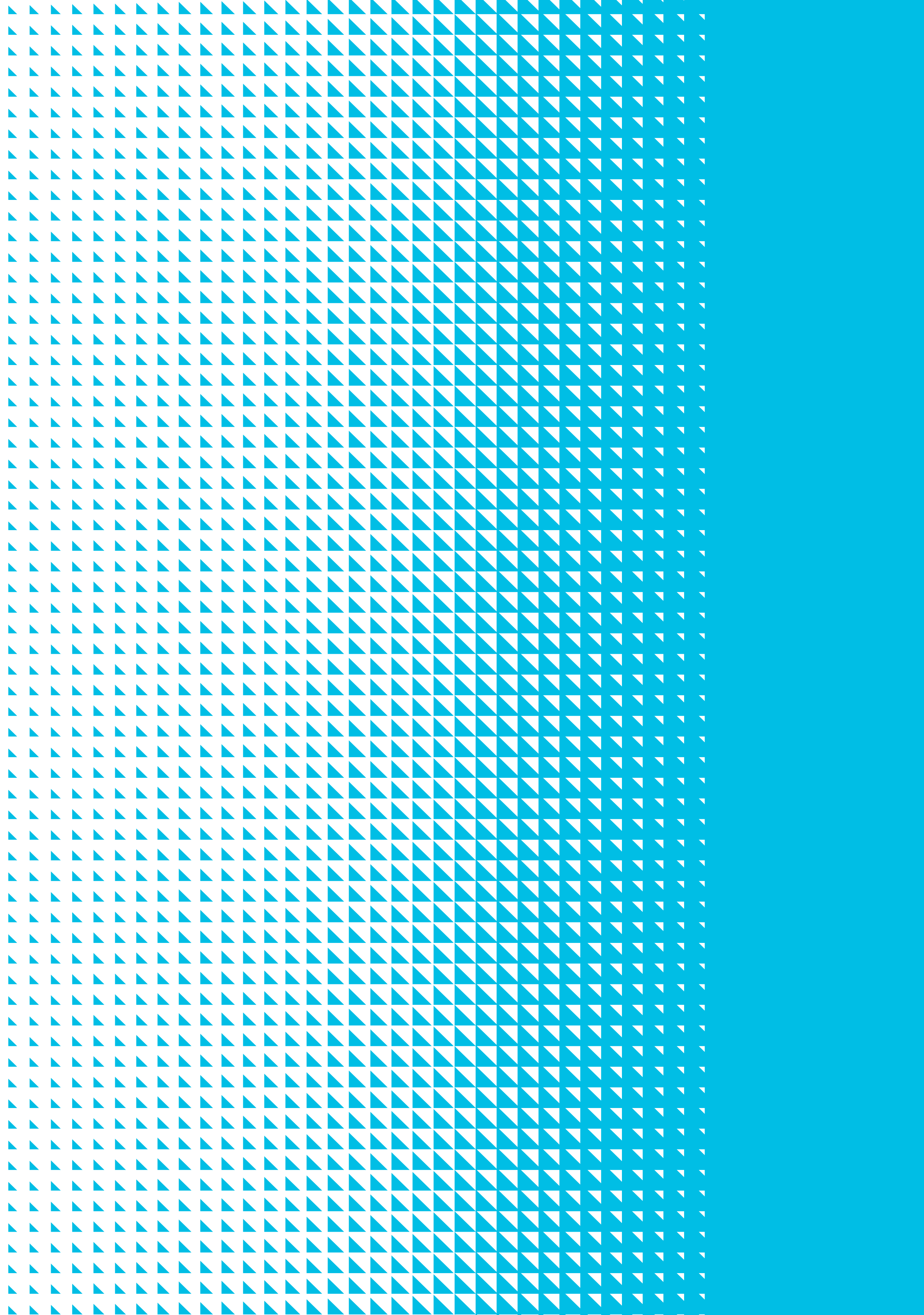
Surgical Options

A Treatment Guide to Parkinson's Disease

Parkinson's Foundation



The aim of this book is to describe surgical treatments that can be used to reduce Parkinson's disease (PD) symptoms in people who may be candidates.

This book will focus on the following therapies:

- **Deep brain stimulation (DBS)**
- **Infusion therapies for advanced PD, including carbidopa/levodopa enteral suspension (Duopa)**
- **Lesion therapy, including focused ultrasound**

ACKNOWLEDGMENTS

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This book has been made possible through generous Parkinson's Foundation donors and a grant from Abbott.

Design: Ultravirgo

This book was designed as a practical guide to explain the complete process recommended for people with Parkinson's and for families considering surgical therapy. The content explores everything from the decision to have surgery to the day of surgery and surgical recovery. While the information contained in this book is intended to facilitate a discussion of surgical options with family, friends and healthcare team members, it is not meant to replace the advice of expert healthcare professionals involved in your care.

GLOSSARY
Definitions for all words underlined with dots can be found in the glossary starting on page 82. A comprehensive Parkinson's disease glossary can be found at Parkinson.org/Glossary.

INDEX
An index of key words and topics can be found on page 86.

PARKINSON'S FOUNDATION RESOURCES
You can find more helpful tips for managing Parkinson's-related symptoms in the books, fact sheets, videos, webinars and podcasts in our PD library at Parkinson.org/Library.

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About Parkinson's Disease

Let's start with some basics about Parkinson's disease (PD).

- Parkinson's disease is a progressive neurodegenerative movement disorder that affects about 1 million people in the U.S. and 10 million people worldwide.
- It is called a movement disorder because of the tremors, slow movements, stiffness, balance issues and muscle cramping that people with PD experience. Collectively, these symptoms are often referred to as "motor symptoms."
- PD can also include non-motor symptoms, such as depression, anxiety, apathy, fatigue, sleep issues, constipation, decreased sense of smell and sexual dysfunction.

PD Symptom Control

During the first several years after a PD diagnosis, medications can provide adequate motor symptom control for most people. As Parkinson's advances, it is common to need ongoing medication adjustments and more frequent carbidopa/levodopa dosing.

Throughout a typical day, you may experience good symptom relief, called "on" time, and periods when symptoms are much more noticeable, or "off" time. This phenomenon, known as "on/off" fluctuations, can occur in both motor and non-motor symptoms.

Around five years after diagnosis, it becomes increasingly common to experience involuntary movements when levodopa levels peak — about an hour after taking each dose. These involuntary movements, called dyskinesia, can happen at other points during a medication cycle, as well.

Optimizing Treatment

There are several strategies to minimize "on/off" fluctuations. Depending on your medications, your doctor may prescribe a higher dose, or recommend taking the same or a smaller dose more frequently. Your doctor might suggest adding or switching to controlled-release levodopa, or adding another medication, like a dopamine agonist, catechol-o-methyl transferase (COMT) inhibitor or a monoamine oxidase-B (MAO-B) inhibitor.

Dyskinesia is often treated by reducing individual doses of levodopa, switching to a different levodopa formulation or adding amantadine.

These strategies are usually effective in minimizing "on/off" fluctuations. When this is not enough, it is important to explore advanced treatment options with your PD specialist.

Read more about "on/off" fluctuations in Appendix A on page 74.

IF YOU ARE CONSIDERING ADVANCED TREATMENT OPTIONS:

Talk with a movement disorder specialist. A movement disorder specialist is a neurologist with specialized training in PD, usually through a two-year fellowship (make sure you ask for credentials). There are also neurologists who have become PD experts through experience and continuing medical education courses.

Discuss your treatment goals with your care team. It's important that your hopes and expectations for a particular treatment match up with what's possible.

Do your homework. Learn all you can about the risks and benefits of the procedure you are considering. Seek out centers with the expertise, technology and resources required to provide specialized, advanced PD treatments.

Consider the future impact on your life. In addition to weighing the risks and benefits of a particular treatment, take into account how your daily routine may be affected. For example, will you need to make frequent follow-up visits after surgery, or will you need to avoid certain activities?

If you are considering deep brain stimulation (DBS), your clinical team should include medically diverse PD experts, such as a movement disorder specialist, neurosurgeon, neuropsychologist, rehab specialists and others. These professionals will evaluate you, meet to discuss your case and work together to coordinate treatment and follow-up care. A collaborative team approach is key to the long-term success of DBS.

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An Overview of DBS

Deep brain stimulation (DBS) is a surgical therapy used to treat Parkinson’s disease (PD).

- During DBS surgery, a special wire, called a lead, is inserted into a specific area of the brain.
- The lead, which has anywhere from four to eight electrode contacts, delivers electrical current to specific brain locations responsible for movement.
- This electrical stimulation regulates the abnormal brain cell activity that causes symptoms such as slowness, stiffness and tremor.

DBS can have a powerful effect on tremor, “on/off” fluctuations and dyskinesia, but is only appropriate for people who meet specific criteria.

> “The last five years before Sam had his brain surgery were very hard. I had to help him with everything and it was emotionally draining. I felt more like a nurse than a wife.
>
> He is like a new man since having the surgery. He can do almost everything for himself now. The surgery gave us both back our independence and our marriage; life is good again. We are truly blessed and grateful.”

Barbara

Symptoms DBS Treats

DBS is not a new therapy. It was first approved by the U.S. Food and Drug Administration (FDA) in 1997 for the treatment of essential tremor and tremor associated with Parkinson's disease. In 2002, DBS approval was expanded to include advanced PD symptoms. Today, DBS is considered a safe and effective treatment for people with Parkinson's who meet specific criteria.

DBS is not a cure. It can be an effective therapy for addressing PD motor symptoms and certain side effects caused by PD medications. DBS may also improve some non-motor symptoms, including sleep, pain and urinary urgency. The impact on mood and energy level is more difficult to predict. For example, these symptoms can worsen after DBS if medication is reduced too much.

As a general rule, symptoms that improve with levodopa therapy will also improve with DBS but in a smoother, more continuous fashion with fewer fluctuations. Tremor is an exception to this rule. Even if tremor fails to improve with levodopa therapy, it often improves with DBS. In contrast, DBS can worsen speech – even if speech improves with levodopa therapy. DBS does not typically address symptoms that do not respond to carbidopa/levodopa such as walking, talking and thinking issues.

