

Disease statistics

UNDERSTANDING PARKINSON'S DISEASE

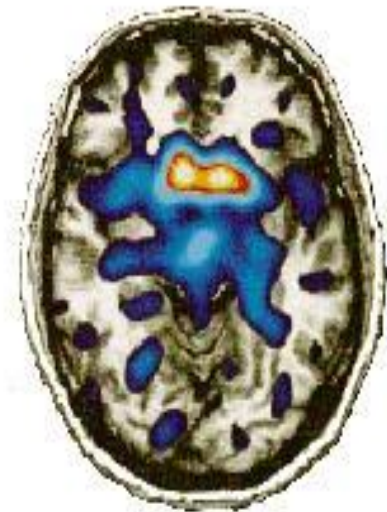


WHAT IS PARKINSON'S DISEASE ?

- A progressive disease of the nervous system marked by tremor, muscular rigidity, and slow, imprecise movement, chiefly affecting middle-aged and elderly people.
- It is associated with degeneration of the basal ganglia of the brain and a deficiency of the neurotransmitter dopamine.



Normal



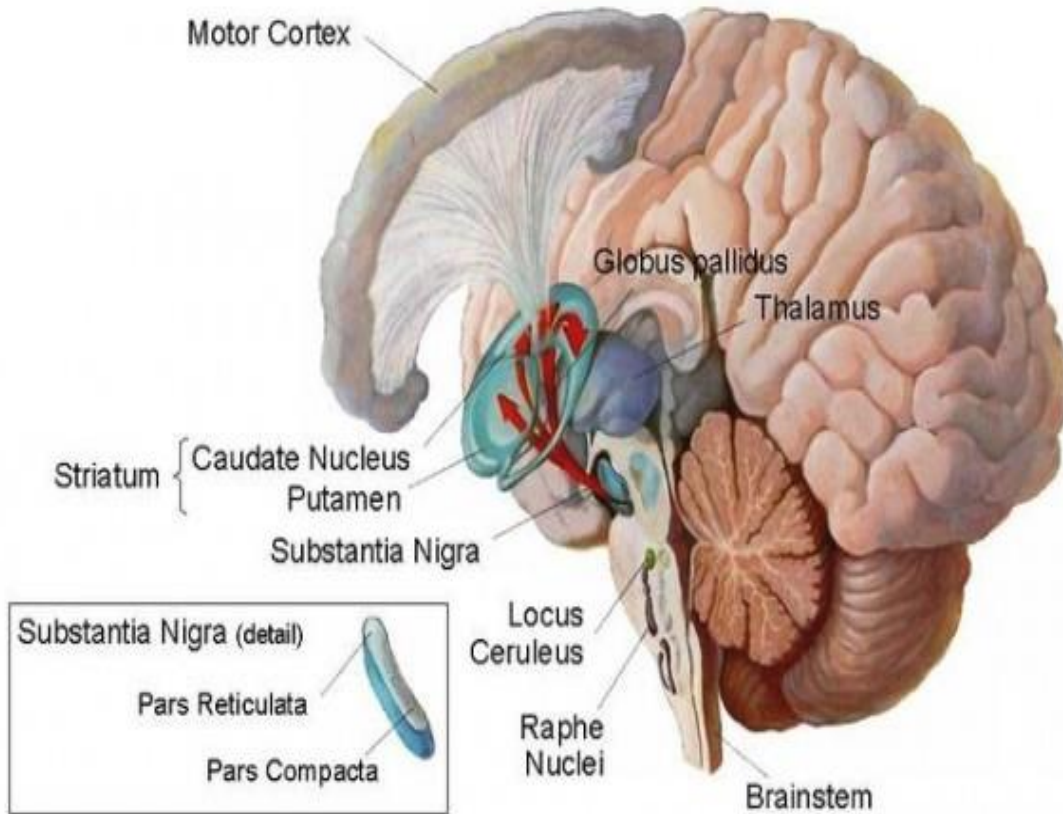
Parkinson's
Disease

PATHOPHYSIOLOGY OF PD

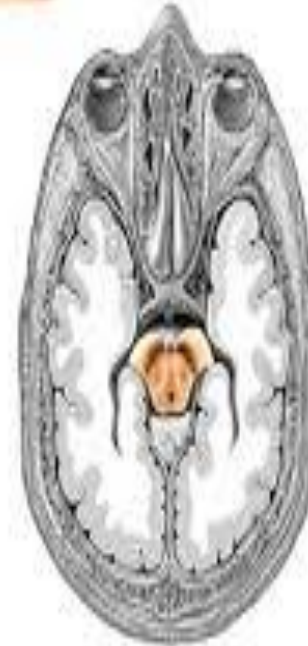
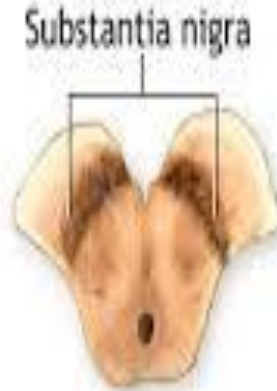
- Progressive loss of pigmented neurons in the *substantia nigra*, decrease in dopamine.
- Symptoms of Parkinson's Disease appear after 60%- 80 % of these cells become impaired or die (striatal dopamine levels have decreased by 20%-50% of normal level).
- Pathological hallmark of Parkinson's Disease is the presence of lewy bodies (intracytoplasmic eosinophilic inclusions) in pigmented neurons of the *substantia nigra*.

PATHOPHYSIOLOGY OF PD

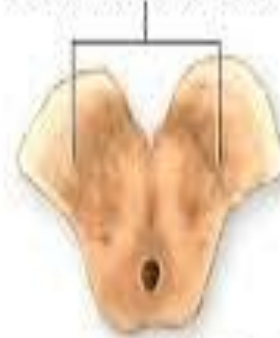
Brain Regions Affected by Parkinson's Disease



Cut section of the midbrain where a portion of the substantia nigra is visible



Diminished substantia nigra as seen in Parkinson's disease



ADAM

Parkinson's disease

EPIDEMIOLOGY OF PD

PD which was first described in 'An essay on the shaking palsy' in 1817 by a London Physician, James Parkinson, has probably existed for thousands of years.

- Affects more than 2 % of the population older than 65. The incidence increases dramatically with increasing age.
- The prevalence of PD is 328 per 100,000 in India. ^[1]
