WHY IS IT DIFFICULT TO DIAGNOSE PARKINSON’S DISEASE?

Etiology Diagnosis and Pathology

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Parkinson’s Disease Symposium

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DISCLOSURE

Dr. Bertoni has no ownership positions but has received support for clinical research trials/lectures/or has served on advisory boards for the following: Abbvie, Acadia, Aventis, Boehringer Ingeleim, Cephalon, Eisai, Elan Pharmaceuticals, KGaA, Kyowa, Merck, National Institutes of Health, Novartis, Pharmacia, Schwarz Pharma, SKB (Smith Kline Beecham), Solvay, TEVA and UCB Pharma
OVERVIEW

• WHERE ARE WE NOW?
• HOW DO WE GET EVEN BETTER?
• 2018 QUALITY MEASURES GOALS
• CURRENT RESEARCH AT UNMC DONS
• SOME RECENT HIGHLIGHTS
  • EXERCISE AND CARDIOVASCULAR RISKS
• PD OVERVIEW
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OTHER TEAM MEMBERS

OCCUPATIONAL THERAPISTS
PHYSICAL THERAPISTS
SPEECH/SWALLOW THERAPISTS
SOCIAL WORKERS
DIETICIAN
SUPPORT STAFF
Dr. James Parkinson, 1755-1824

AN
ESSAY
ON THE
SHAKING PALSY.

CHAPTER I.
DEFINITION—HISTORY—ILLUSTRATIVE CASES.

SHAKING PALSY. (Paralysis Agitans.)

Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured.
10 Commandments For Doctors

1. PLAIN LANGUAGE AND CLEAR, CUSTOMIZED COMMUNICATIONS
   TEACH BACK AND SHOW BACK TECHNIQUES TO MAKE IT CLEAR
   USE DRAWINGS, MODELS OR DEVICES TO DEMONSTRATE POINTS
2. ENCOURAGE PATIENTS TO ASK QUESTIONS
3. EMPHASIZE THE IMPORTANCE OF PATIENT EDUCATION
4. GIVE PATIENTS INFORMATION ABOUT ALL OF THEIR MEDICATIONS,
   DIAGNOSES, TEST RESULTS, AND PLANS FOR FOLLOW-UP CARE
5. IMPROVE SAFETY AND EFFECTIVENESS OF PRESCRIBED MEDICATIONS
   AND REVIEW CURRENT MEDICATIONS AND DOSAGES
6. FOSTER A SAFE, PATIENT-CENTERED ENVIRONMENT
7. DEVELOP PATIENT-CENTERED EDUCATIONAL MATERIALS AND
8. HELP INFORM THE PATIENT TO MAKE OWN MEDICAL DECISIONS
9. MANAGE DISEASE AND INFECTION RISKS WITH GOOD PRACTICES
10. ADOPT THE MULTI-DISCIPLINARY TEAM APPROACH TO IMPROVE
    HEALTH OUTCOMES AND REDUCE ERRORS
Never never never never never never
GIVE UP
WHAT DO WE NEED TO KNOW ABOUT PARKINSON’S DISEASE?

• HOW TO DEFINE PD?
• HOW TO DIAGNOSE PD?
• WHAT CAUSES PD?
  • GENETIC PREDISPOSITION
  • ENVIRONMENT
• HOW MANAGE PD?
  • MEDICATION
  • THERAPIES
  • SURGERY
PARKINSON’S DISEASE

4%

LIFETIME RISK
Parkinson’s Disease: age-specific prevalence rates
AGE & SEX

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Parkinsonism</th>
<th>PD</th>
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<tr>
<td>Age (1-y increment)</td>
<td>1.09</td>
<td>1.10</td>
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<tr>
<td></td>
<td>(1.05–1.15)</td>
<td>(1.04–1.16)</td>
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<tr>
<td>Male gender</td>
<td>1.66</td>
<td>2.13</td>
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<tr>
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<td>(1.02–2.70)</td>
<td>(1.11–4.11)</td>
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ILSA = Italian Longitudinal Study on Aging.
UNMC
MOVEMENT DISORDERS
CLINIC

6000
Patient encounters every year
4% LIFETIME RISK OF PD AND PARKINSONISM

PARKINSON’S DISEASE
MEN 2.0%  WOMEN: 1.3%

PARKINSONISM:
MEN 4.4%  WOMEN: 3.7%

Elbaz et al. Risk tables for parkinsonism and Parkinson's disease
How Do We Get PD?