DBS can reduce dyskinesia – either directly by stimulating specific parts of the brain, or indirectly, as a result of being able to reduce carbidopa/levodopa dosages after DBS is turned on.

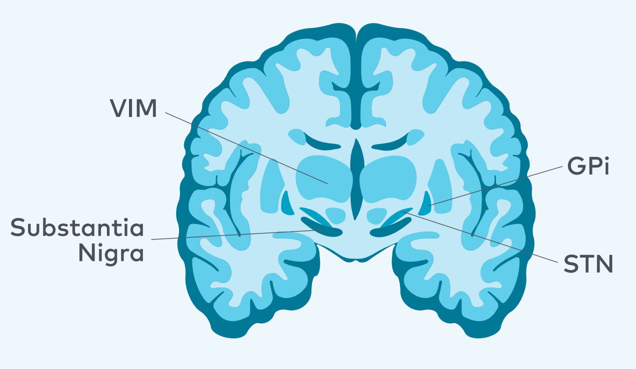
For some people, DBS will lead to more independent lives, while others may need some level of support to complete activities of daily living.

DBS HELPS TREAT THESE MOTOR SYMPTOMS:

- Complete or partial tremor improvement
- Rigidity, or stiffness
- Bradykinesia, or slowness of movement
- Dystonia — persistent muscle contraction causing repetitive, twisting movements and abnormal body positions

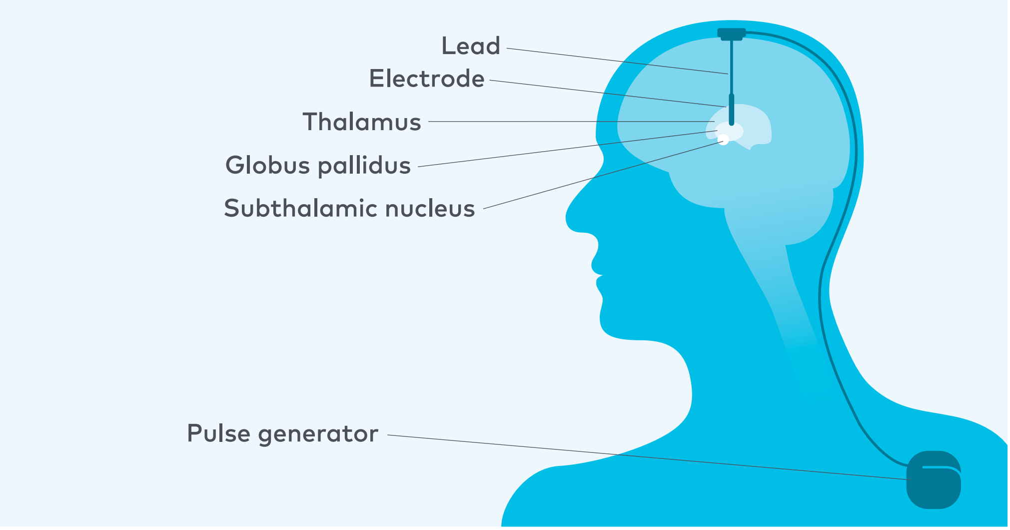
The Science Behind DBS

There is an area deep in the brain called the substantia nigra pars compacta (SNc) where there are more than 400,000 dopamine-producing brain cells. In Parkinson's, these brain cells can become injured and slowly die over time. This process reduces the natural production of dopamine, which, in turn, results in the development of PD symptoms. PD also impacts other regions of the brain. The SNc is of particular interest because it indirectly connects to two key areas of the brain that control both motor and non-motor functions: the globus pallidus internus (GPi) and the subthalamic nucleus (STN). These brain areas send signals that affect arm, leg and neck movements as well as other functions, including thinking and mood. Placing DBS leads (wires with tiny electrodes) in either the GPi or the STN changes the electrical signals in these areas. In most cases, this results in smoother, more fluid movement.



The ventral intermediate nucleus (VIM) area of the thalamus is another DBS target. The following table summarizes the therapeutic effects of each site:

DBS SITE	EFFECT OF THERAPY
Globus pallidus (GPi)	Reduces tremor, rigidity, bradykinesia, dyskinesia (direct effect); improves "on/off" fluctuations
Subthalamic nucleus (STN)	Reduces tremor, rigidity, bradykinesia, dyskinesia (indirectly through medication reduction); improves "on/off" fluctuations
Ventral intermediate nucleus (VIM)	Reduces tremor but usually not other PD symptoms



Leads may be placed on one side of the brain (unilaterally) or on both sides (bilaterally). Once the lead is placed, it is attached to an extension wire that runs under the scalp and just beneath the skin of the neck. It is then connected to an implantable pulse generator (IPG), also called a neurostimulator.

The neurostimulator is typically inserted just below the collarbone and under the skin on one side of the chest, though occasionally can be implanted in other areas like the abdomen. Similar to a pacemaker, the neurostimulator sends electrical impulses to the lead implanted in the brain. Most neurostimulators can be connected to two or more leads. A neurostimulator can be adjusted or turned on and off wirelessly by a patient controller device. The clinician can use a more advanced DBS programmer to adjust the DBS settings to one of millions of combinations to achieve the best possible symptom improvement.

Once the DBS system is turned on, the electricity the lead creates will work to normalize signals in affected areas of the brain. In some cases, stimulation can worsen balance, speech and cognition. If this happens, the programmer will use different strategies to try to reduce or eliminate these temporary side effects.

DBS Devices

The Basics

There are several companies that make DBS systems. Each DBS system has the same basic components: a DBS lead, an implantable pulse generator (IPG), or neurostimulator, and an extension cable.

The Lead

The DBS lead is a thin wire, just over a millimeter in diameter, that is inserted into the brain.

- Leads are currently available with four to eight electrode contacts with different configurations, depending on the company.
- All companies now offer directional leads with electrodes that are divided into segments, allowing the clinician to direct stimulation towards areas of the brain that may result in increased symptom relief or decreased side effects.

The Neurostimulator

The neurostimulator contains the battery and serves as the "brain" of the device. It is programmed and stores the settings the clinician chooses for stimulation.

- The neurostimulator is typically placed in the chest, in a position similar to a cardiac pacemaker. When necessary, it can also be implanted in other locations such as the abdomen.
- Different manufacturers make rechargeable and non-rechargeable batteries for their neurostimulators. Rechargeable batteries must be periodically charged wirelessly above the skin. Non-rechargeable batteries do not require upkeep but need to be replaced more frequently.
- Changing the neurostimulator is a far more minor procedure than the initial DBS surgery. It can often be carried out with the use of local anesthesia rather than sedation (being put to sleep) with general anesthesia. Neurostimulator batteries can be swapped out for rechargeable or non-rechargeable batteries at the time of replacement.

Extension Cable

The extension cable/wire connects the DBS lead to the neurostimulator.

- The extension cable is flexible, and the surgeon typically leaves a little bit of excess cable between the neurostimulator and the DBS lead to ensure that the wires do not disconnect or unplug during normal head movements.

Other Device Features

Additional features, depending on the type of DBS device, include new ways to provide stimulation, such as the ability to stimulate electrode contacts individually with a specific amount of electricity. This allows the clinician to create an individualized DBS setting that can shape the size of the stimulated area based on your clinical needs.

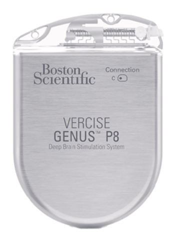
Other new technology can monitor and record brain signals. This feature provides clinicians with feedback that might eventually help them match brain signals with specific symptoms and side effects, such as tremor, slowness of movements and dyskinesia.

Lastly, remote DBS programming is now an option for people with certain DBS devices and will become increasingly available in the coming years. Remote programming enables people to communicate with their clinician using a smartphone, tablet or computer via the internet (telehealth), and receive programming adjustments without needing to go to the clinic or hospital.

Patient Controller

The last part of the system, the patient controller, is not implanted into the body. All three manufacturers provide patient controller options that allow the individual to turn the neurostimulator on and off and to check battery status. They also allow the individual to make some adjustments specified by the clinician.

THE CURRENTLY AVAILABLE NEUROSTIMULATORS (IPGS) ARE BELOW:

IPG MODEL	LEAD TYPES	BATTERY TYPE
ABBOTT INFINITY		
Sizes 5 and 7  Image courtesy of Abbott	Directional	Non-rechargeable
BOSTON SCIENTIFIC VERCISE		
Genus  Image courtesy of Boston Scientific	Directional and Non-directional	Rechargeable and Non-rechargeable
MEDTRONIC		
Percept PC  Image courtesy of Medtronic, Inc.	Directional and Non-directional	Non-rechargeable
Activa SC  Image courtesy of Medtronic, Inc.	1 lead (2 IPGs needed for bilateral stimulation) Non-directional	Non-rechargeable
Activa RC  Image courtesy of Medtronic, Inc.	Non-directional	Rechargeable

BATTERY LIFE*	PATIENT CONTROLLER	UNIQUE FEATURES
4-7 years	App compatible with Apple mobile devices or iPod Touch	Remote (telehealth) adjustment with the internet
Minimum of 15 years 3-5 years (respectively)	Remote connects via Bluetooth to IPG	Able to stimulate different contacts individually with a certain amount of electricity (current). Remote support allows clinicians to receive programming support.
Up to 5 years (Use of brain signal recording feature affects battery life)	Samsung handheld with receiver	Can record brain signals
3-5 years	Standard remote	
Up to 15 years	Standard remote	

**Actual battery life can vary significantly from estimates depending on the stimulation settings required for a given person.*

Q Is DBS neuroprotective?

A While DBS doesn't directly protect cells against damage, it can help people continue functioning and exercising. Growing evidence shows exercise eases Parkinson's symptoms and offers neuroprotective benefits.

Q Is it better to have DBS on one side of the brain or both sides?

A Because Parkinson's typically affects both sides of the body within several years after diagnosis, DBS surgery often involves implantation of two leads to target both sides. Unilateral (one-sided) DBS, which mainly helps symptoms on the opposite side of the body, is considered when symptoms dramatically affect one side, or when surgical risk is high.

