed to ease the outflow of the cerebrospinal fluid system. Often a neurosurgeon will place a temporary drain in the lower spine for three days during a brief hospitalization in order to see if improvement in walking occurs. If so, a permanent shunt is placed.

The most important aspect of NPH and the best predictor of success of shunting is that patient has the typical history for the syndrome. At times the syndrome is suggested by an MRI brain scan where a pattern of multiple small strokes looks like the fluid shifts that take place in NPH or the patient has large fluid spaces since childhood as a coincidental finding. However, unless the classical history for this disorder exists, it is rare to get any material benefit from shunting.

**Psychogenic Parkinsonism**, or a disorder of movement based on unconscious psychological difficulties, is more common than one might think. Two or three percent of patients seen in a movement disorders clinic have symptoms that are ultimately judged not to be a neurological illness. These symptoms are variable and do not follow known patterns of neurological disease.

These may be tremor on action or at rest, alterations of posture, slowness, jerking, incoordination, imbalance, walking and speech dysfunction and strange inconsistent movements of all sorts.

There is no easy explanation as to why this syndrome occurs. It is well recognized that stress can cause an ulcer; a disruption of the stomach lining that can have serious health consequences. What is less well recognized is that stress may be associated with a whole host of other kinds of symptoms including movement disorders that are a reflection of underlying psychological unrest. Non-judgmental explanation of the nature of the disorder helps pave the way for mental health intervention. Referral to a clinic with experience in the recognition and treatment of stress related disorders is the best solution for the patient, when combined with regular supportive care from the primary healthcare provider.

**Essential Tremor** (also known as **ET** or **benign familial tremor**) is mentioned here because it is frequently mistaken for PD. It is one of the most common movement disorders and is characterized by a tremor that comes out during action. Recall that the PD tremor is a resting tremor, that is, it lessens or goes away with performing an action. ET is also not associated with rigidity or slowness, and the tremor can occur in the head, voice and hands most commonly. Rarely, after many years of illness, some 30% of patients with ET may develop a mild Parkinsonism. It remains unknown whether this is coincidental or if there is a biological connection between these two illnesses.

## How accurate is the diagnosis of Parkinson's Disease?

One of the major problems in the clinical practice of neurology is that there is no single test that is diagnostic of PD. The diagnosis is made by clinical criteria, that is, a whole list of physical findings that must be present or absent on your examination for the diagnosis to be certain. If this list is fulfilled then the likelihood of having PD will be high, and this has been confirmed by studies that have examined the patient's brain after death.

However, at the very beginning of many Parkinsonian syndromes it is difficult to know in what direction a patient may evolve. For this reason, the accuracy of diagnosis the first time a patient is seen in a specialty clinic devoted to movement disorders may only be 75%. This doesn't mean, however, that one thinks it's PD and it turns out to be something very different. It is really about distinguishing one Parkinsonian syndrome from another. By the time the patient has reached their fifth year of disease, the certainty goes up to 90% or better. Why? Because the symptoms have evolved and are more evident, and response to treatment indicates what path the disease will follow. As a result, it is easier to say with certainty what illness the patient has.

## Tests your doctor might want

If your healthcare provider thinks you have typical PD, there may not be any medical tests required.

A second opinion from a neurologist or movement disorders specialist might be helpful to assure a correct diagnosis. However, there is no single blood test or brain scan that can prove PD. For example, structural MRI and CT brain scans are normal in PD. Brain wave tests (EEG or electroencephalogram) and tests of nerve and muscle (electromyography or EMG) do not reveal any specific abnormality. These tests may be useful if an atypical form of Parkinsonism, such as MSA or PSP is suspected, but often these tests may be normal in early stages of atypical Parkinsonism as well. We often do tests to rule out all the other brain causes of motor troubles, such as stroke or brain tumor.

Even when the brain imaging studies are abnormal in atypical Parkinsonism, the changes are subtle and can be missed by radiologists who have little exposure to such disorders. For this reason, it is always worthwhile to bring the actual images of the brain scans (either on film or a computer disc), and not just the written report, to a neurological consultation. More recently, a new type of brain scan, called a **dopamine transporter (DAT)** scan, has become available and can be useful to help in the diagnosis of Parkinsonism.

This type of scan is unnecessary if you have already received a diagnosis from an expert, and are responding well to dopaminergic therapy. However, in some tricky situations where the expert is not sure of the diagnosis, or where a potentially risky procedure is being considered (e.g. deep brain stimulation surgery), it is reasonable for your doctor to recommend a DAT scan.

This is how it works: First, the person receives an injection of an imaging agent called a tracer that binds to the dopamine transporter in the brain. After a while, this tracer can be detected and visualized by a scanner with the use of a gamma camera. This makes it possible for the radiologist and neurologist to quantify the amount of dopamine available in certain brain areas. If dopamine is reduced, less of the imaging tracer is visible on the scan.

This would mean that the patient has Parkinsonism opposed to ET where dopamine would be normal. What the DAT scan cannot do is to distinguish between the various parkinsonian syndromes. It is also not a 100% reliable tool. There can be false positive and false negative results. It is important to put the results of the scan in context with the examination by a movement disorders specialist in order to derive the most accurate diagnosis.

One useful laboratory blood or urine test rules out a rare disorder of copper metabolism called Wilson's disease in persons with Parkinsonism under the age of 50. This is easily done with a blood and/or urine test. In this illness, the MRI of the brain is also very abnormal. Otherwise, tests looking at levels of vitamins, metals and minerals are usually not revealing in cases of Parkinsonism.

## **Treating Parkinson's Disease**

The treatment of PD involves many different modalities including medication and non-drug interventions and therapies. Unfortunately, there are also treatments available which are touted as useful but have not undergone any formal testing of their worth in this illness. Some costly treatments of unproven effectiveness are often peddled to patients who are desperate for a "cure" or other miraculous relief which may not be found in the traditional medical community.

Among physicians and scientists in the field of Parkinson's disease there are different approaches to the treatment of PD. We present one approach here. This is crucial for any patient who receives medical treatment; they should understand the reason for the proposed course of treatment, what they may expect to gain, what the risk of side effects might be, and what reasonable alternatives exist. Only then can you give what is known as your "informed consent".

Every interaction with a health care provider is guided by these principles. In certain circumstances informed consent is formalized into a written statement which is signed and witnessed. This is routine before surgery, for example, but also before you may participate in an experimental treatment program. However, the interaction which provides you with knowledge of the risks, benefits, and alternatives to any course of action is the heart of your visit with your healthcare provider. Giving your consent is also a continuous process. If you should change your mind, you may withdraw consent and stop any course of action at any time. You are never tied to a plan.

If your physician can clearly explain to you why a certain path is taken, or why a certain medication is used, then we are enhancing your knowledge of your illness, increasing your chances of using medication correctly, and helping your ability to monitor your own condition. This will encourage you to stick with a treatment that often takes time to give you noticeable benefit.

The mainstay of the treatment of PD is medication. Before the discovery of effective medication for PD, patients survived seven to ten years on average after the start of the illness. Nowadays, we often say that the first ten years of medication treatment in PD is just the beginning, the "honeymoon", and it is only after this that it becomes trickier to avoid side effects of medication and to maintain

smooth motor function for patients. Nevertheless, there are treatment strategies for every stage of illness, and these are explained below.

There have been incredible advances in the treatment of PD in the last few decades. How we care for PD patients now is different than ten years ago, and even more different than the decades before that. Compared to just forty years ago, we are truly living in the world of science fiction, where electrical devices are implanted deep within the brain, and of experimentation with transplantation of human brain cells and genetically engineered viruses.

