INTRODUCTION

When James Parkinson wrote about the “shaking palsy” – the condition that would later come to bear his name – he believed, “there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be stopped.” However, almost two centuries of research, although shedding light on the underlying cause of Parkinson’s disease (PD) and developing symptomatic treatments, have failed to provide a cure for this progressive, neurodegenerative disease. There are an estimated 127,000 people living with Parkinson’s in the UK, with the highest prevalence among those aged over 75. Furthermore, overall UK prevalence is expected to rise by more than 26% by 2020.

In the absence of a cure, the focus of treatment for chronic diseases such as PD becomes long-term management with the goals of secondary and tertiary prevention, encouraging patient self-management, and improving patients’ quality of life. However, although practitioners’ clinical decisions will inherently be based on evidence-based medicine, the complexities of individuals’ personal circumstances and state of health at any given time demand an intuitive, experience-based decision-making process that can justifiably be considered an art. This essay sets out to demonstrate the art as well as the science of geriatric medicine as exemplified by its approach to Parkinson’s disease.

DISCOVERING THE CAUSE OF PARKINSON’S DISEASE

As life expectancy has increased, research into the causes of chronic diseases has expanded commensurately. In the case of PD, it was found that the dopaminergic neurons in the substantia nigra, specifically in the pars compacta, become damaged in PD. This causes a decrease in the availability of dopamine in the nigrostriatal pathway, producing both motor and non-motor symptoms. Moreover, the presence of Lewy bodies (inclusions containing accumulations of the protein alpha-synuclein) in the substantia nigra as well as other areas of the brain was pinpointed as the pathological hallmark of the idiopathic form of PD. In addition, it has been found that non-dopaminergic (e.g. serotonergic) neurotransmitter systems are also affected by PD and play an important role in the development of PD symptoms. However, what causes the initial deterioration of dopaminergic neurons remains unclear. Although several monogenic causes of idiopathic PD have been discovered, these represent less than 10% of PD cases in most populations. It is postulated that genetic susceptibility factors interact with environmental exposures (e.g. certain toxins) to begin the process of neurodegeneration.
**THE CHALLENGE OF DIAGNOSING PD**

Although the neuropathology of PD is well understood, there are only a handful of useful diagnostic tools, so diagnosis remains largely clinical. Apart from the presence of the cardinal features of bradykinesia, muscular rigidity, rest tremor, and postural instability, the patient must respond to drug therapy (levodopa), the course of the disease be progressive, and atypical features be absent in order for a PD diagnosis to be made.\(^5\) This complexity is due to several degenerative (e.g. multiple system atrophy) and non-degenerative diseases (e.g. vascular parkinsonism) mimicking PD. Accordingly, diagnosing idiopathic PD requires considerable clinical skill and expertise, and a recent study calculated that PD is still incorrectly diagnosed in around 25% of patients.\(^6\)

**PHARMACOLOGICAL MANAGEMENT**

Similar to multiple other chronic conditions encountered in geriatric medicine, PD can only be treated palliatively. At present, there are no treatments to prevent, halt, or slow the progression of PD, let alone reverse the damage caused to midbrain dopaminergic neurons. Neuroprotection in particular has sparked considerable research interest, with neuroprotective agents mainly targeting inflammation, oxidative stress, excitotoxicity, apoptosis, and mitochondrial dysfunction. Despite many clinical failures, several potential agents including Minocycline, creatine, and Rasagiline have demonstrated substantial neuroprotective effects and are now in Phase III clinical trials.\(^7\)

Pending conclusive results in the field of neuroprotection, dopamine replacement via levodopa (L-DOPA) remains the gold standard for treatment. L-DOPA is a precursor of dopamine, and unlike the latter, is able to cross the blood-brain barrier, where it is subsequently converted to dopamine. L-DOPA improves both the primary motor symptoms of resting tremor, bradykinesia, muscle rigidity, and postural instability as well as secondary motor symptoms such as gait problems (freezing, festination), dystonia, speech and swallowing disturbances, and hypomimia. Unfortunately, even though L-DOPA is very effective at controlling the motor symptoms of PD, prolonged use and the need for increasing the dose as PD progresses entail increasingly disabling motor side effects. These include dyskinesia as well as “on-off” periods, in which response to the medication fluctuates unpredictably.