1. Environment
2. Genetics
3. Both
## Genetic PD

<table>
<thead>
<tr>
<th>Locus</th>
<th>Gene</th>
<th>Chromosome</th>
<th>Inheritance</th>
<th>Type of parkinsonism</th>
<th>Mutation/variant type</th>
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<td>PARK1/PARK4</td>
<td>SNCA</td>
<td>4q21</td>
<td>AD</td>
<td>LOPD/EOPD, dementia</td>
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<td>6q25-27</td>
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<td>EOPD</td>
<td>Re-arrangement, point</td>
<td>Re-arrangement: convinced; point: unconvenced</td>
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<td>PINK1</td>
<td>1p36</td>
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<td>LRRK2</td>
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<td>ATP13A2</td>
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<td>-</td>
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<td>1q21</td>
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<td>LOPD</td>
<td>Point</td>
<td>Convinced</td>
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<tr>
<td>-</td>
<td>BST1</td>
<td>4p15</td>
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<td>LOPD</td>
<td>Point</td>
<td>Unconvenced</td>
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<tr>
<td>-</td>
<td>MAPT</td>
<td>17q21</td>
<td>Risk</td>
<td>LOPD</td>
<td>Haplotype</td>
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<tr>
<td>-</td>
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<td>12q12</td>
<td>Risk</td>
<td>LOPD</td>
<td>Trinucleotide expansion</td>
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<td>14q32</td>
<td>Risk</td>
<td>LOPD</td>
<td>Trinucleotide expansion</td>
<td>Unconvenced</td>
</tr>
</tbody>
</table>

AD: autosomal dominant; AR: autosomal recessive; EOPD: early-onset Parkinson’s disease; LOPD: late-onset Parkinson’s disease; PD: Parkinson’s disease

Chao-Dong Wang, Piu Chan, *Neuroimmunol Neuroinflam*; 1:115-126 Clinicogenetics of Parkinson’s disease 2014
LRRK2

• Associated with familial and idiopathic PD
• Large, multidomain protein
• Autosomal dominant
• Most prevalent gene associated with PD
  • Among Caucasian patients
    • Up to 5% of familial cases
    • 1%-2% of idiopathic cases
• Its physiologic function and its role in PD etiology are unclear
  • May have a role in lysosomal pathways

PARK2: Parkin

- Autosomal recessive
- Juvenile Parkinsonism

Significance
- Gene most commonly found in early onset
- Up to 50% of recessive familial patients <45 years express mutation
- Onset age range 16-72
- Lewy bodies not a characteristic
- Positive response to LD


SNCA: a-Synuclein

• The first gene associated with PD (1997)
• Autosomal dominant
• Causal gene
  • Critical mutations or overproduction of α-synuclein causes misfolding of the protein and subsequent accumulation, resulting in cell toxicity
• Linked to both familial and idiopathic PD
  • Altered the course of research to focus on genetics
  • Originally linked with early onset (40s)
  • PD due to SNCA mutations is very rare

α-Synuclein

• α-Synuclein is a protein primarily expressed in neural tissue

• Main function may be the control of neurotransmitter release

• Associated with the development of PD
  • α-Synuclein is the main component of Lewy bodies
  • Disrupts synaptic messaging

• Level of causality in PD is unknown

• α-Synuclein toxicity is considered a possible therapeutic target for PD

PARKINSON’S DISEASE
IS A SYNDROME

• Many Subtypes
• Many Genetic Risk Factors
• Many Environmental Risk Factors
• Tremor Dominant Type
• Akinetic Rigid Type
• Long Prodromal Course
• Major Challenge: Disease Modifying Therapy
WHEN DOES PD START?
Figure 1: Clinical symptoms and time course of Parkinson’s disease progression

Diagnosis of Parkinson’s disease occurs with the onset of motor symptoms (time 0 years) but can be preceded by a premotor or prodromal phase of 20 years or more. This prodromal phase is characterised by specific non-motor symptoms. Additional non-motor features develop following diagnosis and with disease progression, causing clinically significant disability. Axial motor symptoms, such as postural instability with frequent falls and freezing of gait, tend to occur in advanced disease. Long-term complications of dopaminergic therapy, including fluctuations, dyskinesia, and psychosis, also contribute to disability. EDS=excessive daytime sleepiness. MCI=mild cognitive impairment. RBD=REM sleep behaviour disorder.
Conceptual Diagram of the Phases of PD

Disease Onset

Increase

Decrease

Premotor Phase

Motor Phase

Time (y)

Dopaminergic Neurons

Nonmotor Symptoms

Motor Symptoms

PARKINSON’S DISEASE IS A SYNDROME

- Many Subtypes
- Many Genetic Risk Factors
- Many Environmental Risk Factors
- Tremor Dominant Type
- Akinetic Rigid Type
- Long Prodromal Course
- Major Challenge: Disease Modifying Therapy
Environment-Gene Interplay in PD

**Environmental risk factors**

- Increased risk (OR >1)
  - Pesticide exposure
  - Prior head injury
  - Rural living
  - Beta-blocker use
  - Agricultural occupation
  - Well water drinking

- Decreased risk (OR <1)
  - Tobacco smoking
  - Coffee drinking
  - NSAID use
  - Calcium channel blocker use
  - Alcohol consumption

**Genetic risk factors**

<table>
<thead>
<tr>
<th>Increased risk (OR &gt;1)</th>
<th>Decreased risk (OR &lt;1)</th>
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<td>BST1</td>
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<td>GPNMB</td>
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<td>MIR4697</td>
<td>SREBF1-RAI1</td>
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<tr>
<td>BCKDK-STX1B</td>
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</table>
PATIENTS CONTROL
BEST CARE

• CAN DO ATTITUDE
• GET SMART ABOUT PD
• GET TOGETHER
• GET STRONGER
• EAT AND SLEEP WELL
• DON’T GET MAD OR DEPRESSED-GET EVEN!
• LET’S IMPROVE LIFE AND BEAT PD
Increased Melanoma Risk in Parkinson Disease