- The average age of onset is 62.4 years with the majority of cases occurring between 50 and 79 years; 10 percent of cases occur before the age of 40.

1. Gupta B M, Bala A. Parkinson's disease in India: An analysis of publications output during 2002-2011. Int J Nutr Pharmacol Neurol Dis 2013;3:254-62

ETIOLOGY OF PD

- Parkinsonism: Refers to a group of disorders that produce abnormalities of basal ganglia (BG) function.
- Parkinson's Disease or IDEOPATHIC PARKINSONISM is the most common form.
- Secondary Parkinsonism results from a number of identifiable causes including virus, toxins, drugs, tumors.
- Parkinsonism refer to those conditions that mimic PD in some respects, but the symptoms are caused by some other neurodegenerative disorder.

CLINICAL MANIFESTATIONS OF PARKINSON'S DISEASE

CARDINAL FEATURES

- Rigidity
- Bradykinesia
- Tremor
- Postural instability

MOTOR SYMPTOMS

- Start hesitation.
- Freezing episodes.
- Poverty of movement.
- Hypophonia.
- Slow shuffling gait
- Stooped posture.
- Micrographia

NON-MOTOR SYMPTOMS

- Memory thinking problem/ Dementia.
- Constipation / Bladder Urgency
- Sleep disturbances.
- Anxiety/Akathisia
- Depression/ Apathy
- Akathisia
- Dysarthria
- Dysphagia

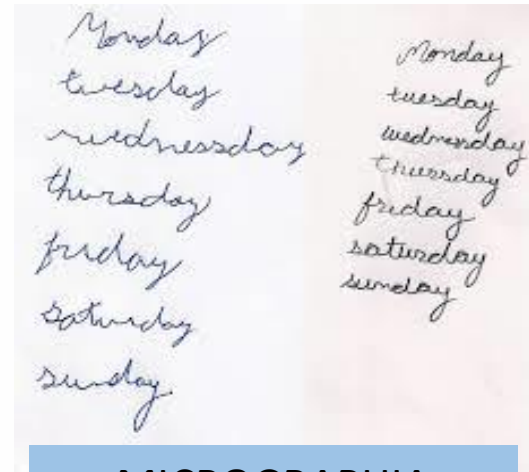
CLINICAL MANIFESTATIONS OF PARKINSON'S DISEASE



POSTURAL INSTABILITY



TREMOR



MICROGRAPHIA

DIAGNOSIS OF PARKINSON'S DISEASE

- There is no standard diagnostic test for Parkinson's.
- The best objective testing for PD consists of specialized brain scanning techniques that can measure the dopamine system and brain metabolism.
- The diagnosis is made on the basis of history and clinical examination, handwriting samples, speech analysis, interview questions that focus on developing symptoms.

