Parkinson’s is a slowly progressive disease; thus the symptoms get worse over time. Therefore the symptoms you have will change and evolve. The pattern of symptoms can vary for each person, so everyone’s experience with the condition is different.

Fortunately the symptoms of Parkinson’s do respond well to medical treatments. Over a number of years however, the response you get from your medication and the way it controls your symptoms will change. These changes are commonly known as motor fluctuations.

“Wearing-off happens when a dose that previously used to help symptoms does not last as long and your next dose is needed sooner.

Symptoms of wearing-off include changes in movement and mobility, thoughts and feelings, sensations and sense of well being.”

(Pink Working Group - UK)

These include;

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>wearing-off</td>
<td>i.e. symptoms returning before your next dose of medication</td>
</tr>
<tr>
<td>dyskinesia</td>
<td>i.e. twisting/turning movements</td>
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<tr>
<td>dystonia</td>
<td>i.e. prolonged muscle cramping</td>
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This section looks at the long term problem of “wearing-off” or “symptom re-emergence”. It also examines how you can work with your doctor to recognise the signs and symptoms of wearing-off and explains the possible management options.
WHAT IS WEARING-OFF?

One of the principal drug treatments for the management of the symptoms of Parkinson’s is levodopa. Levodopa is converted to dopamine in the brain replacing the missing chemical, thus relieving the symptoms of Parkinson’s. It has been considered the cornerstone of Parkinson’s disease therapy for nearly 40 years and is normally very effective when it is first used to treat the symptoms of Parkinson’s. However as the disease progresses you may find that the length of time in which you have a good response to levodopa (known as “on” time) shortens, and the time that you have a poor response to levodopa (known as “off” time) may lengthen. This is known as wearing-off. Symptoms of wearing-off include changes in movement and mobility, thoughts and feelings, sensations and sense of well being. Wearing-off can occur with all drugs but it is most commonly noticed and associated with levodopa. The symptoms of wearing-off may be very subtle initially.
WHY DOES WEARING-OFF OCCUR?

In the early stages of the disease, when you take a dose of levodopa, the brain is able to store any excess dopamine. This can be released at a later stage when dopamine levels are low. This ensures a good continuous supply of dopamine throughout the day and consequently effective control of most of the symptoms of Parkinson’s.

However, as Parkinson’s progresses, the brain has fewer cells that can:

- a) take up levodopa and store it as dopamine
- b) produce dopamine

Because of this reduced ability to store dopamine in the brain and release it when required, there is greater dependency on the availability of levodopa and you may now be more aware of symptoms returning after shorter periods of time (i.e. “wearing-off”). Also, because excess amounts of the drug can’t be stored, you may experience dyskinesias when you take your medication.

Over the years many attempts have been made to improve the availability of levodopa (i.e. increase the length of time that levodopa remains active in your body). Most of each dose of levodopa does not reach the brain as it is broken down by enzymes in the gut and bloodstream. Levodopa is now routinely combined with enzyme inhibitors to prevent this excessive breakdown of the drug before it reaches the brain, where it is needed. This means that more levodopa is available to provide better symptom control for longer periods each day.

Carbidopa and benserazide are DDC enzyme inhibitors that reduce the breakdown of levodopa in the gut. Entacapone is a COMT enzyme inhibitor that prevents the breakdown of levodopa in the bloodstream.

Levodopa is available as:

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
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<tbody>
<tr>
<td>Sinemet</td>
<td>a combination of levodopa and carbidopa</td>
</tr>
<tr>
<td>Madopar</td>
<td>a combination of levodopa and benserazide</td>
</tr>
<tr>
<td>Stalevo</td>
<td>a combination of levodopa, carbidopa and entacapone</td>
</tr>
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</table>
HOW IS WEARING-OFF IDENTIFIED?

Because Parkinson’s disease is a movement disorder, doctors tend to focus on problems with movement known as motor symptoms.

**MOTOR SYMPTOMS**

Motor symptoms of Parkinson’s relate to movement and mobility such as:

- Hands shaking
- Trouble using your hands
- Trouble getting out of a chair
- Muscle cramping
- Trouble speaking
- General slowness
- General stiffness

Doctors identify “wearing-off” mainly by focusing on the return of these motor symptoms. However, you may find that you also have other symptoms when your medication “wears-off” that have nothing to do with movement.

These types of symptoms are known as **non-motor symptoms**. They may affect your thinking, the way you feel and your general sense of well-being.
NON-MOTOR SYMPTOMS

Anxiety
Feeling restless
Panic attacks
Trouble breathing
Insomnia or sleep disturbances
Excessive sweating
Trouble thinking clearly
Slowness of thinking
Lack of energy
Aching and numbness

“Wearing-off” can include both motor and non-motor symptoms. Your doctor may not recognise the non-motor symptoms of “wearing-off” as easily as motor symptoms. They are less obvious because you cannot see them. You can help your doctor to identify non-motor symptoms by telling him or her how and when these symptoms occur.

HOW IS WEARING-OFF IDENTIFIED?

TIP

Fill out the “Wearing-off” card enclosed with this pack and bring it with you to your next appointment with your doctor.
When are you likely to experience “wearing-off”?