A Prospective Clinicopathological Study

John M. Bertoni, MD, PhD; John Philip Arlette, MD, FRCPC; Hubert H. Fernandez, MD; Cheryl FitzAttas, PhD; Karen Frei, MD; Mohamed N. Hassan, MD, PhD; Stuart H. Isaacson, MD; Mark F. Lew, MD; Eric Molho, MD; William G. Ondo, MD; Tania J. Phillips, MD; Carlos Singer, MD; James P. Sutton, MD; John E. Wolf Jr, MD; for the North American Parkinson’s and Melanoma Survey Investigators

Objective: To evaluate the possible association of Parkinson disease (PD) and melanoma in North America.

Design, Setting, and Patients: Thirty-one centers enrolled patients with idiopathic PD. At visit 1, a neurologist obtained a medical history. At visit 2, a dermatologist recorded melanoma risk factors, performed a whole-body examination, and performed a biopsy of lesions suggestive of melanoma for evaluation by a central dermatopathology laboratory. We compared overall prevalence of melanoma with prevalence calculated from the US Surveillance Epidemiology and End Results (SEER) cancer database and the American Academy of Dermatology skin cancer screening programs.

Results: A total of 2106 patients (mean [SD] age, 68.6 [10.6] years; duration of PD, 7.1 [5.7] years) completed the study. Most (84.8%) had received levodopa. Dermatological examinations revealed 346 pigmented lesions; dermatopathological findings confirmed 20 in situ melanomas (0.9%) and 4 invasive melanomas (0.2%). In addition, histories revealed 68 prior melanomas (3.2%). Prevalence (5-year limited duration) of invasive malignant melanoma in the US cohort of patients with PD (n = 1692) was 2.24-fold higher (95% confidence interval, 1.21-4.17) than expected in age- and sex-matched populations in the US SEER database. Age- or sex-adjusted relative risk of any melanoma for US patients was more than 7 times that expected from confirmed cases in American Academy of Dermatology skin cancer screening programs.

Conclusions: Melanoma prevalence appears to be higher in patients with PD than in the general population. Despite difficulties in comparing other databases with this study population, the study supports increased melanoma screening in patients with PD.

Arch Neurol. 2010;67(3):347-352
North American Parkinson’s and Melanoma Survey Investigators

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<td>Sex</td>
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<td>Female</td>
<td>669 (31.8)</td>
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<tr>
<td>Male</td>
<td>1437 (68.2)</td>
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<td>Race</td>
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<td>White</td>
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<td>Asian</td>
<td>58 (2.8)</td>
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<td>Other</td>
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<td>Age, y</td>
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<tr>
<td>≥65</td>
<td>1383 (65.7)</td>
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<tr>
<td>Mean (SD)</td>
<td>68.6 (10.6)</td>
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<td>Tobacco use</td>
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<td>1199 (57.0)</td>
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<tr>
<td>Former</td>
<td>834 (39.7)</td>
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<td>Current</td>
<td>69 (3.3)</td>
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<td>Duration of PD, mean (SD), y</td>
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<td>Hoehn and Yahr stage, mean (SD) c</td>
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<td>Use of dopaminergic drugs (past and current)</td>
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<tr>
<td>Any prior use</td>
<td>2035 (96.6)</td>
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<td>Levodopa</td>
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<td>No dopaminergic agent</td>
<td>71 (3.4)</td>
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a Unless otherwise indicated, data are expressed as number (percentage) of patients.

b Includes 2102 patients.

c Includes 2030 patients.
Figure. Proportions of patients with known melanoma risk factors (N=2106). PUVA indicates psoralen–UV-A. *Includes 1 patient for whom the date of melanoma diagnosis was missing.
Table 2. Prevalence of Melanoma and Other Skin Lesions

<table>
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<th>Dermatologic Finding</th>
<th>No. of Reports</th>
<th>Patients, No. (%) (N=2106)</th>
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<tr>
<td>Prior melanoma based on history</td>
<td>72 (3.4)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Malignant melanoma in situ</td>
<td>39 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Invasive malignant melanoma</td>
<td>27 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Unclassified melanoma</td>
<td>6 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Lesions suggestive of melanoma on examination</td>
<td>519 (24.6)</td>
<td></td>
</tr>
<tr>
<td>Patients with pigmented lesions suggestive of melanoma</td>
<td>346 (16.4)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Significant biopsy findings&lt;sup&gt;c&lt;/sup&gt;</td>
<td>656</td>
<td></td>
</tr>
<tr>
<td>Malignant melanoma in situ</td>
<td>20 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Invasive malignant melanoma</td>
<td>4 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>117</td>
<td>86 (4.1)</td>
</tr>
<tr>
<td>Actinic keratosis</td>
<td>31 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>28 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Melanocytic nevus (including simple lentigo)</td>
<td>289</td>
<td>179 (8.5)</td>
</tr>
<tr>
<td>Pigmented lesions (nonmelanocytic)</td>
<td>124</td>
<td>95 (4.5)</td>
</tr>
<tr>
<td>Other skin malignant neoplasms&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1</td>
<td>1 (0.05)</td>
</tr>
<tr>
<td>Other skin lesions</td>
<td>42 (1.9)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Date of the melanoma diagnosis was missing for 1 patient, who was not included in the Table. Four patients with a history of melanoma were also diagnosed as having melanoma during the initial dermatologic evaluation.

