2022 WAI Annual Update in Alzheimer's Disease & Related Dementias

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Diagnosis and Management of Dementia

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Disclosure Statement

- I have no relevant financial relationships with the manufacturers of any commercial products and/or providers of commercial services discussed in this CME activity

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Common Terms

- Mild neurocognitive disorder/Mild cognitive impairment = MCI
- Major neurocognitive disorder = MNCD/dementia
- Amnestic = cognitive impairment in memory

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Learning Objectives

Review diagnostic criteria for MCI and dementia

Discuss clinical workup for dementia

Management of dementia

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Normal Aging

- Decline in processing speed
- Memory: longer to retrieve
- Attention
- Executive Function

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DSM-5 Criteria for Mild Neurocognitive Disorder (MCI)

A. Evidence of modest cognitive decline from baseline in one or more cognitive domains based on:
   i. Subjective history of cognitive decline
   ii. Objective findings of cognitive decline on neuropsychological testing

B. Functionally independent

C. Cognitive deficits not due to delirium

D. Cognitive deficits not explained by another mental disorder

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DSM-5 Criteria for Major Neurocognitive Disorder (Dementia)

A. Evidence of significant cognitive decline from baseline in one or more cognitive domains based on:
   i. Subjective history of cognitive decline
   ii. Objective findings of cognitive decline on neuropsychological testing

B. Functional impairments (IADLs &/ADLs)

C. Cognitive deficits not due to delirium

D. Cognitive deficits not explained by another mental disorder

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Delirium

A. Disturbance in attention and awareness
B. Acute change from baseline that **fluctuates** in severity during the day
C. Additional disturbance in cognition (memory, disorientation, language, visuospatial ability or perception)
D. Disturbances in Criteria A & C not explained by pre-existing, established or evolving neurocognitive disorder
E. Evidence of direct physiological consequence of another medical condition, substance intoxication or withdrawal or multiple etiologies

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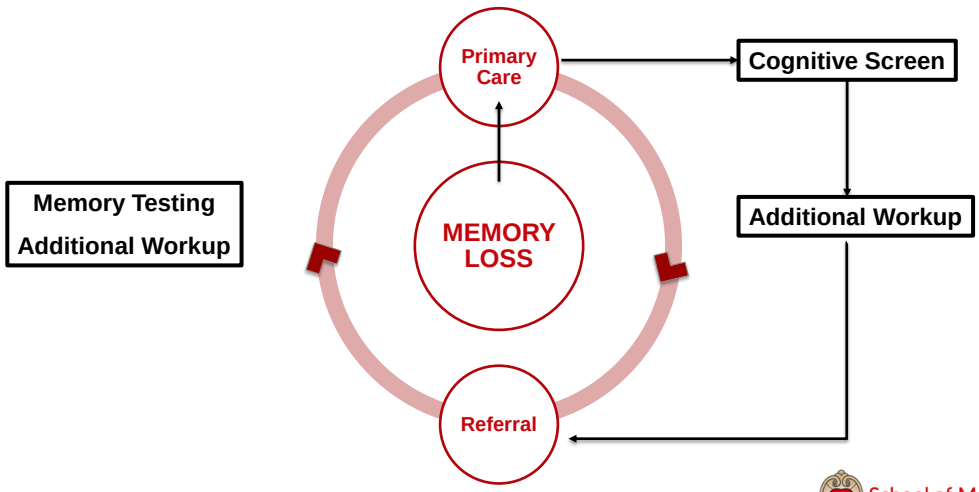
Diagnostic Workup



