DEMENTIA FOR THE PRIMARY CARE PROVIDER

Gabriella Good MD

Geriatrician

Medical Director – UNM Senior Health Center

Assistant Professor of Geriatrics, University of New Mexico School of Medicine

OBJECTIVES

- By the end of this lecture you will know and understand
  - The risks for and causes of dementia
  - How to evaluate a patient for dementia
  - Formulate a treatment plan
  - Know when and where to refer

TOPICS

- Epidemiology
- Risk factors and prevention
- Assessment
- Treatment
- Resources

DEFINITION OF NEUROCOGNITIVE DISORDER (PREVIOUSLY DEMENTIA)

Major neurocognitive disorder, known previously as dementia, is a decline in mental ability severe enough to interfere with independence and daily life. It is a syndrome – a group of symptoms that has a number of causes.

DEFINITION OF NEUROCOGNITIVE DISORDER IN DSM-5

- Focuses less on memory impairment than the former DSM-IV criteria for dementia
- Allows for variables associated with conditions like frontotemporal dementia (FTD), which sometimes begin with declines in speech and language and do not necessarily affect memory immediately.
- Individuals with major neurocognitive disorder have cognitive deficits that interfere with independence
- People with mild neurocognitive disorder may retain the ability to be independent.

DSM-5 CRITERIA FOR MAJOR NEUROCOGNITIVE IMPAIRMENT

- **A.** Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains:
- - Learning and memory
- - Language
- - Executive function
- - Complex attention
- - Perceptual-motor
- - Social cognition

DSM-5 CRITERIA FOR MAJOR NEUROCOGNITIVE IMPAIRMENT

- **B.** The cognitive deficits interfere with independence in everyday activities. At a minimum, assistance should be required with complex instrumental activities of daily living, such as paying bills or managing medications.
- **C.** The cognitive deficits do not occur exclusively in the context of a delirium
- **D.** The cognitive deficits are not better explained by another mental disorder (e.g. major depressive disorder, schizophrenia)

TYPES OF NEUROCOGNITIVE DISORDER

- Alzheimer's disease
- Vascular dementia
- Lewy Body dementia
- Parkinson dementia
- Frontotemporal dementia
- Mixed dementia (mostly AD and VaD)
- Creutzfeldt-Jacob disease
- Huntington's desease
- Vernicke-Korsakof syndrome
- Normal pressure hydrocephalus

EPIDEMIOLOGY OF DEMENTIA

- From WHO 2017 - Worldwide, around 50 million people have dementia, with nearly 60% living in low- and middle-income countries. Every year, there are nearly 10 million new cases.
- The estimated proportion of the general population aged 60 and over with dementia at a given time is between 5 to 8 per 100 people.
- The total number of people with dementia is projected to reach 82 million in 2030 and 152 in 2050. Much of this increase is attributable to the rising numbers of people with dementia living in low- and middle-income countries.2

EPIDEMIOLOGY OF DEMENTIA

- An estimated 5.5 million Americans of all ages have Alzheimer's disease.
- Of the estimated 5.5 million Americans living with Alzheimer's dementia in 2017, an estimated 5.3 million are age 65 and older and approximately 200,000 individuals are under age 65 and have younger-onset Alzheimer's.
- One in 10 people age 65 and older (10 percent) has Alzheimer's dementia.
- Almost two-thirds of Americans with Alzheimer's are women.