Experts may also postpone treating a second location due to someone's overall health or to reassess whether further action is needed. A second DBS lead may be associated with adverse or negative events, such as walking, talking and thinking issues.

Q How long do the benefits of DBS last?

A In most cases DBS benefits – including effectiveness against tremor, motor fluctuations and dyskinesia – last many years. If PD symptoms still respond to levodopa and other dopaminergic medication, DBS will generally continue to work.

DBS settings are typically changed the most during the first year of therapy. Postoperative programming visits are most frequent during the first six months following implantation. Once the programmer determines the best settings, most changes will be made to medications, though occasional neurostimulator adjustments may occur.

Q Will I be able to stop taking my PD medications after I have DBS?

A DBS is not a substitute for medication and does not stop PD progression. It helps to control symptoms.

Once programming has maximized benefits, your PD doctor might gradually lower medication doses. Most people need to continue taking medications, but many – especially those who have subthalamic nucleus (STN) DBS – might be able to decrease their total daily dose by 30-50% and/or take medications less frequently throughout the day.

People with globus pallidus (GPi) DBS, which can reduce dyskinesia, may not be able to significantly reduce medications, but can often increase medication as PD progresses.

Exercise continues to be key for motor symptom management, as do support therapies for symptoms not treated by DBS, such as speech, cognition or balance issues.

Q How do I know if I am a good candidate for DBS?

A It's important to talk with a movement disorder specialist (a neurologist with specialized PD training) to decide if DBS is the right choice for you.

A movement disorder specialist – the best resource for confirming you have PD prior to surgery – may recommend medication adjustments and therapy before exploring DBS. DBS could be harmful when applied to other conditions that mimic PD, such as vascular parkinsonism, dementia with Lewy bodies, progressive supranuclear palsy, multiple system atrophy and corticobasal syndrome.

The best candidates for DBS therapy will have most of the following:

☐ A PD type that responds to levodopa (though it may not be as effective as earlier in the course of PD)

☐ "On/off" fluctuations, with or without dyskinesia

☐ Tremor that does not adequately respond to medications

☐ A history of trying different combinations of carbidopa/levodopa and dopamine agonists under supervision of a movement disorder specialist

☐ A history of trying other PD medications – such as entacapone, tolcapone, selegiline, apomorphine, amantadine or "rescue" medications – without beneficial results

☐ PD symptoms that interfere with daily activities

☐ Motivation to follow through with the different stages of DBS

DBS is generally not a good choice for people with Parkinson's who have:

☐ Significant symptoms related to balance, walking or freezing that are not helped by PD medication

☐ Speech trouble as a main symptom

☐ Confusion, disorientation or daily memory and thinking difficulty

☐ Depression, anxiety or other psychiatric symptoms that don't improve or stabilize with proper therapy, such as medication and counseling

☐ A questionable PD diagnosis. DBS is not recommended in cases of atypical Parkinson's.

Note: Even if positive, a dopamine transporter scan (DaTscan) can not provide a definitive PD diagnosis.

☐ Another serious health condition, such as severe heart or lung disease, making neurosurgery dangerous

Q When should I get DBS?

A The right time varies from person to person. If you have motor fluctuations or dyskinesia that do not improve with medication adjustments and negatively impact your quality of life, it's generally a good idea to start exploring surgical options.

Though you don't have to wait a specific amount of time, it can take several years or longer to determine whether your PD symptoms respond to levodopa – a determining factor in DBS success – or to rule out atypical Parkinson's.

Q What if DBS doesn't work?

A Though DBS failure is possible, most reasons are preventable – including lead placement issues or hardware malfunction, as well as programming, medication management or disease progression problems. DBS can also fail if someone is not a good candidate.

If you have not improved within six months of DBS surgery, ask your doctor if you need a complete workup to discover the cause of failure and whether it can be fixed.

Q Are there activities I should avoid following DBS therapy?

A You can generally resume normal daily activities within a few months of DBS surgery. Always ask your neurologist for instructions specific to your device. Try to avoid massaging and excessively touching components implanted in the neck and chest. Also avoid activities that put you at a high risk for falls – such as climbing or reaching for objects above shoulder level. This can damage or dislodge hardware, requiring further surgery. Though swimming is generally OK, never swim alone, as people have drowned after having DBS.

Q Can I exercise after having DBS?

A Like medication, exercise should be considered a vital part of PD treatment. It is important to return to regular exercise after waiting four to six weeks following DBS surgery. Avoid contact sports or exercise that may dislodge the neurostimulator or the connecting wire.

Q How long will the battery last? What should I do when it stops working?

A Non-chargeable batteries can last between three and five years, while some rechargeable batteries can last 15 years but require daily or weekly charging. Each device has a specific battery level when replacement is recommended. Your DBS programmer should check battery life at every visit and tell you when the neurostimulator needs to be replaced – an outpatient procedure. You can also monitor the battery level with your handheld device.

Note: If battery power runs out, your symptoms will likely worsen. More medication than usual may be needed until the neurostimulator is replaced.

Q Can the DBS stop working suddenly after several months or years?

A Yes, the DBS system can stop, usually if battery power runs out or device hardware malfunctions – for example, a break occurs in the connecting wire in the neck or scalp.

If your PD symptoms suddenly worsen, there may be a problem with the DBS system. Contact your neurologist immediately.

Q Can I have the DBS system removed?

A Yes, you can have the leads and neurostimulator taken out. DBS wires may be left in place if they are not causing problems, as removal involves added surgical risk.

With DBS you can try any new Food and Drug Administration-approved treatment for PD symptoms. However, most clinical trials exploring the safety and effectiveness of new therapies exclude people who have had DBS or other neurosurgery.

Q Will my insurance cover DBS costs?

A DBS surgery and hardware can be costly. Because DBS is approved by the FDA for the treatment of PD, Medicare, Medicaid and most private U.S. insurance carriers generally cover most of the operation costs. Your personal insurance policy will have a DBS coverage section. Ask your DBS center if you can also meet with a financial counselor to know what to expect.

Q Will my neurostimulator activate the metal detector at the airport?

A It may possibly set off the alarm, but security equipment rarely turns the neurostimulator off. Most airports make special accommodations for people with medical devices and allow them to go around the metal detector. Consider bringing your Parkinson's Foundation Aware in Care Kit when traveling. It contains tools to keep you safe when you travel or go to the hospital. Also carry the card provided by the DBS manufacturer explaining the neurostimulator and how the detector may affect it. Share this information with security personnel.

Q Will I feel the electricity when the neurostimulator is turned on?

A Most people with DBS report feeling a brief tingling sensation, nausea or dizziness for a few seconds after the device is turned on. You may temporarily feel a more intense electric sensation while the stimulator is being programmed.

HALYARD

3

DBS Risks, Complications, Special Information and Warnings

Deep brain stimulation (DBS) involves making small holes in the skull and surgically implanting a lead (small wire) into the tissue on one or both sides of the brain in order to provide electrical stimulation through electrodes. Another surgery is required to implant the neurostimulator with the battery under the skin of the chest.

As with any surgery, there is the risk of complications with DBS. These complications can be serious and permanent or temporary and reversible. Ask your DBS team to explain the risks.

Serious or Permanent Complications

The risk of serious or permanent complications from DBS therapy is very low.

Stroke

There is a small risk of stroke from bleeding in the brain during surgery (1-3%). People with a history of bleeding problems will have a higher risk for a stroke during DBS surgery.

Serious Complications and Risk of Death

Serious complications and death are rare. Most complications are temporary, although some people may experience lasting effects from stroke, such as weakness, numbness, problems with vision or slurred speech.

Temporary or Reversible Complications

Temporary or reversible complications may result from the surgery or electrical stimulation and include the following:

Changes in Mood, Memory and Thinking

DBS can worsen memory and thinking and may cause anxiety, depression, apathy, confusion, hallucinations or an overly excited state. These psychiatric symptoms usually get better within days or weeks of the surgery and typically disappear completely. If these symptoms persist, medication or stimulation adjustments can improve or resolve them.

Suicidal thoughts and suicide are rare. These types of neurobehavioral symptoms may also occur when medications are reduced too much after DBS.

People with known cognitive or psychiatric problems, such as dementia or severe depression, are at a much greater risk for these complications, and they typically do not qualify for DBS therapy.

Seizures

Some people who undergo DBS will have a surgery-related seizure during or within the first week after surgery. These will usually go away. Continuing seizures are more likely related to a stroke, brain infection or irritation from the DBS lead. In these cases, seizure medications may be prescribed.

Infection

Antibiotics are administered during surgery to minimize the chance of infection at the brain, scalp or chest surgery sites. If a serious infection does develop, the lead, connecting wire and/or neurostimulator may need to be removed.

Other Complications

Dyskinesia, temporary movement worsening, balance problems and slurred speech can follow surgery. Expert DBS programmings can sometimes improve these symptoms. In other cases, they are permanent.

When headache, dizziness, face or limb tingling or electric shock-like sensations occur, it may be helpful to turn off the stimulator using the patient controller. Though adjusting the stimulator settings may improve these problems, medication adjustments may also be needed.

Even with the best equipment, skills and highly trained DBS center experts, there is always the possibility that the lead may not be placed in the best location in the brain. A second surgery may be needed to adjust placement or correct a faulty device.

Malfunctioning DBS Components

Problems can occur, including:

- Lead movement, or migration away from the target site
- Connecting wire breakage, disconnection or damage
- Neurostimulator malfunction or damage

Touching or rubbing DBS system implants can damage the system or skin, sometimes requiring surgery.

Other Risks of Surgery

There can be pain, inflammation or swelling at the surgery sites, as well as a very small risk of swelling or an allergic response to the implanted materials.


ALL RISK

4

Before, During and After DBS Surgery

If you decide to pursue deep brain stimulation (DBS), the next step will be to plan and prepare for your surgery and recovery. Select a center that has a staff of experts who specialize in DBS therapy for the treatment of Parkinson's disease.

For assistance finding a DBS center near you, call the Parkinson's Foundation Helpline at 1-800-4PD-INFO (473-4636).

Having a strong support network of family and friends throughout your DBS journey will also help you to get the care and resources you need.