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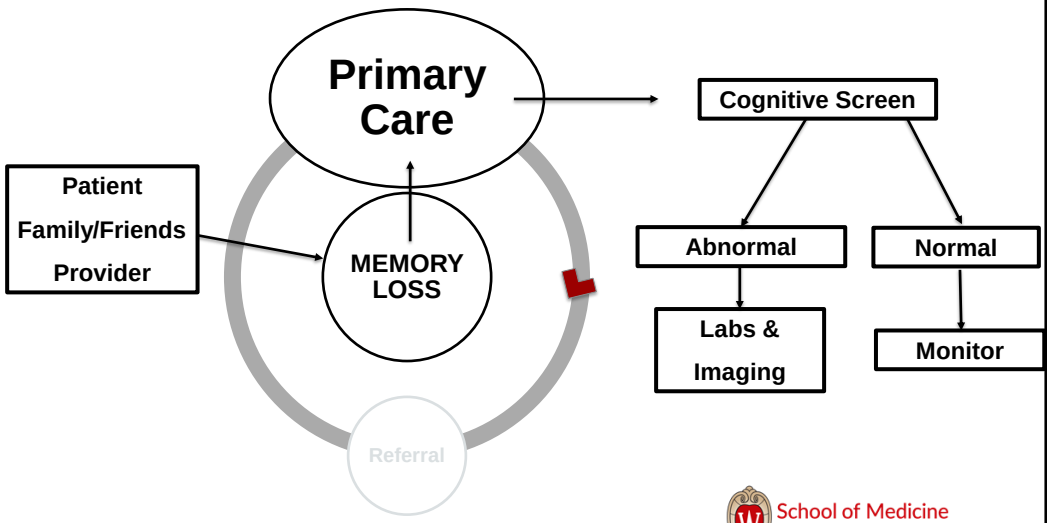
Diagnostic Workup



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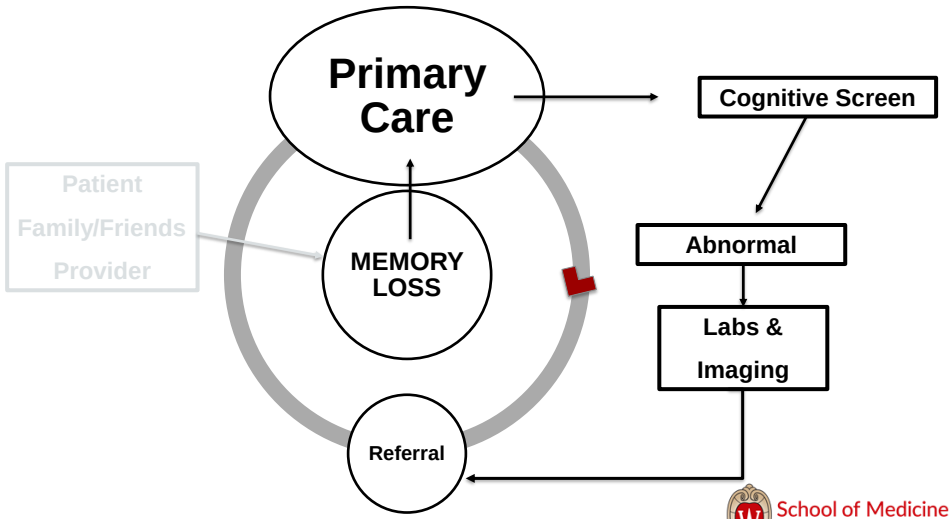
Diagnostic Workup



