PARKINSON’S DISEASE: A NEED TO ATTENTION

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ABSTRACT
Parkinson’s disease (PD) is the most common neurodegenerative movement disorder, characterized by a specific loss of dopamine (DA) neurons in the substantia nigra pars compacta. The degeneration of dopamine containing neurons causes a consequent reduction of dopamine levels in the striatum. Parkinson’s disease is more than a disorder of dopamine neurotransmitter system; additional neuronal fields and neurotransmitter systems are also involved, including the amygdala, hippocampus, the autonomic nervous system and the cerebral cortex leading to depletion of noradrenaline, serotonin and acetylcholine. Dopamine deficiency appears to be responsible for the motor deficits of the disorder but Parkinson’s disease cannot be treated directly with dopamine or related catecholamine’s due to their inability to cross the blood brain barrier (BBB). This article reviews on the different aspects of Parkinson disease like causes, sign and symptoms, useful drugs and surgery for the treatment of Parkinson’s disease.

Key Words: Neurological Disorder, Substantia Nigra, Parkinson’s Disease, Trembling.

INTRODUCTION
The disease was first described in 1817 by Dr James Parkinson. He wrote his ‘Essay on the Shaking Palsy’ based on his observations of certain people who passed by his window each day, and using data from his own patients. At that time the disease was referred to as ‘Paralysis Agitans’, which literally means ‘the shaking paralysis. Years later, Charcot, a famous French physician, named it after Dr. Parkinson. ¹

The effects of the disease were purely physical. In fact, it can slow the mind and impair the memory in some cases. Its more obvious signs are that it causes people to move slowly, their limbs feel stiff and they notice a tremor, or trembling, especially when relaxing. Also they may feel their posture is bent or a little unbalanced. It must be stressed that every person with Parkinson’s disease reacts differently and not everyone will necessarily experience all the possible symptoms. For example, some people may initially only notice a tremor affecting one arm or leg. Where this is the case, it is likely that the disease will get worse over time and more of the symptoms will become
noticeable. However, this will take place over years rather than months, and there are medicines to help maintain a good quality of life.\(^2\)

New medicines and techniques are constantly being developed as researchers all over the world continue to look for the causes of the disease and search for a cure. The outlook for people with Parkinson’s disease is much brighter today than it was 40 years ago - now modern medicine offers realistic hope that the symptoms of the disease can be controlled. The disease affects people from all walks of life. On average, it affects one person in every 1,000 of the population, but for people in their seventies and eighties that rises to at least two people in every 100. People as young as 20 have developed Parkinson’s disease, but this is uncommon. It is one of the most common neurological conditions affecting older people, and over 100,000 people in the UK have the disease at any one time. Men and women are affected equally, but the disease is more common in Caucasian people than in people of Asian or African origin. People of different races tend to develop slightly different symptoms.\(^3\)

**Parkinson’s disease**

Parkinson’s disease is a chronic, progressive neurological disorder, which is characterized by damage to an area of the brain called the substantia nigra. This area influences all voluntary movements. Nobody truly understands what causes this damage, and no cure has yet been found for the disease, but the symptoms can be controlled using a combination of drugs, therapies and occasionally surgery.\(^4\,^5\)

**Causes for Parkinson’s disease**

It is still not known what causes Parkinson’s disease, but research has led to some theories, which shed at least some light on the disease. Recently, scientists have discovered that certain families may be more likely than others to develop Parkinson’s disease because of an abnormality in their genes. The main evidence for this comes from research done on a large Italian family in which many members developed the disease. Tests on their chromosomes revealed an abnormality in chromosome four that could be passed on to future generations. However, the presence of this genetic abnormality did not necessarily mean that the disease would develop in all members of the family. What complicates the picture still further is that this abnormality is not necessarily present in other families where the disease affects more than one member, or in isolated cases of the
disease. Unfortunately, there is as yet no test that allows doctors to find out if a person is going to develop the disease or not. In the mid 1980’s some intravenous drug users in America were trying to make a drug called meperidine and accidentally produced a toxic substance called MPTP, which when injected caused them to rapidly develop the signs and symptoms of Parkinson’s disease. This led many people to believe that the disease is caused by a similar toxin (poison) found in the environment or in food. Research into this is still going on, but a link has never been proven. If a toxin is the cause, it is unlikely to be a modern one, since the disease itself has been around for so long. On the positive side, however, this incident did give scientists a method of inducing the signs and symptoms of Parkinson’s disease in the laboratory, which has benefited research into the treatment of the disorder.6

