Purpose of this presentation

Gain awareness of symptoms and treatments of dementias not caused by Alzheimer’s disease

My Background

- Caregiver for my husband who had Lewy body dementia
- Difficult to get specific diagnosis; got PD diagnosis in 2009
- But – it was obvious to me that PD was not the biggest problem
- It was hard to find information on what was happening, what I should know, what I should do, and what I should expect
- Now volunteer with Alzheimer’s Association, Lewy Body Dementia Association, and the Lexington Area Parkinson’s Disease Support Group
- Hope to provide useful information to others dealing with the challenge of caring for a person with dementia
A note about terminology

DSM 5 (Diagnostic and Statistic Manual of Mental Disorders) removed the term “dementia” and replaced it with major neurocognitive disorder (NCD)

Major NCD is an acquired neurocognitive decline (as opposed to developmental)

Definition: cognitive decline serious enough to interfere with a person’s ability to live independently

For this presentation, I’ll continue to use the term dementia

Major neurocognitive disorder (NCD)

Neurocognitive domains include

- Complex attention
- Executive function
- Learning and memory
- Language
- Perceptual – motor
- Social cognition

Diagnosis no longer requires memory impairment – this was an important change because not all of the dementias exhibit that in early stages

Dementia refers to symptoms of brain disease or injury

- Dementia is NOT synonymous with Alzheimer’s Disease
- Alzheimer’s Disease is the most common cause of dementia, but not the only one
- Other diseases or injuries can also result in dementia
Causes of dementia – potentially treatable (some of these appear in a short time frame)

- Infections of the nervous system (such as meningitis)
- Chronic drug or alcohol use
- Depression
- Hydrocephalus
- Brain tumors

- Interactions of prescribed medications
- Metabolic disorders (such as a vitamin B12 deficiency)
- Underactive thyroid
- Low blood sugar
- PTSD

Four causes of irreversible dementias

- Alzheimer’s Disease (AD) is the most common cause
- Lewy Body Dementias (LBD)
  - Dementia with Lewy bodies (DLB)
  - Parkinson’s Disease Dementia (PDD)
- Vascular cognitive impairment (VCI)
  - (Severe form sometimes called vascular dementia (VaD))
- Frontotemporal lobar degeneration (FTD)

Some other irreversible causes of dementia

- Huntington’s Disease (HD - rare)
- Creutzfeldt-Jakob disease (CJD - very rare – fast progression)
- Traumatic Brain Injury (TBI)
  - (e.g., chronic traumatic encephalopathy, CTE)
AD, LBD, VCI/VaD, and FTD account for more than 90% of irreversible dementias.

They are the diseases specifically named in the National Plan to Address Alzheimer’s Disease.

They are the subject of this presentation.

Why talk about “other” dementias?

- LBD, PDD, VaD, and FTD are not well known to the general public (or even to some medical personnel).
- The more the caregiver and patient know about what’s going on the better they can plan and maximize quality of life.
- The symptoms, treatment, and prognosis for these “other dementias” aren’t necessarily the same as those for Alzheimer’s.
- Getting an accurate diagnosis can help improve treatment.
- Can identify people who might participate in clinical trials.

Just in the past few years, there has been a definite increase in attention given to these other dementias (and to the needs of caregivers!)

- At the national policy level
- By the medical community, both in research and clinical settings
- By caregiver groups
- By organizations, such as the Parkinson’s Foundation
Examples

- Lewy Body Dementia was recognized as a separate disorder in DSM 5, and there are now clinical trials specifically for LBD
- The 2013 Alzheimer’s Disease Research Summit was the first time a national research strategy was developed for LBD, along with recommendations for FTD, VaD, and mixed dementias
- There are more research articles in journals specifically addressing the non-Alzheimer dementias
- There is more attention to use of terminology at all levels so that use of the term “dementia” is not equated to AD
- Parkinson’s Disease websites (such as MJ Fox and Parkinson’s Foundations) now have sections devoted to cognitive issues

Examples – attention to caregivers

- The Recognize, Assist, Include, Support, and Engage (RAISE) Family Caregivers Act was passed in January 2018
  - requires the Secretary of Health and Human Services to develop, maintain and update a strategy to recognize and support family caregivers.
- A Research Summit for Caregiver issues was held in Fall, 2017
  - Sponsored by U.S. Department of Health and Human Services and the Foundation for the National Institutes of Health
  - Focused on research needed to improve quality of care and outcomes, including quality of life and the lived experience of persons with dementia and their caregivers.
  - The final report was issued in May, 2018