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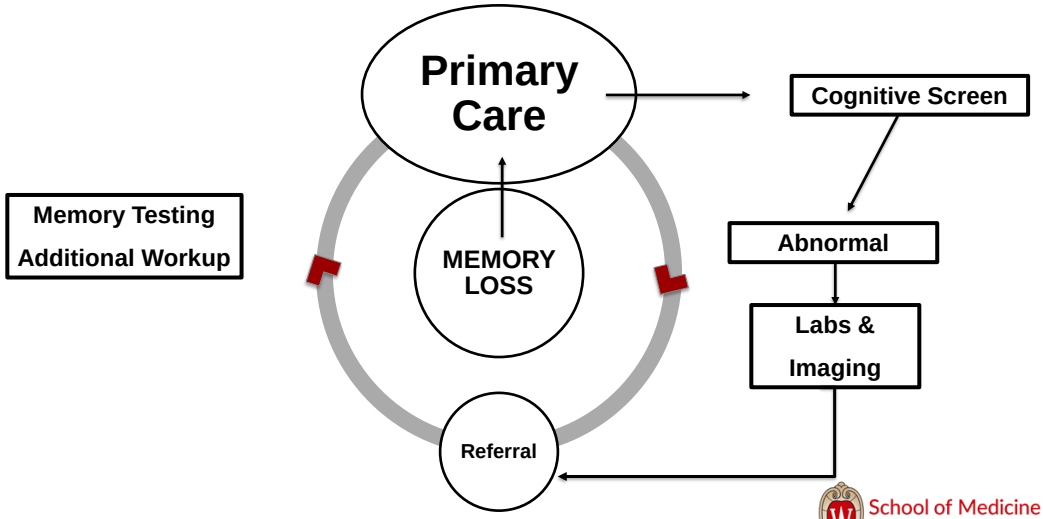
Diagnostic Workup



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Cognitive Screening

- Recommended during annual Medicare Wellness exam (≥ 65)

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Cognitive Screening Tools

- Mini- Cog: sensitivity of >80% and specificity of 60-80%
  - Normal: ≥ 4
- MOCA: less sensitive for MCI or mild dementia
  - Normal: 26-30 (add 1 pt if < HS education)
- SLUMS: better at detecting MCI
  - Normal: 27-30

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Diagnostic Workup

- Labs:
  - Vitamin Levels
  - TSH
  - Blood Count
  - Chemistry
- Structural Imaging:
  - CT/MRI
- Functional Imaging:
  - FDG-PET
- Medication Review
- Depression Screen
- Anxiety Screen
- STOPBANG

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Neurocognitive Disorders

Alzheimer's Disease

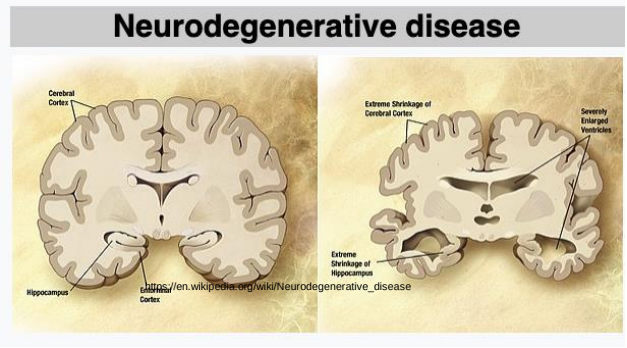
Frontotemporal Dementia

Dementia with Lewy Bodies

Parkinson's Disease

Vascular Dementia

Mixed Dementia



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Neurocognitive Disorders

Normal Pressure Hydrocephalus, NPH

Traumatic Brain Injury, TBI

Chronic traumatic encephalopathy

Cerebral amyloid angiopathy

Infectious Diseases (HIV, Neurosyphilis)

Prion Disease

Substance Abuse

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Neurocognitive Disorders (Reversible Causes)

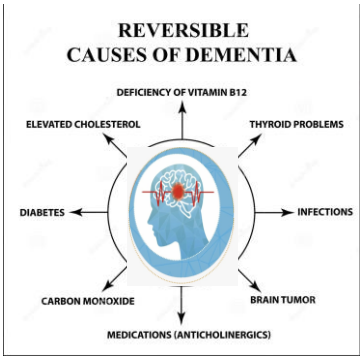
Depression, “Pseudodementia”

Metabolic or endocrine disorders

Medication side effects

Vitamin Deficiencies

Autoimmune



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Common Neurocognitive Diseases

Alzheimer’s Disease:

- Most common neurodegenerative disorder
- 6th most common cause of death in US
- Strongest risk factor: age

- Early onset disease (< 65 yo)
  - Associated with a gene mutation:
    - Autosomal dominant inheritance:
      - Amyloid precursor protein (APP)
      - Presenilin 1 (PSEN1) &
      - Presenilin 2 (PSEN2)

