Dementia with Lewy Bodies

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Disclosures

- No financial or other conflicts of interest
- Funding for the Montefiore-Einstein Center for the Aging Brain from the NYS Centers of Excellence for Alzheimer Disease program
- I am on the Medical Advisory Board for the Lewy Body Resource Center (uncompensated)
- Most treatments for dementia are off-label, especially for Lewy

Goals

1. Know when to suspect Dementia with Lewy Bodies
2. Understand basics of Lewy Body management
3. Know when to refer to a specialist for diagnostic challenges and advanced symptom management

Case: Mr S.

- “My brain’s slowed down!”
- 74M w HTN, OA, w progressive slowed thinking and decr organization x3 years. No trigger at onset. Retired “early” last yr, trouble w bills
- Memory ok: not repeating himself or forgetting events; recalls appts
- Visuospatial: Hitting curbs when parking
- Language & navigation intact
- Medically: walking has slowed, beyond OA. Only fall was out of bed, from sleep. Sleep getting worse at night, and tired during the day. Wife adds: Acting out dreams. No other abnormal movements.

Case: Mr S.

- Meds: amlodipine, oxybutynin
- Soc: HS grad. Former hardware store owner. No toxic habits. Lives w wife. No tob, drug use, concerning alcohol
- Psych: Frustration, no depression or anxiety. May have seen animals in the house a few times. Wife suggests irritability and some VH
- Exam: Ox3. Gives a great history. Memory screen intact. Non-focal
  - Wife: Looking good now, but he got confused w the paperwork 20min ago
- Labs: ok
- MRI brain: ok

Case: Mr S.

- Should we be concerned about the cognition? Memory is good.
  - *Yes, otherwise you wouldn't have used the case to introduce your talk*
- Is this neurological?
- Is this degenerative?

