Parkinson's Disease 101
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Suggested internet resources:
www.cmdg.org
http://www.parkinson.org
http://www.davisphinneyfoundation.org
http://www.parkinson.ca

Parkinson's Disease

2-3% of the population will have Parkinson features by age 80. The average age of onset is 59-60. The range covers all decades with >50% being affected before retirement age.

Early features:

Although the patient most frequently notices the changes that lead to the diagnosis, their family or doctor are commonly the ones that notice the changes first. Family and friends will notice the tremor, loss of facial expression, the tendency to appear depressed (even when not), more rapid aging, quieter voice, slow walking and loss of clarity of writing. The patient may note the tremor, shoulder aching, loss of dexterity, fatigue, a long standing problem with constipation, loss of sense of smell, need to repeat to be heard, change in writing size (micrographia) and drooling especially at night.

The Diagnosis:

There are no blood tests or routine xrays that can confirm Parkinson's disease. This is a diagnosis based on clinical features. There must be slowness of movement along with either tremor at rest or muscular stiffness or both. Characteristically these features start on 1 side of the body and on average take 2 years to start to affect the other side.

Additional clues on exam will be a stooped posture, shuffling gait with reduced stride length, loss of facial expression, quieter voice, reduced arm swing, along with the history of loss of sense of smell and constipation.

The key feature is slowness of movement (Bradykinesia), which is associated with further reduction of speed and rhythm with repeated movements. The patient will require multiple steps to make a turn ("turning en block") and with progression gait initiation will become difficult. Balance gradually becomes impaired and the ability to maintain an upright posture becomes abnormal due to a loss of knowing where the center of gravity is.

The brain chemicals and non motor symptoms:

The primary deficit is an inability to produce normal amounts of dopamine. This mainly affects movement ability but can also lead to cognitive and emotional changes as well as a reduction in motivation. Norepinephrine and serotonin production is also impaired affecting mood, sleep, appetite, sexual desire, pain sensitivity, and motivation.

The collection of non-motor symptoms are frequently present and tend to be associated with more impact on disability and quality of life than the motor symptoms.

Normal brain function:

There is a structure deep in the brain, on both sides, that activates movement called the thalamus (thee “motor”). Another deep structure, the basal ganglia, acts to inhibit the thalamus to actively slow down movement (the “brake”). Dopamine, which is produced in the brainstem, normally is carried by nerve cells to the basal ganglia where it inhibits it, thereby releasing the thalamus to stimulate movement (the Brake regulator”).

Parkinson Pathology:

In Parkinson’s disease the nerve cells that produce dopamine die off at a faster rate than normal. This leads to a inability to inhibit the brake causing the basal ganglia to actively slow down the movements.

Researchers identified an abnormal protein collection appears in those nerve cells prior to death called “Lewy Bodies”. The protein was identified to be alpha synuclein. In 2003 a Dr Braak studied 110 brains and determined there was a pattern of spread of this protein. The initial changes occur in the nerve to smell (olfactory nerve) and the area of the lower brainstem that regulates bowel motility. The pathology then over time spreads to affect the higher brain stem causing the typical Parkinson features, followed by involvement of even more widespread regions of the brain leading to memory changes.

Parkinson’s disease timeline:

The average life span of Parkinson’s disease after dx based on motor signs is 20 years. It is now known though that a collection of “Premotor” features can develop as far back as 20 years earlier including; constipation, loss of sense of smell, sleep disorders, anxiety and depression, fatigue, and weight change.

Atypical Parkinsonism's:

Other conditions besides Parkinson's disease can cause a person to look Parkinsonian, or have "Parkinsonism". Side effects of certain medications is a common explanation. Other neurodegenerative diseases which referred to as "Atypical Parkinsonism" or "Parkinson plus" syndromes and tend to progress more quickly and respond less well to medications.

Brain damage from infections, head trauma, or stroke can also mimic Parkinson's but tend not to respond to medications.

