

Terms highlighted in **bold italic** are defined in the glossary at the end of this information sheet.

### What is drug-induced parkinsonism?

About 7 percent of people with parkinsonism have developed their symptoms following treatment with particular medications. This form of parkinsonism is called “drug-induced parkinsonism”.

People with idiopathic Parkinson's disease and other causes of Parkinsonism may also develop worsening symptoms if treated with such medication inadvertently.

### What drugs cause drug-induced parkinsonism?

Any drug that blocks the action of dopamine (referred to as a dopamine antagonist) is likely to cause parkinsonism. Drugs used to treat schizophrenia and other psychotic disorders, such as behaviour disturbances in people with dementia, (known as neuroleptic drugs), are probably the major cause of drug-induced parkinsonism worldwide. Parkinsonism can occur from the use of any of the various classes of neuroleptics. (See *Table 1 at the end of this information sheet*).

The atypical neuroleptics, clozapine (*Clozaril*) and quetiapine (*Seroquel*), and to a lesser extent olanzapine (*Zyprexa*) and risperidone (*Risperidal*), appear to have a lower incidence of **extrapyramidal side-effects**, including parkinsonism. These drugs are still generally best avoided by

people with Parkinson's, although some of them may sometimes be used by specialists to treat some symptoms, such as hallucinations occurring with Parkinson's. However, risperidone and olanzapine should be used with caution to treat dementia in people at risk of stroke (the risk increases with age, hypertension, diabetes, atrial fibrillation, smoking and high cholesterol) because of an increased risk of stroke and other cerebrovascular problems. It is unclear whether there is an increased risk of stroke with quetiapine and clozapine. (See *PDS information sheet FS11 on Hallucinations*.)

While these drugs are used primarily as antipsychotic agents, it is important to note that they can be used for other non-psychiatric uses, such as control of nausea and vomiting. For people with Parkinson's, other anti-sickness drugs, such as domperidone (*Motilium*) or ondansetron (*Zofran*) would be preferable.

As well as neuroleptics, some other drugs can cause drug-induced parkinsonism. These include some older drugs used to treat high blood pressure such as methyldopa (*Aldomet*); medications for dizziness and nausea such as prochlorperazine (*Stemetil*); and metoclopramide (*Maxolon*), which is used to stop sickness and in the treatment of indigestion. See *Table 2 at the end of this information sheet*. One Parkinson's specialist who commented on this information sheet placed particular emphasis on prochlorperazine (*Stemetil*) and metoclopramide (*Maxolon*) because in his experience these were two of the

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commonest causes of drug-induced parkinsonism in the elderly. Something which is not always recognised.

Calcium channel blocking drugs used to treat high blood pressure, abnormal heart rhythm, angina pectoris, panic attacks, manic depression and migraine, may occasionally cause drug-induced Parkinsonism. The drugs of this type that are most well-documented as causing drug-induced parkinsonism are cinnarizine (*Stugeron*) and flunarizine (*Sibelium*). Calcium channel blocking drugs are however widely used to treat angina and high blood pressure and it is important to note that most common agents in clinical use probably do not have this side effect. These drugs should never be stopped abruptly without discussion with your doctor.

A number of other agents have been reported to cause drug-induced parkinsonism but clear proof of cause and effect is often lacking. Amiodarone, used to treat heart problems, causes tremor and some people have been reported to develop Parkinson's-like symptoms. Sodium valproate, used to treat epilepsy, and lithium, used in depression, both commonly cause tremor which may be mistaken for Parkinson's. Some reports have linked **SSRI** antidepressant drugs such as fluoxetine (*Prozac*) to drug-induced Parkinsonism but hard evidence of cause and effect is unsubstantiated. This type of drug is increasingly used to treat depression in Parkinson's. (See *PDS information sheet FS56 Depression and Parkinson's for more information.*)

### **What are the characteristics of drug-induced parkinsonism and how does it differ from idiopathic Parkinson's disease?**

Drug-induced parkinsonism is more likely to be symmetrical (on both sides of the body) and less likely to be associated with tremor, although it can sometimes present asymmetrically and with a tremor. **Akinesia** with loss of arm swing can be the earliest

feature. **Bradykinesia** can be an early common symptom, causing expressionless face, slow initiation of movement and speech difficulties.

### **Other drug-induced movement disorders**

Tardive dyskinesia is another drug-induced movement disorder that can occur in people who are on neuroleptic drugs. This refers to excessive movement of the lips, tongue and jaw (known as oro-facial dyskinesias). The term 'tardive' means delayed or late appearing and this refers to the fact that the person may have been treated with the neuroleptic for some time before the dyskinesia becomes apparent. Tardive dyskinesia can be difficult to treat and may sadly be permanent in some people.