Parkinson’s disease does not affect everyone in the same way. There is no way to tell if, or when, you might experience “wearing-off.” However, nearly half of all patients experience “wearing-off” within one or two years of starting levodopa treatment. So, if you are taking levodopa, it is important to be aware of your symptoms.

Your doctor may already have determined that you were experiencing “wearing-off.” If so, he or she may have increased your medication.

**TIP**

If you are now taking more than three doses of levodopa a day, you may have begun to experience “wearing-off.”
What if you think you are experiencing “wearing-off”?

Any regular symptoms that you are experiencing may be due to “wearing-off”, particularly if they improve after your next dose of medication.

If you believe that you are experiencing “wearing-off”, discuss the changing symptoms with a healthcare professional. Your symptom control is unlikely to get better on its own, and may worsen.

Are you experiencing wearing-off?

Tell your doctor about any symptoms that you may be experiencing so that he or she can modify your treatment.
How is “wearing-off” treated?

If you are experiencing “wearing-off” your Doctor can manage this in many ways. Your Doctor may review your current medication and may do one of the following:

Switch you to a new treatment

a. Stalevo is a newer levodopa therapy. Stalevo is a combination of levodopa and two other agents (carbidopa and entacapone), which reduce the breakdown of levodopa in the gut and bloodstream. This increased availability of levodopa should lead to smoother and steadier levels of dopamine in the brain providing better symptom control for longer periods each day.

b. Controlled release preparations of levodopa were first developed as a way of trying to extend the control of Parkinson’s symptoms. Such preparations can be beneficial, especially for night-time problems, but the response during the day can be less predictable.

Add in another drug to supplement the ones you are already taking

COMT Inhibitor e.g. entacapone (Comtess) is an agent that reduces the breakdown of levodopa in the bloodstream.

Dopamine agonist e.g. ropinirole (Requip), pramipexole (Mirapexin), pergolide (Celance): These mimic the action of natural dopamine rather than replacing it the way levodopa does.

MAO-B inhibitor e.g. selegiline (Eldepryl), rasagiline (Azilect): These drugs act by blocking one of the enzymes that breaks down dopamine in the brain, thus prolonging and enhancing the effect of the remaining dopamine.

Alter the dose of your current medication

Your doctor may increase the strength of your tablets or increase the number of tablets you take per day.

Alter the times when you take your medication.

For some people with Parkinson’s, protein intake can reduce levodopa absorption. So it may be advisable to take your levodopa one hour before or two hours after meals. It is also recommended to increase your fibre and fluid intake to avoid constipation, which may also reduce levodopa absorption.

NOTE

You need protein as part of a healthy diet, so under no condition should you eliminate protein from your diet. You will need to discuss your diet and protein intake with your doctor or dietician.
COMT
Catechol-O-Methyl Transferase, is an agent that reduces the breakdown of levodopa in the bloodstream.

DDC
Dopa-DeCarboxylase is an agent that reduces the breakdown of levodopa in the gut.

Delayed on
Delayed on is when you take your medication but it does not seem to work, or takes an extra long time to kick in.

Dyskinesia
Abnormal involuntary movement.

Dystonia
Abnormal involuntary movement causing a prolonged, often twisted posture of the affected part of the body.

Freezing episodes
Not to be confused with being off, freezng is literally becoming stuck to the floor. It quite often happens when approaching a doorway, or in restricted areas like between a sofa and coffee table.

Honeymoon period
The length of time during which you are able to function perfectly while taking medication. This is the period of time during which you get all the benefits of the medication without any of the potential drawbacks.

Motor fluctuations
occur after the “Honeymoon period”. You become aware of the effect of your medication i.e. the effect of your medication does not last as long and your symptoms start to reappear before the next dose of medication is due. Motor fluctuations include wearing-off and dyskinesias.

Non-motor fluctuations
Dips in between doses that affect things other than your ability to move. They include slowness of thought, feeling down, sweating, and are relieved when your next dose kicks in.

GLOSSARY OF TERMS

Motor fluctuations
occur after the “Honeymoon period”. You become aware of the effect of your medication i.e. the effect of your medication does not last as long and your symptoms start to reappear before the next dose of medication is due. Motor fluctuations include wearing-off and dyskinesias.
WEARING-OFF

GLOSSARY OF TERMS

**Off-time**
The time when your medication has worn off between doses and movements are more difficult.

**On-time**
The time when your medication (Sinemet/Madopar/Stalevo) is working well and your movements are easier. You may also have dyskinesia for a while in the middle of this time.

**Rigidity**
Abnormal increased stiffness.

**Tremor**
The typical shake of Parkinson’s. Tremor is a rhythmic trembling movement of an arm or a leg that mainly occurs when you are not doing anything, and is one of the primary signs of Parkinson’s.

**Wearing-off**
This happens when a dose that previously used to help your symptoms does not last as long and your next dose is needed sooner. Symptoms of wearing-off include changes in movement and mobility, thoughts and feelings, sensations and sense of well being.
Contact Information
Parkinson’s Association of Ireland
Carmichael House,
North Brunswick Street
Dublin 7

freephone 1800 359 359
www.parkinsons.ie

PALS (Parkinson’s Active Liaison and Support)
Phone 01 851 0040