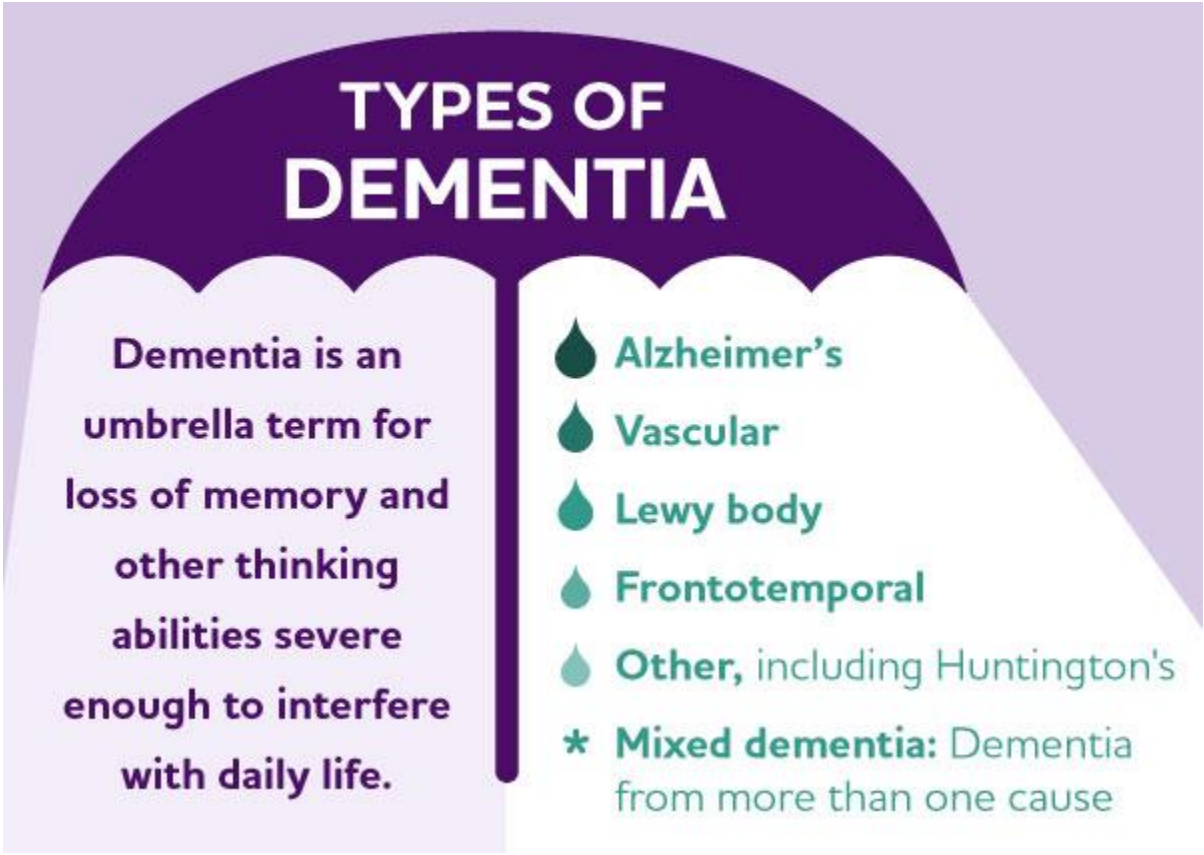
Outline

- Definitions & Epidemiology
- Diagnosis
- Symptoms
- Basic Management
- Caregiver Support
- When to Refer

Dementia

- A syndrome, not a diagnosis
- Cognitive decline from baseline
- Impairing daily function
- Not exclusively due to delirium or 1° psych disorder
- Memory impairment NOT necessary

