Parkinson's Disease Registry Advisory Committee Meeting Minutes

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Date: Friday, March 4th, 2022 (1:00 – 3:00 pm)

Location: Zoom (https://umass-amherst.zoom.us/j/93968180415)

Materials Provided: Meeting agenda.

Committee Members:

Brett Miller (co-chair), Cathi Thomas (co-chair), Dr. Samuel Frank, Lauren Fogarty, Dr. Anindita Deb, Dr. Terrell Johnson, Dr. Glenn Tucker, James Cornell, Matt Keswick

Others Present:

Mary Lou Woodford

Call to Order by co-chair Cathi Thomas

Roll Call:

- Cornell, present
- Deb, present
- Fogarty, present
- Frank, present
- Johnson, present
- Keswick, present
- Miller, present
- Thomas, present
- Tucker, present

I. Welcome

Motion to accept minutes from the 1/26/22 meeting by member Frank. Seconded by Deb.

Unanimously accepted proposed minutes.

II. Overview of Parkinson's Disease

Presented by Dr. Samuel Frank

Parkinson's Disease: An Overview

Samuel Frank, MD
Associate Professor of Neurology, HMS & BIDMC

Epidemiology

- Worldwide prevalence
  - 1% of population greater than 65 years
  - 3% of population greater than 85 years
  - 187/100,000
- US prevalence
  - 1.6% of population over 6
  - In MA = 860,000 x 1.6% = 13,760 people
- North American prevalence
  - ~1 million people
- Annual incidence (new cases) of 20/100,000

Epidemiology

- M:F about 2:1
- Less common in blacks and Asians
  - HOWEVER, PD is generally not well studied in diverse populations
- Average onset age = 63
- 5–10% of people have symptoms < 45

PD Projection

- In the most populous nations will double by 2030 from 4.3 million to 9.5 million worldwide
- Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease
- Enormous public health challenge
- We need to plan for diagnosis, treatment and research purposes

Dorsey et al, Neurology 2007;68:384386

Cardinal Signs

- Onset of (at least 2):
- Tremor
  - Rigidity
  - Bradykinesia
  - Postural instability
    - Later in the course
- Typical asymmetrical
- Absence of another cause

Probable & Possible Diagnostic Criteria

- Group A Features: Characteristic of Parkinson disease
    - Resting tremor
    - Bradykinesia
    - Rigidity
    - Asymmetric onset
- Group B features: suggestive of alternative diagnoses
- Features unusual early in the clinical course
    - Prominent postural instability in the first 3 years after symptom onset
    - Freezing phenomena in the first 3 years
    - Hallucinations unrelated to medications in the first 3 years
    - Dementia preceding motor symptoms or in the first year
    - Supranuclear gaze palsy (other than restriction of upward gaze) or slowing of vertical saccades
    - Severe symptomatic dysautonomia unrelated to medications
    - Documentation of a condition known to produce parkinsonism and plausibly connected to the patient's symptoms (such as suitably located focal brain lesions or neuroleptic use within the past 6 months)

    Gelb, Arch Neur. 1999

MDS 2015 Revised Criteria

Associated Problems - Early

- Loss of smell
- Depression/anxiety
- Sleep disturbance
    - REM behavior d/o
- Small handwriting
- Constipation
- Dizziness
- Urinary urgency
- Blurred vision/dry eyes
- Pain in shoulders/hip
- Dystonia

How to Make the Diagnosis

- Clinical
    - Based on symptoms and exam findings
- Confirmatory tests
    - May be needed to evaluate for other diseases

        - MRI of brain or cervical spine, EMG (PD is NOT a “pinched nerve”)
    - DaTscanSPECT
    - Skin biopsy
        - >90% sensitivity and specificity

DaTscan

What Causes Parkinson’s Disease?

- Unknown
- Probable combination of factors:
    - Genetic (<10% of cases)
    - Toxic
    - Infectious
    - Other/unknown
- First degree relatives have increased risk of developing PD in their lifetime.