<sup>b</sup> Fifty-two of 346 patients with pigmented lesions suggestive of melanoma did not undergo a biopsy, leaving 294 who did.

<sup>c</sup> The 392 patients who underwent biopsies consisted of the 294 patients with pigmented lesions and 98 patients with nonpigmented lesions, all suggestive of melanoma. Some patients underwent more than 1 biopsy and had more than 1 finding.

<sup>d</sup> Excludes malignant melanoma, basal cell carcinoma, and squamous cell carcinoma.
<table>
<thead>
<tr>
<th>Correlate</th>
<th>Patients Without Melanoma (n=2014)</th>
<th>Patients With Any Melanoma at Any Time (n=92)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SE), y</td>
<td>68.4 (0.2)</td>
<td>72.6 (0.9)</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Male, %</td>
<td>68.0</td>
<td>74.2</td>
<td>.15&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>PD duration, mean (SE), y</td>
<td>7.1 (0.1)</td>
<td>7.2 (0.5)</td>
<td>.84&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hoehn and Yahr score, mean (SE)</td>
<td>2.2 (0.02)</td>
<td>2.4 (0.1)</td>
<td>.009&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>No. of melanoma risk factors, mean (SE)</td>
<td>2.9 (0.1)</td>
<td>5.3 (0.3)</td>
<td>&lt;.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Receiving levodopa therapy, %</td>
<td>84.9</td>
<td>82.8</td>
<td>.55&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Calculated using the 2-sample t test.

<sup>b</sup> Calculated using the $\chi^2$ test.

<sup>c</sup> Calculated using the Wilcoxon 2-sample test.
Is PD A Slow Virus Disease?

A

PrP<sub>C</sub> → PrP<sub>Sc</sub> → Prion rods → PrP amyloid plaques

B

α-Syn → α-Syn → α-synuclein fibrils → Lewy body
Pathology of Parkinson’s disease:

- Gross: Loss of pigment in substantia nigra.
- Neuronal loss, degeneration,
- Loss of neurons replaced by gliosis (microglia)
- Loss of neuromelanin.
- Neuronal degeneration
- Reactive gliosis.
- Lewy bodies (α-synuclein) in neurons.
How Does PD Make Us Sick?

1. Dopamine is Low
   • Motivates and moves us
2. Disability related to inactivity
3. Depression
4. Determination is needed to move
5. Discouragement
6. Depression

“YOU MAY HAVE PD. DON’T LET PD HAVE YOU!”
Why do I need a prescription from a doctor to take a drug that boosts my dopamine...

...but I don't need a doctor's approval to use an app that is designed to do the same thing?

Are you ignoring me and playing with your phone?

I wasn't getting any dopamine from listening to you.
HYPOTHESIS:

MOST OF THE DISABILITY IN PD IS DUE TO...

INACTIVITY?
CAN EXERCISE SLOW CLINICAL PROGRESSION OF PARKINSON’S DISEASE?
EXERCISE FOR EVERY PATIENT

DOPAMINE MOTIVATES US

DOPAMINE MOVES US
Clinical Diagnosis of PD

- SLOW  Bradykinesia
- SHAKE Rest Tremor
- STIFF Rigidity
- SHUFFLE Unsteady Gait
- SINEMET Helps
- SOLE Explanation

- Experts are correct 90-95% of the time
- SCAN DAT SCAN
Idiopathic PD Based on UK Parkinson’s Disease Society Brain Bank Criteria

Step 1—Diagnosis of Parkinsonian syndrome

• Bradykinesia and ≥ 1 of the following:
  • Muscular rigidity
  • 4 to 6 Hz rest tremor
  • Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction


*Importantly, bradykinesia is not just slowness of movements. It is meant as *progressive and decrement of repetitive alternating movements* during finger or foot tapping

Queen Square Brain UK PDS Bank Criteria for the diagnosis of Parkinson’s disease 2013

Idiopathic PD Based on UK Parkinson’s Disease Society Brain Bank Criteria

Step 2 – Exclusion criteria

- History of repeated strokes with stepwise progression of parkinsonian features
- History of repeated head injury
- History of definite encephalitis
- Oculogyric crises
- Neuroleptic treatment at onset of symptoms
- More than one affected relative (*)
- Sustained remission
- Strictly unilateral features after 3 yr
- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Early severe dementia with disturbances of memory, language, and praxis
- Babinski sign
- Presence of cerebral tumor or NPH on imaging study
- Negative response to large doses of levodopa
- MPTP exposure

Queen Square Brain UK PDS Bank Criteria for the diagnosis of Parkinson’s disease 2013
Idiopathic PD Based on
UK Parkinson’s Disease Society
Brain Bank Criteria