- *Vs:* Mild Cognitive Impairment

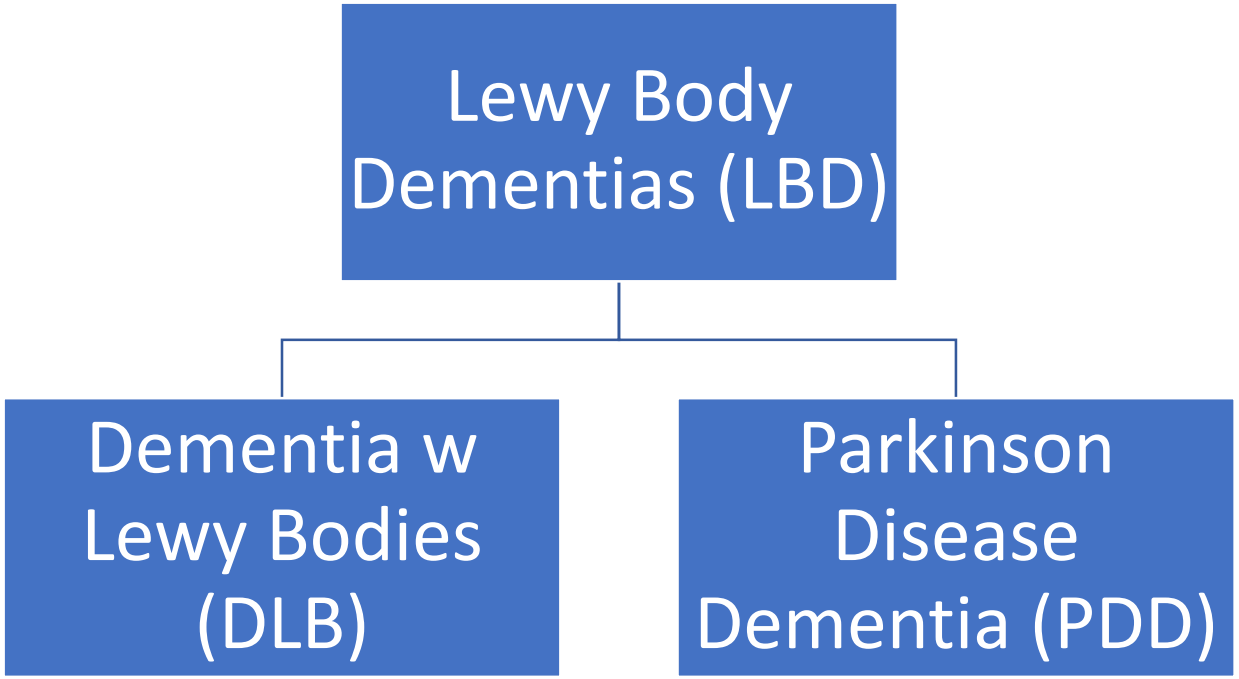


Dementia Epidemiology

- Alzheimer Disease (AD) is most common dementia in US:
  - 6.9 Million age ≥65 w AD dementia now and 6-8 Million w AD-MCI
  - Prevalence increases w age: ~11% of those ≥65yr, ~33% of those ≥85yr
  - NY State: 426,000 w AD, 12.7% of those age ≥65
  - Bronx County: 32,000 w AD, 16.6% of those age ≥65
- Lewy Body Dementia: at least 1.4 Million
  - 4.2-7.5% of all dementia cases
  - Second most common degenerative dementia
- Mixed dementia very common

Dhana 2023, Alz Assn 2024 Facts & Figures, LBDA.org, Goodman 2017, Vann Jones 2014

Nomenclature



- "1 year rule"
- What about Parkinson without dementia?
- What about Mild Cognitive Impairment due to Lewy Body? (Lewy Body Dementia without the dementia) → "prodromal"

This talk will focus on DLB

Yamada 2020

Diagnosis

- Required: Dementia
  - Chronic, progressive cognitive decline affecting daily activities
  - Usually executive function, attention, visuospatial. Memory usually later
- Definite DLB: via pathology
- Probable DLB: 2 core features or 1 core + 1 indicative biomarker
- Possible DLB: 1 core feature or 1 indicative biomarker
- Core features:
  - Cognitive fluctuations (attention, alertness)
  - Recurrent visual hallucinations
  - REM sleep behavior disorder
  - Parkinsonism (bradykinesia, rest tremor, rigidity)

McKeith 2017

Core Feature: Cognitive Fluctuations

- Marked variability in attention and alertness
- Hour to hour, or even minute to minute
  - Not just sundowning or good day/bad day
- Looks like delirium
  - And there is overlapping neurological basis for both
- Can look like a seizure, or even a stroke

Core Feature: Visual Hallucinations

- Recurrent formed visual hallucinations
  - Not illusions, though these may also be present
- Small animals and people are most common
- Often not threatening or upsetting
- Insight into hallucinations is variable

Core Feature: REM Sleep Behavior Disorder

- Acting out of dreams during REM sleep (dream enactment)
  - Complex movements, clear speech, or yelling that convey dream content
  - Clues: Partner no longer shares the bed, falls out of bed while asleep
- May be confused w seizure, restless leg, sleep apnea
- Can also be a side effect of psychotropic meds (esp SSRIs)
- Definitive diagnosis via polysomnogram; not usually done
- May precede other Sx by years or even decades
- >90% of idiopathic RBD develop a degenerative dementia

St Louis & Boeve 2017

Core Feature: Parkinsonism

Only 1 is required:

- Bradykinesia = slow movement
- Rigidity = increased tone (*vs spasticity*)
- Rest tremor = Present when limb is completely at rest, and typically resolves with movement
  - Though pts w DLB can have action and position tremors too
  - Cogwheeling = Rigidity + rest tremor

- *If there is significant parkinsonism first, then Dx = Parkinson Dementia*

Supportive Features

Non-diagnostic but suggestive, though poor specificity:

- Severe neuroleptic sensitivity
- Postural instability, repeated falls
- Syncope or recurrent transient unresponsiveness
- Severe autonomic dysfunction (e.g., orthostasis, constipation, urinary Sx)
- Hypersomnia
- Hyposmia
- Non-visual hallucinations or delusions, incl delusions of presence
  - Isolated olfactory? Think seizure
- Mood Sx: anxiety, apathy, depression