Complexity of the dementias

- AD, LBD, PDD, VaD, and FTD occur as a result of complex interactions among numerous risk factors, so their study is complicated and lengthy
- Neurological changes begin years before clinical signs are apparent
- Still no way to preclinically predict who will develop dementia
- Still no single definitive diagnostic test for any of these dementias
- Mixed dementia is very common, especially for older age groups
Diagnosis of dementias is difficult

- Difficult diagnosis, especially for physicians who don’t work with dementias on a regular basis
- Caregiver observations can help the clinician
- A variety of tests can help with diagnosis
  - Clinical examinations and quick mental status tests
  - Diagnostic criteria exist for the dementias
  - Neuropsychological testing
  - Medical imaging techniques (CT, MRI, PET, SPECT)
  - Testing for biomarkers in body fluids
- Only examination of brain tissue after death can confirm diagnosis

For each of the dementias

- Brief general description
- Early symptoms that might be observed by family or friends
- Will group symptoms into
  - Cognitive
  - Behavioral/psychiatric
  - Physical symptoms
- Treatments

Lewy Body Dementias (LBD)

- Second most common cause of dementia
- Characterized by Lewy bodies within the neuron
  - Alpha-synuclein misfolded protein
  - Location of affected neurons in the brain determines observable symptoms
If cognitive problems appear a year or more after a diagnosis of PD, PDD should be diagnosed.

**Lewy Body Dementias (LBD)**

- Dementia with Lewy Bodies (DLB)
- Parkinson's Disease Dementia (PDD)

If cognitive problems apparent before or within a year of motor symptoms, DLB should be diagnosed.

**Behavioral/Psychiatric Issues** in LBD that may be observed by the caregiver in early stages:

- **LBD**
  - REM sleep disorder (acting out dreams) may occur many years before other symptoms
  - Hallucinations and delusions prominent early in the disease
  - Mood changes (apathy, depression, anxiety)

- **Alzheimer's Disease**
  - REM sleep disorder not usually present
  - Hallucinations and delusions don't occur until later stages, if at all
  - Mood changes (apathy, depression, anxiety)

**Cognitive Issues** in LBD that may be observed by the caregiver in early stages:

- **LBD**
  - Memory relatively spared
  - Significant deficits in visuo-spatial ability

- **Alzheimer's Disease**
  - Early symptoms include prominent memory problems
  - Deficits in visuo-spatial ability typically less severe
Cognitive Issues in LBD that may be observed by the caregiver in early stages

<table>
<thead>
<tr>
<th>LBD</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficits in attention prominent</td>
<td>Attention deficits less prominent</td>
</tr>
<tr>
<td>Deficits in executive function are a common early symptom</td>
<td>Deficits in executive function not as noticeable as memory problems</td>
</tr>
</tbody>
</table>

Physical / Movement Issues in LBD that may be observed by the caregiver in early stages

<table>
<thead>
<tr>
<th>LBD</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia</td>
<td>Significant autonomic dysfunction not apparent early</td>
</tr>
<tr>
<td>Some features of parkinsonism (slow movement, resting tremor, or rigidity)</td>
<td>No early symptoms of parkinsonism</td>
</tr>
</tbody>
</table>

Clinical Diagnostic Criteria for LBD

- Presence of dementia is an essential criterion, especially in the following areas:
  - Paying attention
  - Reasoning and problem solving, called executive function
  - Understanding how objects relate in three-dimensional space, called visuospatial skills
  - Memory may not be affected in early stages

- At least two of the following core clinical symptoms are required:
  - Delirium-like fluctuating cognition; unpredictable changes in thinking, attention and alertness
  - Repeated visual hallucinations
  - REM sleep behavior disorder (which may appear long before the dementia)
  - One or more features of Parkinsonism, specifically slowed movements, tremor when limbs are at rest, and muscle rigidity

- Other supporting symptoms include:
  - Loss of sense of smell
  - Excessive daytime sleepiness
  - Some others
Diagnosis from the Caregiver perspective

- Early symptoms can be vague so any diagnosis is often hard to get, especially if specialists are not readily available
- Preliminary diagnosis is frequently either Alzheimer’s Disease or Parkinson’s Disease

Treatment of LBD / PDD

- There are no FDA-approved medications now specifically for LBD
- Use medications designed for Alzheimer’s for cognitive problems
  - E.g., rivastigmine, donepezil, galantamine, memantine
  - Excelon (rivastigmine) is FDA approved for PDD for cognitive function
- Use medications for Parkinson’s to treat motor problems
  - Various carbidopa/levodopa formulations
  - Nuplazid (pimavanserin) is FDA approved for PDD for hallucinations
- BUT – often the drugs that treat cognitive problems can worsen movement disorder; drugs that improve movement disorder may worsen cognitive problems