Step 3 – Supportive prospective positive criteria PD

≥ 3 required for diagnosis of definite Parkinson’s disease

• Unilateral onset
• Rest tremor present
• Progressive disorder
• Persistent asymmetry affecting side of onset most (*)
• Excellent response (70% to 100%) to levodopa
• Severe levodopa-induced chorea
• Levodopa response for ≥ 5 yr (*)
• Clinical course of ≥ 10 yr (*)
• Hyposmia
• Visual hallucinations
Dopamine Transporter (DaT) Scans
Dopamine Transporter (DaT) Scans
Dopamine Transporter (DaT) Scans

• In conclusion, in cases where the diagnosis is uncertain (e.g. Parkinson’s disease versus essential tremor), a DaT or PET scan can be very useful. But patients and their families need to be aware that in general, these scans cannot reliably separate Parkinson’s disease from parkinsonism (multiple system atrophy, corticobasal degeneration, progressive supranuclear palsy), and thus if you seek a scan you will still need an expert to sort out your clinical picture and diagnosis. If you have already been diagnosed, if your symptoms are progressing, and you have an adequate response to medications, most likely a PET or DaT scan would add little new information and therefore not be necessary.
WHEREAS, Parkinson’s disease is the second most common neurodegenerative disease in the United States behind Alzheimer’s; and
WHEREAS, Nebraska has one of the highest number of individuals with Parkinson’s disease on average in the nation; and
WHEREAS, Parkinson’s disease is becoming an increasing concern as the population is aging; and
WHEREAS, The Nebraska Parkinson’s Disease Registry Act was passed in 1996 and has been collecting data since 1997; and
WHEREAS, The Nebraska Parkinson’s Disease Registry was the first and only population-based Parkinson’s disease registry until 2015; and
WHEREAS, At least 700 individuals are diagnosed with Parkinson’s disease every year; and
WHEREAS, Over 16,000 patients have been diagnosed with Parkinson’s disease since the registry began collecting data in 1997 in Nebraska; and
WHEREAS, Many researchers have used the registry data to study Parkinson’s disease and their papers have been published in academic journals, in addition, Nebraska DHHS routinely uses the data for public health surveillance activities.

NOW, THEREFORE, I, Pete Ricketts, Governor of the State of Nebraska, DO HEREBY PROCLAIM the 30th day of October, 2017 as PARKINSON’S DISEASE AWARENESS DAY in Nebraska, and I do hereby urge all citizens to take due note of the observance.

IN WITNESS WHEREOF, I have hereunto set my hand, and cause the Great Seal of the State of Nebraska to be affixed this Twenty-fifth day of October, in the year of our Lord Two Thousand Seventeen.

Attest:

Secretary of State

Governor
PD MANAGEMENT

PATIENT CENTRIC
TEAMWORK
PATIENT AS AUTONOMOUS ATHLETE
TREATMENT TEAM AS COACHES
WIDE SUPPORT SYSTEMS
Treatments for PD

- Attitude: Teamwork and Determination
- Education is critical
- Support groups, family support
- Health maintenance – activity
- Physical Intellectual and Spiritual
- OT PT ST are ESSENTIAL
- Personal Trainer if possible
- Risks: Falls, low B12 or D, Melanoma
- Prevent Postpone Get Well
- Encouragement Medication Surgery
- Research Research Research!
PD TREATMENT

PREVENTION
AVOID/INACTIVATE THE TOXIN
VACCINE/INACTIVATE GENE/TRANSPLANT
REVERSE/SLOW THE DISEASE/DELAY ONSET ¿30 YRS

SYMPTOMATIC THERAPY: PRECURSORS/AGONISTS

ALTERNATIVE THERAPY

SURGERY: ABLATIVE/DBS

AVOID FALLS FRACTURES WEAKNESS
Disease-Related *Motor* Complications Despite Optimal Levodopa Therapy

- Postural imbalance
- Freezing
- Dysarthria
- Dysphagia
HOW DO WE GET EVEN BETTER?

NEW YEARS RESOLUTIONS
What’s the Goal?

Best Quality of Life
As Long as Possible
PARKINSON’S DISEASE

WHAT IS QUALITY CARE?
PD QUALITY MEASURES
AMERICAN ACADEMY OF NEUROLOGY

1. RECONFIRM DIAGNOSIS YEARLY
2. RULE OUT PSYCHIATRIC PROBLEMS
3. RULE OUT DEMENTIA
4. RULE OUT AUTONOMIC PROBLEMS
5. RULE OUT SLEEP DISTURBANCE
6. RULE OUT FALLS
7. RULE OUT NEED FOR REHAB
8. RULE OUT SAFETY ISSUES
9. RULE OUT MEDICATION PROBLEMS
10. REVIEW MEDICAL AND SURGICAL OPTIONS
PD QUALITY MEASURES

MORE AT UNMC

1. MELANOMA SCREENING
2. NUTRITION/VITAMIN ASSESSMENTS
3. EXERCISE PROGRAMS FOR LIFE
4. PREVENTION OF COMPLICATIONS
5. HOME SAFETY: NIGHT LITES, CO TESTING
6. DRIVING SAFETY ASSESSMENTS
7. MONITOR CAREGIVER BURNOUT
8. PROVIDE ANNUAL EDUCATION PROGRAMS
9. PATIENT EMPOWERMENT
10. MANY RESEARCH TRIAL OPPORTUNITIES
Nebraska Parkinson’s Disease Registry

Ming Xu MD
Parkinson’s Disease Registry Director

Jill Krause
Parkinson’s Disease Registry Coordinator
1996 - LEGISLATION PASSED – GRASS ROOTS EFFORT BY PD INTEREST GROUPS AND RESEARCHERS. THE STATE VOTED NEUTRAL.