ONCE YOU HAVE CHOSEN OR BEEN REFERRED TO A DBS CENTER

- Plan to bring a family member or friend with you to your appointments.
- Make sure you meet with all the members of your DBS care team (movement disorder specialist, neurosurgeon, neuropsychologist, nurses, etc.). In many cases, a physical therapist, occupational therapist and speech language pathologist will be necessary members of your team. Some centers also include social workers, dieticians and financial counselors in their DBS team.
- Be prepared to ask questions about DBS, and make sure they are answered to your satisfaction before the procedure takes place. Ask the staff if there are other patients who have had the surgery that you can speak to about their experiences. Talking to more than one person can give you a more balanced view.

> “My doctor recommended DBS to me for two years before I decided to go to a DBS center for an evaluation. I would tell someone who thinks they might need DBS to go to a good center and get a lot of information about it.”

José

The following are suggested questions for your DBS team. Bring this booklet with you to your pre-appointments and write down answers to each question as you ask them, using the space provided below.

What level of experience does the center have with performing DBS? Does the center perform regular DBS surgeries?
Large, well-established DBS centers perform multiple surgeries each month, which can lower the risk of adverse events (unwanted and unexpected medical events resulting from the surgery).

How does your care team work together to ensure the best care for you?
Your care team should communicate with each other to determine and coordinate your treatment and follow-up care. A team approach is key to the success of DBS surgery.

Do I need DBS surgery on both sides of the brain? If so, how much time can I expect between each surgery?
It is common to need stimulation on both sides of the brain. In some cases, only a single side is needed. Typically, when this is the case, each lead will be implanted in separate surgeries that are separated by weeks or months – sometimes even years.

Will my DBS team implant the neurostimulator in my chest at the same time the lead is implanted, or will that be done later?

Some centers require that you have the neurostimulator implanted under the chest wall several days or several weeks after the lead is placed, while most centers will place the neurostimulator on the same day as the brain lead(s).

Who will program my DBS system and adjust my PD medications after the surgery?
For the first several months, it is best to return to the center where the surgery was performed for programming and adjustments. In many cases, monthly visits are necessary to adjust stimulation settings, medications and monitor for mood and thinking changes. When the programming is working, and frequent adjustments aren't needed, most people can return to their regular neurologist for care.

After surgery, how long will it be before I am able to go home?
Most patients are hospitalized for one night following implantation of the brain leads. Confusion or other concerns could delay your discharge.

Will I be awake or asleep for the procedure?
Different centers use different techniques. Ask your DBS team about their approach.

Pre-surgery Tests and Evaluations

There are several important evaluations that all centers should perform prior to surgery. Some of the evaluations are specific to DBS, while others are standard tests prior to any type of surgery.

A Baseline Evaluation

Several visits to the DBS center may be required. The movement disorder specialist should perform a baseline Unified Parkinson's Disease Rating Scale (UPDRS) when you are on medications and again when you are off. This helps your neurologist evaluate which symptoms DBS is likely to improve.

Memory and Thinking Tests

You will also have a series of memory and thinking tests, called a neuropsychological battery, to make sure that you do not have confusion, memory issues, untreated mood problems or depression. These tests should be carried out by a neuropsychologist who has experience with PD. You may also be required to see a psychiatrist for treatment of depression, anxiety or other psychiatric conditions.

Support Network Assessment

A social worker may complete an assessment of your network of family and friends to make sure that there is someone to help you before and after surgery. It is very important that that you have a care partner or someone with you full-time after the surgery.

Preparing for the Surgery

As the day of surgery approaches, it is normal to be nervous or anxious, as well as excited. After the approval process is finalized some people find themselves especially worried or scared about the actual event. This is normal and expected. Talking to other people who have had the surgery may help. Being organized, planning ahead and knowing what to expect will also help prepare you for the surgery. Asking a friend or family member to be with you before, during and after the surgery can be reassuring.

Here is a checklist to help you stay organized and prepare for DBS:

A Few Weeks Before Surgery

☐ **Make sure you know where to go the day of surgery.** Write down the address, phone numbers and parking instructions for the center. You may wish to practice a rehearsal trip.

☐ **If traveling from out of town, make arrangements to arrive a day early and stay near the hospital.** Check with the DBS center for lodging recommendations and any available discounts.

☐ **Confirm when to take your PD medication with the DBS staff.** Most doctors will give you instructions to take your last dose of PD medication the night before the surgery and to not take PD medication the day of your surgery.

Packing List for the Hospital Stay

Bring the following items:

☐ All medicines, along with a list of the exact medication names, dosages and times taken. Pack at least a week's worth of medication in the original, labeled bottles.

☐ List of names and phone numbers of people to contact in case of an emergency.

☐ Aware in Care kit. If you need to order your hospital kit, visit Parkinson.org/AwareinCare or call the Helpline at 1-800-4PD-INFO (473-4636).

The Night Before Surgery

Get a good night's sleep and follow the instructions you received from the DBS staff for the night before surgery. These will include not eating or drinking after midnight.

The Surgery

There may be differences in what people experience during the surgery process from one center to the next. There is no single "correct" or standard way for the surgery to be performed. DBS procedures vary throughout the world. Some centers utilize a robot. Some procedures are performed awake while others are performed asleep. A headframe may or may not be used. The best technique is the one your team is comfortable with and has experience doing.

Prior to the surgery, high-resolution imaging is typically completed to help with precisely identifying the target and the path the wire will take to get to the area in the brain that will be stimulated. This often requires the use of screws or a "frame" fastened to your skull under local anesthesia. While it is necessary to shave a portion of the head for the surgery, the amount of hair removed can be minimized, and if this is a concern, it should be discussed with the neurosurgeon prior to going for surgery.

Surgical Methods

Traditional Microelectrode Recording vs. MRI- or CT-Guided DBS

There are two approaches your neurosurgeon can use to place your DBS lead(s):

- **Microelectrode recording (MER-guided):** In this method, the surgeon plans the surgery using MRI or CT scans but then verifies that the lead is in the right place by listening to signals from your brain cells using microelectrode recording.
- **MRI or CT scans in the operating room (imaging-guided):** In this technique, the surgeon plans the surgery using MRI or CT scans but then also uses a scanner during the surgery to watch the progress of the placement of the lead into the brain, making sure that the lead is correctly placed within the original target region. This method can be completed with the patient asleep (under anesthesia).

The surgery itself may be done with the initial portion awake, utilizing anesthesia only when needed to control pain and anxiety. In addition, learning relaxation techniques like meditation, mindful breathing or listening to music can help create a calm experience and may reduce your anxiety prior to and during surgery.

The surgery may be completed under full sedation (asleep) with various forms of anesthesia.

The neurostimulator is placed either at the time of the first surgery or several weeks later. The recovery period after the brain surgery is usually overnight to monitor for any signs of bleeding, confusion or stroke. When the neurostimulator is not placed the same day as the lead placement, it is typically done as an outpatient or same-day surgery.

Since the stimulator is normally not turned on until it can be rigorously tested and programmed, it is important to take your PD medication as instructed before and after the surgery. In most cases, PD medication is held the night before surgery. Check with your surgeon if your medication schedule will be changed on the day of surgery.

Although PD symptoms may temporarily lessen (called a honeymoon effect) before the stimulator has actually been turned on, this is usually due to the surgery itself or the swelling resulting from the surgery. These benefits usually last several hours to several weeks. The neurostimular is typically turned on and programmed once these effects have faded.

Care After Surgery

At the end of your hospital stay, the DBS staff will provide you with home care discharge instructions. These provide detailed information about how to care for your incisions (surgical cuts), follow-up appointment dates and PD medication dosing information. These instructions should also include phone numbers to call in case of emergency.

You will be issued a patient controller or download a software application on your mobile device that will allow you to turn the DBS system on and off and monitor your device's battery power. You will also receive a charger If your device battery is rechargeable.

Sometimes these items are given upon discharge from the hospital, but may also be provided at a follow-up visit. Once you receive these devices, be sure that you understand how to properly use them.

You will also receive a wallet-size card in the mail that includes information about the DBS device, as well as your doctor's name and phone number. Carry these items with you when traveling or for doctor's appointments. Keeping them in your Aware in Care kit when they are not in use is a good way to remember to take them with you to your next doctor's appointment.

You can expect to schedule follow up appointments for the removal of sutures (stitches) or staples, the placement of the neurostimulator, if it has not been implanted at the time of the brain surgery, and for your first neurostimulator programming session.

It's important to watch for signs of infection, changes in mood, stroke-like symptoms or seizures.

Complications can develop during the first few weeks or even months after surgery.

For more guidelines around avoiding post-surgical infections, be sure to review Appendix B: Avoiding Infection After Surgery on page 77.

Mood Changes

Tell your doctor immediately if you feel depressed, anxious or experience other mood changes. There are reports of people who become severely depressed or suicidal after DBS. If you have suicidal thoughts, tell a friend or family member. Have someone take you to the nearest emergency room or call 911. DBS-related depression symptoms are likely reversible with appropriate treatment and can include:

- ☐ Feeling sad, irritable, anxious or panicked, or episodes of tearfulness or crying
- ☐ Not feeling like doing your normal daily activities
- ☐ Wanting to be alone, or thinking and talking negatively
- ☐ Sudden sleeping habit changes – sleeping too much or not enough
- ☐ Appetite changes and weight gain or loss
- ☐ Extreme loss of energy, tiredness or fatigue

DBS usually improves impulse control issues – such as inappropriate shopping, gambling, eating or sexual behaviors – when medications are reduced. Improvement of dopamine dysregulation syndrome (craving dopaminergic pills) is harder to predict. Contact your doctor immediately if you notice worsening behavioral side effects, including irritability and apathy.

Stroke-like Symptoms

Seek medical attention immediately if you experience signs and symptoms of a stroke or brain bleed, including:

☐ Sudden severe headache, nausea and vomiting

☐ Sudden confusion, thinking and memory problems, or difficulty talking

☐ Numbness and weakness on one side of the body

☐ Worsening balance or falling to one side

☐ Loss of vision

A brain scan can uncover bleeding or a stroke and can check DBS lead placement.