TREATMENT CURRENTLY AVAILABLE FOR PARKINSON'S DISEASE

- There is no cure for Parkinson's Disease. However, treatment can help control the symptoms.
- **MEDICINE**
 - Medical treatment help control shaking and movement symptoms. Drugs like Levodopa, Dopamine Agonists like Permax (Pergolide), Parlodel (bromocriptine), Apomorphine, Cabergoline, Ropinerole are currently being used that increases dopamine in the brain.
- **SURGERY**
 - Surgery may be an option for some people. Surgery does not cure Parkinson's disease, but may help ease symptoms. Types of surgery include:
 - ✓ Deep Brain Stimulation (DBS)- This involves placing electric stimulators in areas of the brain that control movement.
 - ✓ Pallidotomy.
 - ✓ Thalamotomy

COMPLICATIONS AND LIMITATIONS OF DRUG THERAPY FOR PARKINSON'S DISEASE

- **Levodopa** is the most effective drug treatment for Parkinson's disease (PD). However, its chronic use is associated with dyskinesia, motor fluctuations, and hallucinations.
- **Dopamine Agonists** drastically improve the motor symptoms and quality of life of patients in the early stages of the disease. Sooner or later, they suffer from "dopa-resistant" motor symptoms (speech impairment, abnormal posture, gait and balance problems), "dopa-resistant" non-motor signs (autonomic dysfunction, mood and cognitive impairment, sleep problems, pain) and/or drug-related side effects (especially psychosis, motor fluctuations, and dyskinesias).

- Reference: [Rascol O](#)¹, [Payoux P](#), [Ory F](#), [Ferreira JJ](#), [Brefel-Courbon C](#), [Montastruc JL](#).

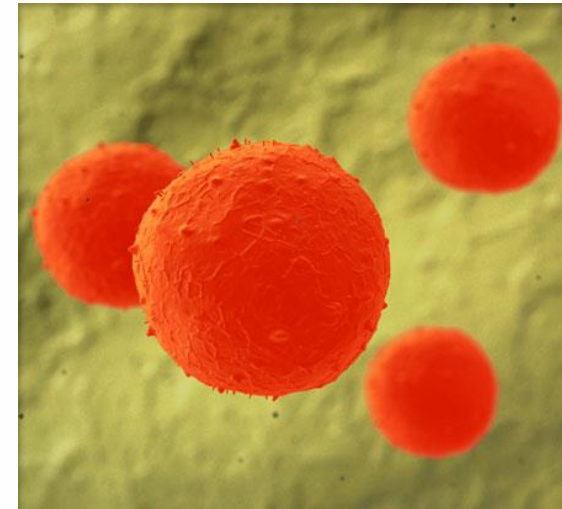
¹Clinical Investigation Centre and Department of Clinical Pharmacology, Toulouse, University Hospital France.

CAN STEM CELLS TREAT PARKINSONS DISEASE?

- Stem cells offer the potential to provide a virtually unlimited supply of optimized dopaminergic neurons that can provide enhanced benefits in comparison to fetal mesencephalic transplants. Stem cells have now been shown to be capable of differentiating into dopamine neurons that provide benefits following transplantation in animal models of Parkinson's Disease.