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Common Neurocognitive Diseases

Alzheimer's Disease

- Insidious onset
- Gradual progression
- Amnestic
- Age ≥ 65 yo

- Cognitive deficits:
  - Memory
  - Language
- Imaging Findings:
  - Mesiotemporal atrophy
  - Hippocampal atrophy
  - Temporoparietal hypometabolism

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Common Neurocognitive Diseases

Vascular Dementia

- 2nd most common neurocognitive disease
- Occurs at any age, increased prevalence after 65

- Risk Factors:
  - Vascular Disease
    - Hypertension
  - Cerebral amyloid angiopathy
  - Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, CADASIL

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Common Neurocognitive Diseases

Vascular Dementia

- History of stroke related to cognitive decline
  - Stepwise decline with focal deficits
- Cerebral small vessel dx
  - White matter lesions
  - Lacunar infarcts
    - Cognitive slowing
- Cognitive Deficits:
  - Difficulty with speeded task
  - Executive dysfunction
- Neuroimaging:
  - Infarcts
  - Hemorrhages
  - White mater hyperintensities

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Common Neurocognitive Diseases

Frontotemporal Dementia

- 2nd most common for early onset
- 50-60% sporadic
- 2 Variants:
  - Behavioral
  - Language
- Most common risk: genetic mutations
  - 40% autosomal dominant pattern
  - Remaining cases are sporadic
- Cognition: Intact learning, memory and perceptual motor function
- Imaging: disproportionate frontal &/temporal lobe involvement

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Common Neurocognitive Diseases

Frontotemporal Dementia

- Insidious onset, gradual progression
- Behavioral variant: (≥3)
  - Disinhibition
  - Apathy or inertia
  - Loss of sympathy or empathy
  - Perseverative, stereotyped behavior
  - Hyperorality and dietary changes
- Language variant
  - Semantic variant
  - Agrammatic/nonfluent variant
  - Logopenic variant

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Common Neurocognitive Diseases

Lewy body Dementia (LBD)

- Dementia with Lewy bodies: cognitive decline ~ 1yr prior to motor symptoms
- Parkinson's disease: motor symptoms

- 2nd most common cause of dementia

- Features:
  - Cognitive Impairment
  - Motor Dysfunction
  - Behavioral
  - Autonomic dysfunction
  - Sleep Disorders

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Common Neurocognitive Diseases

Lewy body Dementia (LBD)

- Insidious onset
- Gradual progression
- Fluctuating cognition with pronounced variation in attention and alertness
- Recurrent visual hallucinations
- Cognition: impairments in visuospatial perception, executive function, memory varies, attention, psychomotor speed
- Imaging: parietal and occipital hypoperfusion/hypometabolism

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Traumatic Brain Injury, TBI

- Prevalence: 1.7 million TBIs annually
- More common in males, 59% in US
- Most common etiology:
  - Falls
  - Car accident
  - Being struck on the head
- Recovery variable depending on injury, age, prior history of damage, substance use, etc..

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Traumatic Brain Injury, TBI

Evidence of ≥ 1 of the following:

- Loss of consciousness
- Posttraumatic amnesia
- Disorientation and confusion
- Neurological signs

Cognition: deficits in complex attention, executive function, learning and memory

- Disturbances in emotional function
- Personality changes
- Headaches, fatigue, sleep disorders, vertigo, dizziness

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Neurodegenerative Disorder	Age of Onset	Disease Progression	Cognitive Deficits	Treatment
Alzheimer's Disease	65 yo	Gradually progressive Insidious Onset	Memory & Language	Acetylcholinesterase inhibitors & NMDA-R antagonist
Frontotemporal Dementia	45 – 64 yo	Gradual progression of behavior/language pathology	Executive dysfunction with sparing of memory and visuospatial domains	Symptomatic, avoid acetylcholinesterase inhibitors.
Vascular Dementia	Any age Increased incidence with age	Step-wise progression	Executive dysfunction, difficulty with speeded task	Control risk factors
Dementia with Lewy body	≥ 50 yo	Gradually progressive Insidious Onset Parkinsonisms @ least 1	Attention, visuospatial construction	Acetylcholinesterase inhibitor (Rivastigmine) Avoid antipsychotics

