Parkinson's Disease: Choices and Challenges
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Learning Objectives
• List four hallmark features of Idiopathic Parkinson Disease, and identify distinguishing features of atypical Parkinson syndromes
• Implement and initial and ongoing pharmacotherapy plan
• Guide patients and caregivers in making key treatment decisions in early, mid- and advanced stage PD.

Epidemiology of PD
• Approximately 1.2 million patients in US, with 50,000 new diagnoses each year
• Average age of onset is 60 years
• Affects up to 0.3% of the general population, but 1%–3% of those >65 years
• Prevalence increasing as the population ages

Parkinson Disease: More Than Meets the Eye
• Parkinson disease in the elder care spectrum
  – Under-reported
  – Under-treated
  – Under-estimated
• Options in medical management
  – Neurologist vs. real doctor
  – Medication timing is critical to motor function
  – Support services must be customized

Basal Ganglia

Hallmark Symptoms in PD
• Resting tremor
• Bradykinesia
• Rigidity
• Loss of Postural Reflexes
Common Symptoms in PD

- Reduced arm swing affected side
- Pain or tingling, “bursitis”
- Asymmetric resting tremor
- Slow, shuffling, stooped gait
- Slow dressing/bathing
- Low, muffled voice (dysarthria)
- Night-time Drooling
- Fine motor limitations (cutting/buttoning/fastening)
- Incredibly small handwriting (micrographia)
- Difficulty getting out of chair/car
- Difficulty turning in bed

Increasing the Odds of Diagnostic Accuracy

- + Resting tremor
- Initial asymmetry
- Masked facies
- Good response to levodopa treatment
- Lack of atypical symptoms

Caution Signs for Atypical Syndrome

- Absence of tremor at onset
- Rapid disease progression
- Autonomic nervous system dysfunction
- Symmetrical onset
- Lack of responsiveness to levodopa
- Early axial rigidity
- Postural instability, early falls
- Diplopia/presyncope/apraxia/dementia

Drug-Induced Parkinsonism

- Careful medication history
- Common offending drug types
  - Antipsychotics
    - haloperidol, chlorpromazine, thioridazine, perphenazine
    - risperidone, olanzapine, ziprasidone, aripiprazole
  - Anti-emetics: metoclopramide, prochlorperazine
  - Dopamine depletors: methyl dopa, reserpine, tetrabenazine
  - Antidepressants: fluoxetine, sertraline
- Treatment
  - Stop offending medication
  - Use alternative medications
  - Parkinsonism may linger over 30 days

Hoehn and Yahr Staging of PD

- Scale was originally designed to describe the untreated patient. Most appropriate current use is to evaluate patients for clinical trials or other research endeavors.
  - Stage I – symptoms detectable, unilateral
  - Stage II – symptoms are detectable bilaterally
  - Stage III – significant impairment of postural righting reflex
  - Stage IV – major gait impairment, cannot live alone
  - Stage V – bed to chair transfers, cannot walk
### Unified Parkinson Disease Rating Scale (UPDRS)
- Part I – cognition, behavior and mood
- Part II – subjective report of ADLs
- Part III – objective assessment of motor function
- Part IV – rating complications of therapy

### Pharmacotherapy of PD
- **Dopaminergic**
  - Carbidopa/levodopa
  - Dopamine agonists
- **Reduced catabolism**
  - MAO-B inhibitors
  - COMT inhibitors
- **Anticholinergics**
- **Amantadine**
- **Emerging therapies**

### Dopaminergic Agents
- **Levodopa-based agents**
  - Carbidopa-levodopa tablets
  - Carbidopa-levodopa sustained-release tablets
  - Carbidopa-levodopa-entacapone combination tablets
- **Ergot-derived dopamine agonists**
  - Bromocriptine
  - Pergolide
  - Apomorphine (injection)
- **Non-ergot (2nd-generation) dopamine agonists**
  - Ropinirole
  - Pramipexole

### Levodopa
- Levodopa has been the cornerstone of the treatment of PD for over 35 years
- Treatment associated with decreased morbidity and mortality over pre-levodopa era
- Most effective drug in the treatment of PD
- *Virtually all patients with Idiopathic PD (IPD) have clinically significant, often robust improvement*
Dopamine Agonists

- Act by direct stimulation of dopamine receptors
- Effectively treat PD symptoms
- Reduced risk of dyskinesia compared to L-dopa
- Consensus recommends as initial monotherapy
- Effective adjunctive therapy to levodopa

Risk Factors for Developing Motor Fluctuations

- Young age at onset
- Longer duration of illness
- Greater severity of illness
- Short half-life of dopaminergic agent, leading to pulsatile stimulation of striatal receptors
- Higher dosage of levodopa

Differential Assessment of Key Motor Features

- Dystonia vs. dyskinesias
  - "off" dystonia is a contorted posture, generally indicative of too little dopamine
  - Early morning dystonia manifests as toes cramping and curling downward (beware podiatry referral)
  - Dyskinesia is a writhing movement, typically indicative of too much dopamine
- Tremors
  - Poor barometer of overall motor function
  - Affected by stress, being in public, exhaustion
  - Self-limiting

Levodopa Motor Complications Occur in up to 80% of Treated Patients

- End-of-dose "wearing-off"
  - 1 to 3 years post initiation of levodopa
  - Response duration (~4 h) becomes shorter
  - Symptoms may re-emerge 1–3 h of each dose ("off" state)
- Dyskinesias
  - Usually take the form of abnormal involuntary choreoathetoid movements
  - Usually appear in peak dose “on” period
  - Occur months to years post initiation of levodopa