The main subtypes include;

PSP – Progressive Supranuclear palsy - Recognized by early falls, neck rigidity, a startled facial expression, poor speed and range of eye movements.

DLB - Dementia with Lewy bodies is a parkinsonism associated with early dementia, fluctuating degrees of confusion and hallucinations

MSA - Multiple system atrophy is a parkinsonism associated with failure of the automatic bodily functions (Autonomic) including blood pressure control, bladder and bowel and sexual function as well as strained breathing.

CBD – Cortical basal degeneration (or syndrome) is a parkinsonism associated with mainly one sided symptoms, associated with higher level dysfunction due to an inability to figure out how to use the limbs involved in addition to the parkinsonism. Memory loss is also common.

All of these have a more severe prognosis due to their more rapid progression and poor medication response.

Cause of Parkinson's Disease:

Most of the time Parkinson's disease does not run in families and is thought of as a sporadic condition. There are definite exceptions to this and ~ 16 % of cases will identify a family history of their condition. This means 84% of the time the condition can't be explained on a genetic basis and must be caused by something the patient has come into contact with over their life.

There are many different genes now linked with Parkinson's. If your parent or sister or brother has it there is a 5-6% chance you will also. If your parent and your brother or sister have it there is a 20-40% chance you will get it.

There are also many environmental triggers that have been confirmed. These include;

Pesticides, Plant toxins, Effects of viruses, fungi and bacteria, heavy metals including manganese, carbon monoxide poisoning, epoxy resin exposure and head injuries.

The analogy is "genetics loads the gun and the environment pulls the trigger".

Parkinson's Management:

Canadian guidelines recommend this condition be cared for in an interdisciplinary specialty clinic. In Manitoba, the Deer Lodge Movement Disorder Clinic provides specialty care for Parkinson's disease. There is a "pre-appointment problem profile" to assist patients and clinic staff in getting the most out of clinic visits. There are many issues that can be managed without resorting to medications. Medications should be introduced if the quality of life is significantly affected.

Management - Non-Medication:

Exercise is strongly encourages. 3 hours per week of cardiovascular fitness or restrictive exercise is a good way of fighting back and is thought to slow the rate of progression of the disease by up to 30% per year. Education is a must to better understand the disease. Allied health input will assist in managing with a variety of challenges including problems with diet, speech, swallowing, general fitness, fitness to drive, and linking up with other support networks. Counseling can be provided to assist coping and maintaining independence. Advise is also available to help with advance life planning.

Management - Medications:

There are no medications that halt or slow the progression of Parkinson's disease. One, Rasagiline showed some encouraging results in this regard but the conclusion by the FDA was this goal was not achieved.
As a result all medications for Parkinson's are used in attempt to improve the symptoms. There is no proven need to start them as soon as a diagnosis is made. They are introduced to try to maintain function and quality of live – both at work and home.

The aim is to resolve the dopamine deficiency state. This can be done by dopamine replacement using either regular release Levodopa / Carbidopa (Levocarb / Sinemet / Prolopa) or long acting Sinemet CR (erratically absorbed), or by changing the chemical imbalance in favour of Dopamine by blocking acetylcholine with "anticholinergics (eg. Trihexyphenidyl). Amantadine acts to block acetylcholine as well but also seems to have other effects on Dopamine receptors making it useful to treat Parkinson symptoms as well as the excessive movements levocarb can sometimes cause (Dyskinesia).