However, even with the dramatic improvements in the effectiveness of our therapies, certain guiding principals in treatment remain the same: we can only change one thing at a time. Otherwise when something happens, good or bad, you can't know what it was due to. In treating the brain, you start medication at low doses and increase slowly. It makes the side effects much more tolerable and it decreases the chance of missing the lowest possible dose of medication that gives you the desired effect.

This is important because all medications active in the nervous system have both good and bad effects.

Consider that we are spreading medication throughout the entire brain in order to get the desired effect in just one small brain circuit. This excess medication will have different effects in different people. Some will tolerate it well, and others will not tolerate it at all and have a variety of side effects. This can be due to individual differences in how we digest, absorb, distribute, and eliminate medication, as well as differences in the underlying disease process found in patients' brains.

This approach also takes into account the fact that the brain is a special place when it comes to medication. It is not like taking an aspirin and getting four hours of relief; it is more like filling up the gas tank of a car with an eyedropper. It can take weeks for the effect of a medication to become fully evident, especially when just beginning the early stages of PD treatment.

## **Beginning treatment**

While general guidelines exist for the treatment of Parkinson's disease, in fact, every patient is different and every patient requires a treatment regimen that is customized to their individual needs, their symptoms, and their special sensitivities to side effects.

Let us first begin by describing the treatment of a patient whom most people would think of as the typical Parkinson's disease patient. This could be a middle-aged man or woman who presents with the typical beginning symptoms of Parkinson's disease. They might have a foot cramp with toe curling on one side in association with resting tremor of the hand; diminished dexterity and fine motor skills may quickly follow. The spouse may notice a reduced arm swing when walking and diminished facial expression. These symptoms and their associated loss of functioning bring the patient to the doctor.

The healthcare provider then is faced with making decisions based on two elements of each person's disease. The first is to eliminate the symptoms in order to get the person back to full functioning capacity. The other is to create a treatment regimen that will assume that the patient is going to have a normal lifespan for someone who presents with the illness at age 55 (the average age of onset). This means taking into account that that person may very well live another 20 to 30 years.

To understand what your choices might be in this regard, it is worthwhile taking the time to tell you the story of how modern day treatment of Parkinson's disease has evolved.

## **L-DOPA and dopamine agonists in Parkinson's Disease**

To sum up two centuries of scientific inquiry in a few pages, we will begin at the time when it was discovered that the signs and symptoms of Parkinson's disease were caused by the loss of dopamine-producing cells. These cells originate deep in the brain in a part called the brainstem, and they project up to other circuits higher up in the center of the brain. It was discovered that the cells that die in Parkinson's disease produce dopamine, but until 1968, there was no way to replenish this lost chemical that drives the motor system.

It is interesting that prior to 1968, Parkinson's disease was in essence a surgical disorder; that is, there were no effective medications and it had been discovered through "accidents of nature" that surgical procedures could reduce some symptoms. It was observed that small strokes in damaging certain central parts of the brain, improved shaking or rigidity. What followed in the early to middle 20th century was the development of neurosurgical techniques to reliably destroy small parts of the brain in order to provide relief for certain Parkinson's patients. The procedures for stopping tremor and reducing rigidity were quite effective and in fact, knowledge based on that experience is used today in the deep brain stimulation treatment of Parkinson's disease.

However, in the 1960s, there were attempts to replenish dopamine in the brain. One could not give dopamine directly to patients as it would not be absorbed and the stomach would breakdown the chemical.

But, it was discovered that a naturally- occurring substance called **L-DOPA** or **levodopa** could be given in large enough quantities that it would be absorbed and converted to dopamine and act in the brain's motor circuit to restore function, which was later made into a very good motion picture. It should be noted, however, that the patients recounted in that tale were in fact not Parkinson's disease but a form of Parkinsonism which was quite different, a result of the influenza epidemic ("Spanish flu") in the early part of the 20th century. You may be aware of this history as recounted in a wonderful book by Oliver Sacks called **Awakenings**.

In any case, the effect of slowly building up L-DOPA in patients who had Parkinson's disease to the point where they would be taking 3000 to 5000 milligrams (mg) daily was quite remarkable. Nursing facilities, which were filled with PD patients in advanced stages of the disease, literally emptied out. However, there were a number of features that were noted as complications to levodopa therapy very early on. These results are still concerns today and have molded the direction of advances in the drug therapy of Parkinson's disease in the ensuing four decades since levodopa was introduced.

In 1968 levodopa was first introduced in the United States to a large population of Parkinson's disease patients with a variable range of disease duration and severity. There were those who were initiating treatment at the beginning of their disease as well as people who had been frozen in nursing homes for a number of years and were starting their treatment quite late. In addition, the progress of PD is considerably variable and there were severely affected patients who had progressed to that stage of their illness both slowly and quickly.

When treatment was first begun with just levodopa alone, it was often associated with drops in blood pressure, dizziness, and nausea.

These were related to the fact that L-DOPA was being converted to dopamine throughout the entire body. The capacity to convert levodopa to dopamine exists virtually everywhere. Every blood vessel has the enzyme that can do it. It also can occur inside the brain in the appropriate neurological compartments. The effect of converting L-DOPA to dopamine outside the nervous system has considerable side effects. It will slow down the movement of the gut and constipation results. It will also act like a mild diuretic (or “fluid pill”) and people will have less fluid volume in their bloodstream than they normally would. This is at least one mechanism by which levodopa drops blood pressure, but it may also make it more difficult to constrict the blood vessels in your legs, which helps control blood pressure when going from a lying to a standing position. In addition, it can make people nauseated by acting on brain centers which control that sensation.

Nevertheless, it was found that by starting at very small doses and very slowly building up over time that one could get to a large enough dose of L-DOPA in the brain that would begin to have an effect by being converted to dopamine in the right place. Symptoms would slowly melt away over weeks. Ironically enough, some people experienced increased shaking and this would result from rigidity and stiffness improving first. Naturally, if you are very, very stiff and you shake as well, the stiffness actually interferes with the tremor. As this improves, you may shake more, but as the medication builds up effect, your tremor is reduced as well. In fact, levodopa is a potent anti-tremor agent when it is present with the full blown symptoms of Parkinson’s disease.

For patients who have had their illness for a period of time, often 10 years or more, it was noted that they went through a brief honeymoon where the stiffness, slowness, and shaking of Parkinsonism would be remarkably reversed. However, within a period of weeks to months, it was noted that the patient became very much dependent upon each dose of the medication. There seemed to be poor storage of the medicine in the brain and each dose of medication would take time to take effect. It would last for only a few hours and then it would wear off.

At times, the wearing off of the anti-Parkinson effect of L-DOPA was so precipitous and random, it was like switching off a lamp. This was the origin of the term **on-off syndrome**. Associated with this was the fact that, over time, the L-DOPA did not just return the patient to a normal motor state, but actually gave them extra involuntary movements of a writhing or jerking nature, called **chorea** or **dyskinesia** or **involuntary movements**. So, this new miracle cure was a double-edged sword, and in the early years of L-DOPA treatment, most PD patients developed this on-off syndrome with levodopa-related involuntary movements within 7 years of beginning drug treatment.

At the same time, more was being learned about L-DOPA. For example, it was used in other conditions and, in one experiment, was even given to normal subjects, the spouses of Parkinson's disease patients! Levodopa-related dyskinesia developed in none of these other conditions. Therefore, these involuntary movements were not caused by the drug but rather were a particular interaction between L-DOPA and the brain of a Parkinson's disease patient.

When L-DOPA was given to patients with recent onset of their disease, the situation was not as dire. These patients in stage I and stage II illness would have a remarkable response to the levodopa and often do well for a number of years.

It was even noted that early in the illness, the effect of the medication lasted all day and there were papers in scientific journals that talked about using levodopa every other day for the treatment of early Parkinson's disease. It was evident that early in the illness, the brain had considerable capacity to store up the medication's effect.