EPIDEMIOLOGY OF DEMENTIA

- African-Americans are about twice as likely to have Alzheimer's or other dementias as older whites.
- Hispanics are about one and one-half times as likely to have Alzheimer's or other dementias as older whites.
- Because of the increasing number of people age 65 and older in the United States, particularly the oldest-old, the number of new cases of Alzheimer's and other dementias is projected to soar. Today, someone in the United States develops Alzheimer's dementia every 66 seconds. By mid-century, someone in the United States will develop the disease every 33 seconds.(3)

THE IMPACT OF DEMENTIA

Economic

- $604 billion annually for direct costs of medical and social care and informal care
- Medicare, Medicaid, private insurance provide much of the direct costs — remaining costs with families and/or caregivers ($220.2 billion in US)

Emotional

- Direct toll on patients
- Nearly half of caregivers suffer psychological distress, especially depression, and have more physical health issues

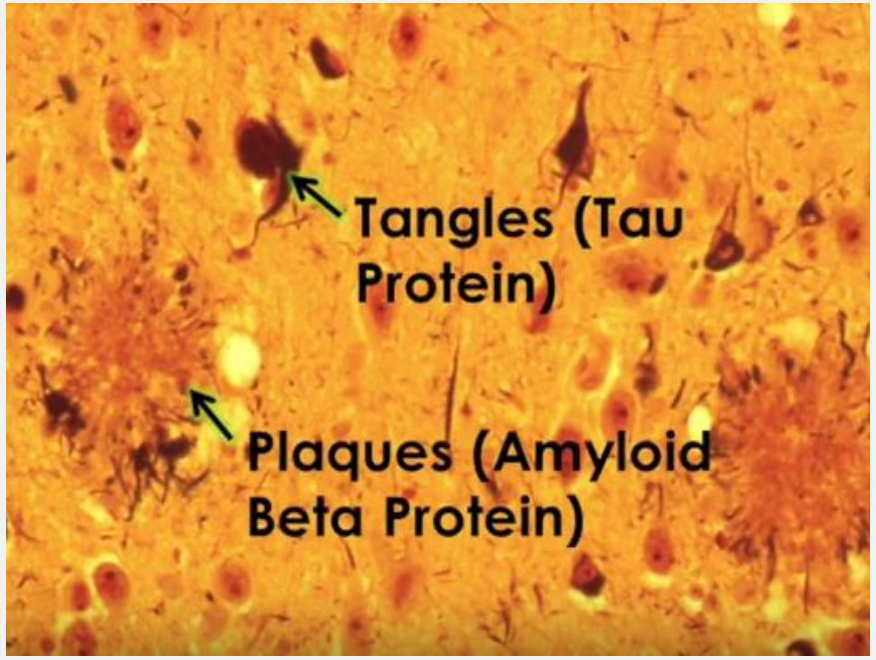
ETIOLOGY OF DEMENTIA

- Alzheimer's Disease
  - Amyloid Plaques/oligomers
  - Tau neurofibrillary tangles
- Lewy Body and Parkinson Dementia
  - Cytoplasmic a-synuclein inclusion bodies
- Frontotemporal dementia
  - Tau or ubiquitin proteins

HALLMARK CHANGES IN THE BRAIN WITH ALZHEIMER'S

- Plaques, microscopic clumps of a protein fragment called beta-amyloid
- Tangles, twisted microscopic strands of the protein tau
- Loss of connections among brain cells
- Inflammation, triggered by the body's immune system
- Eventual death of brain cells and severe tissue shrinkage

HALLMARK CHANGES IN THE BRAIN WITH ALZHEIMER'S



TAU FORMS TANGLES

- Tangles destroy a vital cell transport system made of proteins.
- A protein called tau helps the neuron tracks stay straight.
- Tau collapses into twisted strands called tangles.
- The tracks can no longer stay straight. They fall apart and disintegrate.
- Nutrients and other essential supplies can no longer move through the cells, which eventually die.

RISK FACTORS

PROTECTIVE

- Unknown
- Possible
  - NSAIDS
  - Antioxidants
  - Intellectual Activity
  - Physical Activity
  - Statin

RISKS

- Age
- Family history
- APOE4 allele
- Down syndrome
- Possible: head trauma, fewer years of formal education, history of depression cardiovascular risk factors.

