INTRODUCTION
Parkinson’s disease (PD) is a common, chronic and incurable neurodegenerative disorder of the brain. It presents with a resting tremor, slowness of movement, rigidity, and problems with walking. The pathology within the brain is widespread but there is critically a loss of dopaminergic neurons in an area of the brain called the substantia nigra. Replacement of this transmitter with drugs (such as L-dopa or dopamine agonists) has been possible since the 1960s and produces great clinical benefit. This approach suggests that treating PD by transplanting dopaminergic neurons should work as well as these medicines.

RATIONALE FOR USING CELL BASED THERAPIES FOR PD
The most logical and obvious cellular replacement therapy (CRT) approach for PD is the engraftment of dopaminergic cells of the type lost to the disease process, the A9 nigral midbrain dopamine cells. Implanting these cells in the brain of patients with PD will need to be done at the site where dopamine normally works and should give a clinical response that is equivalent to that seen with dopamine drugs. This CRT, while not curing patients of PD, has the theoretical advantage over drug therapies that the grafted nerve cells will release dopamine in a physiological way at the site where it is needed, and by so doing should avoid the side effects seen with dopamine drugs.

WHERE ARE WE WITH CELL BASED THERAPIES FOR PARKINSON’S DISEASE?
Beginning in the 1980s, attempts have been made to repair the PD brain using dopamine-producing cells, of which the most successful to date used human fetal ventral mesencephalic tissue. These cells, when grafted into patients with PD, can survive long-term in large numbers, release dopamine, make synapses with the host brain, as well as significantly improve PD for years. This approach, however, has quality, logistical and, to some, ethical issues as well as side effects in some trials. As such a more acceptable and reliable source of dopamine cells are needed. Over the last 10 years, technologies and protocols have evolved to the point that midbrain dopamine neurons can now be made from both embryonic stem (ES) and induced pluripotent Stem (iPS) cell sources which show good survival in animal models of PD and demonstrate functional benefits. This work is now at the point that first in-human clinical trials are fast approaching.

WHEN WILL TRIALS BEGIN?
The first in-human clinical trials will probably start with ES-derived dopamine-producing cells in the US (most notably by the group of Lorenz Studer) and with iPS cell-derived dopamine-producing cells in Japan (lead by Jun Takahashi) in 2018/19. In Europe, this work is likely to enter trial for the first time around 2020/1. Trials have already begun in Australia using a parthenogenetic stem cell source but issues relating to aspects of this trial have been raised.

MAJOR CENTERS WORKING ON THE CLINICAL APPLICATION OF STEM CELLS FOR PD
The groups leading this work have formed a global alliance called G-FORCE PD. Their website is www.gforce-pd.com and their latest publication was at the end of 2017.
REFERENCES


USEFUL WEBSITE
https://www.eurostemcell.org/
http://www.closerlookatstemcells.org/

Roger A Barker, PhD, MRCP, University of Cambridge, and the ISSCR Clinical Translation Committee

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