### Rapid Recognition of Motor Fluctuations
- Diminished facial expression (hypomimia)
- Increased dysarthria
- Decreased amplitude of finger tapping
- Marked upper limb rigidity, greater on primary side of involvement
- Decreased leg agility (gauged by heel tapping)
- Gait instability
  - Increasing difficulty with balance
  - Freezing and festination

### Management of Early and Midstage PD
- No harm in delaying pharmacologic treatment if symptoms are mild
- Initiate dopaminergic replacement therapy with a dopamine agonist
- Supplement with levodopa if clinical control with dopamine agonist not optimal
- Add COMT inhibitor when motor fluctuations appear, or perhaps when beginning levodopa

### Management of Later Stage PD
- Minimize peaks by lowering levodopa at each dose
- Reduce “off” time by decreasing dose intervals of levodopa, or adding dopamine agonist, COMT inhibitor, or MAO-b inhibitor
- Rescue strategies: apomorphine, liquid levodopa/carbidopa, soda
- Monitor dyskinesias, psychosis, cognitive impairment
- Monitor risks of constipation, dysphagia, falls

### Allied Health Strategies
- PT and OT evaluations
- Aquatic exercise
- Massage to reduce rigidity and dyskinesias
- Lee Silverman Voice Therapy for dysarthria
- Support groups
- Individual and family counseling
- SLP dysarthria & swallowing assessment
- Palliative care as an option in advanced PD

### Comprehensive Management of PD
- Individualize therapy: age, cognition, symptoms, response to treatment
- Focus on wellness (eg, exercise, stress reduction, balanced diet)
- Monitor functional ability
- Introduce dopaminergic therapy when symptoms require treatment
- Evaluate response and modify treatment

### DBS Considerations
3 slides from Stuart Isaacson
still to come
Non-motor “Wearing-Off” Symptoms

- **Sensory:** pain, paresthesias, akathisia
- **Psychiatric:** apathy, depression, anxiety, panic, paranoia, hallucinations, cognitive changes
- **Autonomic:** BP changes, shortness of breath, tachycardia, sweating, pallor, laryngeal stridor, drooling, dysphagia, belching, abdominal bloating, urinary disturbances

Mood Disorders in PWP

- **Anxiety**
  - Non-specific anxiety is common in PD
  - Manifests as brooding, excessive worrying, fidgeting, S.O.B., sleep disturbances, agitation
  - Observe symptoms 4-6 months prior to classification and treatment.
- **Apathy**
- **Depression**
  - Clinical depression occurs in > 50% of patients sometime over the course of their disease.
  - Low mood for > 2 weeks warrants pharmacotherapy.
  - Anti-depressant medication + counseling offers superior outcome over medication alone.

Apathy as a Syndrome: *Who Cares?*

- Lack of motivation; failure to initiate goal-directed behavior
- Involves three domains
  - Cognitive
    - loss of interest in new experiences
    - lack of concern about personal problems
  - Affect
    - flattened affect
    - no reactivity to positive or negative events
  - Goal Direct Behavior/Action-Initiation
    - requires other to structure activities
    - Lack of effort

Laura Marsh, MD, Johns Hopkins

Sources of Confusion in PD

- Medication
- Depression
- PD-related
  - 40%+ of patients have cognitive impairment
- Concurrent neurological disease
  - Lewy body dementia
  - Alzheimer’s disease
Behavioral Approaches to Dementia

- Simplify communication and complex sequences.
- Do not argue.
- Reinforce desired behaviors every time.
- Anticipate physical needs.
- Incorporate music, rhythm, repetitive motion and high-touch strategies into daily activity plan.
- Modify environment to minimize disorientation.

Sleep Disorders in PD

- Comprehensive sleep evaluation may be warranted to define specific sleep problems associated with PD. (beware unintended SE of polysomnogram)
- Sleep disruption is more common in PD than sleep-onset insomnia.
  - Valerian root and Calms Forte are safe OTC sleep aids to try vs. diphenhydramine or Rx agents.
- Sleep hygiene is a powerful tool, under-emphasized
  - Establish a regular going-to-bed routine
  - Get up at the same time every morning
  - Maintain comfortable sleep environment
  - Stop watching the News!
LNAAs and Levodopa Absorption

When the concentration of LNAAs is high, only a small amount of levodopa is transported into the brain. When the concentration of LNAAs is reduced, more levodopa is transported into the brain.

Nutritional Interventions

- Adequate hydration is fundamental to medication absorption
- Determine most appropriate timing of meals to avoid interference with levodopa absorption.
- Crystallized ginger can relieve medication-induced nausea
- Deal pro-actively with constipation
  - PD drastically slows the entire GI process
  - Mobility problems limit weight-bearing exercise
  - Useful OTC agents to prevent acute constipation:
    - Stool softeners such as docusate sodium
    - Triphala, an Ayurvedic adaptogen and anti-oxidant
    - Miralax
    - Infant glycerin suppositories
    - MOM, Fleet enema for occasional use
Nutraceuticals for PWP

- Lactobacillus acidophilus – GI probiotic
- Ginger for nausea
- Triphala for constipation
- Parsley for GERD

Nutraceuticals for PWP

- St John’s Wort – antidepressant
- Valerian root – anxiolytic/sedative
- Ginkgo biloba – alerting properties
- Milk thistle – improves liver function
- Coenzyme Q10 - antioxidant

Quality of Life Predictors

- Predictive elements for positive adjustment for persons and families living with chronic illness
  – Commitment to maintain optimal health status
  – Ability to cope with losses
  – Intellectual curiosity
  – Sense of engagement
  – Support system (people, pets)
  – Safety net
  – Tactile needs met
  – Sense of humor