REASON FOR LEGISLATION OF REGISTRY/IMPORTANCE OF THE REGISTRY

AN INCREASING PUBLIC HEALTH CONCERN AS THE POPULATION IS AGING

ESSENTIAL FOR PUBLIC HEALTH PROFESSIONALS AND RESEARCHERS

TO STUDY THE INCIDENCE OF AND POSSIBLE RISK FACTORS CONCERNING PARKINSON’S

TO PLAN FOR HEALTH CARE REQUIREMENTS AND EDUCATION OF HEALTH CARE PROVIDERS

NE WAS THE FIRST AND ONLY FULLY FUNCTIONAL POPULATION-BASED REGISTRY UNTIL 2015

1997 - DATA COLLECTION BEGAN

SUSPENDED OCTOBER, 2004 – FEBRUARY, 2006 DUE TO LACK OF FUNDING
Required Data Elements

Per Nebraska Statute 81-6,102
From PHYSICIANS within 60 days of initial diagnosis:
(a) Name;
(b) Social Security number;
(c) Date of birth;
(d) Gender;
(e) Address at time of diagnosis;
(f) Current address;
(g) Date of diagnosis;
(h) Physician;
(i) Identification of reporting source; and
(j) Any additional information the department demonstrates is reasonable to implement the Parkinson's Disease Registry Act.

Per Nebraska Statute 81-6, 103
From PHARMACIES for whom they dispense one or more drugs from the State’s ‘Reportable List of Drugs’:
Name
Address
Social Security number
Name and address of the prescribing physician
2017 Reportable List of Drugs (brand name or generic):
Azilect
Carbidopa/levodopa
Mirapex
Neupro
Requip
Selegiline
Stalevo
Data Flow Chart

Physician verification/initial reporting

Pharmacists patients

Patient self-reporting

Nebraska Parkinson's Disease Registry

State death file

Hospital Discharge Data
Patients per County Map Pre-1997 - 2016

Legend
Parkinson's Disease Patients

- 0 - 19
- 20 - 67
- 68 - 147
- 148 - 292
- 293 - 600
- 601 - 2815

The registry began collecting data in 1997.

Diagnosis of PD based on physician office confirmation or death certificate.

Nebraska 15,053
Out-of-State 574
Total Cases 15,627

Registry was terminated from Oct. 2004 - Feb. 2006 due to lack of funding.
CONTACT INFORMATION

http://www.dhhs.ne.gov/ced/parkinsons
Basic information about Parkinson’s disease
History of the registry
Statute and Rules and Regulations
Reporting forms and file formats
Parkinson’s data reports

Jill.Krause@nebraska.gov
Table 1. Comparisons of the most commonly diagnosed comorbid conditions between PD cases and non-PD referent subjects admitted to hospitals in Nebraska between 2004 and 2012.

<table>
<thead>
<tr>
<th>Essential Hypertension</th>
<th>Delirium, Dementia, Amnestic and Other Cognitive Disorders</th>
<th>Disorders of Lipid Metabolism</th>
<th>Coronary Atherosclerosis and Other Ischemic Heart Disease</th>
<th>Fluid and Electrolyte Disorders</th>
<th>Cardiac Dysrhythmias</th>
<th>Thyroid Disorders</th>
<th>Mood Disorders</th>
<th>Gastrointestinal Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>1799 PD group vs. 9459 non-PD group</td>
<td>976 PD group vs. 2133 non-PD group</td>
<td>926 PD group vs. 6301 non-PD group</td>
<td>901 PD group vs. 6587 non-PD group</td>
<td>881 PD group vs. 4576 non-PD group</td>
<td>838 PD group vs. 5764 non-PD group</td>
<td>636 PD group vs. 3004 non-PD group</td>
<td>631 PD group vs. 2016 non-PD group</td>
<td>630 PD group vs. 2734 non-PD group</td>
</tr>
</tbody>
</table>

| Age at Admissions | 0.95 (0.83–1.10) | 4.23 (2.43–7.37) | 0.77 (0.63–0.95) | 0.62 (0.46–0.83) | 0.72 (0.54–0.96) | 0.77 (0.54–1.09) | 1.73 (1.30–2.30) | 1.78 (1.45–2.19) | 0.92 (0.67–1.25) |
|<65 | (0.78–0.93) | (5.03–7.72) | (0.62–0.79) | (0.50–0.67) | 0.99 (0.85–1.15) | 0.65 (0.55–0.78) | 1.10 (0.91–1.33) | 1.78 (1.51–2.09) | 1.36 (1.14–1.62) |
| 65–74 | 0.85 (0.94–1.02) | 6.23 (1.86–2.14) | 0.77 (0.69–0.80) | 0.72 (0.67–0.77) | 0.98 (0.91–1.05) | 0.74 (0.69–0.79) | 1.00 (0.92–1.10) | 1.45 (1.30–1.61) | 1.13 (1.03–1.24) |
| >=75 | 0.98 (0.79–0.99) | 1.99 (0.94–1.02) | 0.96 (0.69–0.80) | 0.72 (0.67–0.77) | 0.91 (0.91–1.05) | 0.74 (0.69–0.79) | 1.06 (0.92–1.10) | 1.59 (1.34–1.74) | 1.27 (1.14–1.42) |