Various Inheritance Patterns

- Autosomal recessive (11 genes): ATP13A2, DNAJC6, FBXO7, PRKN/PARK2, PARK7, PINK1, PLA2G6, SLC6A3, SPR, SYNJ1, VPS13C
- Autosomal recessive (4 genes): CHCHD2, LRRK2, SNCA, and VPS35
- X-linked recessive (2 genes): RAB39B and TAF1
- AD or AR: Pathogenic variants in GCH1
- Susceptibility genes: GBA and MAPT, EIF4G1, GIGYF2, HTRA2, UCHL1

Source: Prevention Genetics

Some Causes of “Parkinsonism”

- Drugs
    - Anti-psychotics
    - Anti-nausea
    - Illicit drugs
- Multi-Systems Atrophy
    - Shy-Drager
    - Striato--nigral degen
    - OPCA
- Progressive Supranuclear Palsy
- CBGD
- Vascular disease
- Dementia with Lewy Bodies
- Normal Pressure Hydrocephalus

- Wilson's disease
- Huntington's disease
- Alzheimer's Disease
- Dystonia
- Structural lesion

PD vs. ET

- James Parkinson:
    - "In the real Shaking Palsy, the agitation continues full force whilst the limb is at rest and unemployed; and even if sometimes diminished by limb is at rest and unemployed; and even if sometimes diminished by calling the muscles into employment."
- He noted tremors liable to be confused include those due to alcohol abuse, tea and coffee abuse, and old age.

Time Course of PD Progression

Kalia & Lang Lancet 2015

Non-motor Symptoms of PD

- Psychiatric
    - Mood disturbance
    - Depression
    - Agitation
    - Anxiety and panic attacks
    - Dementia
    - Hallucinations
    - Delirium
- Autonomic
    - Orthostatic hypotension
    - Constipation
    - Urinary problems
    - Sexual problems
    - Sweating and thermoregulation
- Sleep disorders
    - Parasomnias
    - REM Sleep behavior disorder
    - Insomnia —maintenance or early awakening
    - Sleep fragmentation
    - Restless legs syndrome
    - PLMS
    - Excessive daytime sleepiness

    - Sudden onset of sleep
- Sensory
    - Hyposmia
    - Pain
    - Paresthesias
    - Altered sensation
    - Restless legs

FDA-Approved Medications for PD

- Carbidopa/levodopa
    - Sinemet®
    - (10/100), 25/100, 25/250
    - Sinemet CR®
    - 25/100, 50/200
    - Rytary®
    - Stalevo® (carbidopa/levodopa/entacapone)
    - Duopa®
    - Parcopa® (dissolvable carbidopa/levodopa)
    - Inbrejia®
- COMT Inhibitors
    - Entacapone
    - Tolcapone
    - Opicapone
- Dopamine agonists
    - Ropinirole (and XL)
    - Pramipexole (and ER)
    - Rotigotine(topical patch)
    - Apomorphine (injectable and SL)
- MAOB Inhibitors
    - Selegiline
    - Zydis® selegiline
    - Rasagiline
    - Safinamide
- Anti-cholinergic
    - Trihexyphenidyl
    - Benztropine
- Amantadine
    - Immediate release
    - GoCovri®
    - OsmolexER®
- Adenosine A2A Receptor Antagonist

    - Istradefylline
- Other
    - Rivastigmine
    - Pimavanserine
    - Droxidopa

When to Start What

- Treatment should start anytime function is impaired by physical manifestations of PD.
- Levodopa remains most effective symptomatic therapy.
- Delayed use of levodopa may delay onset of dyskinesias and response fluctuations, particularly in young onset (<40)
- LD vs. DA agonist: controversial
    - No difference in quality of life after 6 years

Complications of Medical Therapy

- 50% after 5 years, 80% after 10 years
    - Dyskinesia
    - Wearing off
    - Freezing
    - Dystonia
    - On/Off

Motor fluctuations and dyskinesias in Parkinson's disease: Clinical manifestations

Movement Disorders, Volume: 20, Issue: S11, Pages: S11-S16, First published: 08 April 2005, DOI: (10.1002/mds.20458)

Surgery for PD

- Deep Brain Stimulation (DBS)
    - Patient selection important
    - Does not alter course of disease
    - STN vs. GPi
- Other approaches under investigation
    - High frequency ultrasound
    - Gene transfer/therapy

Other Treatments

- Education of patient and family
- Support for patient and family
- Counseling (professional, legal and financial)