Important note about antipsychotics for LBD

- People with LBD should not be prescribed the “traditional” antipsychotics, such as chlorpromazine (Thorazine) and haloperidol (Haldol)
- People with LBD may have very severe reactions to these medications
  - Cognitive symptoms can become worse
  - Parkinsonism can worsen
  - In rare cases, antipsychotic medications may cause a condition called “neuroleptic malignant syndrome” (NMS)
- The atypical antipsychotics, such as clozapine and quetiapine, may be helpful for people with LBD
- ER physicians might not be familiar with this problem in LBD; caregivers should be alert
Genetics

- Still needs more research – LBD has been under-diagnosed and there are few studies
- A 2018 genome-wide association study estimated heritability at about 36%
- The study also noted that LBD has a genetic risk profile that is different from AD or PD

Guerreiro et al. Lancet Neurology Jan 2018

Frontotemporal Lobar Degeneration (FTD)

- **Group** of rare, progressive neurological diseases that affect the frontal and temporal lobes of the brain
- These are the parts of the brain that regulate speech, behavior, emotions
- Affects about 50,000-60,000 people – but about 60% of cases occur in people 45-64 years old
  - Probably the most common cause of dementia for this age group

Frontotemporal Degeneration (FTD)

- The hallmark of FTD is a gradual, progressive decline in behavior and/or language
- Several protein malformations are involved in the various subtypes
- It’s very challenging to diagnose and to treat
  - The disease is not well known
  - It can present in many ways clinically
  - Often mistaken for psychiatric disorder
  - Dementia not usually associated with people in their 50’s and 60’s
Subtypes of FTD

1. Behavioral variant FTD (bvFTD) – most common (about 50%)
   - Previously referred to as “Pick’s Disease” or “frontotemporal dementia”

2. Language variant – this is referred to as “primary progressive aphasia (PPA)” (aphasia = problems with language/speaking not due to physical issues)
   - Nonfluent / agrammatic
   - Semantic
   - Logopenic

3. FTD with Motor Neuron Disease (FTD/MND)

Behavioral/Psychiatric Issues in FTD that may be observed by the caregiver in early stages

<table>
<thead>
<tr>
<th>FTD</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disinhibition, leading to inappropriate or bizarre social behavior; may lead to criminal behavior</td>
<td>Typically retain appropriate social behavior in early – mid stages</td>
</tr>
<tr>
<td>Apathy – loss of interest in work, family, personal care, initiative</td>
<td>May be present but probably not the main behavior noticed by a caregiver</td>
</tr>
<tr>
<td>Emotional blunting - often exhibit lack of concern for social norms or other people, lack of insight into their own behaviors</td>
<td>Typically retain appropriate social behavior in early – mid stages</td>
</tr>
</tbody>
</table>

Behavioral/Psychiatric Issues in FTD that may be observed by the caregiver in early stages

<table>
<thead>
<tr>
<th>FTD</th>
<th>Alzheimer’s Disease</th>
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</thead>
<tbody>
<tr>
<td>Compulsive behavior (pacing, pointless repetitive activity)</td>
<td>Compulsive behavior not commonly observed</td>
</tr>
<tr>
<td>Changes in eating habits or diet (binge eating, change in food preference, consumption of inedible objects)</td>
<td>Not a common symptom</td>
</tr>
</tbody>
</table>
### Cognitive Issues in FTD that may be observed by the caregiver in early stages

<table>
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<th>Alzheimer's Disease</th>
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</thead>
<tbody>
<tr>
<td>Retain important features of memory (keeping track of day-to-day events, orientation to space and time, etc)</td>
<td>Memory loss is a key early indicator; worsens as disease progresses</td>
</tr>
<tr>
<td>Deficits in Executive Function - Poor decision-making, judgment, problem-solving, and organizational skills</td>
<td>Not a pronounced early symptom</td>
</tr>
</tbody>
</table>

### Language variant FTD displays serious difficulties with names and words

<table>
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<th>FTD</th>
<th>Alzheimer's Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language variant FTD displays serious difficulties with names and words</td>
<td>Milder problems with recall of names and words in early stages</td>
</tr>
</tbody>
</table>

### Movement/Physical Issues in FTD that may be observed by the caregiver in early stages

<table>
<thead>
<tr>
<th>FTD</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typically begins from age 40-60</td>
<td>Usually seen in people over 65</td>
</tr>
<tr>
<td>May display early motor problems such as rigidity, tremor, difficulty walking</td>
<td>Motor problems mild or non-existent</td>
</tr>
</tbody>
</table>
FDA-Approved Treatments for FTD