THE GENETICS OF DEMENTIA

Early onset (<60 years old)

- Amyloid precursor protein (APP)
- Presenilin proteins (PS1 and PS2)

Late onset

- Apolipoprotein E gene (*APOE 2/3/4*) — chromosome 19
  - *APOE4* — two alleles confers greatest risk, decreasing age of onset in dose-related fashion
  - *APOE2* — protective
- Genome-wide association studies have identified other genes that confer risk of AD

SCREENING

- The US Preventive Services Task Force concludes the evidence is insufficient to recommend for or against routine screening for dementia in all older adults.
- If a patient or family member expresses concerns about cognitive decline, or a provider notices dementia warning signs, a mental status assessment and dementia evaluation is indicated.
  - Possible warning signs include unkempt appearance, poor historian, difficulty following directions, repeating the same question, lost in familiar places

DIFFERENTIAL DIAGNOSIS

NORMAL AGING	MILD COGNITIVE IMPAIRMENT	ALZHEIMER'S DEMENTIA (DSM-5)
Mild decline in memory More effort/time needed to recall new info New learning slowed but well compensated by lists, calendars, etc. Decreased efficiency in divided attention tasks (ie multi-tasking) No impairment in social and occupational functioning	Subjective complaint of cognitive decline in at least one domain of memory, executive function, language or visuospatial perception Cognitive decline is noticeable and measurable (see screening instruments) No impairment in social and occupational functioning	Significant objective decline in memory and learning in one or more cognitive domain of disturbed executive functioning, language, visuospatial ability, perceptual motor ability The cognitive decline is steady and progressive. The cognitive deficits interfere with independence in everyday activities. Other medical and psychiatric conditions, including delirium, have been excluded

DIFFERENTIAL DIAGNOSIS

	ALZHEIMER'S DEMENTIA	VASCULAR DEMENTIA	LEWY BODY DEMENTIA	FRONTOTEMPORAL DEMENTIA
ONSET	Gradual	Sudden or stepwise	Gradual	Gradual (age of onset <70)
COGNITIVE DOMAINS AND SYMPTOMS	Memory, difficulty learning, language, visuospatial, managing complex tasks	Depends on location of ischemia	Memory, visuospatial, visual hallucinations, fluctuating symptoms; extreme sensitivity to neuroleptic medication	Executive dysfunction, personality changes, disinhibition, language, ± memory
MOTOR SYMPTOMS	Rare early Apraxia later	Correlates with ischemia	Parkinsonism, present at time of onset of cognitive changes; frequent falls	None
PROGRESSION	Gradual (over 8-10 yr)	Gradual or stepwise	Gradual, but faster than Alzheimer's disease	Gradual, but faster than Alzheimer disease
IMAGING	Possible global atrophy	Cortical or subcortical ischemic changes on brain MRI	Possible global atrophy	Atrophy in frontal and temporal lobes

NORMAL AGING

- Occasionally forgetting where you left things you use regularly, such as glasses or keys.
- Forgetting names of acquaintances or blocking one memory with a similar one, such as calling a grandson by your son's name.
- Occasionally forgetting an appointment or walking into a room and forgetting why you entered.
- Becoming easily distracted or having trouble remembering what you've just read, or the details of a conversation.
- Not quite being able to retrieve information you have "on the tip of your tongue."

MILD NCD/MCI

- MCI: Subjective complaint of decline in at least one cognitive domain: noticeable and measurable
- No impairment in independent living
- 9.4 to 14.3/1000 person-years convert to Alzheimer disease; higher in amnestic MCI
- ~50% with amnestic MCI maintain stable level of impairment or return to normal cognitive status in 3–5 yr

ALZHEIMER DISEASE

- Onset: gradual
- Cognitive symptoms: memory impairment core feature with difficulty learning new information, language, visuospatial
- Motor symptoms: rare early, apraxia later
- Progression: gradual, over 8–10 yr on average
- Lab tests: normal
- Imaging: possible global atrophy, small hippocampal volumes