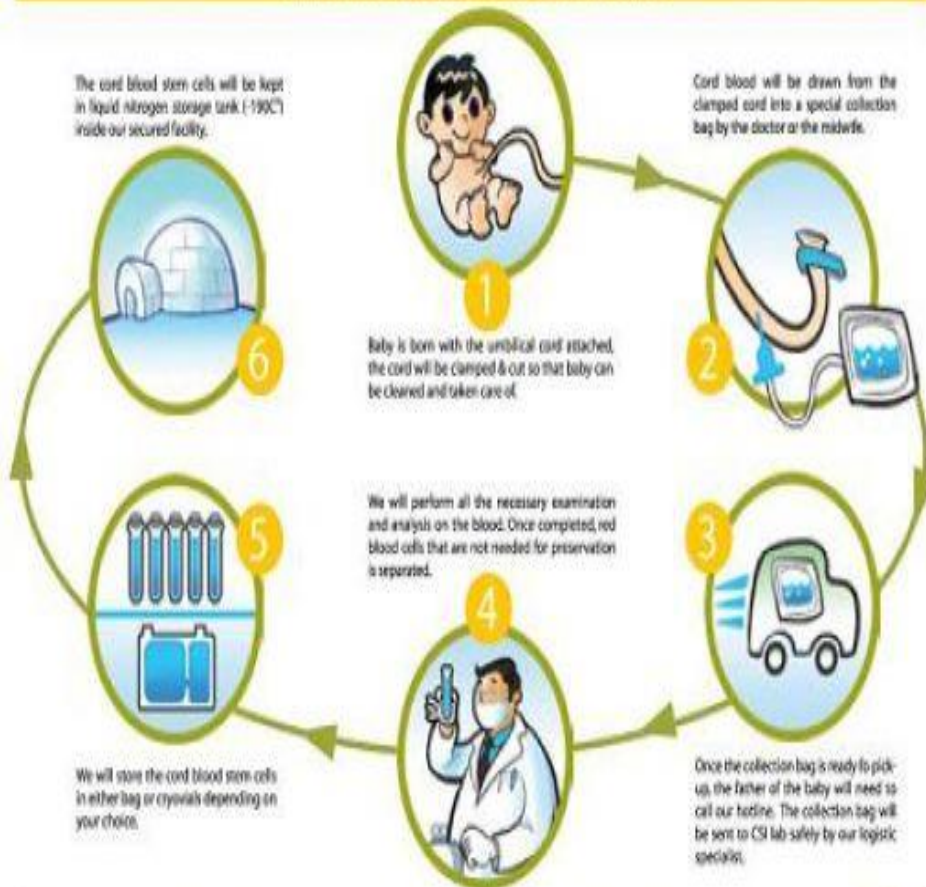
Journal: [Lippincott Williams & Wilkins, Inc.](#)

- Scientists have also considered whether a patient's own (endogenous) stem cells could be mobilized to repair the damage caused by Parkinson's. Adult neural stem cells are located in the brain's white matter and can multiply and form all the major brain cells, including neurons.
- Mesenchymal stem cells offer an intriguing approach to treating Parkinson's disease. These stem cells can be harvested directly from a patient's bone marrow, as well as from other tissues, and therefore when injected back into the patient, they may be able to minimize the likelihood of transplant rejection. Studies have shown that it is possible to differentiate mesenchymal stem cells into neurons but the real power of these cells likely resides in their ability to produce growth factors that support damaged neurons.



BENEFITS OF UMBILICAL CORD STEM CELLS

How do we collect cord blood stem cells?



- ✓ Stem cell harvest from umbilical cord blood and cord tissue is a painless and non-invasive process.
- ✓ Cord blood stem cells are immature and therefore more tolerant to HLA mismatches, posing low risk of Graft versus Host Disease (GVHDs).
- ✓ Cord blood derived stem cells have high rate of engraftment.
- ✓ Finding match is very easy and its immediately available .
- ✓ Cord blood stem cells are young and unexposed to external environment.

IMPORTANT PUBLICATIONS ON APPLICATION OF UCSCs IN PARKINSON'S DISEASE

- ✓ Cell transplantation is a strategy with great potential for the treatment of Parkinson's Disease, and many types of stem cells, including neural stem cells and embryonic stem cells, are considered candidates for transplantation therapy. Mesenchymal stem cells are a great therapeutic cell source because they are easy accessible and can be expanded from patients or donor mesenchymal tissues without posing serious ethical and technical problems.

Reference: Parkinson's Disease and Mesenchymal Stem Cells: Potential for Cell-Based Therapy. <http://www.hindawi.com/journals/pd/2012/873706/>

- ✓ Immature stem cells in human cord blood may be able to ameliorate the effects of Parkinson's Disease. Symptoms and death in mice models of Parkinson's Disease were postponed the most in those animals given mononuclear cells from human umbilical cord blood mononuclear cells.