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Management

Pharmacological Treatment

- Acetylcholinesterase Inhibitors
  - Donepezil (all stages)
  - Rivastigmine (mild-moderate)
  - Galantamine (mild-moderate)
- NMDA receptor antagonist
  - Memantine (mod-severe)

Non-Pharmacologic Strategies

- Lifestyle Changes
  - Diet
  - Exercise
  - Sleep
  - Cognitive Stimulation

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Management

- Symptom Management
  - Antidepressant (SSRI's)
  - Sleep (sleep hygiene, melatonin)
  - Dangerous behaviors (antipsychotics)

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Case Presentation

- A 72 year old accountant
- PMH: chronic history of depression
- PCP: concern of difficulties expressing thoughts, forgetting what he's saying midsentence and forgetful of recent events as well as details. He was unable to do calculations in his head and noted making the wrong turn while driving. It's been taking longer for him to think about information and his gait has started slowing down. Wife notes a gradual decline in symptoms.
  - Family also notes word retrieval difficulties, short term memory loss, forgetting recent conversations. Significant changes from patient's baseline

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Case Presentation

- A 72 year old accountant
- Meds: antidepressant
- Labs: insignificant
- PE: insignificant
- ROS: insignificant

- Functional Assessment: scammed out of $50K, forgetting bills and missing appointments

- Neuropsychological Testing:
  - Deficits in learning new information, short term memory and language
  - Impairments with IADLs (medication management, finances and appointments)
  - MMSE: 15/30

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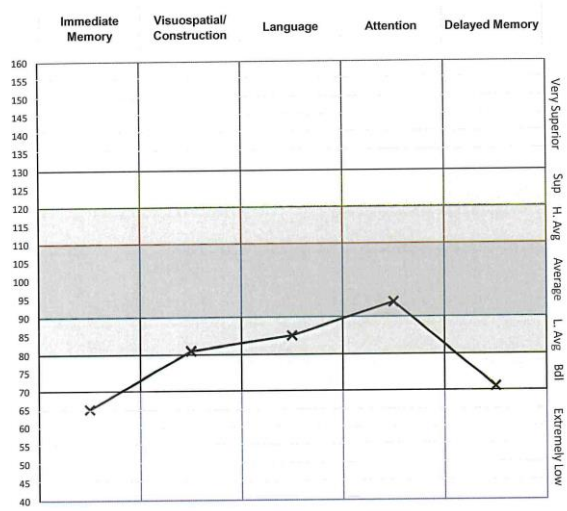
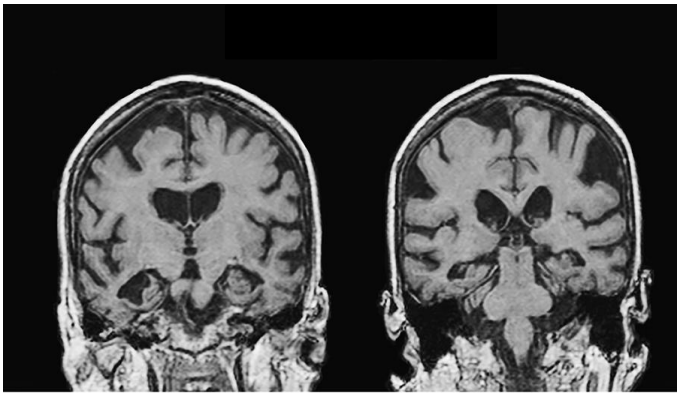
Case Presentation

MAC Summary Sheet (RBANS Form A)