Nevertheless, over time, patients would begin to develop this on-off syndrome as their illness progressed, and by the time levodopa had been used for treating patients for a decade, it was a well-recognized complication of Parkinson therapy.

Out of this observation came the controversy concerning when to begin levodopa treatment in Parkinson's disease. Some experts thought that it should be held back for the time when one really needed it because the effect would "eventually wear off." Of course, the effect did not wear off; every Parkinson's disease patient, no matter how advanced, continued to get some benefit from L-DOPA. It was simply erratic and taking place in an abnormally wired nervous system.

Another school of thought felt that people should be treated earlier and that they would maintain their function for longer. There was good data to support both schools of thought. What was most interesting, however, was that if you looked at when patients began L-DOPA treatment, it was begun at virtually the same time in the illness regardless of whether their physician's philosophy was to treat sooner versus later. The explanation for this is simple. Physicians treat their patients individually and when the patient needs treatment because they are incapacitated, it is given. One's philosophy obviously did not get in the way of taking care of people.

At that time, no one understood why patients should lose their beneficial L-DOPA effect into this inconsistent on-off syndrome.

It was noted that if you stopped the medication and allowed the patient to become parkinsonian again, you would regain some sensitivity to the medication and you would have less fluctuation in drug response. This led to the use of “drug holidays,” where patients would be hospitalized and taken off their medications for a few days to weeks. Unfortunately, the benefit from this kind of strategy was often short-lived and, at times, it could have terrible results. If the patient went into what was called an akinetic crisis, severely rigid parkinsonian state, there were times when one could no longer rescue the patient with medication. In those patients, it was evident that the benefit of levodopa had in fact allowed the patient to survive past the time they would have been able to without the L-DOPA therapy. Under the cover of L-DOPA, the pathology of the illness continued to progress. And this is still true for all the medications we have for PD; no medication has yet been proven to change the natural history of the progression of this illness.

The quest then became to try and develop medications that would stimulate the places in the brain that needed dopamine, but were not subject to the influences that affected L-DOPA. L-DOPA was poorly absorbed from the gut and this was easily interfered with by food. It had to be converted to an active ingredient that could be chewed up by the body in large measure before it got to the brain. It lasted in the blood a very short time and while it was incredibly effective, its chemical properties actually made it a poor medication.

It was attempted then to create medications that would stimulate dopamine receptors that were easily absorbed and lasted a long time in the blood stream and the brain. As a group these are known as **dopamine agonists**.

The first such drug was **bromocriptine** (Parlodel), introduced in the late 1970's. **Pergolide** (Permax) was the next of these artificial drugs which mimic the effect of dopamine. It entered clinical trials in the early 1980's and was approved for use in Parkinson's disease by the end of the decade. It is no longer prescribed because it could cause damage to the heart valves.

By the 1990's, it had been clearly established that starting the treatment of Parkinson's disease with a long-acting dopamine agonist would delay the development of wearing off of levodopa effect due to poor storage in the nervous system and the development of levodopa-related involuntary movements after that.

These studies showed that patients could start on dopamine agonists and use this as sole treatment for up to 3 years before requiring the more effective therapy of levodopa.

Dopamine agonists were discovered to be a little bit less potent and that they also had more side effects, especially in the behavioral sphere. Today, a more advanced class of dopamine agonists exists called non-ergots, which are associated with less side effects. These are **ropinirole**, **pramipexole** and **rotigotine**. Ropinirole and pramipexole are oral agents which are also available in extended release once daily formulations, and rotigotine is a patch which slowly releases the drug over a twenty four hour period.

Nevertheless, when one looks at a group of Parkinson's disease patients today in any movement disorders clinic, it is remarkably different than the population of 30 years ago. In the past, a Parkinson's clinic was filled with patients with severe fluctuations and poor control of the disease, associated with wild gyrating motions which would begin with the onset of drug effect.

Today, while there are still fluctuations in drug response and involuntary movements, they are qualitatively much less than we would have seen in the past. This has represented a true advance for the maintenance of physical function in Parkinson's disease patients, not to mention greatly improved quality of life.

## Helpful medications in Parkinson's disease

As we discussed above, L-DOPA is changed to dopamine throughout the body in many different structures including the gut and blood vessels. For this reason, **carbidopa** (Lodosyn) is given in combination with it. Carbidopa is a large molecule that does not enter the brain across the blood-brain barrier, which serves as an effective barrier to the passing of some chemicals from the blood to the brain.

Carbidopa prevents much of the levodopa from being converted to dopamine outside the nervous system. For example, prior to the development of carbidopa, patients would take 3000 to 5000 mg of levodopa each day in order to get an effective dose into the nervous system. With carbidopa, this is reduced to 600 mg to 1000 mg daily illustrating just how much was lost before it became active in the nervous system.

The combination of **carbidopa/levodopa** into a single pill was originally marketed under the brand name **Sinemet** and comes in various combinations of milligrams: 25/100, 25/250, and 10/100. It is also in an extended release form: (**Sinemet CR** 25/100 and 50/200). The fact that there is both a regular and controlled release form of the 25/100 demands much attention from the patient: sometimes these can be mistaken for one another at the drugstore.

Know what your pills look like!

**Rytary** is an extended-release formulation of carbidopa-levodopa that was approved by the FDA in 2015. Compared to the prior extended-release formulation, **Sinemet CR**, **Rytary** has more consistent absorption in the body, and is more appropriate for taking during the daytime hours. **Rytary** is also known as **carbidopa-levodopa ER**, in various combinations of milligrams: 23.75mg/95mg; 36.25/145mg; 48.75mg/195mg; 61.25mg/245mg. For patients who have wearing off between doses of the standard, short-acting carbidopa-levodopa (**Sinemet**), they may try switching to **Rytary**, which is taken 3-4 times per day, spread over waking hours. **Rytary** has a very similar profile in terms of benefits and potential side effects as the short-acting carbidopa-levodopa, as they both are ultimately providing L-DOPA to the brain.

A more recent advance in using levodopa for the treatment of PD is a medication pump system called “Duopa”. With the help of this pump, a gel form of levodopa is infused continuously at very small doses directly into the gut. This way, the blood level of levodopa remains fairly constant over time, thus reducing or eliminating the fluctuations patients often experience when they use levodopa in pill form.

The Duopa pump will be considered for patients with off time between doses, and those with involuntary movements (dyskinesias). A gastroenterologist will insert a small tubing system called a “PEG tube” via a scope into the patient’s gut, and this PEG system will allow the patient to connect their pump through a small button like device on the left side of their abdomen to the tubing inside the gut. Nothing but the small plastic button will be visible from the outside. Many patients like the more predictable medication levels that this pump can achieve.

**Catechol-O-methyl transferase (COMT) inhibitors** like entacapone (Comtan) or tolcapone (Tasmar), or opicapone (Ongentys) also help to ensure that more of the levodopa that is ingested actually gets to the nervous system rather than being disposed of before it gets there, and helps it stay there without being digested. Another class of compounds called **MonoAmine Oxidase B (MAO-B) inhibitors** also block the breakdown of dopamine once it is formed. These medications, selegiline (Eldepryl or Zelapar), rasagiline (Azilect), and the most recently approved, safinamide (Xadago) are all useful in extending the time in which dopamine remains present and able to communicate from one nerve cell to the next. Istradefylline (Nourianz) is the most recent addition to the drugs used to treat wearing off. Using a different pathway than all other drugs, it can give people more functional "on" time when used together with carbidopa/levodopa.

