COMPREHENSIVE CARE CENTRE FOR MOVEMENT DISORDERS

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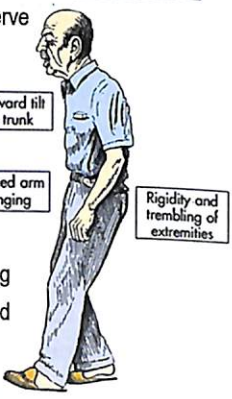
PARKINSON'S DISEASE AND ITS TREATMENT

"A life long friend"

Brain is an organ subserving a wide variety of functions like perception of sensations, initiation, control and co-ordination of movements of the body, maintenance of consciousness, intellectual functions etc.

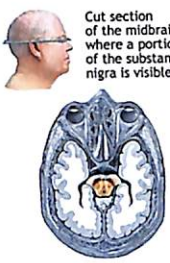
Parkinson's disease (PD) is a degenerative disease affecting the brain. Degenerative diseases are a group of disorders which result from progressive and premature death of nerve cells in the brain. Degenerative disorders show predilection for certain areas /functions of the brain. For example Alzheimer's disease is a degenerative disease which predominantly affects nerve cells subserving memory and cognitive (intellectual) functions. In Alzheimer's disease, the patients' main symptom will be loss of memory and intellectual dysfunction. In PD, the nerve cells predominantly affected are those concerned with posture of the body and movement. So the patients with PD will have predominantly movement related symptoms. However the disease process in PD is not solely confined to the areas of brain controlling movement. Other areas like those concerned with sleep, mood, autonomic functions (like control of blood pressure and urinary bladder functions), behavior and intellect could

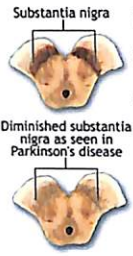


onate medicines for them!"

also get affected to a variable degree. Abnormal functioning of these areas of the brain can result in 'non-motor' manifestations like a variety of sleep disturbances, depression, anxiety, psychiatric symptoms, and incontinence of urine and memory dysfunction, in addition to the well-known movement-related (motor) dysfunction in PD.

What causes PD?





What causes PD is not fully clear to scientists even now. It could be due to defects in certain genes (which mean macro-molecules inside cells which control the properties and functions of the cell and also play an important role in heredity). Genetic problems directly causing PD is rare (1-2% of cases only). Genetic factors may only predispose the subject to PD, rather than causing PD directly. Certain factors in the environment are also thought to contribute to PD. For example, exposure to insecticides and drinking well water, have been found to have a role in the genesis of PD in some patients. Most of the times, environmental and genetic factors interact and result in PD. It is often very difficult to point out the factor which has caused the disease in individual patients.

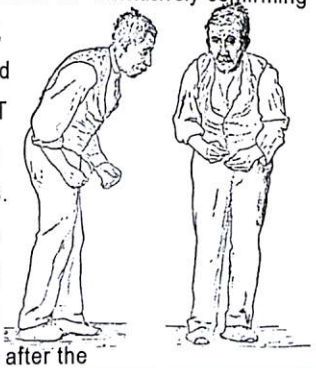
What are the clinical features of PD?

Patients with PD usually have tremor of limbs, stiffness of limbs (rigidity), slowness of activities (bradykinesia) and stooped posture with a tendency to loose balance. All of them need not be present in all patients. For example some patients have tremor as their predominant symptom, while others may have no tremor at all. The symptoms usually begin on one side and gradually spread to the other side. Some patients can have a phenomenon called freezing of gait, in which the patient feels that his feet are glued to the ground, on trying to walk. Freezing can significantly interfere with mobility. Patients with later stages of the disease can have difficulty in speaking, swallowing food etc. Other symptoms, unrelated to movement can occur, even in early stages ("non-motor symptoms"). They include reduced sleep,

depression of mood, anxiety, urinary bladder dysfunction leading to involuntarily passing urine, sexual dysfunction etc. Non-motor symptoms which occur in some patients in late stages include memory and intellectual problems, psychosis (Symptoms of psychosis include the patient seeing animals, objects or persons who are not actually present. This phenomenon is called 'hallucination') repeated falls etc. Other 'non-motor' manifestations of PD, which have been identified recently by researchers include the "Impulse Control disorders" ie. patient's inability to control the urge to do certain pleasurable activities (like gambling, eating, shopping, sexual activities) and a fascination for stereotyped, purposeless, complex activities (like repeatedly arranging and re-arranging books in a shelf, repetitive manipulation, disassembly and then assembly of machines etc), called "Punding".

How is PD diagnosed?

PD is diagnosed clinically, that is, from a detailed history of the onset and evolution of the patient's symptoms and the signs detected by the doctors on examining the patient. How the patient is responding to treatment also helps diagnosis. It may not always be possible for doctors to make the diagnosis at the first visit itself, especially if the patient is in the early stages of the disease and clinical examination findings are scanty. Follow-up visits to examine how the disease is progressing and responding to treatment may be required to reach a correct diagnosis. Currently there is no imaging study (scan) or blood test, commercially available to doctors for conclusively confirming the diagnosis of PD. However, researchers use certain advanced types of scans like PET/SPECT scans, to diagnose PD more accurately in research projects. Even these scans do not give a 100% ful-proof confirmation of diagnosis. A confirmed diagnosis of PD is currently possible only after the



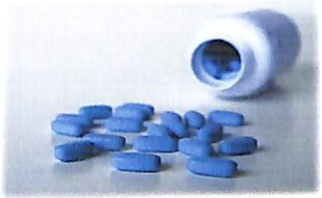
patient's death by examining the patient's brain under the microscope to see the characteristic changes in the dying nerve cells.