8 ALZHEIMER'S BEHAVIORS TO TRACK

- Signs of poor judgement. Worrisome spending, not noticing a safety issue.
- Reduced interest in leisure activities, less interest in favorite hobbies
- Repeating oneself
- Difficulty learning something new
- Forgetting the year or the month
- Difficulty managing money or finances
- Problems with appointments or commitments
- Daily struggles with memory or thinking

VASCULAR DEMENTIA

- Onset: may be sudden/stepwise
- Cognitive symptoms: depend on anatomy of ischemia, but dysexecutive deficits and slowing common
- Motor symptoms: correlates with ischemia
- Progression: gradual or stepwise with further ischemia
- Lab tests: normal
- Imaging: cortical or subcortical changes on MRI

DEMENTIA (OR NCD) WITH LEWY BODIES

- Onset: gradual
- Cognitive symptoms: memory, visuospatial, hallucinations, fluctuating symptoms
- Motor symptoms: parkinsonism
- Progression: gradual, but faster than AD
- Lab tests: normal
- Imaging: possible global atrophy

FRONTOTEMPORAL DEMENTIA

- Onset: gradual, usually age <60
- Cognitive symptoms: executive, disinhibition, apathy, language, +/- memory
- Motor symptoms: none (rare genetic forms associated with ALS)
- Progression: gradual but faster than AD
- Lab tests: normal
- Imaging: atrophy in frontal and temporal lobes

DELIRIUM VS. DEMENTIA

- Delirium and dementia often occur together in older hospitalized patients

- The distinguishing signs of delirium are:
  - Acute onset
  - Cognitive fluctuations throughout the course of a day
  - Impaired consciousness and attention
  - Fluctuating levels of alertness
  - Altered sleep cycles

- Search for underlying dementia once delirium cleared

DEPRESSION VS. DEMENTIA (1 OF 2)

- The symptoms of depression and dementia often overlap.
  - Presents diagnostic challenges

- Patients with primary dementia commonly experience symptoms of depression, and may minimize cognitive losses

DEPRESSION VS. DEMENTIA (2 OF 2)

- Patients with primary depression are generally unlike those with dementia in that they:
  - Demonstrate ↓ motivation during cognitive testing
  - Express cognitive complaints that exceed measured deficits
  - Maintain intact language and motor skills
- ~50% presenting with reversible dementia and depression progress to dementia within 5 yr

HISTORY OF PRESENT ILLNESS

- Document cognitive domains affected; interview patient and family or other informant.
- Document time course of onset and progression of cognitive and motor symptoms.
- Document time course of onset and progression of impairment in social and occupational functioning.
  - Impairment in social and occupational functioning may be evidenced by impairment in activities of daily living (ADLs) and instrumental activities of daily living (IADLs).
- Exclude depression
- Exclude delirium

HISTORY OF PRESENT ILLNESS

Ask both the patient and a reliable informant about the patient's:

- Patterns of substance use or abuse
- Living arrangements

PAST MEDICAL HISTORY

- Possible risk factors for Alzheimer disease
  - include advancing age
  - history of head trauma
  - Late-onset major depressive disorder,
  - Fewer years of formal education
- risk factors for cardiovascular disease.

FAMILY HISTORY

- Most commonly Alzheimer disease begins late in life.
- Rare forms of familial Alzheimer disease begin before age 60.

SOCIAL HISTORY

- educational level
- work history
- substance use and abuse
- driving
- firearms
- caregiver stress

REVIEW OF SYSTEMS

- Screen for behavioral disturbances such as wandering, self-neglect, physical aggression, psychosis

MEDICATIONS

- Thoroughly review medications and decrease or discontinue medications that increase cognitive, physical, or functional disability
- Anticholinergic medications such as diphenhydramine, and other 1st generation antihistamines, drugs such as tricyclic antidepressants, and for overactive bladder.
- Benzodiazepines
- Beers List for more detail.