It is likely that Parkinson’s disease is caused by a combination of these factors. A particular genetic make-up may make a person more likely to get the disease if they come into contact with certain, as yet unidentified, toxins or environmental triggers. However, if a person who does not have this genetic make-up comes into contact with the same toxin or trigger, they could also go on to develop the disease. In short, particular genetic profiles appear to increase the chances of developing the disease, but not by a great deal. Researchers have found no viral or bacterial cause for the disease, so on present evidence we can say that it is not infectious. It is also not fatal. Severe stress or anxiety do not cause Parkinson’s disease, but states of severe anxiety, alcoholism, thyroid disease and a variety of rare metabolic and structural disorders can mimic some of the signs and symptoms of the disease. Doctors carry out tests to rule these disorders out before making a diagnosis of Parkinson’s disease.

Inside the brain in Parkinson’s disease

In people with Parkinson’s disease there is a degeneration of a specific area of the brain called the substantia nigra. This is a small cluster of cells found within an area called the basal ganglia deep in the centre of the brain. This cluster of cells is usually black in colour, but in people with Parkinson’s disease, this colouring is lost. This can only be seen when doctors examine the brain tissue after death. Usually, chemicals called neurotransmitters are produced by this area of the brain. They are responsible for helping to send messages between cells within the brain and the rest of the nervous system. In
people with Parkinson’s disease there is a substantial reduction in the production of a chemical messenger called dopamine, which is responsible for helping the motor (or movement) coordination centres of the brain (the basal ganglia and the striatum) work efficiently. A loss of dopamine in people with Parkinson’s disease means that the brain circuits that control movement stop working efficiently. Messages sent by the brain to the muscles do not pass through smoothly, and so ordinary movements like walking, getting up from a chair and putting on clothes become slow and difficult.

The end result is the emergence of the typical signs of the disease: slowness, stiffness and tremor. Doctors tend to refer to slowness of movement as bradykinesia and slowness in starting movements as akinesia, while the stiffness is referred to as rigidity. Normally, the ageing process itself causes the level of dopamine to drop mildly, but in people with Parkinson’s disease around 80 per cent of dopamine has been lost by the time the disease produces physical signs.

In the brain and nervous system there is normally a balance between dopamine and another chemical messenger called acetylcholine. In people with Parkinson’s disease, acetylcholine is relatively more active because of the lack of dopamine, which creates tremor. This is a simplified explanation of what goes wrong in the brain. In reality things are more complicated. Many other chemical messengers are also involved and many pathways within the brain and nervous system stop working properly.7

Signs and symptoms

The main symptoms of Parkinson’s disease were mentioned earlier. They are: trembling (tremor), stiffness (rigidity), slowness (bradykinesia/akinesia), problems with posture and problems with balance.8

Tremor

This is the commonest problem that leads people to seek medical advice. It affects around seventy per cent of people with Parkinson’s disease. One hand or leg alone may shake, or it may even be just the thumb. The shake is most noticeable when relaxing and usually disappears when sleeping. This symptom also tends to disappear when the limb is being used, for example while eating a meal or exercising the hand. Tremor can be very embarrassing to sufferers, but it is rarely disabling. Sometimes it is not noticeable to others but can be felt inside. It is very important to note that tremor is not unique to
Parkinson’s disease. There is another condition called Benign Essential Tremor which also causes the shakes.

**Essential Tremor Rigidity**

The doctor may notice rigidity or stiffness when he or she moves your arm around at the elbow or wrist. This is described as ‘lead-pipe’ rigidity when the limb is just generally difficult to bend or straighten - as if it were a metal pipe.

Where tremor is also present it is referred to as ‘cog-wheel’ rigidity, as movement in the joints feels like a ratchet. The latter can be especially noticeable at the wrist joint. This rigidity may cause the limbs to feel clumsy, weak or heavy and if severe may result in the affected person losing the use of one or more limbs.

**Slowness**

Technically, this is described as ‘akinesia’ or ‘bradykinesia’. These words mean ‘no movement’ and ‘slow movement’ respectively. In real terms the affected person will notice that they take longer to start and carry out tasks; they will walk more slowly and without swinging their arms; they may experience difficulty getting up out of chairs and they will also get tired easily when carrying out repetitive tasks. In addition to moving slowly, they may have particular problems with starting or controlling movements.

