The DETECT Initiative in Early Alzheimer's Disease: Optimizing Collaboration and Multidisciplinary Care to Facilitate Timely Diagnosis

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Disclosures

- **Dr. Dickerson discloses the following:**
  - He receives royalties from Oxford University Press, Cambridge University Press, and Elsevier.
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Learning Objectives

- Evaluate the burden of Alzheimer's disease (AD), including the process of prolonged decline in cognitive function
- Use cognitive assessments, biomarkers, and imaging to distinguish between normal aging and cognitive impairment
- Select and use the best therapeutic options for patients with AD, based on up-to-date clinical data on established and emerging disease-modifying therapies
- Employ best practices for multidisciplinary care coordination, workflows, and best practices for referral of patients

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Pre-read Material

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Risk Factors for Dementia

Modifiable risk factors for dementia	
• Diabetes • Hypertension • Dyslipidemia • Metabolic syndrome and obesity • Cerebral hypoperfusion cerebrovascular injury or stroke • Side effects of medications • Excessive alcohol and substance intake • Severe or repeated head trauma or traumatic brain injury	• Smoking • Air pollution • Depression and mood disorders • Sleep disorders • Low physical activity • Low social contact • Hearing loss • Low cognitive reserve • Poor nutrition

Non-modifiable risk factors for dementia	
• Age • Genetics (APOE, other probabilistic; Down's; rare autosomal dominant)	• Gender (F>M RR ~1.5) • Race (AA/Hispanic > White RR ~1.5-2)

Livingston G, et al. *Lancet.* 2020;396:413-446. McDade EM. *Continuum.* 2022;28:648-675. Alzheimer's Association. Facts and Figures 2022 (www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf). Accessed 11/19/2022. Atri A. *Med Clin North Am.* 2019;103:263-293.

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Challenges Related to Temporal Course of Neurodegenerative Diseases

- If a person has a stroke, recovers to the extent possible, and then come to the PCP and not only has trouble walking but is struggling to manage medications and finances and other IADLs, it may be obvious that the person has mild dementia—in part because of how different that individual is now compared with baseline a month or two ago
- If a person develops AD/ADRD, changes are usually gradual, making it difficult to determine whether the person has changed relative to baseline, since adaptations and adjustments are typically made incrementally over time
  - A clock-drawing test or MMSE will not tell you that a person has changed from baseline; ***a history from the patient and an informant who knows the person well regarding independence in complex daily activities is crucial for making this determination***

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Referral for Neuropsychological Assessment

- Outstanding utility at characterizing cognitive-functional status and cognitive-behavioral syndrome
- When initial evaluation is borderline or in individuals with unusual clinical profiles or with high premorbid abilities
- Establish a baseline and track longitudinal change
- Clarify patterns of cognitive impairment and strengths
- Help distinguish between depression/ mood disorders and dementia
- Help determine competency
- Assist in next steps, eg, diagnostic evaluation, interventions, treatments, referrals, and counseling:
  - Determination of disability
  - Delineate specific weaknesses and strengths
  - Recommendations for further diagnostic workup, referrals (early-onset, atypical features, rapidly progressing), and management
  - Recommend strategies for safety and more efficient functioning

Atri A. *Dementia: Comprehensive Principles and Practice*. Oxford University Press, 2014. Atri A. *Med Clin North Am.* 2019;103:263-293. Atri A. *Semin Neurol.* 2019;39:227-240. Shaughnessy L, et al. *J Clin Psychiatry.* 2019;80:MS18002BR2C.

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Referral for Specialist Assessment—
Neurologist, Geriatric Psychiatrist/Neuropsychiatrist, Geriatrician

- Very mild impairment
  - Memory or other cognitive symptoms of concern without impairment on office testing
  - Overall high function but with notable instances of problems with cognition
- Conflicting information
  - Concerning symptoms without impairment on testing
  - Impairment on testing without symptoms reported in daily life
  - Very high or low education; English is second language
- Atypical presentations
  - Young onset (<65 years)
  - Language or visuospatial dysfunction
  - Prominent behavioral symptom presentation
  - Accompanying motor or sensory symptoms, or sleep disturbance
  - Fluctuating course
  - Rapid progression

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Amyloid Imaging Taskforce: Appropriate-Use Criteria

Appropriate-use criteria for amyloid imaging	
Appropriate	**Inappropriate**
1. A cognitive complaint with objectively confirmed impairment	1. Used for evaluation of individuals without cognitive complaints; however, preclinical AD may become an indication for amyloid imaging if preventive treatments are proved to be effective
2. Performed only after full standard workup is completed	2. When standard recommended clinical diagnostic testing has not been ordered for initial assessment
3. AD is a possible diagnosis, but it is uncertain	3. As a stand-alone diagnostic for AD dementia
4. Knowledge of Aβ pathology would increase diagnostic certainty and alter management	4. To assess disease progression
5. Should only be ordered by experts in dementia	

Johnson KA, et al. *Alzheimers Dement*. 2013;9:e1-e16. Johnson KA, et al. *J Nucl Med*. 2013;54:1011-1013.

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CSF Taskforce: Appropriate-Use Criteria

Appropriate-use criteria for cerebrospinal fluid	
Appropriate	**Inappropriate**
• Patients with SCD (cognitively unimpaired based on objective testing) who are considered to be at increased risk for AD	• Cognitively unimpaired and within normal range functioning for age as established by objective testing; no conditions suggesting high risk and no SCD or expressed concern about developing AD
• MCI that is persistent, progressing, and unexplained	• Cognitively unimpaired patient based on objective testing, but considered by patient, family informant, and/or clinician to be at risk for AD based on family history
• Patients with symptoms that suggest possible AD	• Patients with SCD (cognitively unimpaired based on objective testing) who are not considered to be at increased risk for AD
• MCI or dementia with an onset at an early age, ie, <65 years	• Symptoms of REM sleep behavior disorder
• Meeting core clinical criteria for probable AD with typical age of onset	• Use to determine disease severity in patients having already received a diagnosis of AD
• Patients whose dominant symptom is a change in behavior (eg, Capgras syndrome, paranoid delusions, unexplained delirium, combative symptoms, and depression) and where AD diagnosis is being considered	• Individuals who are APOE ε4 carriers with no cognitive impairment
	• Use of LP in lieu of genotyping for suspected ADAD mutation carriers
	• ADAD mutation carriers, with or without symptoms

Shaw LM, et al. *Alzheimers Dement*. 2018;14:1505-1521.

SCD = subjective cognitive decline; REM = rapid eye movement; LP = lumbar puncture; ADAD = autosomal-dominant AD.

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