- No FDA-approved drugs specifically for FTD
- Existing drugs can be used to address symptoms and contribute to patient and caregiver quality of life
- Cholinesterase inhibitors used for AD (donepezil, rivastigmine, galantamine) may help cognitive symptoms
- Memantine not shown to help FTD patients
- Anti-depressant drugs can improve some behavior symptoms
- Psychostimulants and antipsychotics drugs should be used with caution
- Movement disorder aspect often doesn’t respond well to Parkinson’s drugs (L-dopa)

Genetics

- There seems to be a strong familial link in FTD
- About 40% of individuals with FTD have a family history that includes at least one other relative who also has or had a neurodegenerative disease
- In approximately 15-40% of all FTD cases, a genetic cause (e.g., a gene mutation) can be identified as the likely cause of the disease and in most cases it is an inherited mutation.
- But there is still a lot of research needed to explain the heritability of FTD

Vascular Cognitive Impairment (VCI)

vascular: related to blood vessels
Types of Vascular Damage

- Blood vessels in the brain may
  - Be blocked
  - Be narrowed
  - Burst
- The resulting lack of blood flow can kill the cells
  - This area of dead tissue is called an “infarct”
- Effects of these infarcts depend on what part of the brain is affected
- The presence of infarctions is very common in older people and they may have no signs of cognitive impairment

Vascular cognitive impairment: fast or slow

Fast:
- When the blood flow to the brain is interrupted due to a major blockage or rupture we call it a stroke
- Cognitive problems after a stroke are sometimes called post-stroke dementia

Slow:
- But - small blockages and ruptures also can occur over a long period of time in many small blood vessels
- This is harder to diagnose as a cause of dementia

VCI Has Variable Symptoms

- AD, LBD/PDD, FTD have definite brain lesions in specific areas of the brain that can be related to symptoms
- But - any part of the brain could be affected by clots or ruptures, so symptoms are variable
- MRI and CT scans can give some information about vascular damage, and damaged areas should be related to symptoms observed
- It is common in older people for vascular damage to co-exist with other dementing diseases, especially Alzheimer’s
### What a caregiver might observe in VaD

- Trouble paying attention and concentrating
- Reduced ability to organize thoughts or actions
- Decline in ability to analyze a situation, develop an effective plan and communicate that plan to others
- Difficulty deciding what to do next
- Problems with memory
- Restlessness and agitation
- Unsteady gait
- Sudden or frequent urge to urinate or inability to control passing urine
- Depression

### Progression of VaD can be stepwise

- Most of the diseases causing dementia progress steadily and slowly
- Vascular dementia can sometimes be stable for some time and then suddenly deteriorate due to mini-strokes

### Treatments

- No treatment can repair the effects of vascular dementia
- Treatment aimed at preventing future events by controlling cardiovascular risk factors
  - High blood pressure
  - Cholesterol level
  - Diabetes
  - Smoking
- Drugs effective for AD (cholinesterase inhibitors and memantine) don’t benefit most people with VaD
Where to Find Information and Help

Alzheimer’s Association (alz.org)
- Web site has LOTS of information for both caregiver and patient
- There is a 24-hour help line (800 272 3900)
- Local offices provide community education

Lewy Body Dementia Association (LBDA) (www.lbda.org)
- LBD Caregiver Link
  - Toll-free: 800-539-9767
  - Email: support@lbda.org
- LBD Support Groups
- LBDA Forums
  - To join, email: forum@lbda.org
- LBD Awareness Movement
  - October of each year
Association for Frontotemporal Degeneration (AFTD)
http://www.theaftd.org/

- Information about FTD
- Helpline: 866-507-7222
- Email: info@theaftd.org

Vascular Dementia

No specific organization related only to VaD

Information about VaD found on websites related to stroke and heart disease

- http://memory.ucsf.edu/education/diseases/vascular
- http://www.strokeassociation.org/STROKEORG/

References (all publicly available online)

- National Plan to Address Alzheimer's Disease: 2017 Update

- National Research Summit on Care, Services and Supports for Persons with Dementia and Their Caregivers, final report
References (all publicly available online)

- A 2016 report on the state of the science for LBD

- National Parkinson’s Foundation “mind guides” to cognition, mood, and psychosis in PD

- Links to resources for information about frontotemporal degeneration from the NIA
  https://www.nia.nih.gov/health/frontotemporal-disorders-resource-list

- Information on vascular dementia from the American Heart Assn and American Stroke Assn
  http://strokeconnection.strokeassociation.org/Summer-2016/Understanding-Vascular-Dementia