### **Are there any other risk factors for drug-induced parkinsonism?**

The incidence of drug-induced parkinsonism increases with age. Drug-induced parkinsonism is more prevalent in elderly patients and twice as common in women than men. Other risk factors include a family history of Parkinson's and **affective disorders**. There may be a genetic predisposition to drug-induced parkinsonism. Younger people may develop sudden onset of dystonia (abnormal muscle postures) and abnormalities of eye movements if treated with drugs that cause drug-induced parkinsonism.

### **How quickly will the symptoms of drug-induced parkinsonism appear after someone starts taking a drug that may cause it?**

It depends on the properties of the drug. The symptoms generally occur within one month of starting neuroleptics in 50% of cases. In some elderly people, features can be identified as early as the fourth day of treatment and sometimes after one dose. However there can occasionally be a delayed development of parkinsonism.

## How does drug-induced parkinsonism progress?

Drug-induced parkinsonism tends to remain static and does not progress like idiopathic Parkinson's disease but this is not usually all that helpful in making the diagnosis.

## If the offending drug is stopped, will the drug-induced parkinsonism improve and if so, how long will this take?

Generally, 60% of people will recover within 2 months and often within hours or days of stopping the offending drug. However some people may take two years. One study reported that 16% of cases went on to be confirmed to have idiopathic Parkinson's disease. These people were probably going to develop Parkinson's at some stage in the future in any event but the offending drug 'unmasked' an underlying dopamine deficiency. This theory is supported by research studies with specialist *PET scans*.

## What other treatment is available?

In many cases the first approach to treatment will be to try either stopping the offending drug for a sufficient length of time, reducing it or changing it to another drug which may be less likely to cause drug-induced parkinsonism. **NB: No drug should be withdrawn because you think it is causing drug-induced Parkinsonism, or worsening existing Parkinson's disease without first discussing the situation with your doctor. Some drugs need to be withdrawn slowly, particularly if the person has been taking the drug for a considerable time and problems can arise if they are withdrawn abruptly.**

Sometimes, for medical reasons, the person cannot stop taking the drug that causes drug-induced parkinsonism. Where this is the case, the benefits of the drug need to be weighed up against the side-effects of parkinsonism. Sometimes adjusting the dose of an neuroleptic drug downwards to a level that does not cause parkinsonism may

help. However sometimes it is not possible to do this without taking the dose to a sub-therapeutic level (i.e. a level where it is not as effective at treating the psychotic illness for which it is prescribed). Usually changing the medication to an atypical neuroleptic is the best approach.

If stopping the offending drug is not possible, then anticholinergic drugs may be used. However, these should not be used in elderly people because they may cause confusion as well as worsening tardive dyskinesia.

Amantadine (*Symmetrel*), another drug used to treat Parkinson's, can also be used to treat drug-induced parkinsonism if the person cannot stop the offending drug. However, like anticholinergic drugs, amantadine also causes confusion and sometimes psychosis in older people, and therefore is only really suitable for younger people with drug-induced parkinsonism.

## Can these drugs aggravate existing idiopathic Parkinson's disease?

Yes. Stopping the medication (where possible) may be enough to relieve the drug-induced parkinsonism, although improvements can take several months.

## Can illegal drugs such as heroin cause drug-induced parkinsonism?

In the late 1970s drug addicts in California were making their own drugs as a cheap alternative to heroin. One of these addicts aged 23 years became ill and over several days developed symptoms of parkinsonism, such as tremor, rigidity and akinesia. When he was treated with anti-Parkinsonian drugs he improved dramatically. When he died sometime later from an overdose of other drugs, a post-mortem was carried out and they found that severe damage had been done to the dopamine containing cells in the basal ganglia, similar to that seen in Parkinson's disease. He was obviously very young to have developed Parkinson's disease, so doctors suspected that the

drugs he was taking had caused his condition. They analysed the material that he had been making and found it contained a chemical called MPTP. Further research showed that a breakdown product of MPTP was capable of producing severe damage to the dopamine-containing cells in the basal ganglia.

Since this first case, many other drug addicts have developed a similar syndrome after injecting themselves with drugs contaminated by MPTP.

Although research into other illegal drugs is limited, theoretically cocaine, ecstasy and other illegal drugs may also be possible causes of drug-induced parkinsonism. More research in this area is needed.

### **I have read that some illegal drugs may actually improve the symptoms of Parkinson's. Is this true?**

A BBC TV Horizon programme, broadcast in the UK in February 2001, featured a person with Parkinson's who found that some of his Parkinson's symptoms were improved temporarily when he took ecstasy. Ecstasy is known to affect a **neurotransmitter** called serotonin. The levels of serotonin are abnormal in brains of people with Parkinson's and the findings of the BBC Horizon programme have suggested that further research into the relationship between serotonin and Parkinson's is needed and may lead in the future to new non-dopaminergic treatments for the condition. These treatments will not however use ecstasy which remains an illegal drug and is known to have long-term adverse effects associated with its use. Also, although ecstasy gave temporary relief to the person in the programme, there is no evidence to suggest that anyone else with Parkinson's would benefit in the same way from the drug. *(Please see the PDS information sheet FS47 Ecstasy and Parkinson's for further information.)*

Media attention in the last couple of years has also focussed on the role that cannabis may play in the management of pain in neurological conditions like multiple sclerosis. This is now being researched. At present there is no information available on research into cannabis and Parkinson's.