| Gender | 0.96 (0.91–1.01) | 2.64 (2.40–2.91) | 0.74 (0.69–0.80) | 0.73 (0.68–0.79) | 1.03 (0.93–1.12) | 0.72 (0.66–0.78) | 1.13 (0.99–1.30) | 1.53 (1.34–1.74) | 1.27 (1.14–1.42) |
| Male | 0.94 (0.90–0.99) | 1.99 (1.81–2.19) | 0.72 (0.66–0.79) | 0.59 (0.53–0.67) | 0.91 (0.83–0.99) | 0.74 (0.67–0.82) | 1.02 (0.93–1.12) | 1.59 (1.43–1.77) | 1.04 (0.93–1.17) |
| Female | 0.95 (0.92–0.99) | 2.29 (2.14–2.45) | 0.73 (0.69–0.78) | 0.68 (0.64–0.73) | 0.96 (0.90–1.03) | 0.73 (0.68–0.77) | 1.06 (0.98–1.14) | 1.57 (1.44–1.70) | 1.15 (1.06–1.25) |
| Overall | 0.77 (0.54–0.96) | 0.54–1.09 | 0.65 (0.55–0.78) | 0.99 (0.85–1.15) | 0.91 (0.83–0.99) | 0.74 (0.67–0.82) | 1.02 (0.93–1.12) | 1.59 (1.43–1.77) | 1.04 (0.93–1.17) |

*P < 0.001. b 0.001 ≤ P < 0.01. c 0.01 ≤ P < 0.05.

Color salmon: PD patients had an increased risk.
Color blue: PD patients had a decreased risk.
Table 2. Comparisons of the most commonly diagnosed comorbid conditions between PD cases and non-PD referent subjects received outpatient clinic services in Nebraska between 2004 and 2012.

<table>
<thead>
<tr>
<th>Essential Hypertension</th>
<th>Connective Tissue Disease</th>
<th>Spondylosis; Intervertebral Disc Disorders; Other Back Problems</th>
<th>Diabetes Mellitus without Complication</th>
<th>Disorders of Lipid Metabolism</th>
<th>Coronary Atherosclerosis and Other Ischemic Heart Disease</th>
<th>Genitourinary Symptoms and Ill-defined Conditions</th>
<th>Gastrointestinal Disorders</th>
<th>Non-traumatic Joint Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>590 PD group</td>
<td>330 PD group</td>
<td>328 PD group</td>
<td>295 PD group</td>
<td>292 PD group</td>
<td>278 PD group</td>
<td>256 PD group</td>
<td>238 PD group</td>
<td>210 PD group</td>
</tr>
<tr>
<td>vs. 3710 non-PD group</td>
<td>vs. 1578 non-PD group</td>
<td>vs. 1336 non-PD group</td>
<td>vs. 1888 non-PD group</td>
<td>vs. 2168 non-PD group</td>
<td>vs. 2013 non-PD group</td>
<td>vs. 867 non-PD group</td>
<td>vs. 747 non-PD group</td>
<td>vs. 1045 non-PD group</td>
</tr>
</tbody>
</table>

### Age at visits

| <65        | 0.90 (0.68–1.19) | 1.00 (0.76–1.32) | 1.37 (1.02–1.84)c | 0.72 (0.49–1.04) | 0.75 (0.52–1.06) | 0.38 (0.22–0.67)a | 1.38 (0.83–2.27) | 1.11 (0.71–1.72) | 0.84 (0.57–1.24) |
| 65–74      | 0.69 (0.58–0.82)a | 1.13 (0.91–1.41) | 1.28 (1.02–1.61)c | 0.69 (0.55–0.87)b | 0.62 (0.49–0.77)a | 0.63 (0.48–0.81)a | 1.78 (1.33–2.38)a | 1.63 (1.20–2.20)b | 1.04 (0.79–1.38) |
| >=75       | 0.82 (0.75–0.91)a | 1.02 (0.88–1.19) | 1.17 (1.00–1.36)c | 0.84 (0.72–0.97)c | 0.69 (0.59–0.80)a | 0.75 (0.65–0.87)a | 1.41 (1.20–1.66)a | 1.69 (1.42–2.01)a | 1.03 (0.86–1.25) |

### Gender

| Male       | 0.80 (0.71–0.89)a | 1.23 (1.05–1.44)b | 1.28 (1.08–1.51)b | 0.74 (0.63–0.87)a | 0.73 (0.63–0.85)a | 0.69 (0.60–0.79)a | 1.48 (1.24–1.77)a | 1.90 (1.57–2.29)a | 1.00 (0.81–1.22) |
| Female     | 0.79 (0.71–0.89)a | 0.89 (0.75–1.05)  | 1.18 (1.00–1.39)c | 0.84 (0.70–1.00)  | 0.60 (0.49–0.73)a | 0.70 (0.56–0.88)b | 1.47 (1.19–1.82)a | 1.28 (1.03–1.60)c | 1.01 (0.83–1.24) |
| Overall    | 0.80 (0.73–0.86)a | 1.05 (0.93–1.17)  | 1.23 (1.09–1.38)a | 0.78 (0.69–0.88)a | 0.67 (0.60–0.76)a | 0.69 (0.61–0.78)a | 1.48 (1.29–1.69)a | 1.59 (1.38–1.84)a | 1.00 (0.87–1.16) |

*p < 0.001. ^0.001 ≤ P < 0.01. ©0.01 ≤ P < 0.05.