Reference: Ende N and Chen R. Parkinson's Disease Mice and Human Umbilical Cord Blood. *Journal of Medicine* 2002; 33(1-4): 173-180.

IMPORTANT PUBLICATIONS ON APPLICATION OF UCSCs IN PARKINSON'S DISEASE

- ✓ In this study Human mesenchymal stem cells isolated from Wharton's jelly of the umbilical cord were induced to transform into dopaminergic neurons in vitro through stepwise culturing in neuron-conditioned medium, sonic hedgehog, and FGF8.
- Reference: Fu YS, Cheng YC, Lin MY, Cheng H, Chu PM, Chou SC, Shih YH, Ko MH, Sung MS. Conversion of human umbilical cord mesenchymal stem cells in Wharton's Jelly to dopaminergic neurons in vitro - Potential therapeutic application for Parkinsonism. Stem Cells 2005; Aug 11

<http://onlinelibrary.wiley.com/doi/10.1634/stemcells.2005-0053/full>

CASE STUDY OF APPLICATION OF MESENCHYMAL STEM CELLS IN PARKINSON'S DISEASE

Treating Parkinson disease using umbilical cord blood mesenchymal stem cell

Wu Li-ke, et al, Journal of Clinical Rehabilitative Tissue Engineering Research October 1, 2009 Vol.13, No.40

A total of 30 Parkinson patients in Beijing Wu Stem Cells Medical Center, from January to December 2008, were selected, including 19 males and 11 females, aged 45-66 years, mean aged 58 years, 2-4 grade according to Hoehn-Yahr classification. All patients received MSCs implantation by lumbar puncture via subarachnoid space, the 3, 4 lumbar was served as puncture points. Totally 5 mL (5 000 000 cells) MSCs were slowly injected within 10 minutes, once per week, for 4 successive weeks. Unified Parkinson's Disease Rating Scale (UPDRS) was used to evaluate those Parkinson patients' neural function, the greater scores, the severe damage.

Compared to before transplantation, the UPDRS was significant decreased at 3 month after treatment ($P < 0.01$). The clinical symptoms, such as tremor, rigidity, slow movement, unstable posture had obvious improvement, in addition, there was no graft versus host disease occurred.

CONCLUSION: MSCs implantation can ameliorate clinical symptoms, as well as improve life quality of Parkinson patients in some extent.

CLINICAL TRIAL CASE STUDY

Successful second implant of NTCELL for Parkinson's Disease

- Living Cell Technologies Limited, 18 August 2014 – Sydney, Australia and Auckland, New Zealand – Living Cell Technologies
- Limited today announced that a second patient has been successfully implanted at Auckland City Hospital in the clinical trial of the regenerative cell therapy NTCELL® for Parkinson's disease.
- The Phase I/IIa clinical trial is an open-label investigation of the safety and clinical effects of NTCELL in patients who can no longer respond to current therapy.
- Dr Ken Taylor, CEO of LCT says, "A great deal of hard work, preclinical research and scientific endeavour has gone into the discovery and development of NTCELL. Our innovative approach is the first to target regeneration of brain cells for patients who are failing the current conventional treatment for Parkinson's disease."

Reference: [CHINA TROPICAL MEDICINE 2010 10, 9:1043-45.](#)

CASE STUDY IN INDIA

Manipal Hospital discovers cure for Parkinson`s disease (April 4th, 2007)

Mr Andrew Kisana, a 58-year-old patient affected by Parkinson`s Disease has shown positive signs of cure with stem cell therapy.

With the success in treating this patient, India-based Manipal Hospital has proved that stem cell therapy could be a potential option for easing out symptoms in a patient suffering from Parkinson`s Disease.



REFERENCES:

- Parkinson Society Canada <http://www.parkinson.ca/>
- National Parkinson Foundation (US): <http://www.parkinson.org>
- European Parkinson's Disease Association <http://www.epda.eu.com>
- Parkinson's Disease Society (UK): <http://www.parkinsons.org.uk>
- The Michael J. Fox Foundation <http://www.michaeljfox.org>
- Journal: *Nature* 441, 1094-1096 (29 June 2006) | doi: 10.1038/nature04960; Published online 28 June 2006.
- <http://www.slideshare.net/apekshabesekar/parkinsons-disease-23892325>
- <http://onlinelibrary.wiley.com/doi/10.1634/stemcells.2005-0330/full>

Thank you