**Problems with posture**

People with Parkinson’s disease tend to stoop forwards. They also hold their arms in a flexed position at the elbows and at the wrists. The knees sometimes become permanently bent. Because Parkinson’s disease usually affects one side of the body more than the other, they may lean over to one side. Poor posture puts stress and strain on different areas of the body, and this leads to pain.

**Loss of balance**

Poor posture often leads to poor balance. It alters the centre of gravity in the body, giving the affected person a tendency to fall. Even when standing still they may have a tendency to stumble forwards or backwards if nudged. When they try to walk they may find that they are constantly trying to compensate for this alteration in the centre of gravity. They walk with small, fast shuffling steps (called festination) and constantly look as if they are about to topple forwards.

**Loss of facial expression**
Parkinson’s disease slows all movements, and the muscles of the face are also affected. A person with Parkinson’s may look depressed or sad; they won’t blink as much as before and they sometimes appear to be staring; they also may not appear to smile or laugh as readily as before.

**Speech problems**
Parkinson’s disease can cause the voice to become much softer, and the affected person may lose their ability to speak to a room full of people. Sometimes the voice becomes hoarse and the words a little slurred. Often words seem to tumble out on top of each other much too quickly. Swallowing becomes slower, and in advanced cases the person cannot deal with their own saliva.

**Small writing**
This is technically termed micrographia. An example is shown below. This is very common. In many cases it can be shown that Parkinson’s disease has been developing for many years by the fact that handwriting in diaries or on cheque book stubs has become progressively smaller.

**Greasy skin and sweating**
The skin can become very greasy, even in people who previously had a very good complexion. It is important to pay particular attention to personal hygiene so that other problems do not develop. Unfortunately, the combination of Parkinson’s disease and its treatments can cause excessive sweating, so much so that a bed can become completely drenched.

**Memory problems**
Contrary to what was first thought, it is now accepted that Parkinson’s disease can cause some memory problems, even in the early stages. Small things like forgetting where you put your keys are typical. Patients may also be a little slow to respond to questions, or not be able to add up a column of figures as quickly as before. These symptoms should not to be confused with the early signs of dementia that occur in Alzheimer’s disease.

**Pain**
Pain is not a common feature of Parkinson’s disease. It does sometimes occur, as do other sensory symptoms that are difficult to explain, such as pins and needles or numbness. These symptoms usually respond better to adjusting the Parkinson’s disease drug.
treatment than to pain-killers. Sometimes, other groups of drugs such as tricyclic anti-depressants can be useful.

**Night-time/sleep problems**

People often have problems with turning over in bed, and night-time visits to the toilet can be a nuisance. Cramp is common, and people sometimes suffer from something called ‘Dystonia’, a cramp-like symptom that causes them to hold themselves or part of their body in an unnatural posture. What this amounts to is that sleep can often be disrupted. Drug treatment can help, so discuss these problems with your doctor or specialist.

**Drugs used in Parkinson’s disease**

Drugs used for Parkinson’s disease can be divided into five main groups. Most of the medicines used to treat the disease have only been around since 1970.

**Drugs which replace dopamine**

These are the mainstay of treatment for Parkinson’s disease. Their names are Sinemet (Co-careldopa) and Madopar (Co-beneldopa). They come in much different strength as tablets, capsules, dissolvable instant-action preparations or controlled-release formulae. Each one has a specific use in the treatment of Parkinson’s disease.\(^9\)

Both drugs are a combination of levodopa and a chemical known as a dopa decarboxylase inhibitor. Levodopa given by mouth is absorbed into the system and is eventually converted into dopamine within the nerve cells in the brain.

It is then used by these cells, as naturally occurring dopamine would be, to send messages from one cell to the next. The function of the dopa decarboxylase inhibitor in each case is to make sure that as much of the levodopa reaches the target cells as possible by stopping it from being digested on the way.