Finally, there is one other class of medication that is used in Parkinson's disease that is effective against tremor but little else. **Anticholinergic** drugs were first isolated from plants and were administered to Parkinson's disease patients in the 19th century. They have remarkable effect on tremor but also have considerable side effects. They interfere with memory. They can cause dryness and constipation and sometimes outright confusion and hallucinations. Nevertheless, for the patient who can tolerate them (particularly our younger patients), they are often useful in their ability to help the shaking of Parkinson's disease. The most common ones in use today are **benztropine (Cogentin)** and **trihexyphenidyl (Artane)**.

**Amantadine** or its extended-release form, Gocovri, is an interesting drug with multiple mechanisms of action including an anticholinergic effect, a dopamine effect, and an effect on the glutamate neurotransmitter system. Amantadine is used in early Parkinson's disease, can be used to treat tremors later on, and is currently the only drug shown to be effective for the treatment of dyskinesias. Unfortunately, this class of medication can be associated with a withdrawal syndrome and needs to be carefully weaned off.

## Rescue Medications

Some off episodes tend to be unpredictable or occur sporadically, rather than at the end of each dose. People might experience sudden slowness, stiffness, or are suddenly unable to walk. They might be in need for a quick rescue medication that kicks in faster than a pill taken by mouth. There are currently 3 choices of therapy that you can ask your doctor about: An inhaler, a sublingual (under the tongue) film, and an injection treatment.

### **Levodopa inhaler (Inbrija)**

People who choose the levodopa inhaler will use a small handheld device similar to one used for asthma attacks or other breathing conditions. They “load” the inhaler with a capsule of levodopa powder, take a deep breath, then “load” another capsule and repeat the process. This form of levodopa kicks in rather quickly and can bridge until the next by mouth dose of medication is due.

### **Apomorphine sublingual film (Kynmobi)**

While the inhaler contains actual levodopa, the sublingual film contains a dopamine agonist, called apomorphine. People place this film under their tongue at the first onset of an off episode. It is important to note that this medication will cause nausea and vomiting unless your doctor also prescribes an anti-nausea drug for you. But with the anti-nausea treatment, most people tolerate this very well.

## **Apomorphine s.c. injection (Apokyn)**

Another way to use apomorphine is with a subcutaneous (under the skin) injection. The device used for these rescue shots looks somewhat similar to an EpiPen. Injectable apomorphine kicks in quickly, but again, it is associated with nausea if you do not also take an anti-nausea medicine with it.

## Medication sensitivity in Parkinson's disease

While the scenario described above is useful for the typical Parkinson's disease patient, it is unfortunately common that this regimen is troublesome because of medication side effects.

Some of these are expected and unavoidable because the drugs affect many different processes in the body, in addition to the beneficial medication effect desired in the brain. The therapeutic window that separates the good effects from the bad ones may be quite narrow, and in some patients you can't get benefits without unacceptable adverse effects. These unfortunate patients have a lowered threshold to side effects of most PD medication. It especially makes them much more sensitive to the effects of anti-Parkinson drugs on thinking processes. For this reason, we describe here another common scenario involving the patient who is sensitive to behavioral side effects of medicines.

There are patients in whom one will have a suspicion of early cognitive dysfunction in Parkinson's disease. While anti-Parkinson drugs, if used in high enough doses, will cause behavioral changes in virtually everyone, it is the patient with thinking troubles who will have a much lower threshold for this. Very often, this person will not be able to use anything but carbidopa/levodopa from the very beginning of treatment.

These patients are often **elderly**, and this happens more frequently in the patient with the fairly symmetric postural disability gait disorder form of PD. In addition to their Parkinson's disease motor complaints, they will complain of difficulty in certain kinds of mental functions such as calculations (for example, keeping the checkbook organized), difficulty remembering directions to places, difficulty with carrying

out complex tasks that they used to be able to do with ease, or even the early development of visual illusions or hallucinations.

Almost all patients will have some complaint of memory trouble with the anticholinergic medicines mentioned above. **Acetylcholine** is a neurotransmitter that is important in the memory system. While blocking this neurotransmitter helps control tremor, the actions of these medicines in other parts of the brain (which cannot be avoided) mean that patients will have difficulty remembering things. While trihexyphenidyl and benztropine are the most potent members of this class, **amantadine**, which is quite useful in Parkinson's disease for reducing levodopa-induced involuntary movements, also has significant anticholinergic properties. If a person has pre-existing memory difficulties and is given these medicines, then a profound confusional state can develop quite quickly.

Dopamine agonists similarly have psychical side effects in susceptible individuals. These can often be subtle and of a sort that are not intuitively linked with the medication. It may not occur at the beginning and it may only develop with time as the medication is titrated to a higher dose. Even very early on in the development of L-DOPA treatment of Parkinson's disease, strange impulsive behavior was noted. This was initially characterized as hypersexuality, a greatly increased preoccupation with sexual thoughts and activity.

Since then, it has been recognized that obsessive thoughts and compulsive behaviors may occur affecting a wide range of human activities. In addition, when levodopa was first introduced in the patient care, it was tried in many patients who may have had atypical Parkinsonism and other neurological disorders at higher risk for behavioral side effects. This greatly added to the "mythology" surrounding levodopa effects.

We do know, however, that levodopa in adequate doses in susceptible individuals will cause impulsive behavior, though at a lesser rate than the dopamine agonists. These may be associated with spending or compulsive shopping, especially of lottery tickets or collectibles. People may gamble, buying lottery tickets or even traveling to casinos, and they can experience a wide variety of sexual thoughts and behavior. Even people who had never had any such interests are suddenly surfing the Internet for pornography or buying hours of adult movies on their cable television network.

Research has tried to find what predisposes patients to these kinds of behaviors and it may be that levodopa accentuates previous behavioral tendencies so that if one were fond of spending money as in shopping or gambling, it may become uncontrollable and impulsive with medication.

Another unusual phenomenon is called punding. This is repetitive pointless behavior such as keeping detailed notes of no real use or attempting to accomplish repetitive small tasks that one gets stuck on and cannot give up. The origin of this interesting term is a Swedish word for being “block-headed.”

About 1 out of 15 patients being treated with levodopa is at risk for these kinds of behaviors. This occurs more commonly in people who take dopamine agonists (pramipexole, ropinirole, rotigotine), occurring in 1 out of 7 patients when given adequate doses to produce this psychic phenomenon. While it is generally at higher doses, there have been cases where these behaviors also began at very low doses.

These behaviors may be insidious and come on imperceptibly. The spouse, who had always enjoyed spending money, suddenly can go through the family’s entire savings before it may be detected.

We are careful to warn anybody we start on these medications about the potential for these kinds of behavioral side effects. Everyone understands that constipation or dry mouth or some physical symptom could result, but we are less inclined to identify psychological changes as an obvious drug side effect.

The presence of behavioral symptoms in a patient at the start of their Parkinson's illness means that we will usually treat them with a more levodopa dominant medical regimen, using MAO-B's and COMT's but avoiding dopamine agonists altogether.

Thankfully, however, most of these patients are older than the average PD patients and, therefore, their natural life expectancy may mean that they never get to the point of having the failures of levodopa therapy and the development of fluctuations.

## **Summarizing treatment strategies**

To recap: There is not a typical Parkinson's patient, and there is not a typical treatment plan for a Parkinson's patient. Every patient is affected by the disease in a completely different way, has different sensitivities to medications and different expectations from therapy. We do have many effective medical therapies for the treatment of Parkinson's disease, and we know these medications well, so the rule with medical treatment of Parkinson's is now to use multiple medications at lower doses to extract every drop of benefit from them, and keep the side effects low. The argument of starting dopamine agonists first and delaying dopamine therapy has been ongoing for over thirty years. The bottom line is that there is no right answer for everyone. You should not think of levodopa therapy as something that should be "saved for a rainy day".