McKeith 2017

Indicative Biomarkers

➢ *Referral to Neurology is recommended*

- Reduced dopamine transporter uptake – e.g., DaTSCAN (SPECT)
- Abnormal MIBG Cardiac Scintigraphy
- Polysomnogram confirming REM sleep without atonia (the measured phenomenon in REM sleep behavior disorder)

McKeith 2017

Supportive Biomarkers

- Relative preservation of medial temporal lobes on CT/MRI
- SPECT or PET w reduced uptake occipitally
  - +/- cingulate island sign on FDG-PET
- Prominent posterior slow waves on EEG with fluctuations

McKeith 2017

Back to Mr S.

- Does he have Lewy Body?
  - Dementia (Progressive cognitive decline impairing function) → Yes
  - Cognitive fluctuations (attention, alertness) → Maybe
  - Recurrent visual hallucinations → Yes
  - REM sleep behavior disorder → Yes
  - Parkinsonism (bradykinesia, rest tremor, rigidity) → Yes

Back to Mr S.

- Not everyone is as straightforward
- Without his wife present:
  - Dementia (Progressive cognitive decline impairing function) → Yes
  - Cognitive fluctuations (attention, alertness) → No
  - Recurrent visual hallucinations → Maybe
  - REM sleep behavior disorder → No
  - Parkinsonism (bradykinesia, rest tremor, rigidity) → Maybe

Diagnostic Challenges

- Many cognitive screeners are memory focused
- >20% do not have visual hallucinations
- >15% do not have parkinsonism
- Many do not have bed partners to relate RBD Sx
- Some symptoms may present years later
- Some patients do not have insight into their symptoms
- MRI typically normal, or shows co-pathology

McKeith 2017

Diagnostic Challenges, Neurologist Edition

- >50% of DLB are +Amyloid
  - Co-pathology is common
  - Age is the biggest risk factor for amyloid positivity
- DaTSCAN has higher specificity (>90%) than sensitivity (76%)

Probability of Amyloid+				
AGE:	**60**	**70**	**80**	**90**
Normal memory	21%	29%	38%	48%
Subjective symptoms	23%	32%	41%	50%
MCI	44%	55%	65%	73%
Alzheimer Dementia	87%	85%	83%	80%

McKeith 2007, Petrou 2015, Jansen 2022, Bouteloup 2024

Lewy Body Composite Risk Score

- Have slowness in initiating and maintaining movement or have frequent hesitations or pauses during movement?
- Have rigidity (+/- cogwheeling) on passive range of motion in any of the 4 extremities?
- Have a loss of postural stability (balance) with or without frequent falls?
- Have a tremor at rest in any of the 4 extremities or head?
- Have excessive daytime sleepiness and/or seem drowsy and lethargic when awake?
- Have episodes of illogical thinking or incoherent, random thoughts?
- Have frequent staring spells or periods of blank looks?
- Have visual hallucinations (see things not really there)?
- Appear to act out his/her dreams (kick, punch, thrash, shout or scream)?
- Have orthostatic hypotension or other signs of autonomic insufficiency?

Galvin 2015

Lewy Body Composite Risk Score

- Signs present/absent within the last 6 mos
- Symptoms present/absent at least 3x within 6 mos
- Positive Score: ≥3
- Differentiates DLB from AD, all-cause dementia (AUC 0.94, 0.94)
- Differentiates MCI-DLB from MCI-AD (AUC 0.96)

Galvin 2015

Recommended Basic Dementia Workup

- History from patient & knowledgeable informant
- Review for potentially inappropriate medications
- Depression & anxiety screening
- Obstructive sleep apnea screening questionnaire
- Cognitive screening tool
- Chem, CBC, LFT, TSH, B12 (+MMA if <400 & >200), Syphilis*
- Structural brain imaging: MRI > CT > nothing