PHYSICAL EXAM

Examine:

- Neurologic status
- Mental status
- Functional status (direct observation or informant report)

Include:

- Quantified screens of cognitive function
  - For example, Mini-Cog, SLUMS, MoCA
- Neuropsychological testing when presentation is atypical or if results are confounded by a high level of education or subtle changes

PHYSICAL EXAM

- Comprehensive physical exam with focus on neurologic exam to characterize dementia subtype or exclude treatable conditions that cause or exacerbate cognitive impairment:
- Gait (Lewy body dementia, normal-pressure hydrocephalus)
- Motor function (vascular dementia)
- Reflexes (vascular dementia)
- Extrapyramidal signs: rigidity, tremor, bradykinesia (Lewy body dementia)

EXAMPLES OF SCREENING INSTRUMENTS FOR THE EVALUATION OF COGNITION

Instrument Name	Cognitive Domains Assessed	Available
Mini-Cog	Visuospatial, executive function, recall	http://geriatrics.uthscsa.edu/tools/MINICog.pdf
St. Louis University Mental Status (SLUMS) Examination	Orientation, recall, calculation, naming, attention, executive function	http://medschool.slu.edu/agingsuccessfully/
Montreal Cognitive Assessment (MoCA)	Orientation, recall, attention, naming, repetition, verbal fluency, abstraction, executive function, visuospatial	www.mocatest.org
Folstein Mini–Mental Status Examination	Orientation, registration, attention, recall, naming, repetition, 3-step command, language, visuospatial	Copyrighted document for purchase: www.minimental.com

MINI-COG

- 3-minute instrument to screen for cognitive impairment in older adults in the primary care setting.
- The Mini-Cog uses a three-item recall test for memory and a simply scored clock-drawing test (CDT).
- Less affected by subject ethnicity, language, and education, and can detect a variety of different dementias.
- Detects many people with mild cognitive impairment
- Tests visuospatial, executive function, recall
- http://geriatrics.uthscsa.edu/tools/MINICog.pdf

ST LOUIS UNIVERSITY MENTAL STATUS EXAM (SLUMS)

- The SLUMS is a 30-point, 11 question screening questionnaire that tests orientation, memory, attention, and executive function, with items such as animal naming, digit span, figure recognition, clock drawing and size differentiation.
- Takes approximately 7 minutes to complete.
- The maximum score is 30 points, with the point values for correct answers written on the exam for easy scoring.
- Cut-off scores for dementia or mild neurocognitive impairment are based on the education level of the patient (high school and above or less than high school).

- http://medschool.slu.edu/agingsuccessfully/pdfsurveys/slumsexam_05.pdf

MOCA TEST

- The Montreal Cognitive Assessment takes approximately 10 minutes to administer and was designed to detect mild cognitive impairment in elders scoring in the normal range on the MMSE,
- Tests short-term memory, visuospatial abilities, executive functioning phonemic fluency (1 point), and verbal abstraction, attention, concentration, and working memory, language and orientation to time and place (6 points)
- Using a cutoff score 26, the MMSE had a sensitivity of 18% to detect MCI, whereas the MoCA detected 90% of MCI subjects. In the mild AD group, the MMSE had a sensitivity of 78%, whereas the MoCA detected 100%.
- Specificity was excellent for both MMSE and MoCA (100% and 87%, respectively). (5)

MINI MENTAL STATE EXAM

- The maximum score on the MMSE is 30 points.
- A score of less than 24 points is suggestive of dementia or delirium. Using a cutoff of 24 points, the MMSE had a sensitivity of 87 percent and a specificity of 82 percent in a large hospital-based sample
- Test is not sensitive for mild dementia, (18% sensitivity)
- Scores may be influenced by age and education, as well as language, motor, and visual impairments .

