Parkinson’s Disease
Over the Years:
A Brief History
Andrew Duker, MD
Neurologist, University of Cincinnati
Gardner Center for Parkinson’s Disease
and Movement Disorders, UC Neuroscience Institute

Why is history important?
• “Those who cannot remember the past are condemned to repeat it.”
  - George Santayana, philosopher

  • “There is no cure for birth and death save to enjoy the interval”

Was Parkinson the first?
• Tremors had been defined for some time – the ancient Greek physician Galen described tremor in 175 AD as an “involuntary alternating up-and-down motion of the limbs” resulting from partial “weakness of the force that supports and moves the body”

• Even earlier, the ancient hindu healing science called Ayurveda details the presence of a condition with tremor, called “Kampavata” in approximately 1000 BC

Ayurveda
• According to Ayurvedic concepts, there are three categories or humors, namely, doshas, dhatus, and malas.
• Doshas govern the physiological and physicochemical activities of the body, and these are three in number, namely, vata, pitta, and kapha.
• Vata is responsible for all movements and sensations, including motor actions.
  - Kampa = tremor
  - Kampavata = tremor humor

Ancient Parkinson’s disease - Kampavata
• Ayurvedic literature describes kampavata as:
  - no inclination for movement (probable akinesia/bradykinesia)
  - drooling of saliva
  - love of solitude (probably due to depression)
  - constant somnolence
  - whiteness and fixation of the eyes (possible reptilian stare or masked facies)
Ancient Treatment

- It also appears this condition was treated with formulations including mucuna pruriens (a herb now known to contain levodopa).

An Essay on the Shaking Palsy

- Parkinson's essay was unique in that it was the first in modern western literature to put together the clinical symptoms of the whole syndrome rather than focusing solely on tremor.

Who was James Parkinson?

- Parkinson did not initially receive much attention for his essay.
- “English born, English bred, forgotten by the English and the world at large, such was the fate of James Parkinson.”
  - L.G. Rowntree

James Parkinson’s London

- No photograph exists of James Parkinson.
- He lived and practiced medicine at No. 1 Hoxton square, London.
- He was famous not only for his contributions to medicine but also for several textbooks of geology.
- He died in 1824 at age 69 following a stroke.

Why is it called Parkinson’s disease?

- Jean-Martin Charcot, one of the first neurologists, recognized the elegance of James Parkinson’s description of this condition from his essay and attached Parkinson’s name to the condition in the 1860s.
Encephalitis lethargica
- Also known as von Economo's encephalitis
- First described in Romania in 1915, it resulted in pandemics around the world in the 1920s
- The mortality rate came close to 40%
- Many of those who survived developed neurologic symptoms
- Parkinsonism was quite common, although different from idiopathic Parkinson's disease in that oculogyric crises were common and the disease progression was much slower

Awakenings (1990)

Early treatment of Parkinson's
- Charcot used atropine
- Other medications like Artane and Cogentin (anticholinergic drugs) helped mainly the tremor but not the other symptoms of PD
- Neurosurgical procedures were developed, some serendipitously

Early surgical treatment
- In 1952, Irving Cooper was forced to tie off the anterior choroidal artery while he was performing an operation on a patient with parkinsonism
- When the patient woke from anesthesia, his tremor and rigidity had disappeared
- He began to purposely repeat this procedure to improve symptoms for patients with Parkinson's disease

Before and after Irving Cooper's surgery

Stereotactic surgery for movement disorders
- Originated in 1947 with an apparatus designed by Spiegel and Wycis
- Used to target specific deep targets in the brain, including the globus pallidus (supplied by the anterior choroidal artery) and also the thalamus
Curing parkinsonian rabbits

- In the 1950s, the Swedish scientist Arvid Carlsson discovered that D,L-dopa reversed the parkinsonian syndrome caused by reserpine in rabbits.

Parkinson’s and dopamine

- In 1959, Carlsson speculated that dopamine was somehow responsible for Parkinson’s disease.
- He later won the Nobel Prize in Medicine in 2000 for his work with dopamine.

Using levodopa to treat Parkinson’s

- In the 1960s, researchers began to test intravenous L-dopa as a treatment for Parkinson’s disease, which was helpful but only transiently so; high doses were needed but were often ineffective.
- In 1967, George Cotzias started with low doses and gradually increased the dose up to 16 g/day, with good and sustained results.

Using L-dopa

Sinemet

- Adding carbidopa (a peripheral decarboxylase inhibitor) further increased the potency of levodopa and decreased the associated nausea and vomiting.
- Sinemet (carbidopa-levodopa) was marketed.
- Sinemet = sine (without) – emet (emesis).

MPTP

- In 1982 a group of young drug addicts in northern California developed severe parkinsonism after injecting MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) under the impression it was a new 'synthetic heroin'.
MPTP

The advent of DBS

- In 1997, thalamic DBS was approved in the US for tremor due to Parkinson's disease and essential tremor
- In 2002, DBS of the STN and GPi was approved for the treatment of Parkinson's disease

Advances in genetics

- In 1997, the first gene mutation was identified in PD, alpha-synuclein (PARK1)
- Since that time, many more mutations have been discovered (PARK2-PARK 15)

Progress forward

References