Seizure

Brain cells irritated by head trauma, infection, blood or even DBS lead placement can cause seizures. While rare, seizures from DBS therapy usually occur during surgery or the following 24 hours and can include uncontrolled jerking, unconsciousness, numbness or sudden confusion.

If you suspect you have had a seizure, seek immediate medical care. Your doctor may prescribe anti-seizure medications. Seizures usually will not happen again.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FH 29 head

5

DBS Programming

During the programming process, the clinician will use a DBS programmer to adjust the system, testing different stimulation locations and settings. The goal is to map out locations and stimulation settings that provide the best symptom control with the fewest side effects. In addition to location, there are ways to change the intensity and characteristics of the electrical field that can affect how stimulation is felt.

Programming of the neurostimulator system usually happens in the clinic or doctor's office several weeks after the DBS surgery to allow time for brain swelling to go down around the DBS lead. Sometimes the system is turned on and programmed before leaving the hospital. Depending on the DBS device, virtual or telehealth visits over the internet may also be an option for communicating and receiving programming adjustments.

DURING THE INITIAL PROGRAMMING PROCESS THE CLINICIAN WILL:

- Examine you and ask you questions about how you are feeling.
- Look for improvements in your tremor, rigidity (stiffness), bradykinesia (slowness), dyskinesia (uncontrolled, involuntary movements) and dystonia (sustained muscle contractions).
- Check for stimulation side effects such as numbness, tingling, spots in your vision, muscle cramping or pulling, electrical shock-like sensations, and possibly a worsening of PD symptoms.

> “I can move my right side much better than before having DBS and I am taking less medicine now. I did have some trouble with tingling on the right side of my face, and with slurred speech, so they had to change the settings a couple of times. After a few programming sessions, the numbness and speech were better.”

Mike

MEDICATIONS DURING AND AFTER DBS PROGRAMMING

You will likely need to continue taking Parkinson's medications after DBS surgery, although possibly smaller or less frequent doses. Ask if you should take your usual medication before a programming appointment. Symptoms are more obvious when you are 12 or more hours off your medication, and programming is often more successful. Always bring your PD medications to a programming session is case you are asked to take them during or after the session.

Some PD symptoms might improve immediately, especially tremor. Others may take hours or days to respond. Similarly, some stimulation side effects such as tingling may be immediate. Others show up after a medication dose or develop days later.

Stimulation side effects commonly go away as your brain adjusts.

Finding the best settings takes time: there are multiple setting combinations and people respond to stimulation differently. Many centers ask you to return periodically for the first six months to continue improving programming. You may also go to a rehabilitation facility for closer evaluation of how you respond to DBS programming and medication adjustments.

Higher settings aren't necessarily better. They can result in side effects, such as tingling or slurred speech. Each person requires a unique combination of low and high settings for best symptom control. Appreciating the benefits or noticing side effects from a particular DBS setting may take several days to a few weeks.

You will be advised to NOT turn off your DBS system once the ideal settings are determined. If the device is turned off for some reason, you can use your patient controller device to turn it back on.

After your initial programming appointment, you will be asked to return for routine follow-up appointments. Your follow-up schedule will vary according to your condition and your neurologist's recommendations.

Battery Information

Depending on the settings, the battery life of a non-rechargeable neurostimulator should last from three to five years. Be aware that your PD motor symptoms may worsen when the battery is running low. As the battery life of the neurostimulator nears its end, your neurologist or neurosurgeon will want to schedule you to have it replaced. This is a simple outpatient procedure in which an incision is made to open the area in which the neurostimulator is implanted, the DBS extensions are unplugged and a new neurostimulator is implanted and connected.

It is very important that the programmer check the battery life at each programming session and prepare a plan for replacement. The DBS battery may need to be replaced prior to the estimated timeframe, or it may last several months beyond the estimated timeframe. Unlike non-rechargeable batteries, rechargeable batteries have a fixed life of approximately 10-15 years, depending on the manufacturer.

ADDITIONAL DBS INFORMATION

After your surgery, your DBS team should provide you with a patient controller. All DBS manufacturers provide articles and downloadable guides about their devices for your review.

- Abbott: Neuromodulation.abbott.com
- Boston Scientific: DBSandMe.com
- Medtronic: Medtronic.com/DBS

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Infusion Therapy for Advanced PD

Carbidopa/levodopa (Sinemet) is the gold standard in Parkinson's disease (PD) treatment, however, as the brain continues to change, it can become less effective. Short dose durations and side effects are two of the main challenges. In addition, slow stomach emptying (common in PD) can delay medication delivery and absorption, which may result in unpredictable or reduced symptom relief.

When these issues occur, complex medication strategies are often needed to improve symptom relief, stabilize "on/off" fluctuations and minimize side effects. If these approaches are not successful, infusion therapy may be the next step for some people.

Infusion therapies bypass the stomach since they are delivered either through a needle inserted under the skin or a gastric tube into the small intestine. Unlike oral medication taken in separate doses, infusion therapies deliver medication slowly and continuously throughout the day.

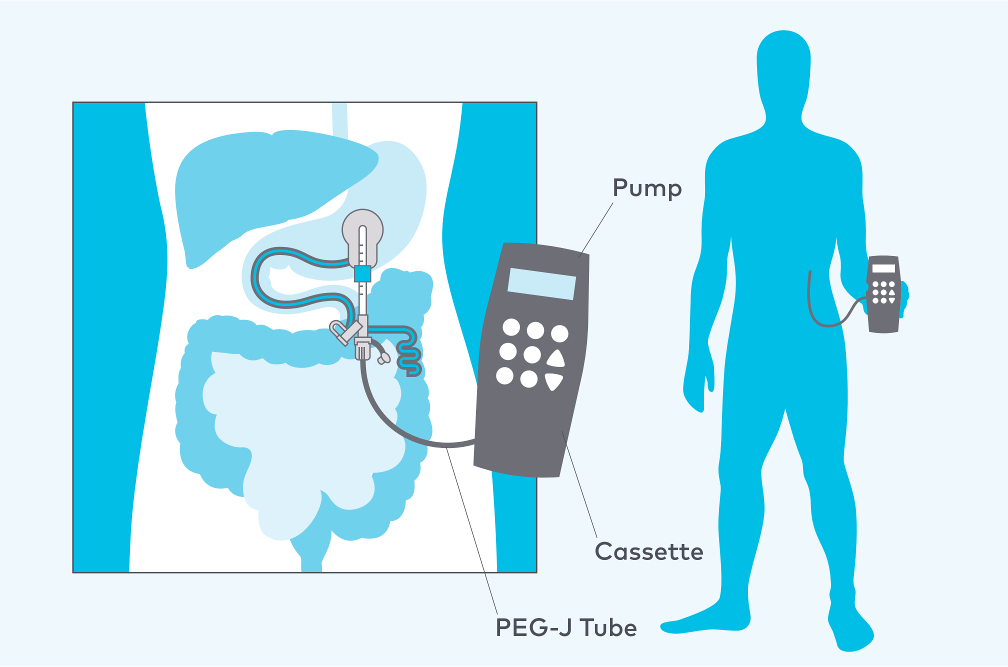
Levodopa and apomorphine (a dopamine agonist) are the main drugs used in continuous infusion therapy for Parkinson's disease. There are two continuous subcutaneous therapies (given through a small needle under the skin) currently being investigated. Of the two, continuous subcutaneous apomorphine is not available in the United States and continuous subcutaneous levodopa is in clinical trials.

The only FDA-approved infusion therapy in the U.S. for advanced PD is carbidopa/levodopa enteral suspension, also referred to by the brand name Duopa or Duodopa outside the U.S.

About Carbidopa/Levodopa Enteral Suspension (Duopa)

Carbidopa/levodopa enteral suspension (Duopa) was approved in 2015 by the U.S. Food and Drug Administration (FDA) for motor fluctuations in advanced PD. Like other forms of carbidopa/levodopa, Duopa temporarily restores dopamine, a neurotransmitter (or chemical messenger) that plays an essential role in our ability to move normally. The levodopa in Duopa converts into dopamine in the brain, which helps reduce motor symptoms, such as bradykinesia (slowness), rigidity (stiffness) and tremor. Carbidopa, combined with levodopa, helps lessen potential side effects, particularly, nausea and vomiting.

Duopa for the most part replaces carbidopa/levodopa in pill form. For this reason, it can be a good choice for people with swallowing issues or who have trouble managing their medication schedule.



Duopa is delivered directly to the small intestine rather than going through the stomach, which makes the absorption of carbidopa/levodopa smoother. This can cut down on "on/off" fluctuations and dyskinesia.

Before starting Duopa, a surgeon or a GI (gastrointestinal) doctor will make a small hole (called a "stoma") in your stomach wall to place a gastrostomy tube. A smaller tube is then fed through this tube so that the medication can flow directly into the small intestine. This system of tubes is called a percutaneous endoscopic gastrostomy with jejunal tube, or PEG-J tube.

The carbidopa/levodopa gel is contained in a small cassette, which is connected to a pump. The pump can be placed in a pouch the size of a small fanny pack and can be worn while doing everyday activities.

> "I have been using Duopa for a year now. For me, it delivers a consistent flow for 16 hours a day. I have had tube migration issues that have been annoyances, but not dangerous. I was reluctant for a year or so before I said yes. Now, I have predictable "on" time so we can plan ahead."

Dianne

Q Am I a good candidate for Duopa therapy?

A You might be a good candidate for Duopa therapy if you:

☐ Have symptoms that respond to carbidopa/levodopa – even if only for short periods throughout the day.

☐ Experience daily motor fluctuations (changes in your ability to move) with three or more hours of "off" time.

☐ Have tried and failed to control your motor fluctuations by adding and adjusting medications.

You may be a good candidate for Duopa if you have gut issues, such as slow emptying of the stomach or constipation, or have difficulty with your meals interfering with the absorption of your levodopa.

Q What does Duopa treat?

A Duopa treats bradykinesia (slowness), rigidity (stiffness) and tremor. It generally helps PD symptoms that improve with your best medication "on" time when taking the pill form of carbidopa/levodopa. It may be helpful in reducing "on/off" fluctuations and other motor complications, like dyskinesia.