Levodopa remains the most effective medical therapy for the treatment of the motor symptoms of Parkinson's disease, and has the best behavioral side effect profile. Our ability to administer this medication has improved remarkably, and newer developments have not overshadowed its efficacy to date. It does carry a higher risk for the development of dyskinesia but these are rarely troublesome to the patient, and when they are, they can be treated. So if levodopa works for you, keeps you active, independent and doing the things you enjoy in your life it should not be withheld, but used judiciously.

If patients on a levodopa heavy regimen begin to wear off, multiple effective therapies are available including extended released levodopa formulation, dopamine agonists (regular and extended release) MAO-B inhibitors, and COMT inhibitors. It is true that the development of dyskinesias limits the clinician in terms of our ability to increase the dose of medication, since this will inevitably worsen dyskinesias. Sometimes the simplest alternative is to reduce the dose and the interval between doses, however, this can lead to taking medication very often which can be a large burden on the patient. Immediate-release amantadine or a new extended-release amantadine formulation (Gocovri<sup>®</sup>) may also be considered when treating dyskinesia.

This is the stage when we consider an evaluation for **deep brain stimulation (DBS)**, or Duopa infusion therapy.

# Deep Brain Stimulation

Deep in the brain are several structures that are all connected together in a circuit to facilitate movement. Consider the analogy that the broken brain circuits in Parkinson's disease are akin to trying to drive a car with the parking break locked in the on position. The effect of DBS is to unlock the parking break. The exact mechanism of how deep brain stimulation works is not entirely clear, but it frees the motor system to operate in a fairly normal fashion. It requires the placement of electrodes deep in the motor structures on both the right and left sides of the brain to adequately treat most patients.

The electrodes are connected to a programmable generator under the skin below the collarbone, much like a heart pacemaker.

Patients who benefit the most from DBS are those who benefit greatly from medications for Parkinson's, however experience wearing off or dyskinesias which limit that benefit. For those patients DBS is able to keep them in the "on" state without dyskinesias. Patients who have a coarse tremor that has not responded to medications can also benefit greatly from DBS. In thinking about DBS, it is important to recognize that it helps only those symptoms which are helped by the medications given for the motor troubles. It does not benefit the non-motor symptoms of PD like memory problems.

The decision to pursue DBS is an individual one which should be carefully made by the patient with physician guidance and family support. DBS is not for everyone. It is important to understand what DBS can do for you, and what it cannot, prior to considering surgery. Once a decision has been made to pursue DBS, consideration then needs to be given to when is the best time in your life and your disease process to make this transition.

DBS is a very specialized treatment which requires a skilled and experienced team approach. For it to be successful, this is absolutely necessary. The critical parts of the team process include selection of the right kind of patient for surgery, choosing the correct target for surgery, placing the electrode in the correct area to maximize benefit and minimize side effects, and programming the device correctly after surgery with the simultaneous medication adjustments.

Patient selection and screening is done by: 1) a movement disorder neurologist who confirms the diagnosis and ensures all reasonable medical therapies have been tried, 2) a neuropsychologist who performs cognitive and psychological testing to ensure there are no conditions that need further treatment or could increase the risk of surgery, and 3) a neurosurgeon who will screen for conditions that may complicate the surgery or put the patient at higher risk. Each case is then individually presented and discussed at the DBS Conference where all findings are carefully considered into a final decision to pursue surgery, and if so, what precautions need to be taken to ensure success.

The day of the surgery it is imperative that the functional neurosurgery team work together with neurologists and neurophysiologists to ensure optimal placement of the DBS electrode. The surgeon targets based on imaging and stereotactic coordinates while the neurologist and neurophysiologist map the region in real time and test the electrodes to ensure it works and does not cause any side effects, prior to permanent placement.

One of the most critical elements for successful DBS is the post-operative period. Here patients have frequent visits with the DBS neurologist and mid-level providers to begin to tailor the stimulation to control each patient's individual symptoms.

At this time medications are often diminished as we transition the treatment from one that relies on medication to one that relies more on stimulation. The experience of the team in programming and managing medications in this period is highly important.

## Special treatment considerations in Parkinson's disease

This next section will discuss particular situations that occur in Parkinson's disease and the treatment choices that may be helpful.

There are times, generally later in the illness, when symptoms arise that are not directly related to the loss of dopamine in the brain. These symptoms can be responsible for a great deal of the unhappiness that comes with Parkinson's disease due to the nature of the symptom itself and because, in some cases, we do not have effective medication to relieve these troubles.

The most important of these is **depression**. There is something about Parkinson's disease that leaves the patient uniquely sensitive to a variety of emotional symptoms often found with the diagnosis of depression.

These include irritability, loss of concentration, loss of enjoyment in the usual things, the desire to be reclusive, and loss of motivation.

The usual medications that are used in the illness called "major depression" are extremely effective at benefiting the depression of Parkinson's disease, which in my experience is seldom resistant to treatment. This is likely the single most important non-motor symptom of Parkinson's disease. The presence of depression makes everything look bad, and the patient feels pessimistic, with a "glass half empty" perspective on the world.

A patient who is otherwise fully functional and doing well with their PD can perceive themselves as very much disabled. As a result, we find that mood elevators are the most beneficial class of drugs for patients after carbidopa/ levodopa and dopamine agonists.

It is important to note that there are multiple neurotransmitters that are deficient in the brain of a Parkinson's patient. Dopamine is the best known neurotransmitter that is diminished, and is thought to have a central role in the motor symptoms of Parkinson's disease. It turns out dopamine also plays a role in mood, explaining why some Parkinson's patients experience depression. Other neurotransmitters like serotonin and norepinephrine, which are targeted by many mood elevating medications or anti-depressants, are also decreased in Parkinson's disease. All in all, patients with Parkinson's disease are at an increased risk for depressed mood and apathy, from the disease itself, and replacing these diminished chemicals in the brain is often a very effective therapy.

**Anxiety** also commonly occurs in Parkinson's disease. While there are tranquilizer medications that are used to help anxiety in the short-term, best control of anxiety over the long-term is also achieved with the same drugs taken for depression. These medicines augment other chemical systems in the brain which are also abnormal in PD. It is a difficult distinction to make, but some patients feel very restless when medication wears off, and have trouble finding a comfortable position. This is different than the psychological sensation of nervousness and is best treated by controlling the PD motor symptoms.

**Sleep disturbances** may be associated with disorders of mood and anxiety or exist by itself due to PD or as a result of PD treatment. Sleep disturbances can come in many different forms.

**Insomnia** is difficulty falling asleep. This is often associated with anxiety or depression. Insomnia can improve by treating the underlying mood disorder, either with medications or cognitive behavioral therapy. Some medications can be activating and contribute to insomnia and these need to be reviewed by your physician and adjusted or discontinued.

Tremor or **restless legs (RLS)** can also contribute to insomnia. RLS is defined as an unusual sensation in the legs associated with an urge to move the legs, relieved by standing or walking, often more common in the evenings or at bedtime.

**Fragmented sleep** can occur from breakthrough motor symptoms like tremor, slowness or stiffness at night. More commonly it occurs from frequency in urination during the night. Many patients describe being able to fall asleep without difficulty, then experience **early awakening** after just a few hour and have difficulty falling asleep again. Other causes of fragmented sleep include **periodic limb movements of sleep** or REM behavior disorder.

**REM behavior disorder (RBD)** is characterized by patients acting out their dreams during sleep. In most people, dream sleep is characterized by little body movement except rapid eye movements (REM). Normally the motor system is cut off. In patients with RBD, they still have an active motor system and it will act out dreams. Actions may be so violent that the patient will strike out or fall out of bed or be talking or laughing or crying or act scared.