MRI Brain Findings



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Case Presentation

- 72 yo M executive with18 years of formal education p/w forgetfulness of recent info, word retrieval difficulties and trouble expressing self. Trouble doing simple calculations, slower thought process, wrong turns w/driving. Wife notes slow, progressive decline but patient's functional abilities fluctuate over hours and days.
- FH: sister and maternal uncle with dementia in 60's
- Sleep: yelling, cursing and shaking limbs for the past 9yr. Moderate OSA on CPAP
- Visual hallucinations of small children in his room stealing from him.
- Mood: stopped socializing, exercising or going out

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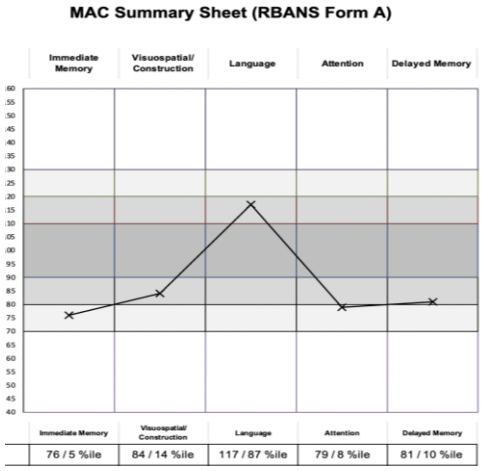
Case Presentation

- Meds: vitamins only
- BP: 160/85 sitting and 107/65 while standing
- PE: tiring with finger tapping, symmetric postural tremor, shuffling gait
- ROS: lightheadedness and near syncope with standing
- IADLs: getting lost, accident 2 months ago
- Labs: within normal limits
- MMSE: 25/30; poor performance on intersecting pentagons



TMT-A: 117 sec, impaired

TMT-B: 178 sec, BRDL

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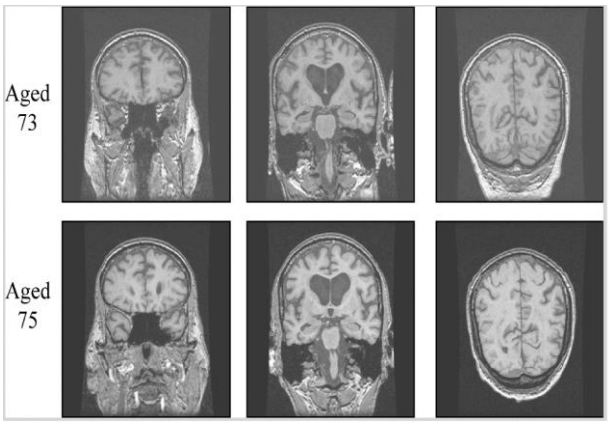
Case Presentation – Dementia with Lewy Bodies



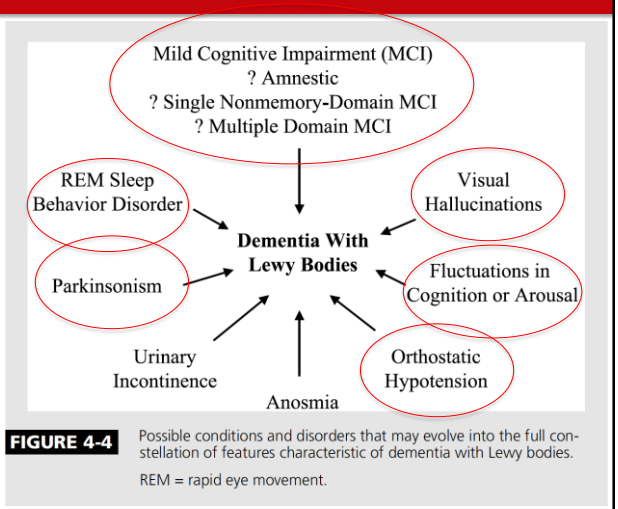


FIGURE 4-4 Possible conditions and disorders that may evolve into the full constellation of features characteristic of dementia with Lewy bodies.

REM = rapid eye movement.