Q Will I still need to take my other PD medications?

A The pump is worn for up to 16 hours per day. In rare cases it's used for 24 hours, for example, when levodopa throughout the night is needed to help sleep quality. Your continuous rate settings will provide most of your daily medication, and you may give yourself extra doses with the pump if needed. Some people continue their other PD medications, such as dopamine agonists or amantadine, although it is common to stop these medications once you have the pump. At night, you can expect to take your medication in pill form as normal.

Q Can I swim or bathe with Duopa?

A You can shower within two days of the procedure if the stoma is healing well – just disconnect the pump and avoid getting the pump wet. You will be able to swim and bathe with Duopa once your stoma heals, which normally takes several months.

Your pump cannot get wet, so you will need to remove it prior to swimming or bathing. Your neurologist may advise you to give yourself an extra dose before you remove the pump. After swimming in a pool, make sure to wipe off the tubing to remove excess chlorinated water. Talk to your gastrointestinal (GI) specialist prior to swimming for additional information about how to keep your tube clean.

Note: Swimming alone is not recommended for people with Parkinson's due to the risk of drowning as a result of freezing.

Q How expensive is Duopa Therapy? Will my insurance cover the costs?

A Most insurance companies pay for Duopa therapy. However, since Duopa is relatively new in the United States, it is available as a name brand drug only – not generic. Out of pocket cost will differ from one insurance plan to another. Obtaining insurance coverage for Duopa may be more difficult if you are living in a long-term care facility. Before deciding whether Duopa is right for you, talk with your doctor and your insurance provider about what you can expect to pay per month and per year. Know that "copay assistance" is not always guaranteed to continue from year to year and is different than the "free drug program" available to some people. Ask your doctor if there is a social worker, pharmacy counselor or financial advisor who can help you make an informed decision.

Q Will my pump activate the metal detector at the airport?

A Yes, you will need to let the TSA agent know that you have a medical device and cannot go through the metal detector. Most airports will make special accommodations for people with medical devices and will allow them to bypass the metal detector. Ask your doctor for a letter explaining your need for the Duopa pump and print out a TSA Notification Card. In addition, bring your Parkinson's Foundation Aware in Care Kit containing tools to keep you safe while traveling or during a hospital stay. The kit includes a medical alert card that you can share with security personnel that explains the pump and how it may be affected by the detector.

Q Why would I pick Duopa instead of deep brain stimulation (DBS)?

A Whether you choose Duopa or DBS is a decision that should be carefully discussed with your neurologist and care team. In some cases when brain surgery is too risky, Duopa can be a reasonable alternative. Some people choose Duopa over DBS because it reduces their daily pill requirement. There are some people who have both DBS and Duopa, so it is important to remember that having one does not rule out the other.

Q How important is having a reliable care partner if I choose Duopa?

A People with Duopa and the experts who manage their care emphasize the importance of having an actively involved care partner. Duopa requires tubes and hardware that live outside of the body and need to be maintained (unlike DBS).

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Duopa: Before, During and After the Procedure

If your neurologist decides you are a good candidate for carbidopa/levodopa enteral suspension (Duopa), you will be referred to see a gastrointestinal (GI) specialist.

The GI specialist will evaluate you to make sure you can have the endoscopic gastrostomy with jejunal tube – or PEG-J – procedure. If you have had certain abdominal surgeries, you may not be eligible for Duopa therapy. Large scars running across your belly also may rule out the PEG-J procedure. If the GI specialist determines you are a good candidate, the next step is to schedule the PEG-J tube procedure.

The procedure usually lasts about an hour, which includes the time you are under anesthesia. The GI specialist will insert an endoscope, or flexible tube, through your mouth that goes down your throat and into your stomach. They will use the endoscope to visualize and locate the correct place for the PEG-J tube, which will be threaded through the skin of your abdomen with a needle and secured in place. In some centers this procedure is performed by a specially trained radiologist.

Most hospitals will send you home on the same day as the procedure. Your neurologist will calculate your pump settings based on the levodopa dosage you are currently taking in pill form. Often your neurologist, nurse practitioner (NP) or physician assistant (PA) will allow your stoma to heal for a few days to a few weeks before starting to administer the gel. During this time, you will take your normal Parkinson's pills like you did before surgery. You may also be scheduled for an office visit to adjust your settings.

Prior to the procedure, your care team will arrange an educational session on how to care for your stoma and tube, as well as how to operate and take care of your pump.

You will need to care for your stoma daily, which will involve keeping your stoma clean by moving your tube a small amount every day. You or a care partner will need to flush the tube twice a day while using the pump.

Shipments of Duopa cassettes and supplies will be mailed directly to your home. Duopa cassettes need to be kept refrigerated.

People using Duopa therapy are assigned a case manager through Abbvie's DuoConnect program who can answer questions, provide education and support and help troubleshoot problems. Call 1-844-DUO-4YOU (386-4968) for more information.

Programming the Pump

Your neurologist, nurse, nurse practitioner or physician assistant will program your Duopa pump settings to deliver the medication specific to your needs. These settings usually include a morning dose that will be delivered when you first attach the pump, followed by medication that will be delivered at a continuous rate throughout the day for up to 16 consecutive hours. Your neurologist may also program additional doses if you need more medication during the day.

Duopa Risks, Complications, Special Information and Warnings

The most common adverse reactions after the PEG-J tube procedure are pain around the stoma where the tube was inserted, nausea and gas pain. In most cases, these issues resolve after 24 to 72 hours. However, serious complications, including infection, bleeding and intestinal blockage can occur, some of which may lead to tube replacement. Your gastrointestinal specialist and neurologist should discuss these risks with you prior to the procedure.

The side effects from Duopa gel are similar to those from carbidopa/levodopa in pill form. These can include dyskinesia, nausea, stomach upset, low blood pressure, hallucinations, dizziness, impulsive behaviors and others.

Similar to DBS, the Duopa hardware can be removed if necessary, although you must wait a minimum of 14 days to remove the PEG-J tube after the initial surgery.

For more guidelines around avoiding post-surgical infections, be sure to review appendix B: Avoiding Infection After Surgery on page 77.

8

Lesion Therapy

Standard (or radiofrequency-based) pallidotomy, thalamotomy and subthalamotomy are types of surgical procedures in which a tiny, heated probe is inserted into a specific region of the brain to lesion (or destroy) tissue.

Pallidotomy targets the globus pallidus internus (GPi) and is the most widely used type of lesion therapy for Parkinson's disease (PD). It has been used over the last several decades to help relieve PD motor symptoms.

Thalamotomy targets the ventral intermediate nucleus (VIM) of the thalamus and is used mainly to treat tremor.

Subthalamotomy targets the subthalamic nucleus (STN). It can provide some of the same benefits as pallidotomy.

Benefits of Lesion Therapy

A pallidotomy lesion has the potential to improve bradykinesia (slowness), rigidity (stiffness), tremor, motor fluctuations, dyskinesia, and in very select cases, freezing. It usually does not improve walking, speech or thinking. Pallidotomies, like deep brain stimulation (DBS), are generally only effective in treating PD symptoms that respond to carbidopa/levodopa, with the exception of tremor. Tremor may respond to pallidotomy (and thalamotomy) even if medications don't work.

Pallidotomy has advantages over DBS – it doesn't require implanted wires, batteries or electronic programming sessions to fine-tune settings. There are no hardware malfunctions and usually no infections resulting from the initial surgical procedure.

For those who might have difficulty traveling for DBS programming, or in cases when DBS is too expensive or not available, pallidotomy may be a reasonable choice. Pallidotomy can be as effective as DBS in treating PD symptoms, however, the lesion must be placed in exactly the right spot. Recent studies have shown that the benefits of pallidotomy when the lesion is well-placed can be long-lasting. A misplaced lesion may lead to persistent side effects or incomplete benefits.

Subthalamotomy has been gaining popularity because it can provide the same types of benefits as pallidotomy. It is performed less frequently than other types of lesion therapy because it requires a high level of precision. There is also an associated risk of developing dyskinesia.

Risks, Complications, Special Information and Warnings

Lesions (cuts) in the brain can cause stroke, seizure, bleeding, weakness, numbness, changes in vision or speech and/or stroke-like symptoms. Lesions on both sides of the brain can affect cognition and speech and have additional effects on walking and balance. Traditionally, lesion therapies have been reserved for treatment on one side of the brain.

Unlike DBS, pallidotomy should not be performed on both sides of the brain in most cases. This is one major limitation of this surgery. Performing two pallidotomies can lead to permanent speech, swallowing and cognitive problems. People with an existing pallidotomy who require a second surgery will usually have DBS on the opposite side of the brain.

A few subthalamotomy patients have developed a side effect called hemiballism (uncontrollable flinging of one arm and/or leg), but in most cases it is temporary.

Despite the benefits, subthalamotomies are still not frequently performed as they carry the risk of lasting adverse effects (unwanted and unexpected medical events) when the lesion is not accurately placed.

9

Focused Ultrasound

In the past, ultrasound was primarily used by doctors to view the brain and body. Sound waves can also make lesions (cuts) when they pass through tissue creating heat.

Scientists discovered that these lesions, when placed in specific areas of the brain, have therapeutic benefits for some neurological disorders. As a result, focused ultrasound (FUS) was introduced in the 1950s as a treatment for brain disorders like Parkinson’s disease (PD). At that time, the procedure required surgically removing part of the bone from the skull to expose the brain in a procedure called a craniotomy, which allowed direct application of ultrasound to the brain.

FUS for Parkinson's disease

Since the 1950s, there have been several important improvements in FUS (also called high-intensity focused ultrasound, or HIFU). It is still not a common procedure for PD in the U.S. Surgeons no longer remove part of the skull. Instead, they use a special helmet that allows the ultrasound energy to be focused on specific areas of the brain. Also, new magnetic resonance imaging (MRI) technology lets doctors directly observe structures and temperatures in the brain.

Focused ultrasound thalamotomy was approved by the FDA in 2018 to treat tremor-dominant PD on one side of the brain. In 2021, the FDA expanded its approval to include focused ultrasound pallidotomy, still on only one side of the brain, for the treatment of other PD symptoms, such as slowness (bradykinesia) and stiffness (rigidity). FUS may also help reduce levodopa complications, such as dyskinesia.