It is often quite traumatic to anyone sharing the bed. If the patient is awakened they will not have a recollection of what they were dreaming and are often surprised to find that they may have hit their partner or even tossed themselves out of bed.

REM behavior disorder is often easily treated with sleep medications such as **clonazepam** or some of the shorter-acting medications used decades ago for sleep such as **temazepam** and **flurazepam**. These are relatives of the same class of drug as diazepam (Valium), which may be more familiar to you. They may be habit forming.

**Melatonin** is a neurotransmitter naturally produced by your brain to control circadian rhythms and can also help with RBD.

Modern sleep medications such as **zolpidem** (Ambien) and **eszopiclone** (Lunesta) may not be as effective for this kind of problem. It is also true that some of the drugs for depression may actually increase REM behavior disorder and so these should be taken in the morning. Two medications that tend to induce REM behavior disorder less than other antidepressants include **venlafaxine** (Effexor) and **bupropion** (Wellbutrin).

Keeping good “sleep hygiene” is very important when treating any sleep disturbance. This includes maintaining a regular bedtime, avoiding any activities in the bedroom aside from sleeping (like watching TV or working on the laptop), and avoiding excessive sleep during the day. It is important to stay active during the day, exercise, and get into a routine where your body knows it is time for sleep and nothing else. If you find your mind ruminating about tasks lined up the next day, it is a good idea to get out of bed, write down your thoughts, and then put them aside. Find a relaxing activity to calm yourself down like reading, then go back to bed.

**Psychosis, hallucinations and delusions** are an important part of PD related symptoms in some patients (as described above). The presence of these mental features signal that many different kinds of medications are best avoided.

As we discussed above, carbidopa/levodopa is generally the best treatment for patients who have the mental aberrations of Parkinson's disease, but there are times when **anti-psychotic** medications are required in order to help the patient to sleep or reduce delusions, visual illusions and / or hallucinations. The difficulty with most anti-psychotic medications is that they block dopamine.

As a result these drugs, while they control the hallucinations and behavioral disturbances, may greatly interfere with the patient's motor system. Newer antipsychotic drugs are "atypical," meaning they block the dopamine system less. The one that is used most often in Parkinson's disease is **quetiapine** (Seroquel). Another option is **clozapine** (Clozaril); however this medication requires regular blood monitoring. Most of the other drugs in this class are contraindicated in Parkinson's disease.

**Pimavanserin** (Nuplazid) is a once daily medication approved by the FDA in 2016 for hallucinations in Parkinson's disease. It works on serotonin receptors in the brain, sparing the dopamine receptors. This means that pimavanserin does not have the side effect of worsening the slowness or bradykinesia in Parkinson's disease. Your physician may want to check an EKG before starting pimavanserin. As of this writing, pimavanserin must be obtained through a specialty pharmacy.

The treatment of psychosis in Parkinson's disease first and foremost requires a close look at all of the medications that a patient is taking including over-the-counter food supplements. A large number of medicines including bronchodilators for chronic lung disease, medications for bladder and prostate, and tranquilizers in general may contribute to the confusion of Parkinson's disease.

The sudden worsening of mental symptoms or onset of confusion in a patient where there has been no recent medication change should prompt a look for other medical illness (bladder infection, blood clot, falling with resultant head trauma, out of control blood sugar in a diabetic, dehydration, or even the common cold). Inadvertent overdosing of PD medication is also common especially if the patient is taking several medications on a complicated schedule. Help with dispensing of medication may be needed to keep such a situation well organized, with pre-loaded pill boxes and family members helping to watch the time interval for medications over the day.

**Bladder and bowel dysfunction** are often problems in Parkinson's disease as well. Consider that the bladder is, in essence, a muscular bag. Just as one moves slowly and with deliberate movement with PD, the bladder is also affected so that it does not contract vigorously and does not always empty fully. This can result in the patient feeling that they have to urinate frequently. Medications that increase the strength of bladder contraction taken together with medicines that reduce prostate related obstruction are useful in combination. One does have to look out for the anticholinergic side effects of these drugs (particularly worsening memory). Some of the newer bladder medications tend to be drugs that do not cross the blood-brain barrier into the nervous system and therefore are more effective without the side effect patterns seen in some of the older medicines.

The bowels are slowed in a number of ways in Parkinson's disease. The autonomic nervous system, which governs contractions in the bowels that move food along, may be affected in PD. In addition, small amounts of levodopa will be changed to dopamine and this neurotransmitter will also slow the bowel. Anticholinergic medications and dopamine agonists also do this and so many patients are constipated, some severely so.

If the bowel is filled with stool it will press on the bladder, reducing its capacity and contributing to urgency and frequency of urination.

One of the bowel's major functions is to reabsorb water. The longer that the stool sits in the colon, the harder it becomes because water is being taken out of it continuously. Common wisdom suggests an increase in dietary fiber and that is good to a degree and works well in normal people. However, in a very slow moving bowel, where you do not have adequate water in the colon, it will simply make a larger, harder bowel movement.

The solution is to increase drinking fluids. To supplement one may consider a preparation that keeps this water in the bowel like **Polyethylene glycol** (MiraLAX) which is an effective powder for this purpose, and available over the counter in pharmacies. This means that the bowel movement will continue to be processed normally in the colon even though the speed of it moving along is much slower than in a normal bowel. Other laxatives or enemas will often not be needed. The dose of MiraLAX can be titrated for adequate effect. Most patients don't need the full dose listed on the label every day.

**Walking difficulties** can occur in later stages of Parkinson's disease. Early on, patients may notice a change in posture, decrease in arm swing, shortening of the steps and overall slower pace of walking. In later stages patients can develop more troublesome walking difficulties. These are generally divided into difficulties with balance or **postural instability**, **festination** and **freezing of gait**. **Postural instability** is your ability to keep your balance in normal walking situations, and to catch yourself when you are thrown off balance. Festination occurs when patients begin to walk faster, feeling propelled forward making short steps unable to effectively stop themselves.

Freezing of gait is defined as an inability to walk despite the intention to do so. Patients often feel “stuck” with the feet “glued to the floor”. This can occur when one first sets out to start walking (on initiation, or start hesitation), when turning, when arriving at a destination, or when going through a threshold like a doorway or a change in pattern on the floor. Freezing is easily overcome at first, and can respond to medication, but in more advanced cases can be quite difficult to overcome. It is important to recognize that almost all patients who complain of difficulty walking have more than one problem contributing to their dysfunction.

Usually we see a combination of freezing or festination with balance impairment that leads to frequent falls. However, orthopedic problems like arthritic knees or hips, nerve problems causing numbness in the feet, spinal cord problems, even difficulties with attention, ability to multi-task, hearing and vision, all contribute to difficulties with walking and the resulting falls. Low blood pressure can sometimes contribute to falls, whereby patients feel lightheaded when they stand up from a chair and sometimes faint altogether. Finally, it is important to use good judgment when considering a walking task: safety first! Remember that falls put you at risk for fractures and hospitalizations which can be difficult to recover from. Sometimes it is easy to forget about walking limitations and take unnecessary risks when walking. It is important to take some time prior to starting to walk to consider if it is safe to do so, and give your body time to adjust to being upright before starting to walk.

At the center of any treatment plan to address difficulty walking is physical and occupational therapy. Physical therapists can spend more time with you determining how each factor is contributing to your walking difficulties.

They can also determine which assist device (cane, walker, etc.) will be most helpful, and teach you how to use them appropriately. There is now good science supporting physical therapy protocols like the Lee Silverman Voice Therapy-BIG (LSVT- BIG) and others that improve many of these gait disturbances. Occupational therapists can make home visits and show you safe and effective ways of keeping your independence at home and with other activities. Medication trials, adjustments, DBS, orthopedic, neuromuscular, cognitive, visual and hearing evaluations may all be considered as part of a multidisciplinary approach to address walking difficulties in Parkinson's disease.