AAN 2001, AAN 2017

The Future of Lewy Diagnosis

➢*Referral to Neurology is recommended*

- MIBG scan – not typically used in US
- Skin biopsy – not yet available in NY, but can apply for a waiver
- CSF biomarkers
- Blood-based biomarkers

Lewy Treatment Basics

- Remove potentially inappropriate medications
- Non-pharmacologic treatment
- Pharmacologic treatment
  - Consider Neuro/ other referral
- Caregiver support & education
- Research studies

Note evidence for some Tx is (very) limited

Potentially Inappropriate Medications

- Anticholinergics – not ideal in older adults, bad in AD, worse in DLB
  - Oxybutynin
  - Benztropine
  - Diphenhydramine, doxylamine (Unisom)
  - Amitriptyline, doxepin (>6mg/day), paroxetine, olanzapine
- Neuroleptics – not ideal in older adults, may be very bad in DLB
  - All besides quetiapine, clozapine, and pimavanserin, including
  - Haloperidol
  - Risperidone
  - Olanzapine

Non-pharma Tx

- Exercise
  - Best studied in Parkinson disease
- Therapy (OT/PT/SLP), including “Big and Loud”
  - Best studied in Parkinson disease
- Healthful diet
  - Best studied in Alzheimer and all-cause dementia
- Control of vascular risk factors
  - Best studied in Alzheimer, vascular, and all-cause dementia
- Cognitive behavioral therapy
  - Anecdotally, for frustration, depression, anxiety

Pharma Tx

- Cholinesterase inhibitors!
  - Any stage, including MCI or more severe stages
  - For cognition, fluctuations, RBD, psychiatric Sx, and more
  - **Donepezil** – start 5mg daily after food, increase after >6 weeks to 10mg
    - May increase further with divided dosing
  - Rivastigmine patch – start 4.6mg/24h in those who cannot tolerate donepezil
- Memantine
  - Moderate stage
  - For cognition and mood
  - Start 5mg/day, increase by 5mg/day/wk to 10mg or 20mg/day (based on CrCl)

Pharma Tx

RBD

- 1st: Cholinesterase inhibitor
- 2nd: Melatonin – start 3mg, increase by 3mg/wk to max 12mg
- 3rd: Clonazepam – start 0.25mg hs
  - Yes, a benzo in older adults with dementia

Mood

- Does it need Tx?
- Is is frustration or depression?
- SSRIs (escitalopram, citalopram, sertraline)

St Louis & Boeve 2017

Pharma Tx

Parkinson / Motor

- Carbidopa-levodopa
- Avoid dopamine agonists

Caregiver Support & Education

- Lewy Body Dementia Association
  - Resources for medical professionals
  - Resources for patients & families
- Lewy Body Dementia Resource Center
  - Includes website in 8 languages
  - Includes 2.5 hours of videos discussing various aspects of the disease
  - Multiple support groups
  - Live helpline
- Alzheimer Association
- County Departments for the Aging

Research Studies

- Via LBDA, LBDRC, Alzheimer Association

When To Refer

- Unclear diagnosis, especially if advanced neuroimaging or other biomarker testing may be needed
- Anything beyond basic medication management
  - Especially for advanced psychotropic medication management
  - Especially for Parkinsonian motor symptoms
- Therapy (CBT, OT, PT, SLP) – low threshold
- Caregiver support – always appropriate

Outline

- Definitions & Epidemiology
- Diagnosis
- Symptoms
- Basic Management
- Caregiver Support
- When to Refer

I hope this talk was more clear than a Rochester sky during a total solar eclipse

Thank you!

- Jessica Zwerling and the Center for the Aging Brain team
- NYS DOH Centers for Excellence in Alzheimer Disease program
- Judy Hazelden and URMC
- Alzheimer Association
- Lewy Body Dementia Resource Center
- Lewy Body Dementia Association