Researchers have been exploring whether bilateral (two-sided) treatments can be safety performed. The use of bilateral FUS in regular practice is not recommended at this time.

Before, During and After the Procedure

The procedure is completed inside a radiology scanner using a high-intensity ultrasound machine. People typically have a computerized tomography (CT) scan of the entire skull to measure skull thickness and an MRI to define the specific area for surgery in advance.

On treatment day, the person's head is shaved and the scalp is inspected for scars and other lesions that could affect the path of the ultrasound. Once a standard head frame is positioned, a silicone plastic helmet is put on top of the scalp to keep the skull bone temperature cool and comfortable. It's rare but possible for the skull to be too thick for this procedure to be performed.

The surgical team monitors vital signs during surgery, which is carried out under local anesthesia (numbing only certain areas). The ultrasound helmet is attached to the person's head, and high intensity ultrasound waves are applied while doctors closely monitor for symptom improvement or side effects. Treatment ends once symptoms have sufficiently improved.

After the procedure, a neurological status check is completed in the recovery room and an MRI is used to review the location and size of the lesion.

Risks, Complications, Special Information and Warnings

Tremor improves in most people when ultrasound lesions are well-placed in the thalamus.

Similar to classical thalamotomies, the most common side effects include face or arm numbness, weakness and poor balance. Procedures on both sides of the brain carry a high side effect risk.

Though persistent side effects have not been reported as common in larger trials at experienced centers, there have been concerns about lasting side effects, even with procedures on one side of the brain.

As with other lesion-based therapies, it is not possible to correct problems, improve benefits or reduce side effects that do not go away over time.

FOCUSED ULTRASOUND VS. DEEP BRAIN STIMULATION

The following are potential **disadvantages** of FUS compared to DBS:

- Not as precise as DBS
- Adjustments cannot be made to improve benefits or reduce permanent side effects once the lesion has been placed in the brain

The following are potential **advantages** of FUS compared to DBS:

- Ability to repeat treatments if needed
- No need to replace batteries or adjust settings
- No incisions or leads in the brain

10

Advances in Surgery

Scientists are continuously studying deep brain stimulation (DBS) to figure out ways to make it a safer and more effective treatment for Parkinson's disease (PD).

Ongoing research continues to push technology into new areas, including:

- New electrical stimulation methods that improve benefits and limit side effects
- Better batteries
- Improved programming and targeting allowing DBS devices to last longer powered by the same batteries
- Applications that facilitate remote programming at home

Although these have been very beneficial, the work of scientists is far from complete.

New Programming Algorithms

DBS programming can be lengthy, challenging and sometimes ineffective. New programming devices are now able to upload a scan of an individual's brain from an MRI and use mathematical concepts to predict where the stimulation will go and what it will do. Other investigations are exploring special MRI scans or connectomes (a sort of atlas or map of brain connections) to see how new brain pathways can guide and streamline DBS programming.

New DBS Targets

Current DBS surgery stimulates a "target"— one part of the brain that has been affected by Parkinson's disease (PD). There are many new targets being researched. Among these are the centromedian nucleus of the thalamus, the zona incerta, the nucleus basalis of Meynert, the motor cortex and the pedunculopontine nucleus. It is possible that stimulating one of these will treat symptoms that do not currently respond well to standard DBS targets – such as walking, balance, talking or thinking. At present, however, researchers cannot confirm that these targets effectively help PD-related symptoms.

Adaptive DBS

Today, DBS devices pulse regularly like a clock. What if they could pulse only when your brain needed the stimulation? What if a computer could listen for signs of trouble and then respond by pulsing to bring the signal back to normal, like a heart pacemaker? If electrodes could be turned on only when needed to treat your symptoms, this could result in fewer side effects and more benefits.

Multiple DBS Leads

Researchers have already begun to implant multiple leads into more than one region of the brain to monitor signals related to PD and to test new stimulation approaches.

Focused Ultrasound Research

Relative to DBS, focused ultrasound (FUS) is still in its early research stages. More time and research are needed to determine how people will respond over different time periods and who may benefit from this procedure.

Currently, FUS is approved by the FDA for one side of the brain. The benefits and risks of FUS on both sides of the brain are being explored in clinical trials. Another area that is being explored in clinical trials is using FUS to get past the blood-brain barrier to deliver new drugs or therapies.

Appendix A

"On/Off" Fluctuations

In early PD, medication can work smoothly to control motor symptoms, and daily life typically continues as normal for many people. As time goes on, symptom management becomes more challenging, which means that you may need to explore different medication and treatment strategies with your doctor to continue living your best life.

Understanding Dopamine and Parkinson's

The nervous system is made up of nerve cells (neurons) that form a "communication network" within the brain and throughout the body. In Parkinson's disease, these neurons stop functioning normally or die in a part of the brain called the substantia nigra.

Neurons in this area of the brain are responsible for producing dopamine, a chemical messenger or neurotransmitter essential for smooth, controlled movement. Levodopa, the main ingredient of the medication carbidopa/levodopa (Sinemet), directly converts into dopamine in the brain. Dopamine agonists work by mimicking dopamine.

Medication Complications

Levodopa medication continues to replace dopamine for many years; however, as the brain changes in PD, it gradually loses some of its ability to store and use the chemical as effectively. As a result, people taking carbidopa/levodopa — typically those who have been taking it for a while — often experience a "wearing-off" effect, or a return of symptoms in between medication doses. Symptoms may return gradually or suddenly — like flipping a switch. After taking the next dose, symptoms usually improve and people feel "on" again. This phenomenon, known as "on/off" fluctuations, may also occur when taking dopamine agonists but to a lesser degree.

For some people, the combination of brain changes and levodopa therapy can lead to dyskinesia (uncontrolled, involuntary movements). Other people never develop dyskinesia. Levodopa therapy can also cause painful muscle contractions (dystonia), fatigue, hallucinations and delusions, as well as low blood pressure. Balancing symptom relief with medication side effects becomes complex, often requiring the expertise of a neurologist with special training in movement disorders, known as a movement disorder specialist.

"On/Off" Fluctuation Symptoms and Timing

As with PD symptoms, each person experiences "off" episodes differently. You may have more slowness (bradykinesia), stiffness (rigidity) or tremor when your medications wear off. Freezing and muscle contractions (dystonia) can also be wearing-off symptoms. In fact, any symptom that improves with carbidopa/levodopa therapy can also worsen or intensify when medication wears off, including non-motor symptoms like anxiety, depression, fatigue, foggy thinking and pain.

"On/off" fluctuations, though more common at the end of a dose cycle, can happen at any time during the day or night. You may experience just one or a combination of the following "off" situations:

- Early morning "off" before your medication has started to "kick in."
- Middle of the night "off" episodes after the evening dose "wears off."
- End-of-dose "off," which usually follows an expected pattern.
- A sudden, unexpected "off."
- An "off" episode following a protein-rich meal. Protein can delay or stop levodopa's effects.
- Constipation-related "off" episodes. Carbidopa/levodopa must travel from the mouth to the small intestine, where it is absorbed. Constipation can slow levodopa absorption and make it less effective.

Treatment for "On/Off" Fluctuations

Treatment for "on/off" fluctuations is individualized. Your doctor will adjust your medications while watching for new or increased medication side effects. Depending on your current medications, your doctor may:

- Optimize your carbidopa/levodopa therapy by increasing or decreasing the dose or adjusting the dosing frequency.
- Add different medications to your current regimen to keep dopaminergic levels more consistent.
  - **Catechol-O-methyltransferase (COMT) inhibitors** can extend levodopa benefits by blocking an enzyme that breaks down levodopa.
  - **Monoamine oxidase-B (MAO-B) inhibitors** promote dopamine in the brain by blocking an enzyme that breaks down dopamine.
  - **Adenosine A2a antagonists** stimulate a receptor in the brain and extend "on" time.
  - **Dopamine agonists**, in general, are not as effective as carbidopa/levodopa. However, they usually last longer and can be helpful in smoothing out the "on/off" effect of levodopa. Dopamine agonist therapy needs to be initiated and monitored with great care as they can lead to serious behavioral changes and impulse control issues.
- Try a controlled-release or extended-release carbidopa/levodopa formulation designed to extend the benefits from the same dose of carbidopa/levodopa. These drugs can be beneficial to take at bedtime to reduce wearing off during the night.
- Supplement your scheduled carbidopa/levodopa doses with a quick-acting "rescue" medication.

If these medication adjustments cause or increase dyskinesia, adding an amantadine formulation may help.

For more information about these medications, download or order our book, Medications, at Parkinson.org/Store.

Appendix B

Avoiding Infection After Surgery

Your doctor may prescribe antibiotics to reduce chances of infection at the incision sites. Other precautions include the following:

- ☐ Carefully follow all your incision care instructions.
- ☐ Wash hands frequently.
- ☐ Keep stitches clean, dry and covered with a dry bandage or gauze, especially while bathing. Use a small amount of antibacterial soap and water for cleaning. Pat them dry with a clean towel or gauze.
- ☐ Do not swim, bathe or get in hot tubs with stitches. Wait seven days after surgery before showering. People with Duopa cannot get in hot tubs even after surgery site has healed.
- ☐ Never scratch, touch or put any pressure on the incision.
- ☐ Keep pillows, sheets and bedding clean.
- ☐ Make sure hats and wigs are clean.
- ☐ Wash hands after handling pets.
- ☐ Go to your follow-up appointment to have sutures and/or staples removed. Most centers will remove sutures seven to 10 days after surgery although some may use dissolving stitches.

Look for the signs of infection:

- ☐ Redness, swelling or warmth at the incision or around stitches.
- ☐ A fever of 100 degrees or higher.
- ☐ Pain or tenderness at the incision.
- ☐ Pus, blood or oozing at the incision.

Report any infections signs immediately to your doctor, who will likely prescribe antibiotics. Early detection and treatment can sometimes prevent removal of system components due to infection.

Appendix C

DBS Device Hospital Plan

If you have a deep brain stimulation (DBS) device, it's important to prepare your Aware in Care Kit before a planned or emergency hospital trip.