**Speech and swallowing disorders** also may come late in PD. There are two parts to swallowing. The first action is the movement of the mouth in chewing the food, making it small, mixing it with saliva, and moving the food from the teeth to the back of the throat. At that point the automatic part of swallowing takes over: a “conveyor belt” that produces the motions that remove the food from the back of the mouth and move it down the esophagus to the stomach.

When the patient has swallowing difficulties, it is important to figure out whether the trouble is in the chewing and moving the food to the back of the throat or whether it is actually the automatic swallowing mechanism itself that is difficult.

When incoordination affects swallowing, a few simple tricks will maintain good swallowing hygiene and avoid aspiration of food or liquid into the windpipe. These include tucking your chin down when swallowing, keeping your head looking straight to the front, taking in small pieces of food, and not placing more food into your mouth until your mouth is empty. It is important to refrain from conversation because it is natural to want to respond.

With food in your mouth, it could end up in the windpipe. These few things will greatly reduce the incidence of choking.

In the same manner that other body parts slow down in Parkinson's, so does swallowing. Parkinson's patients tend to swallow less often than those without Parkinson's disease. However, the glands that produce saliva continue to make saliva at the same rate. This results in excess saliva in the mouth or drooling. This can be severe and troublesome for some patients. This is treatable with anticholinergic medications, patches, atropine drops dissolved in water, or botulinum toxin injections. Medications can have side effects like constipation and memory loss and atropine drops usually don't last very long. If drooling is considerable, botulinum toxin injections can be very effective. Speech and its volume are typically related to the amount of air that passes the vocal cords. The effect of PD on the chest wall means your lungs don't move as much air as they normally would. If one has "stiff bellows" and not much air passes the vocal cords, a softer voice results. It helps to consciously take a deep breath before starting a sentence.

Otherwise you may quickly run out of breath as you begin to say something. Some patients have good breath control but still speak softly. It appears that our ability to automatically know the correct level at which we need to speak to be heard is affected in Parkinson's. This can be effectively overcome by simply practicing, or re-training yourself regarding the correct volume necessary to be heard in normal conversation. Lee Silverman Voice Therapy-LOUD (LSVT-LOUD) is perhaps the best known of these kinds of interventions.

**Physical and occupational therapy (PT and OT)** among other non-drug treatments are also very helpful in order to maintain strength and fine motor control. The important thing to understand about these therapies is that you will be given goals to achieve.

The therapy is not offered to help you maintain a given level of ability. This would be prohibitively expensive and impractical. Rather, you are being taught to exercise, and when you have reached a plateau in your improvement, the therapist no longer continues with you. At that point you are expected to practice these skills and exercises on your own. If you do not, then you will quickly lose whatever benefit you had.

Patients often ask for physical therapy referrals. If in fact what they are really talking about is conditioning and muscle strength building, we prefer to recommend trainers of the sort that are generally found in health clubs. These trained athletes are often better able to help you to attain a higher level of physical strength and conditioning than therapists in PT and OT. Trainers tend to be less sympathetic to all the creative excuses we come up with to try and avoid the exercise that we know will benefit us the most.

Word of mouth at the local gym is a useful way to find a good one.

Alternative forms of exercise are actively being studied. We have patients who have taken part in **Tai Chi** and **Qigong**, among others, and have felt greatly benefited. Yoga is also excellent and there are many different forms, from meditation to balance exercise to cardiovascular aerobic training. Ballroom dancing is also a popular and active diversion among some patients. Exercise can be boring. The only solution is to make it varied and make it fun. There's no prescription for that other than your own.

# Social aspects of Parkinson's Disease

Being told that you or a loved one has Parkinson's disease is a shock, to say the least, and takes some adjustment. We are often then surprised, disappointed, sad, and angry at such happenstance. Often the patients who remain the healthiest are the ones who act in positive ways to find out more about their illness and take action to live healthy lives in general.

After the initial period of adjustment, often the good response to medication illustrates in a dramatic way that one will continue to go on in life and a successful adjustment can be made. In some cases, however, it is difficult to get over the initial hurdles and we encourage mental health or pastoral counseling for the patient and their loved ones because living with a chronic disease does require an adjustment.

Identifying the presence of a mood or anxiety disorder is important to making a successful adjustment. Patients often fear that antidepressants will drug them, be addictive, or otherwise change who they are. The pleasant surprise for these patients is that these medications actually makes them feel more like themselves and make it possible for them to be able to get back to the usual enjoyments of life.

The first practical task is to find a physician who is familiar with Parkinson's disease. This is not as easy as it sounds. There are very few Movement Disorders Centers or specialized treatment programs or physicians who have had advanced training in movement disorders following general neurology training. Such specialists are often found in large regional medical centers attached to medical schools. As a result, most patients will never benefit from having such a resource at a tertiary medical center. It is for this reason that this primer is created.

The next option is to find an effective health care provider, either physician or physician extender (nurse practitioner or physician’s assistant), who is willing to explore treating your illness with you. They will need to be comfortable knowing what they don’t know and at times seeking help from specialists in making decisions with you about your care. We think the best word to describe this important and necessary relationship is “partnership”.

As we have tried to illustrate in treating Parkinson’s disease, it is just as important to know what medications to avoid, as it is to know what to take. Joining a Parkinson’s disease support group may provide you with additional information. Such groups often include patients at all stages of PD, so you may see people with significantly advanced disease, while in other instances be unable to differentiate the patient from the spouse. It is crucial to remember that this disease is quite variable, and each patient’s experience is quite different.

Finding information on the Internet is also useful but the quality of the source needs to be considered. Good quality information may be found from non- profit foundations such as The Parkinson’s Foundation, Michael J. Fox Foundation, and American Parkinson Disease Association. Be wary of sites that are run by individuals; the information they have may be a result of their own bias, or personal experience with the disease. You will also find that some sites are cleverly designed to sell you health related products.

## Diet and exercise

While there is no specific dietary recommendation for people with PD, we remind patients and families to ensure that nutrition is well balanced and that hydration is optimized. In more advanced PD, patients are recommended to take carbidopa/ levodopa on an empty stomach to optimize its efficacy. We suggest taking it approximately 45 minutes before or after a meal. Since protein absorption competes with levodopa to get to the brain, we suggest that the higher protein meals be reserved for later in the day – so that if a dose of levodopa is less effective it is not during the prime time of the day.

The importance of exercise in PD cannot be stressed enough. While many supplements and compounds have been studied in an effort to find an intervention to slow down disease progression, only exercise shows promise to in fact modify disease progression in addition to helping symptoms.

Exercise exerts its benefits on the brain as well as the body. Regular exercise improves quality of life, walking ability, balance, strength, and flexibility. Exercise can improve posture, strength, balance, and walking ability, can limit physical decline, reduces some symptoms, may slow disease progression, may be disease modifying, and may protect your brain from cell loss. The role of exercise evolves through the course of PD. Initially we suggest an evaluation with a physical therapist to help begin an exercise program even if you do not have difficulties with balance, stiffness, etc. In more advanced disease rehabilitative physical therapy reinforces basic skills such as getting out of a low chair or bed, walking better, strategies to get out of a freeze, how to improve your posture, etc.

The key at any stage is to find something you like & stick with it. Join a group – get social & have FUN. We suggest working up to about 150 minutes per week of cardiovascular exercise. This means an activity that gets your heart rate up continuously to about 60-80% of your maximal heart rate (with supervision of your physician to ensure no contraindication). To find a physical therapist near you, go to: [www.APTA.org](http://www.APTA.org) or call the American Physical Therapy Association at 800-999-2782. The mantra is “Use it or lose it!” – so get moving!