ASSESSMENT: LABORATORY

Routine

- CBC
- Na+, Ca++
- BUN/Cr
- Fasting glucose
- RPR
- TSH
- Vitamin B_{12} level

Optional (based on clinical exam and suspicion)

- Liver function
- Folic acid
- Homocysteine/methylmalonic acid
- Urinalysis / Toxicology
- CSF analysis
- HIV testing

ASSESSMENT-BRAIN IMAGING

- The American Academy of Neurology recommends that all patients with newly discovered cognitive impairment undergo at least one CT or MRI as part of the clinical evaluation of dementia
- Other groups, especially in the primary care areas, have favored more selective use of neuroimaging and advocated the use of decision algorithms to choose the patients most likely to have treatable brain abnormalities . Examples of high-risk factors include younger age (<60 years), presence of focal neurologic signs, and short duration of symptoms (eg, <2 years).

ASSESSMENT: BRAIN IMAGING

Consider imaging when:

- Onset occurs at age <65 years
- Symptoms begin suddenly or progress rapidly
- There is evidence of asymmetric or focal neurologic deficits
- Clinical picture suggests normal-pressure hydrocephalus
- Patient has had recent fall or other head trauma

Consider:

- Non-contrast CT head scan
- MRI
- Positron emission tomography (PET) when diagnosis remains uncertain

PRIMARY GOAL OF TREATMENT

To enhance quality of life and
maximize functional performance by
improving or stabilizing cognition, mood, and behavior

NONPHARMACOLOGIC MANAGEMENT (1 OF 2)

- Cognitive rehabilitation (6)
- Supportive individual and group therapy
- Physical and mental activity
- Regular appointments every 3–6 months
- Family and caregiver education and support
- Attention to safety
  - Need for supervision, wandering, driving etc.

NONPHARMACOLOGIC MANAGEMENT (2 OF 2)

- Environmental modification
  - Supportive strategies such as clocks, calendars, to-do list, visual clues, simple and compassionate communication style
  - Structure activities to match patient abilities

PHARMACOLOGIC MANAGEMENT

- *Treatment should be individualized*
- Cholinesterase inhibitors: donepezil, rivastigmine, galantamine
- Memantine
- Other cognitive enhancers
- Antidepressants
- Psychoactive medications

CHOLINESTERASE INHIBITORS (1 OF 2)

- Slow breakdown of acetylcholine
- Clinical trials demonstrate modest delay in cognitive decline compared with placebo in AD
- GI side effects common
  - Mitigated by slow titration curve
  - Maximum dosing of donepezil 23 mg/day creates significant side effects without evidence of improving global function
- No evidence of difference in efficacy among drugs

CHOLINESTERASE INHIBITORS (2 OF 2)

- Use in other dementias
  - Widespread use in vascular dementia *not* recommended
  - Attention and behavioral disturbances in Lewy body dementia can *benefit* from treatment
  - Rivastigmine is *FDA-approved* for mild to moderate dementia in Parkinson dementia
  - Treatment in frontotemporal dementia may *worsen* agitation

MEMANTINE

- Neuroprotective effect is to reduce glutamate-mediated excitotoxicity
- Modest *benefit* on cognition, ADLs, and behavior in AD
- Limited effect on cognition and no evidence to support widespread use in vascular dementia
- FDA-approved for moderate to severe AD
- Common adverse events: constipation, dizziness, headache

OTHER COGNITIVE ENHANCERS

- Vitamin E (α–tocopherol) may lower rate of functional decline, but no evidence of cognitive improvement in AD
  - The clinical efficacy and safety of vitamin E has yet to be fully established
- Selegiline may lower rate of functional decline, but no evidence of cognitive improvement in AD
- Ginkgo biloba offers no benefit in slowing cognitive decline in MCI

SYMPTOM MANAGEMENT (1 OF 2)

- Psychoactive medications
  - Behavioral disturbances best managed nonpharmacologically, eg, reducing overstimulation, environmental modification
  - When meds are required, target symptoms should be identified, and therapy selected accordingly
- Antidepressants
  - Depressed mood, low appetite, insomnia, fatigue, irritability, agitation
  - *Possibly* effective for disinhibition and compulsive behaviors associated with frontotemporal dementia
  - Caution: falls and anticholinergic effects that may worsen confusion (ie, paroxetine)