Order the kit at Parkinson.org/AwareInCare or by calling the Parkinson's Foundation Helpline at 1-800-4PD-INFO (473-4636).

The kit includes an Aware in Care Hospital Action Plan. It explains that a deep brain stimulation device helps to control symptoms and includes a surgically implanted, battery-operated neurostimulator in the brain connected to a pacemaker-like device in the chest.

The kit also contains critical MRI information and other alerts for your healthcare team, including:

- Unless the hospital has experience imaging a DBS device safely, MRI should not be performed.
- MRI is not recommended if the neurostimulator is placed anywhere other than the chest or abdomen, or if there is hardware damage or pieces left in the body.
- In some cases, DBS devices must be turned to 0.0 volts and MRI should not image structures of the body lower than the head. Dangerous heating of the lead could occur.
- Turning off the DBS device enables the best possible EKG or EEG recordings.
- Diathermy and other surgical procedure instruments may need to be avoided.

Always check with your DBS team before having an MRI to make sure it is safe for you. The DBS model and settings will determine if the neurostimulator should be off during the MRI.

Call the prescribing or implanting doctors, the manufacturer (Abbott: 1-800-727-7846; Boston Scientific: 1-833-327-4636; Medtronic: 1-800-510-6735) or the Parkinson's Foundation Helpline (1-800-473-4636) with questions.

Appendix D

Instructions for Other Procedures When You Have DBS

CT scans, DAT/SPECT scans, common X-rays, fluoroscopy, and PET (positron emission tomography) scans are safe for people with deep brain stimulation (DBS) but the quality of the image may be compromised by the DBS leads.

Ultrasound procedures, such as carotid doppler or abdominal ultrasound, can be performed safely.

Cardiac pacemakers can usually be placed in people who have had DBS therapy, as long as the neurostimulator and cardiac pacemaker are 10 inches apart.

Electrocautery, used to stop minor bleeding during surgery, can be used on people with DBS but only with the following safeguards to minimize any flow of the electrical current toward the DBS device:

- Inform the surgeon that you have DBS well before the surgery; contact your neurologist to let him or her know that you are having surgery.
- Just before surgery (in some DBS models) the leads should be turned off and the amplitude settings turned to zero. In other models the DBS device can be turned off.
- Bipolar electrocautery should be used to lessen transfer of electricity (A unipolar device is not recommended.).
- A grounding pad should be placed on one of your legs. Any electrical charges that might transmit from the electrocautery device will be directed to the ground lead on your leg instead of the neurostimulator system.

The surgeon should consult the DBS manufacturer for specific questions about the surgery or surgical equipment.

Miscellaneous procedures

- Any type of medical procedure that will be performed directly over the neurostimulator device or connecting wire is not recommended. It could damage the device.
- Most X-rays can be performed safely.
- Do not allow your dentist to place electric drills or cleaning tools near the neurostimulator, connecting wire or implant site on the scalp. Dental X-rays are okay.
- If you have a mammogram, be sure that the pressure of the machine on the breast does not directly compress the neurostimulator or connecting wires.
- Radiation therapy for the treatment of cancer can be performed as long as it is not too close to the neurostimulator (IPG) and a protective shield is placed over it.
- Lithotripsy, a procedure to break up kidney stones, is not recommended unless it is the only medical option, as the treatment can damage the neurostimulator. When used, protective shielding should be placed over the neurostimulator, which should be turned off and amplitude/voltage set to zero.

Appendix E

Going to the Hospital When You Use a Duopa Pump

If you use a Duopa pump, be sure to have your Aware in Care kit prepared before a planned or emergency trip to the hospital.

Order your Aware in Care kit at Parkinson.org/AwareInCare or by calling our helpline at 1-800-4PD-INFO (473-4636).

The following is an excerpt from the Aware in Care Hospital Action Plan that is designed to share with your doctors:

I HAVE A DUOPA PUMP

Duopa therapy is an enteral gel suspension of the Parkinson's disease medication carbidopa/levodopa. The gel suspension is administered by a pump connected to the body using a percutaneous endoscopic gastrostomy with jejunal tube.

- Duopa therapy is FDA approved for daily use of up to 16 hours.
- Patients using Duopa therapy are assigned a case manager that can be reached through AbbVie's DuoConnect at 1-844-DUO-4YOU (386-4968). Case managers answer questions, provide education and support and help troubleshoot problems.
- If a patient is disconnected from the Duopa pump for more than two hours, the patient will likely need to be prescribed an oral form of carbidopa/levodopa.
- The Duopa pump is not waterproof.
- Do not expose the pump to therapeutic levels of ionizing radiation, ultrasound, MRI or electrocardiogram (ECG). Call DuoConnect for instructions before initiating any imaging.

Glossary

Glossary terms are underlined with dots the first time they appear in this book.

B

Bradykinesia Slowness of movement; one of the cardinal symptoms of Parkinson's.

C

Computerized tomography (CT) scan A medical test hat use a computer linked to an x-ray machine to take pictures of the inside of the body.

D

Deep brain stimulation (DBS) A surgical treatment for Parkinson's disease.

A special wire (lead) is inserted into a specific area of the brain responsible for movement. The lead is connected to a pacemaker-like device implanted into the chest region. This device creates electrical pulses, sent through the lead, which "stimulate" the brain and control abnormal brain cell activity.

Duopa therapy A form of carbidopa/levodopa delivered in gel form – called enteral suspension – rather than a pill. It is used to treat the motor symptoms of PD.

Dyskinesia Abnormal, involuntary body movements that can appear as jerking, fidgeting, twisting and turning movements; may result from levodopa therapy as PD progresses.

E

Electrical currents A movement of positive or negative electric particles (such as electrons).

Electrode A small piece of metal or other substance that is used to take an electric current to or from a source of power. These attach to the lead within a DBS system.

F

Focused ultrasound The use of ultrasound waves to create targeted lesions (cuts) as they pass through tissue in the brain. Used to treat abnormal brain cell activity.

G

General anesthesia The use of medications that put you in a sleep-like state of unconsciousness before a medical procedure.

Globus pallidus internus (GPi) A section of the Globus pallidus partially responsible for sending signals affecting the movement of arms, legs and neck, as well as other functions including thinking and mood. One of three targets for Parkinson's DBS, aimed at reducing tremor, rigidity (stiffness), bradykinesia (slowness), dyskinesia; improves "on-off" fluctuations.

L

Lead A thin, insulated wire inserted through a small opening in the skull and implanted in the brain. The tip of the lead (the portion with the electrodes) is positioned within the targeted brain area.

Lesion therapy A surgical procedure in which a tiny, heated probe is inserted into a specific region of the brain to lesion, or destroy, tissue.

Local anesthesia Numbing of a small site where the pain or procedure will occur without a change to consciousness.

M

Magnetic resonance imaging (MRI) A medical imaging technique that uses magnetic forces to obtain detailed images or pictures of the body. MRI is non-invasive – meaning it does not require surgery, and does not use radiation.

Motor fluctuations Changes in the ability to move, often related to a drop in dopamine levels in the brain and medication timing.

Motor symptoms Parkinson's symptoms related to movement, such as slowness, tremor and stiffness.

Movement disorder A group of neurologic conditions associated with problems with movement including dystonia, Huntington's disease, Parkinson's disease and others.

Movement disorder specialist A neurologist with additional training to treat people with Parkinson's at every stage of the disease.

N

Neurodegenerative disorder A disease characterized by the loss of cells of the brain or spinal cord, which over time leads to dysfunction and disability.

Neuron A brain cell.

Neuroprotective Protects brain cells (neurons) from injury or dying.

Neuropsychological battery A structured assessment of cognitive function that helps doctors assess thinking, memory, perception, problem solving and verbal ability.

Neuropsychologist A licensed psychologist with expertise in how behavior and skills are related to brain structures and systems.

Neurosurgeon A physician who specializes in surgical treatments of the central nervous system.

Non-motor symptoms Parkinson's symptoms unrelated to movement such as depression, cognitive changes and fatigue.

O

"On/off" fluctuations Changes in symptom control when carbidopa/levodopa is either working well or losing its effect.

P

Pallidotomy A type of brain surgery in which a tiny part of the globus pallidus is lesioned.

Percutaneous endoscopic gastrostomy with jejunal tube (PEG-J tube) The tube used in Duopa therapy which allows medication to enter the body through the intestine.

R

Rigidity In Parkinson's, stiffness of the arms or legs beyond what would result from normal aging or arthritis. Some people would call it "tightness" in their limbs.

S

Substantia nigra pars compacta (SNc) A portion of the substantia nigra made up of dopamine neurons.

Subthalamic nucleus (STN) One of the three targets for DBS that is partially responsible for sending signals affecting the movement of arms, legs and neck, as well as other functions including thinking and mood. One of three targets for Parkinson's DBS, aimed at reducing tremor, rigidity (stiffness), bradykinesia (slowness), dyskinesia; improves "on-off" fluctuations.

Subthalamotomy A type of brain surgery in which the subthalamus, a tiny area of the brain, is lesioned or destroyed.

T

Thalamotomy A type of brain surgery in which the thalamus, a tiny area of the brain, is lesioned or destroyed. Primarily effective for tremors.

U

Unified Parkinson's Disease Rating Scale (UPDRS) A universal scale of PD symptoms created to comprehensively evaluate and document an individual's PD progression and establish a baseline comparison for future follow up visits.

V

Ventral intermediate nucleus (VIM) of the thalamus A part of the nucleus targeted in DBS for essential tremor; a less common target of Parkinson's DBS treatment that only aims to reduce tremor.

Index

Notes

ABOUT THE PARKINSON'S FOUNDATION

The Parkinson's Foundation makes life better for people with Parkinson's disease by improving care and advancing research toward a cure.

In everything we do, we build on the energy, experience and passion of our global Parkinson's community. A wealth of information about Parkinson's and about our activities and resources is available on our website, Parkinson.org.

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Your answers will be used to improve our resources and will benefit people with Parkinson's, caregivers, families and others in the Parkinson's community. Thank you for your help.

ONLINE FORM:	Parkinson.org/Feedback

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