Several alternative treatments have been developed in order to delay or reduce the need for L-DOPA. Dopamine receptor agonists mimic the effects of dopamine in the brain and are associated with fewer long-term motor complications. Although less potent than L-DOPA, they can reduce the dose and side effects of L-DOPA and are often administered as a monotherapy in the early stages of PD. Other drugs that are used in conjunction with L-DOPA include monoamine-oxidase-B inhibitors, which delay dopamine breakdown, and catechol-O-methyltransferase inhibitors, which reduce the peripheral breakdown of L-DOPA.

Although PD is classically considered a movement disorder, non-motor manifestations are an integral part of the disease and often deemed by patients to be more disabling than the
motor manifestation. Neuropsychiatric disturbances (depression, dementia, hallucinations, compulsive disorders), autonomic dysfunction, and sleep disorders are just some of the many non-motor symptoms (NMS) patients may experience. Although current dopaminergic treatment does little to alleviate NMS, non-dopaminergic neurotransmitter systems promise to be more rewarding therapeutic targets. Regrettably though, NMS are still underdiagnosed and therefore undertreated: a recent study found that out of a mean of 11 of 30 NMS reported by patients, only an average of 4.8 were recorded in their clinical notes. Furthermore, medication for NMS often interacts with medication for motor symptoms; for example, dopaminergic treatment may induce psychosis, and conversely, antipsychotics may worsen motor symptoms.

Pharmacological management of PD therefore demands considerable clinical expertise. Geriatricians must prescribe drug regimens that strike a balance between symptomatic relief and debilitating side effects, taking into consideration each patient’s general state of health and personal preference.

**SURGICAL TREATMENTS**

In advanced stages of PD, when medical treatment alone becomes inadequate, surgical interventions are an important part of ongoing treatment. Deep brain stimulation is the preferred type of surgery and consists of implanting electrodes in the brain that stimulate the globus pallidus or subthalamic nucleus, thus blocking signals from these areas and reducing motor symptoms. There has also been extensive research into other surgical modalities such as transplantation of neural tissue, gene therapy, and neurotrophic factor infusion. Despite ambiguous and often disappointing study outcomes, it has been suggested that these have been due at least in part to variability and confounding factors in the studies themselves: for example, in the field of neurotransplantation, the highly variable results can be partly attributed to uncontrolled factors such as tissue preparation and post-operative immunotherapy. It is hoped that improved study designs and communication amongst researchers will help develop effective clinical treatments.

**A HOLISTIC APPROACH TO PATIENT CARE**

Since chronic diseases such as PD are very diverse in nature and affected by psychosocial variables, a purely biological approach to care would be incomplete. Geriatric PD patients in particular have complex needs that need to be addressed in a multidisciplinary, holistic way in order to maximize patients’ function and quality of life. One of the most important aspects of patient care is reducing disability and maintaining patients’ independence. Even though elderly PD patients are usually more reliant on caregivers, a recent prospective, longitudinal study showed that 57% of patients over 70 (with PD duration of over 4 years) were still able to live independently. With respect to cultivating and preserving such independence, geriatricians should organize and coordinate complementary therapies, the benefits of which are far-reaching: physiotherapy can help reduce falls, speech therapy assists with hypophonia, occupational therapy helps adapt the home environment, and counseling can help manage depression and anxiety. Furthermore, involving a Parkinson’s
nurse in patient care will improve the continuity of care and the level of patient support. Finally, it is important that patients and carers are involved in medical decision-making and future planning and that psychological, social, and financial support for both patients and carers is made available wherever possible to help them cope with PD.

**CONCLUSION**

In addition to relying on evidence-based treatments, geriatric medicine also depends on the artful skill of evaluating the patient as a whole and integrating all pertinent information in order to make appropriate clinical decisions. With its diverse clinical presentation, heterogeneous progression and problematic management, Parkinson’s disease epitomizes the challenges of treating elderly patients. The science of geriatric medicine – the knowledge gained by experimentation and observation – has given us a deeper understanding of the causes of PD as well as bringing us closer to a cure. However, treatment remains incredibly complex, especially when patients present with comorbidities, multimorbidities and the functional impairment natural to aging. Consequently, it is the geriatric practitioner’s art, i.e. the skill of diagnosing, treating, and collaborating with patients, which provides comfort, support, and hope to PD patients and their families.

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REFERENCES