## **Glossary**

**Affective disorders** – mental illnesses characterized predominantly by marked changes in mood. Includes manic depression.

**Akinesia** – poverty of movement

**Bradykinesia** – slowness of movement

**Extrapyramidal side effects** – term used to describe the development of a variety of movement disorders as a result of taking certain medications such as neuroleptic drugs. These side effects may include akathisia (restlessness), dystonias (muscular contractions or spasms), parkinsonism and tardive dyskinesias (abnormal, involuntary muscle movements).

**Neuroleptic drugs** – drugs used to treat schizophrenia and other psychotic disorders

**Neurotransmitters** – chemical messengers produced by the nerve cells in the brain. Their purpose is to pass messages from the brain to other parts of the body. There are a number of different neurotransmitters which each have a particular function. For instance, dopamine, which is short supply in the brains of people with Parkinson's, is involved in processes that involve the co-ordination of movement. Serotonin has a variety of functions, including being involved in controlling states of consciousness and mood.

**PET Scans** - The PET scan (Positron Emission Tomography) provides anatomical information about the brain. This means that with PET scans it is possible to assess the functioning of different parts of the brain while the individual is carrying out a particular movement or engaging in a

specific mental activity. With PET it is also possible to examine the state of particular neurotransmitter receptor sites in the brain. PET scans require the use of radioactive material in very small quantities, usually the equivalent to the radioactive exposure during a transatlantic flight. The dopamine systems in the brain, which are affected in Parkinson's, can be assessed with PET scanning.

**SSRIs** (Selective Serotonin Re-Uptake Inhibitors) – a newer type of anti-depressant that specifically targets the neurotransmitter, serotonin. Includes fluoxetine (*Prozac*), and paroxetine (*Seroxat*)

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The PDS cannot supply these references but you should be able to obtain them via a public or medical library.

*PDS Information Sheet FS38*

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**Table 1: List of Neuroleptic Drugs available in the UK**

<i>Generic name</i>	<i>Trade name</i>
<b>Amisulpride</b>	Solian
<b>Chlorpromazine hydrochloride</b>	Chloractil/Largactil
<b>Clozapine</b>	Clozaril
<b>Flupenthixol</b>	Depixol
<b>Fluphenazine hydrochloride</b>	Modecate/Moditen/ Motival (includes nortriptyline)
<b>Haloperidol</b>	Dozic/Haldol/ /Serenace
<b>Methotrimeprazine/Levomepromazine</b>	Nozinan
<b>Olanzapine</b>	Zyprexa
<b>Oxypertine</b>	Oxypertine
<b>Pericyazine</b>	Neulactil
<b>Perphenazine</b>	Fentazin, Triptafen (Perphenazine+amitriptyline)
<b>Pimozide</b>	Orap
<b>Pipotiazine</b>	Piportil
<b>Prochlorperazine</b>	Prochlorperazine/Stemetil
<b>Promazine hydrochloride</b>	Promazine
<b>Quetiapine</b>	Seroquel
<b>Risperidone</b>	Risperdal
<b>Sulpiride</b>	Domatil/Sulparex/Sulpiride/Sulpi til Sulpor (Sulparex is discontinued)
<b>Thioridazine</b>	Melleril
<b>Trifluoperazine</b>	Stelazine/
<b>Zuclopenthixol acetate</b>	Clopixol
<b>Zotepine</b>	Zoleptil

**Table 2: Other drugs that can cause drug-induced parkinsonism**

<b>Generic Name</b>	<b>Trade Name</b>	<b>Used to treat</b>
<b>Amiodarone</b>		Heart problems
<b>Cinnarizine</b>	Stugeron	Nausea and vomiting motion sickness vertigo dizziness tinnitus vascular disease and Raynaud's syndrome, high blood pressure, abnormal heart rhythm, angina pectoris, panic attacks, manic depression and migraine
<b>Fluphenazine with nortriptyline</b>	Motival, Motipress	A combination of antidepressant and antipsychotic drug
<b>Lithium</b>		Depression
<b>Methyldopa</b>	Aldomet	High Blood Pressure
<b>Metoclopramide</b>	Maxolon	Sickness and indigestion Also included in some medicines used for migraine such as Paramax (with paracetamol) and Migramax (with aspirin)
<b>Prochlorperazine</b>	Stemetil	Dizziness and nausea
<b>Tranlycypromine</b>	Parnate	Depression