**Drugs which mimic the action of dopamine**

These are called ‘dopamine agonists’. Their names are in Tablets Parlodel (bromocriptine), Celance (pergolide), Revanil (lysuride), Requip (ropinirole), Cabaser (cabergoline), Pramipexol (mirapex) and Injection Britaject (apomorphine). Instead of trying to replace the missing dopamine, these drugs act directly on the receptor sites which dopamine stimulates, hence mimicking its action. They can be used on their own as treatment or in combination with Sinemet or Madopar. It is thought that using them
early on their own may delay the need for levodopa and therefore prevent the long-term side effects of this drug. Each specialist has their own preference regarding treatment and eventually a combination of drugs is used to carefully control the symptoms. Each group of drugs can be very useful and has its place. Agonists essentially have the same side effects as levodopa preparations. They are more likely to cause nausea and dizziness when they are first taken, so antisickness drugs may need to be given initially. Hallucinations, nightmares and confusion are also more common. Careful monitoring of the dosage should prevent these happening. Apomorphine, the injectable agonist, can be used in combination with all the other drugs.10,11

**Drugs which inhibit the action of acetylcholine**

These drugs are known as anticholinergics. The ones that are commonly used are as Artane (benzhexol), Disipal (orphenadrine), Cogentin (benztropine), Kemadrin (procyclidine). All of these are available in tablet form, some as syrup and one as an injection. These drugs work by dampening down the effect of acetylcholine within the brain and the nervous system. They help to restore a balance between the chemical messengers within the basal ganglia of the brain. This group of drugs can be used to help suppress tremor, although with limited success.

**Drugs which prevent the breakdown of dopamine**

The most common drug in this group is selegiline (Eldepryl). It is known as a monoamine oxidase inhibitor or MAOI. Selegiline has been used since the mid 1980’s and it was initially hoped that it might stop the disease progressing. This, however, has proved not to be the case. In reality, because it stops the breakdown of dopamine, it gives a little relief from the symptoms of the disease. It is a mild anti-depressant and has a slight amphetamine effect, which means that it genuinely makes people feel better.12,13

**Others**

Amantidine (Symmetrel) was originally developed as an anti-viral drug and by coincidence was found to help the symptoms of Parkinson’s disease. It is thought that it works by bypassing the need for dopamine in a similar way to dopamine agonists, but the target receptor sites it uses are different. It does not help everyone and only works for a limited length of time in those cases nowhere it does have an effect. Because of how it
works it is particularly useful in treating Parkinsonism, but it can be used to treat Parkinson’s disease as well, particularly where dyskinesias are a problem.

**Surgery for Parkinson’s disease**

Surgery has been used in the treatment of Parkinson’s disease for four decades. Recently it has revived in popularity as new, precise methods of brain surgery have made it more reliable and much safer.

**Thalamotomy**

A tiny area in a part of the brain called the thalamus is destroyed using stereotaxic surgery. This operation is considered when tremor is disabling and interfering with everyday life to the extent that a person requires help with nearly all tasks.\(^\text{14}\)

**Pallidotomy**

A tiny area in a part of the brain called the internal globus pallidus is destroyed using stereotaxic surgery. This operation is used to relieve severe dyskinesia.

**Transplantation**

Midbrain tissue from human foetuses can be transplanted into the diseased area of the brain of the person with Parkinson’s disease. These foetal cells then produce dopamine, which eventually relieves the symptoms of the disease.\(^\text{12}\)

**Deep brain stimulation**

Instead of an area of the brain being permanently destroyed by stereotaxic surgery, a device called a deep brain stimulator is inserted. This uses the same technology as heart pace makers, but sends rapid electrical impulses to specific areas of the brain rather than the heart muscle. The stimulator can be placed in the thalamus, where it is most useful for treating tremor, or in the pallidum or subthalamus, where it is most effective for treating stiffness and dyskinesias.\(^\text{15}\)

**Radiosurgery**

The two main methods of carrying out radiosurgery are by gamma knife and by modified linear accelerator (linac). Both of these procedures use a high energy dose of radiation that can be focused on a very precise point within the brain. Radiotherapy may require a number of visits over weeks or months, but radiosurgery is completed in one visit and usually does not require an overnight stay. This approach is sometimes used to treat deep-
seated lesions or malformations within the brain that may be difficult to reach by conventional methods without causing damage.\textsuperscript{16}

**CONCLUSION**

At last it should be concluding that the Parkinson’s disease sign and symptoms in every single patient is different. It is important to remember that the changes in your brain were happening before the signs and symptoms of the disease became apparent enough to make a diagnosis. Researchers are at present trying to discover why people from different races experience different symptoms. Although common in older people, Parkinson’s disease is sometimes overlooked by doctors as the signs and symptoms may be wrongly put down to old age. When this occurs it is unfortunate since the available medicines can help people of all ages. From the clinical point of view, physician now take a more active interest in the patient’s basically in night time suffering and are increasingly aware of public health issues relative to alertness while driving with Parkinson’s disease.

**REFERENCES**


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