**The Edinburgh Parkinson's Lecture, Thursday 15 May 2014**

# Recent Advances in the Cause and Treatment of Parkinson's

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We were very lucky that Professor Tony Schapira accepted our invitation to deliver the third annual Edinburgh Parkinson's Lecture. The event, held at the Royal College of Physicians in Queen Street, was attended by nearly three hundred people, including many with Parkinson's Disease (PD) and many others with a personal or professional interest in the causes and treatment of the condition. Over a hundred people in the audience were health professionals, and over a hundred had travelled from outside our Branch area. The diversity of the audience, both in terms of experience of PD and of understanding the technicalities of its causes and treatment, would have presented a considerable challenge to any speaker; but Professor Schapira rose to that challenge and there was indeed something for everyone is this lecture.

After a warm welcome from Dr Nicki Colledge to the Royal College of Physicians of Edinburgh, and an introduction outlining Professor Schapira's career and achievements from Professor Siddarthan Chandran, Director of the Anne Rowling Regenerative Neurology Clinic, Professor Schapira set out his agenda, to consider first some recent developments in understanding the **causes** of PD, and then to review current medical approaches to **treatment**, including prospects of new treatments. He stressed the link between the two, and the need to understand more about the causes in order to develop effective new drugs.

In his discussion of the **causes**, key points included:

- the important association between PD and ageing, and the need to factor in how treatment interacts with the ageing process;
- the fact that pathological changes in the brain may begin long before the symptoms are noticeable: for example, the distribution of Lewy bodies starting in the brainstem, spreading to the substantia nigra and then to the whole brain;
- the continuing debate about whether causes are predominantly environmental or genetic. While there are no confirmed **environmental causes**, some modifying factors have been identified: for example, exposure to pesticides or solvents or low Vitamin D levels appear to increase the risk of PD, while smoking, coffee, anti-inflammatory drugs and high urate in the blood appear to decrease the risk. Evidence

suggested that some of these modifying factors may be a reflection of genetics, in ways which we do not yet fully understand.

- the importance of recent advances in the understanding of glucocerebrosidase (GCase), discussed in the context of the **genetic causes** (outlined fully in Professor Schapira's slides which are also available on our website). The process of developing PD may begin early, with metabolic changes starting even in the womb. Research in the 1990s using fetal graft cells had shown that alpha-synuclein could spread from the patient's own brain into the fetal cells. This proof of how alpha-synuclein can spread throughout the brain provided the motivation for subsequent research to find ways of stopping the spread and slowing the development of the disease. Research on Gaucher disease had also helped advance understanding of the link between GCase and alpha-synuclein: if glucocerebrosidase levels increase, alpha-synuclein decreases.

Turning to discussion of **treatments**, Professor Schapira outlined briefly the current drug treatments, highlighting new Levodopa therapies including subcutaneous, slower-acting versions, and Safinonamide, a new drug which is beneficial in improving the motor function without increasing dyskinesias. He then reviewed non-dopaminergic approaches to the treatment of PD, before considering new approaches to neuroprotection, to slow the course of the disease. He stressed again the importance of understanding the causes of PD in order to develop appropriate treatments for all stages of the disease, and that progress is being made for all four stages. LRRK2 inhibitors and GBA modulators are being developed to try to stop the disease from developing in its earliest stages; drugs promoting compensation help delay the onset of dysfunction once PD is established; multi-functional drugs are still being improved to help once degeneration is underway; and cell replacement therapies may help in the later stages.

His own current work is in the area of neuroprotection. Building on the understanding of the link between glucocerebrosidase and alpha-synuclein, research is now testing the hypothesis that increasing GCase activity would reduce alpha-synuclein levels and slow the progression of PD. In a recently published article in the journal *Brain* (2014: 137, pp.1481-95), McNeill and a team including Professor Schapira had demonstrated how Ambroxol improves lysosomal biochemistry in glucocerebrosidase mutation-linked PD cells.

After a lively question and answer session, chaired by Dr Conor Maguire, and some appreciative closing remarks from Dr Katie Le Blond from Parkinson's UK, the evening ended with a vote of thanks from Ken Bowler. The donations from the audience will support further Parkinson's research.