- PT, OT, SLPPT, OT, SLP
- Exercise (including Yoga, Tai Chi, Dance)
- Relaxation Therapy
- Nutritional consultation
- Home Health Services
- Respite
- Palliative Care

Complementary & Alternative Interventions

- Various supplements
    - Beware of amino acid compounds
- Chiropractors and/or massage therapy
- Acupuncture
- Yoga
- Stem cell treatments
    - Caveat emptor

III. Overview of ALS Registry in Massachusetts

Presented by Lauren Fogarty, DPH

Summary and Key Take-Aways from ALS Registry

- In 2002, Massachusetts was one of seven states awarded funds by the U.S. Centers for Disease Control and Prevention to track health conditions thought to be impacted by the environment.
- The statewide registry, initially supported by these CDC funds, was established in 2003 in accordance with legislation supported by ALS patients and advocacy groups calling for more research into the causes of ALS.
- Registry data collection began on January 1, 2008, with retrospective collection going back to 2007. Each year, medical records for Massachusetts residents evaluated for ALS are requested from all neurologists and major hospitals in Massachusetts for confirmation of diagnosis. Medical, demographic, and residential information is collected for all cases.
- DPH was granted the authority to create an ALS Registry by legislation **(**Massachusetts General Laws Chapter 111, Section 25A, as amended by Section 26 of Chapter 140 of the Acts of 2003**).**
- In addition, ALS is considered a reportable disease under DPH regulations (Title 105 of the Code of Massachusetts Regulations (CMR), Section 300.192: Surveillance of Diseases Possibly Linked to Environmental Exposures.**)** This regulation specifically authorizes DPH to collect medical records and other identifiable information from health care providers and other persons subject to 105 CMR 300.000, and/or prepare data, as detailed in 105 CMR 300.190 and 300.191**,** on people evaluated for or diagnosed with ALS and other selected environmental related diseases.
- This how the DPH ALS Registry staff collect data (Below is a summary of what I discussed during the meeting):

- ALS patients are reported annually to MDPH/BEH by hospitals, clinics, physicians, and vital records for any patient diagnosed with or treated for ALS while residing in Massachusetts. A trained MDPH/BEH Registry nurse conducts a full review of the medical records for each patient reported. Before being added to the Registry, all diagnoses are verified by a consulting neurologist.

- In conclusion, only cases reported by medical professionals are included in the state registry.

Committee members posed questions about budget, information collection methods, triggering mechanisms, software, existing uses for the ALS registry data. Lauren Fogarty to follow up with relevant parties to answer questions.

IV. Committee Deliverables and Planning Discussion

Co-chair Cathi Thomas shares the report topics for member research and next steps.

1. What is the purpose, design, and functionality of the registry?
2. What data will be collected? (including but not limited to demographic data to determine incidence and prevalence by areas of the Commonwealth)
3. How will the data be collected and disseminated
4. How to ensure privacy and confidentiality of data?
5. How will the registry be implemented?

Member Frank points out that question four is less substantial for this committee than the others.

Committee members inquired as to the presentation from California's registry guest speaker. Presentation rescheduled to next meeting due to lack of availability per Lauren Fogarty.

Committee members discussed elements of these items.

Member Keswick asks what the deliverable is for this project and what deadline it must be delivered by.

Project manager Mary Lou Woodford clarifies that the deliverable is a report as a precursor to defined action steps for DPH implementation. If the scope of this project cannot be completed, committee may report to that end, but a report must be submitted by May 31st as per legislative mandate.

Members discussed splitting questions 1 and 2 into multiple individual topics and allow the remaining topics to be informed by this research and the presentation from California's registry speaker.

VI. Next Steps

Member Deb to discuss ALS registry insights with colleagues who may interact with the registry.

Members Tucker, Frank, and Miller to report back individually on what data will be collected.

Members Tucker, Deb, and Johnson to report back individually on suggested registry functionality, design, and purpose, respectively.

Project manager Mary Lou Woodford to coordinate member availability to propose an additional meeting date in order to finalized the report as needed.

Motion to adjourn from Tucker, seconded by Johnson.

- Roll call:
  - Affirmed: Fogarty,Frank, Johnson,Tucker, Miller, Thomas, Keswick, Deb
  - Not present: Cornell