- **Color salmon**: PD patients had an increased risk.
- **Color blue**: PD patients had a decreased risk.
Low cardiometabolic risk in Parkinson’s disease is independent of nutritional status, body composition and fat distribution

Emanuele Cereda a, b, *, Erica Cassani a, Michela Barichella a, Angela Spadafranca c, Riccardo Caccialanza b, Simona Bertoli a, b, Alberto Battezzati a, b, Gianni Pezzoli a

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ARTICLE INFO

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Accepted 12 February 2012

Keywords:
Parkinson’s disease
Cardiometabolic risk
Nutritional status
Body composition
Fat distribution

SUMMARY

Background & aims: To investigate if the reduced cardiometabolic risk in Parkinson’s disease (PD) is independent of nutritional status, body composition and fat distribution.

Methods: We designed a case–control study comparing 80 non underweight PD patients with 80 controls matched for sex, age and body mass index (BMI). Nutritional assessment included: anthropometry (BMI and waist circumference [WC]), body composition estimated by impedance and biochemistry (fasting glucose, serum lipids and transaminases). The presence of arterial hypertension, diabetes mellitus and metabolic syndrome (MetS) were noted.

Results: Compared to controls and independently of gender, PD patients showed lower percentage of body fat (P < 0.001) and biochemical parameters (glucose, P < 0.001; total cholesterol, P < 0.001; LDL, P < 0.001; triglycerides, P = 0.002; alanine aminotransferase, P < 0.001 and aspartate aminotransferase, P = 0.015) but similar WC (P = 0.324). The prevalence of hypertension and MetS was similar in the two groups, as well as the frequency and the number of MetS criteria. The relationship between PD and low cardiometabolic profile was independent of age, gender, current smoking and BMI. After adjusting for WC and body fat, most of the associations remained significant.

Conclusions: PD patients seem to have a more favorable cardiometabolic risk profile, independently of nutritional status, body composition and fat distribution.

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Never, Never, Never, Never, NEVER, Give Up
A CASE IN POINT
OCTOBER 2017

85 YEAR OLD PATIENT WITH PD SINCE 2012
“NOT DOING WELL”
WHAT IS THE RIGHT THING TO DO?
SQUEEZE INTO COMPREHENSIVE CLINIC

HISTORY- HEART BLOCK AND PACEMAKER
DOWNSIZING/MOVING
WIFE HAS CANCER
A CASE IN POINT
OCTOBER 2017

85 YEAR OLD PATIENT WITH PD SINCE 2012

EXAM- MMSE 21/30  ANOSMIA DYSARTHRIA
LOSS OF VIBRATION + COLD BELOW KNEES
ROMBERG-UNTESTABLE (FALLS WITH EYES OPEN)
NOW WHAT?
## UPDRS MOTOR SCORES

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34, 33</td>
<td>35</td>
<td>NO SHOW</td>
<td>NO SHOW</td>
<td>45</td>
</tr>
</tbody>
</table>
A CASE IN POINT
OCTOBER 2017

85 YEAR OLD PATIENT WITH PD SINCE 2012

EXAM- MMSE 21/30  ANOSMIA DYSARTHRIA
LOSS OF VIBRATION + COLD TO KNEES
ROMBERG-UNTESTABLE (FALLS WITH EYES OPEN)
UPDRS WORSE _BUT NOT MORE TREMOR OR RIGIDITY_

NOW WHAT?
<table>
<thead>
<tr>
<th>Tests</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
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<tbody>
<tr>
<td>MMSE</td>
<td>29</td>
<td>25*</td>
<td>-</td>
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<td>21</td>
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<td>* HE refused neuropsych testing</td>
<td></td>
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<tr>
<td>MCV (29-97)</td>
<td>97.1</td>
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<td>-</td>
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<td>FOLATE (&gt;5.8)</td>
<td>10.7</td>
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<td>-</td>
<td>-</td>
<td>11.8</td>
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<tr>
<td>B12 (180-914)</td>
<td>457</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>72</td>
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<tr>
<td>B1 (70-180)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>30</td>
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<td>B6 (20-125)</td>
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<td>5.2</td>
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<td>D (30-80)</td>
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</table>
VITAMIN AND NUTRITIONAL RESEARCH PROJECT:

1. WHAT IS THE PREVALENCE OF NUTRITIONAL DEFICIENCY IN PD?

2. WHAT NUTRIENTS ARE MISSING?
Thank You For Your Attention!