There are medications that block the ability of the body to get rid of dopamine which can also provide beneficial effects on their own in the case of Selegiline or Rasagiline or in combination with levodopa in the case of Entacapone. There are also medications that mimic dopamine's effect on dopamine receptors. These "dopamine agonists" include Bromocriptine, Ropinirole, Pramipexole and a unique skin patch that lasts 24 hours, Rotigotine. Unfortunately since these medications came to marked, it was recognized they have a high potential to cause excessive sleepiness (12%) and what has been referred to as "Impulse control" problems. The latter can include gambling, shopping, hypersexuality, binge eating, and other compulsive patterns of behavior in up to 13% of patients. Should these side effects occur it usually becomes necessary to discontinue them.
As a result of the side effects on agonists, levodopa would often be the medication patients initiate.
The goal of medications is to obtain a blood level of dopamine receptor stimulation within the "therapeutic window". Too high a dose can trigger side effects including excessive movements and confusion. Too low a dose will not achieve adequate symptom control. As Parkinson's disease progresses, this therapeutic window narrows. This causes a greater reliance on medications to replace the dopamine that the Parkinson brain becomes less and less able to provide.

Fluctuations in response to medications result in fluctuations of function. Patients are referred to as "ON" when the level is in the therapeutic window and "OFF" when blood levels drop below the effective dose. Involuntary movements "dyskinesia" can occur if the blood level gets too high. Dyskinesia occurs in 50% of young onset cases within 3 years of onset. They become less common with older age of onset. Dopamine agonist are known to be less likely to cause these fluctuations and dyskinesia in comparison to levodopa and as a result are still tried in young patients prior to levodopa after discussion and depending on the patient preference.

Daily diaries of the timing of fluctuations are often needed to guide medication dose and timing to minimize these problems. With progression consistent timing of doses becomes increasingly important. There are a variety of medication alarms available. A good internet source is www.epill.com.

Management - Surgical:

Deep Brain Stimulation (DBS) involves surgically implanting electrodes into the basal ganglia to alter the firing pattern. This has been confirmed in multiple trials to be more effective than available medications once a patient reaches a stage where medications still work but cannot maintain a stable response through the day. This procedure cannot be done safely on elderly cases with cognitive problems.

Surgical implantation of a tube into the small bowel and then infusing levodopa in the form of a gel by a externally worn pump is an additional option for cases with problematic fluctuations who are not able to tolerate surgery. Currently this is only covered by pharmacare by cases seen by Dr Anang a movement disorder specialist at St Boniface Clinic. The cost is $60,000 / year.

Disease progression:

Once diagnosed, this neurodegenerative disease continues to slowly worsen. On average the first 3 years is spent in a honeymoon period when the medications provide an even response all day long. Fluctuations become increasingly prominent after this stage requiring more medications and more frequent dosing. DBS starts to become an option during this stage (3-8 years). From 8-15 years from diagnosis treatment refractory symptoms become increasingly evident. These can but do not always include balance problems, worsening speech and swallowing, bowel and bladder dysfunction, sleep disorders, and fatigue.

Advanced stages of the disease are associated with more frequent confusion, falls, hallucinations, memory loss and loss of independence requiring increasing input from family and home care. Depending on individual situations personal care home placement may enhance patient safety and reduce social isolation. Planning for advances stages of the disease should be done early and communicated with a chosen health proxy.

Other management issues:

MPI needs to be informed of this illness as the combination of a reduced reaction time and with progression cognitive slowing, the risk of an accident increases. Not infrequently periodic road tests will be recommended to ensure safety on the road.

There are several common issues for patients with Parkinson's to deal with. These include constipation (managed with a adequate fluid intake to avoid dehydration, fruit and fiber in the diet, and if needed daily sienna laxatives or an osmotic laxative such as lactulose.

REM sleep disorder wherein patients retain the ability to move during their dreams. This can cause self injury and injury to the bed partner. Melatonin at bedtime often improves this condition.

Depression and anxiety occur in 30% of cases and can precede the diagnosis. This is managed in the same way as anxiety and depression in cases without Parkinson's.

Psychosis typically begins as an illusion of presence – getting the feeling someone is behind you. This can progress to delusions – often paranoid about partner infidelity. True hallucinations can follow. As Parkinson's will be worsened by typical neuroleptics (they block dopamine), management involves reducing causative agents if possible or using quetiapine or clozapine as they won't worsen Parkinson's.