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Case Presentation

- 77 yo F with hypothyroidism, HTN, HLD, coronary artery disease and type 2 diabetes mellitus p/w short term memory loss, word retrieval difficulties and missing medical appointments.
- FH: CVD in parents, 3 siblings
- ROS: constipation, fatigue, headaches, extremely dry, flaky skin
- Mood: apathetic
- Sleep: getting 4-5 hours of sleep, naps during day for 1 hour, snoring, apneic episodes, restlessness
- Meds: amlodipine 10, levothyroxine 125 mcg, metformin 500 mg, atorvastatin 10 mg
- Functionally Independent – IADLs & ADLs

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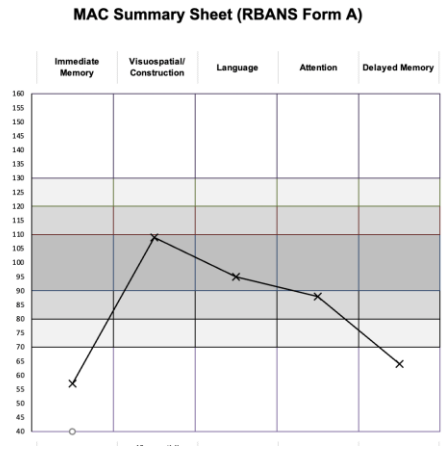
Case Presentation

- Vitals: BMI: 40. BP 175/92 P 55 O2: 98% on RA
- PE: disheveled, dry, flaky skin, skin turgor, slow responses with word retrieval difficulties
- Labs: H&H: 10.3/31. BUN/Cr: 24/1.2 B12: 157 TSH: 25. A1c: 6.5
- MRI: scattered hyperintensities advanced for age, infarct in temporal region
- MMSE: 25/30
- GDS: 10/15



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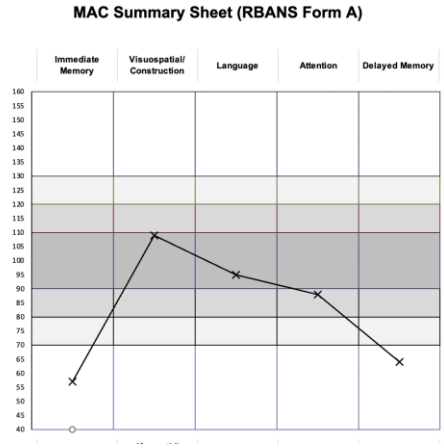
Case Presentation – Cognitive Impairment 2/2 Multiple Etiologies

- Subtherapeutic hypothyroidism
- Moderate Depression
- Uncontrolled HTN
- c/o sleep apnea, STOPBANG 6
- c/o dehydration
- Vitamin B12 deficiency
- Nutrition
- Increased vascular disease with remote infarct noted (silent stroke)



TMT-A: 59 sec, 1 error, low average
TMT-B: 168 sec, 1 error, low average

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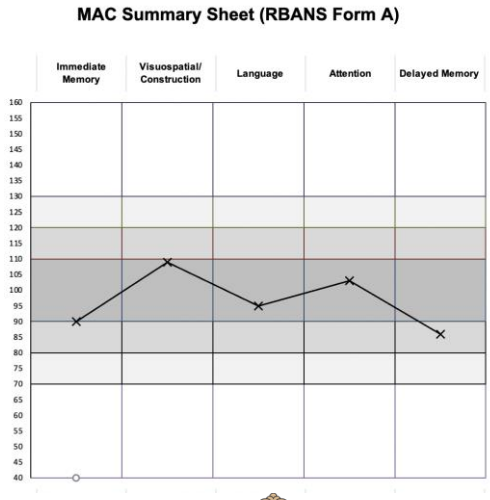
Case Presentation – Cognitive Impairment 2/2 Multiple Etiologies

Correct Underlying Etiologies
- Thyroid Disease
- HTN
- Sleep Apnea
- B12 Supplement
- Hydration
- MIND Diet
- Counseling
- Weekly Pill box with oversight