## Employment

As we are fond of saying in this part of the country, “idle hands are the devil’s playground” and we encourage staying active and engaged. For many of us this means continuing to work.

Deciding to share your diagnosis with your co-workers is a very personal decision. While plenty of newly diagnosed patients can significantly delay this disclosure, over time it becomes difficult to continue to “hide” the symptoms. At some point however, it is too obvious that you shake or fluctuate in response to medication and you will have to say something. The danger of waiting too long, is that others will begin to gossip about what has changed your appearance, and often the conversation turns to suspicions of drug or alcohol abuse.

Many patients find a sense of relief once they discuss their diagnosis with colleagues, while others feel more self-conscious. Be sure to discuss this with your family and physician to help decide what is right for you.

Be aware that The Americans for Disabilities Act is a law that protects you against discrimination that results just because you have an illness. If you can do your job, you are allowed to ask for reasonable accommodation at work. However, if you cannot do your job adequately, it does not fully protect you.

You may find yourself out of work through a general reduction in the work force at your place of work or your position may be eliminated. However, in this case, you will be one of a number of employees being let go. If it is just you who are fired, this may be thinly veiled discrimination. If you suspect this, seek consultation with an attorney who has experience with disability law.

The average PD patient works for seven years after diagnosis. Many work longer and some quit because it has simply become time to retire. But some may not be able to do their job, especially if fine motor skills are required. If this is the case, do not just quit. Seek help from your company's human relations department or Employee Assistance Program, or call the local Social Security Administration office.

# Caregiving

PD affects more than just the patient and is often a family affair. As the disease most often starts after age 60, the role of “caregiver” is often the spouse. This role is ever-evolving. Initially the patient will likely need a support system to help make sense of the new diagnosis. This can come from immediate family members or close friends. Roles in the family may change, and as this slowly progressive disease changes, so does the role of the support network and caregiver(s). In more advanced PD, the patient relies more on the caregiver for a variety of things – from assistance with activities of daily living to house-hold chores. It is crucial to realize that the caregiver must also engage in regular self-care, and must not feel guilty for doing so. Caregivers will not be effective for anyone if they do not take care of themselves as well. No one person is able to care for a patient (with any diagnosis) 24 hours a day, seven days a week.

In our experience, things fall apart especially quickly when the patient no longer sleeps through the night and requires assistance from the caregiver. There is no way that one can be up at night and then expect to function normally the next day, especially if one also has a job or children to care for.

In this circumstance, the phenomenon known as “caregiver burnout” can occur very quickly and a family crisis results. To avoid this, we encourage all available family members to be involved in the patient’s care as well as helping to make plans for the future. As we have discussed before, nothing in PD develops quickly and there is often plenty of time to plan for the difficulties of later stages, if they appear.

If a patient has difficulties at night or is going to need more care than one person can give, one option is to hire a health aide to stay with the patient at night so that the spouse or partner can sleep. Unfortunately insurance does not generally cover aides in the home unless you are one of the fortunate few with long term care insurance. If such resources are not available, alternative living situations such as assisted living (which is covered by Medicare and Medicaid) may offer a better solution. Respite care (a short stay for the patient in a health care facility in order to allow everyone to catch their breath) may provide temporary relief while the family seeks out more permanent solutions.

Spouses and children often promise their loved one with PD (or any other serious illness, for that matter) that they will never “put them in a nursing home.” While nobody wants that to happen, very often a well-selected assisted-living environment removes the day-to-day caregiving responsibilities from the spouse and, in fact, the patient and the spouse once again begin to enjoy a relationship more suited to partners in life. Pathological behaviors such as paranoia and suspicion and accusation need to be treated quickly as does any impulsivity. These can interfere with any care-giver patient relationship. While neurologists are often comfortable with the routine care of such behavior, it sometimes takes consultation with a psychiatrist experienced in geriatric behavioral illness. These behaviors if left unchecked could result in social disaster quite quickly. Patients need to be asked about these behaviors but partners and spouses are often hesitant to bring up the subject lest they feel they are insulting the patient or betraying a trust.

At times, it turns out that the spouse for a variety of reasons (their own health or mental abilities) is incapable of caring for the patient with PD. A patient who is quite dependent may be abused by a caregiver with their own behavioral issues.

There may be two sick partners in the house and no one present to care for them. In these cases, Adult Protective Services, an agency in the local health or social services department should be called to make an appropriate assessment and consider an intervention.

Early intervention on the social isolation and natural reclusiveness that occurs in more advanced Parkinson's disease is the most important action for preventing some of the crises noted above. We encourage the patients to be active, to maintain usual activities, and to socialize. Even if the patient has a lack of motivation, they are generally quite happy to go along with what their spouse will encourage them to do.

There are important life issues that should be addressed even before anyone reaches this stage in life; that is, estate planning. It is never too early for anyone to plan ahead. Estate planning includes a regular will, a living will which helps to guide your family as to how you wish to be treated if you are unable to speak for yourself, and also a power of attorney which gives your trusted representative the right to act for you if you cannot act. These kinds of documents are easy to prepare. There are self-help sites on the Internet, and most attorneys can also help you with this.

Finally, at some point in life it is recognized that one is at the end of their time in this world. Unless you are one of the few who die a sudden death, you will see the end coming and you will have time to prepare for it and say goodbye to your loved ones. In patients with Parkinson's disease who do not have dementia, chances are death will occur from something else, not related to the Parkinson's disease. In patients who do have dementia, however, they often have difficulties with falls and resultant injuries as well as trouble with swallowing and maintaining nutrition.

Most of us do not worry about dying but, very appropriately, worry about what comes before dying. Fortunately, we have hospices - health care agencies designed to help care for patients in the last months of life. Hospice care is generally covered under all insurance policies including Medicare and Medicaid. The dedicated healthcare workers of hospice provide knowledgeable end-of-life service in your home with quality of life while maintaining dignity as the emphasis.

## The power of clinical research

Your doctors and PD researchers will not rest until we have what you are really looking for: **The cure for PD**. However, no amount of research funding or ideas can make up for a lack of volunteers.

Without people with PD participating in clinical trials to teach us what does and does not work, we will not get there, but with all of you on board, we will succeed. Clinical research refers to the stage of research where new medications are tested in people in real life circumstances. Some clinical trials in PD try to find newer and better medications to address stubborn symptoms such as freezing of gait, dyskinesias, and cognitive decline, to name a few. Others evaluate drugs aimed at slowing or stopping the progression of Parkinson's Disease. In some of these trials, you might be randomly assigned to either the real study drug, or a placebo (inactive) pill. The chance is usually 50/50. The way we look at this is that if you do not participate in a clinical trial, you have a zero chance of getting a new medicine that could potentially work. If you participate in a placebo-controlled trial, you have a 50% of getting the new medication and you help all people with PD on their way to the cure. Clinical research participation is at no cost to the patient.

Ethics committees and the FDA strictly oversee and regulate these trials. Participating puts you in a pro- active position to actively do something about PD and not just let it happen to you. This is perceived as extremely positive by our clinical trial participants.

**You can inquire with a Parkinson's Disease Center of Excellence near you about clinical trial opportunities, or you can call us at the MUSC Movement Disorders Research phone line at :**

**843-792 7262, or check out our website: *<https://muschealth.org/medical-services/neurosciences/movement-disorders>* to learn more.**

**Other helpful web-sites to locate clinical trials are:**

**the FOX Trial Finder <https://foxtrialfinder.michaeljfox.org>**

**and the National Institute of Health website [www.clinicaltrials.gov](http://www.clinicaltrials.gov).**

## A final thought

Live in the present.

Worrying about the future will not change it, but you will succeed in wasting precious time. The best way to live a long, happy life with a chronic illness, is to take very, very good care of it.