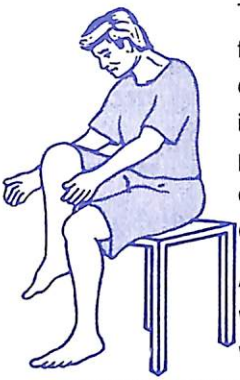
What are the other diseases which mimic PD ?

There are certain other neuro degenerative diseases which have symptoms and clinical signs very similar to PD and may be mistaken for the same, in the initial stages. These include multiple system atrophy (MSA), Progressive supranuclear palsy (PSP) etc. Even though they mimic PD in initial stages, these patients will not have a good and sustained response of their symptoms, to treatment. They also will have a more serious disease course. MRI scans are likely to show changes pointing to the diagnosis of this sort of diseases. Doctors generally advise the patients to get the scan done, if these diseases (collectively called "Atypical Parkinsonism"), rather than PD are suspected.

How is PD treated ?

In PD most of the movement related symptoms and some of the other 'non motor symptoms' result from deficiency of a chemical called 'Dopamine' in the brain. Dopamine is produced by some nerve cells located in a region called 'substantia nigra' in the 'mid-brain'. These nerve cells are the ones undergoing premature death in patients with PD. The mainstay of treatment of PD is replacement of dopamine in the brain. This is achieved by administrating a drug called Levodopa (Syndopa/Tidomet) which, on reaching the brain, is converted to dopamine. There are some medications called Dopamine agonists (like Pramipexole, Ropinirole etc) which mimic the action of dopamine in the brain. They are also useful in the treatment of PD. Some other medications (Entacapone, Rasagiline) act by interfering with the function of the enzymes (enzymes are very large molecules controlling the bio-chemical reactions leading to productions of chemicals inside the brain and their destruction) causing destruction of dopamine. These drugs help dopamine to be present in the brain for longer period of time and act longer.





The selection of the medicine, the dose, the frequency of administration etc have to be carefully decided by the doctors, considering a number of factors like the age of the patient, degree of disability, duration of the disease, co-existing 'non-motor' symptoms etc.

As we saw earlier PD is associated with a wide variety of other 'non-motor' symptoms which may significantly affect (sometimes even more than the movement-related 'motor' symptoms!) the patient's day to day functioning. These often need to be treated with appropriate drugs including medications for depression & anxiety, medications for good sleep, medications to control behavior etc.

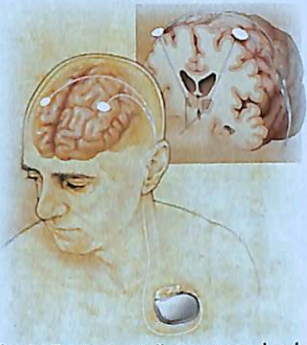
Regular exercise and physiotherapy have an equally important role for relieving muscle stiffness and improving mobility.

Currently there is no treatment available to restore the cells which have died off or to prevent further damage to the brain by arresting further nerve cell death. All the currently available treatment modalities aim at correcting the chemical deficiencies in the brain resulting from death of cells. Thus the currently available treatment modalities only relive the patient's symptoms and improve the quality of life. None of them can prevent the disease from worsening over the course of time.

What are the limitations of medical treatment of PD?

As pointed out earlier, the neuro-degenerative processes (progressive death of nerve cells) happening inside the brain will go on, in spite of all the currently available treatments. Thus the disease is likely to become more severe in due course of time, even though treated early and optimally. As the disease progresses, the patient will require more and more medications to control the symptoms. A condition called 'motor fluctuation' develops - three or four doses of medications fail to give relief to symptoms through-out the day. Each dose of Levodopa will result in a period of "On" characterized by relief of symptoms. This is followed by an "Off" period where all the symptoms recur. The patient will have to take the next dose to turn "On" again. The duration of improvement with each dose of medication gradually comes down and

the patient will require more and more number of doses to remain active throughout the day. Another problem faced with in late stages is 'drug induced dyskinesia'. This is characterized by abnormal, excessive 'dancing' movements of the body during the period when the patient is experiencing the beneficial effect of the drug. At this stage, the treating doctors are put into a dilemma in which a reduction in dose leads to worsening of symptoms of PD and any increase in dose to relive these results in abnormal excessive movements.



Patients with disabling symptoms resulting from such advanced stages of PD, not relieved by optimal medical treatment are considered for surgical treatment. The preferred surgical treatment for patients with PD is "Deep Brain Stimulation", in which a device called the Neuro-stimulator ("DBS Battery") which is similar to a cardiac pacemaker is implanted over the chest wall, under the skin. It is a device containing a battery and microelectronic circuitry. It generates electrical signals that are delivered to the brain via a thin wire with electrodes attached at the tip, to relieve the movement-related symptoms of PD. DBS is not the first option when treating PD patients. It has to be understood that it is not a 'cure' for PD, but a treatment option to relieve the patient's symptoms in advanced stages of the disease, when the treatment with medicines alone fails to give adequate relief of symptoms. The other surgical procedures include stereotactic thalamotomy and pallidotomy. In these procedures, a small surgical "lesion" is produced in the brain target, to alter its function and relieve the symptoms.

The patient is selected for these lesioning surgeries, when symptoms cannot be controlled by medical management alone and DBS is not possible due to technical or other (eg: financial) reasons. These procedures are much less expensive than DBS; however the results are also inferior to those of DBS.

For more details contact:

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