- Retest
  - Underlying Neurocognitive Disorder



TMT-A: 50 sec, low average
TMT-B: 160 sec, low average

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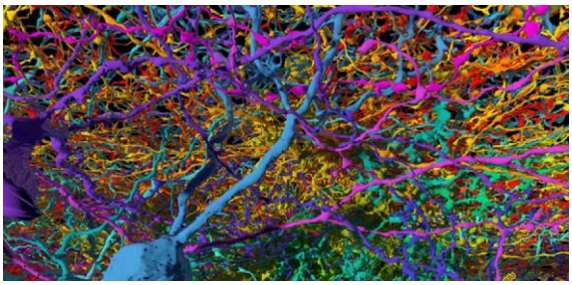
Diagnosis and Management of Dementia

- Early Diagnosis
  - Cognitive Screen in Clinic
  - Rule out Reversible Factors
  - Neuroimaging
- Referral
  - Neuropsychological Testing
  - Additional Work-up



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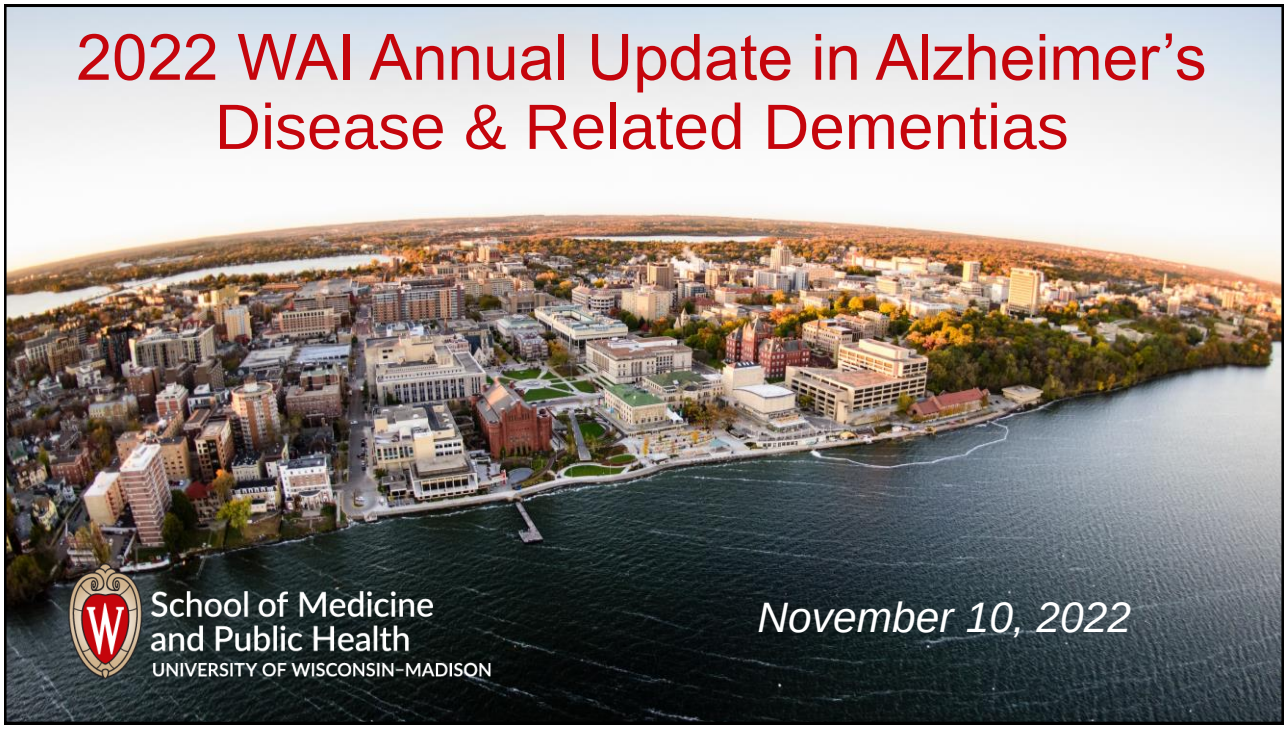
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