**Parkinson’s Disease**

**BACKGROUND**
Parkinson's disease, also known as idiopathic paralysis agitans or shaking palsy, is a chronic progressive neurodegenerative disease. Parkinson’s disease occurs when a part of the brain which contains dopamine (a certain chemical or neurotransmitter) degenerates.

Idiopathic or Classical Parkinson’s disease must be differentiated from secondary parkinsonism associated with other neurodegenerative disorders including Olivopontocerebellar degeneration (OPC), Striato-nigral degeneration, Progressive Supranuclear Palsy (PSP), Multiple System Atrophy (Shy-Drager Syndrome). This distinction is important for treatment and predicting response to surgical intervention. The combination of resting tremor, initial asymmetry of symptoms, slow progression, and good response to levodopa are most diagnostic of classical Parkinson’s.

Relevant Anatomy (Figure 1):

**SIGNS and SYMPTOMS of DISEASE**
Tremor is often the most prominent clinical symptom. It often starts in one limb and may be worsened by stress, cold weather, or fatigue. It is a tremor present at rest. Bradykinesia is another common symptom. Patients may report slowness with common activities including dressing, bathing, or completing chores. Cogwheel rigidity may be seen on exam with a ratchet-like feel of the limb on passive movement.

A certain Mask-like facies and a slow and shuffling gait are also seen frequently. Dementia (loss of memory) is also often present as a significant clinical feature of Parkinson’s in the elderly. The incidence of dementia in patients with Parkinson’s is more than six times greater than in patients without the diagnosis. Parkinson's disease affects approximately 1% of Americans over age 50. Age is the single most important risk factor. The male to female ratio is approximately 3:2. No single environmental or genetic factor has been identified but both are believed to play a role in its development.

A focused exam will help distinguish Idiopathic Parkinson’s from other causes of parkinsonism. Abnormalities in vertical eye movement might suggest PSP. Cerebellar features or autonomic instability might suggest Multiple System Atrophy. Early onset (less than age 40) and the presence of Kayser-Fleischer rings on slit-lamp exam would suggest Wilson’s disease.

**DIAGNOSTIC TESTS**
The diagnosis of Parkinson’s is made clinically. Imaging studies may be helpful in distinguishing Idiopathic Parkinson’s from other causes of parkinsonism.
TREATMENT OPTIONS

- Levodopa - the standard medical therapy. Over 90% of patients with Parkinson's initially respond to Levodopa. The absence of a response may suggest an alternative diagnosis. It is contraindicated in patients with malignant melanoma (dopamine is a melanin precursor and may stimulate tumor growth) and in patients taking MAO inhibitors (hypertensive crisis). Nausea and vomiting are common side effects. Dyskinesias (abnormal movements) may be seen.

- Dopamine Agonists - Useful in patients experiencing on-off phenomena and in those requiring larger doses of Levodopa.

- Anticholinergics - May improve symptoms of rigidity, tremor and akinesia. Side effects are very common. They include organic confusional syndrome, dry mouth, urinary retention, facial dyskinesias.

- Anticholinesterase Inhibitors - Rivastigmine, a dual cholinesterase inhibitor, showed moderate improvement in dementia associated with Parkinson's disease but was associated with increased nausea, vomiting and tremor in a placebo-controlled study.

- Implantation of Dopaminergic Tissue - The first double-blind, placebo-controlled, randomized study of implanted fetal mesencephalic dopaminergic tissue showed no significant difference in any outcome measures between the two groups. Implanted tissue did not reduce the prevalence of dyskinesia and several patients with implanted tissue developed new dyskinesias not relieved by reducing antiparkinsonian medication.

- Deep brain stimulation (DBS) - Electrodes implanted in the brain have been shown to decrease the severity of symptoms during “off medication” periods, with subsequent reduction of levodopa dosage and associated dyskinesias during “on medication” periods in patients with advanced Parkinson's. A prospective, double-blind study has confirmed these findings. This procedure is FDA-approved for treatment of medically refractory Parkinson’s.

SURGICAL TECHNIQUE

Patients may be admitted the night prior to surgery and have anti-Parkinson medications withheld on the morning of surgery. A stereotactic frame (similar to a HALO) is typically used. MRI of the brain may be used for target planning. Electrodes are implanted under local anesthesia with monitoring. Hair is shaved and the head is prepared in a sterile fashion. Two holes are placed in the skull based on the calculated path. Microelectrodes are advanced through a guide to the anatomical target to aid in determining the final electrode position. The surgery can take 3-6 hours for the implants.

Xray of DBS Implant in the head (Figure 2)

SURGICAL RISKS

Recently published data of STN deep brain stimulation suggest that the risks of surgery include device infection (5%), revision (3.1%), cerebral infarct (stroke), bleeding, air embolism, perioperative seizures, confusion (6.8%), and battery failure (8.4%). In a review of 100 patients undergoing STN electrode implantation no patient died or experienced new permanent neurological deficit.
EXPECTED OUTCOME
Average hospital stay is approximately 2-3 days including the day prior to surgery. A long-term follow-up study of patients who had undergone bilateral subthalamic stimulation demonstrated a 27% improvement in activities of daily living indices and a 28% improvement in motor scores in patients who underwent surgery versus baseline. There was also a greater than 50% reduction in the use of levodopa medication doses\textsuperscript{11}. A five year prospective study of patients who had undergone bilateral subthalamic nucleus stimulation showed even more promising outcomes. After five-years, patients’ scores for motor function off medication and for activities of daily living improved by 54 and 49%, respectively. Average scores for cognitive performance and depression, however, did not improve\textsuperscript{12}. These studies suggest that although there are risks of surgery, in the properly selected patient population deep brain stimulation can provide significant and permanent improvement of Parkinson’s related symptoms.

AUTHORS
S. Yadla, A. Sharan, J. Harrop

RELEVANT TERMS
(List with Numbers)
1. Parkinson’s Disease
2. Deep Brain Stimulation
3. Subthalamic Nucleus Stimulation
4. Levodopa
5. Bradykinesia
6. Substantia Nigra
7. Neostriatum
8. Dyskinesia
Figure 1: Areas of the Central Nervous System Affected by Parkinson’s Disease. Courtesy of Lang AE, Lozano AM. Parkinson’s Disease. NEJM 339:1044-1053, 1998.
Figure 2: An X-ray of the skull showing two deep brain electrodes for Parkinson’s disease