SYMPTOM MANAGEMENT (2 OF 2)

- First or Second-generation antipsychotics
  - Limited evidence of efficacy and increased risk of all-cause mortality in dementia
  - Should be used with caution in targeting delusions, hallucinations, paranoia, and irritability — frequently attempt to taper off
- Valproic acid and carbamazepine
  - Possible options, but with limited evidence and increased risk of mortality
- Benzodiazepines and anticholinergic medications should be *avoided*

THE GENERAL PROGRESSION OF DEMENTIA (1 OF 2)

Stage 1: No cognitive impairment	
	Unimpaired individuals experience no memory problems, and none is evident to a health care professional during a medical interview.
Stage 2: Very mild cognitive decline	
	Individuals at this stage feel as if they have memory lapses, especially in forgetting familiar words or names or the location of keys, eyeglasses, or other everyday objects. However, these problems are not evident during a medical examination or apparent to friends, family, or coworkers.
Stage 3: Mild cognitive decline	
	Early-stage Alzheimer disease can be diagnosed in some, but not all, individuals. Friends, family, or coworkers begin to notice deficiencies. Problems with memory or concentration may be measurable in clinical testing or discernible during a detailed medical interview.
Stage 4: Moderate cognitive decline (mild or early-stage Alzheimer disease)	
	At this stage, a careful medical interview detects clear-cut deficiencies. The affected individual may seem subdued and withdrawn, especially in socially or mentally challenging situations.

THE GENERAL PROGRESSION OF DEMENTIA (2 OF 2)

Stage 5: Moderately severe cognitive decline (moderate or mid-stage Alzheimer disease)
Major gaps in memory and deficits in cognitive function emerge. Some assistance with day-to-day activities becomes essential.
Stage 6: Severe cognitive decline (moderately severe or mid-stage Alzheimer disease)
Memory difficulties continue to worsen, significant personality changes may emerge, and affected individuals need extensive help with customary daily activities.
Stage 7: Very severe cognitive decline (severe or late-stage Alzheimer disease)
This is the final stage of the disease when individuals lose the ability to respond to their environment, to speak, and ultimately to control movement.

WHEN TO REFER

- Inconclusive diagnosis
- Atypical presentation
- Behavioral/psychiatric symptoms
- Younger-onset (< 65 years)
- Second opinion
- Patient/family preference
- Family dispute
- Caregiver support

RESOURCES FOR MANAGING DEMENTIA (1 OF 2)

- Specialist referral to:
  - Geriatric psychiatrist
  - Neurologist
  - Neuropsychologist
- Social worker
- Physical therapist
- Nurse
- Pharmacist

RESOURCES FOR MANAGING DEMENTIA (2 OF 2)

- Attorney for will, conservatorship, estate planning
- Community: neighbors & friends, aging & mental health networks, adult day care, respite care, home-health agency
- Organizations: Alzheimer's Association, Area Agencies on Aging, Councils on Aging
- Services: Meals-on-Wheels, senior citizen centers

CHOOSING WISELY®

- Don’t prescribe cholinesterase inhibitors for dementia without periodic assessment for perceived cognitive benefits and adverse gastrointestinal effects.
- Don’t use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia.

SUMMARY (1 OF 2)

- Dementia is common in older adults but is *not* an inherent part of aging
- AD is the most common type of dementia, followed by vascular dementia and dementia with Lewy bodies
- Evaluation includes history with informant, physical & functional assessment, focused labs, & possibly brain imaging

SUMMARY (2 OF 2)

- Primary treatment goals: enhance quality of life and maximize function by improving cognition, mood, behavior
- Treatment may involve both medications and non-pharmacologic interventions
- Community resources should be used to support patient, family, caregivers

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