Cognitive Decline: Evaluation and Treatment of Memory Loss, Alzheimer's, & Dementia
2020 update

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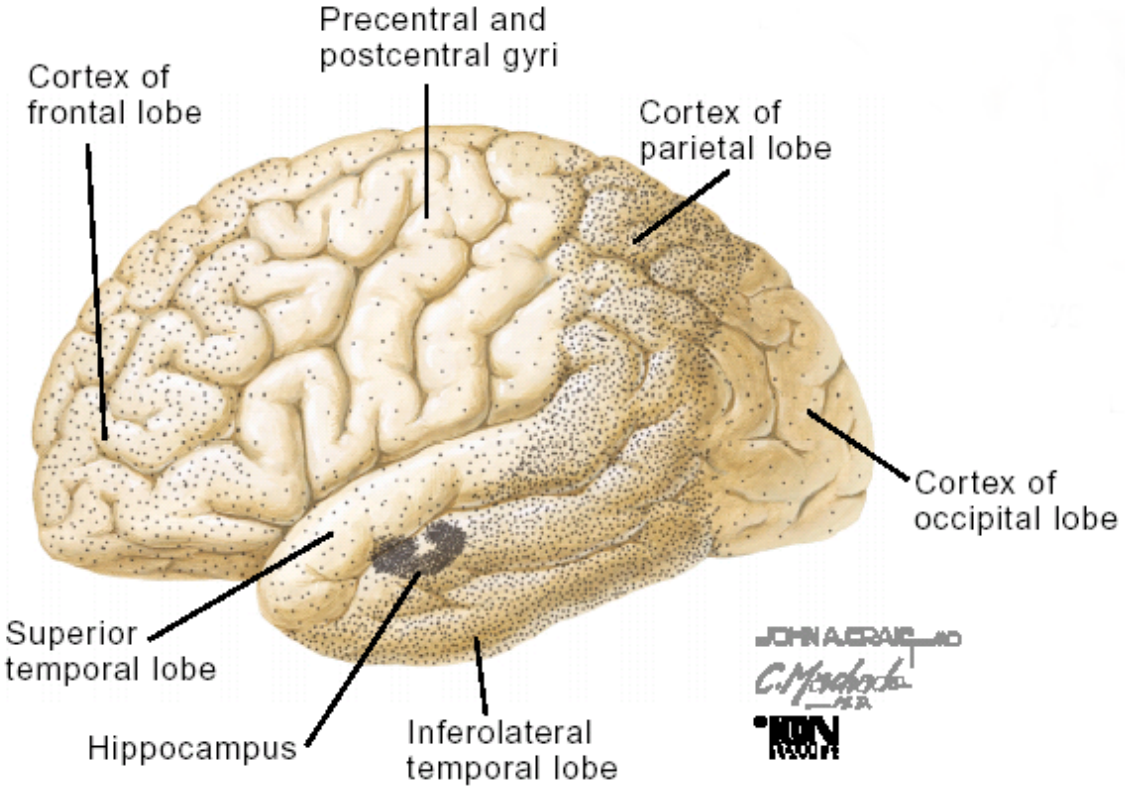
Learning objectives:
1. Understand the Alzheimer's disease pathophysiologic process.
2. Use the new diagnostic criteria to diagnose Alzheimer's disease dementia and mild cognitive impairment (MCI) due to the Alzheimer's disease pathophysiologic process.
3. Distinguish Alzheimer's disease from other common causes of cognitive impairment and dementia.
4. Learn about LATE (Limbic-predominant, Age-related, TDP-43 Encephalopathy)
5. Treat Alzheimer's disease and other common causes of cognitive impairment and dementia.

I. <u>Dementia Prevalence</u>

A. Increases geometrically with age
   1. 5-10% of individuals > age 65
   2. 50% of those > age 85

B. Alzheimer's disease is the most common form of dementia.

C. Distribution of pathology in Alzheimer's disease:



D. LATE (Limbic-predominant, Age-related, TDP-43 Encephalopathy) damages hippocampus and temporal lobes causing episodic memory loss and naming

difficulties that look like Alzheimer's disease. One paper suggested that it may be the cause of 17.3% of cases of dementia of the Alzheimer's type (DAT), compared to 39.4% of cases actually due to Alzheimer's neuropathologic change. BRAIN 2019: 142; 1503–1527

II. Evaluation (to diagnose Alzheimer's disease vs. other dementia). For additional information see Sections I & II of Budson & Solomon, *Memory Loss, Alzheimer's Disease, and Dementia: A Practical Guide for Clinicians*, Philadelphia: Elsevier Inc., 2016.

A. Structure of appointment:

- *With both patient & caregiver*: brief hx per patient's perspective, PMH, All, Meds, SHx including education & occupation, FHx (25-40% of AD patients have at least one other afflicted relative) (10 min)
- *Caregiver alone*: History per caregiver's perspective. Key questions: (1) What was the **first symptom** suggesting impairment, and (2) **when** did it occur? (3) What was the **pace** of the decline? Was it gradual or stepwise? (4) What cognitive areas are **currently** impaired & (5) which are the **most prominent**? (15 min)
- *Patient alone*: Physical, Neurological & Cognitive exam. (20 min)
- *Both patient & caregiver*: Assessment, further work-up and/or treatment plan. (15 min)
- Do in two visits if necessary. (An extra 10 minutes each on the history and cognitive exam is worth at least as much diagnostically as a PET or SPECT scan, neuropsychological testing, expert referral, etc., and is much more cost effective.)

B. History: (Although classically in neurology exam tells where, and history tells what, history often tells where as well as what in dementia.)

****Need to talk with caregiver/child/spouse alone****

General: Gradual and insidious onset over months to years, not stepwise (ask about when retired and why; keep checkbook; do taxes; continue community participation; etc.)

Hippocampal: Inability to learn new information, with striking preservation of older memories initially (repeats self; needs to be told information multiple times; misses appointments).

Temporal: Word finding difficulties. Disruption in the semantic storage and retrieval of linguistic information (anomia, not just for names of people; empty speech).

Parietal: Visuo-spatial deficits (difficulty planning routes; gets lost; cannot draw intersecting pentagons).

Frontal: (late) Dysexecutive syndrome (disinhibition; aggression; agitation; also much worse memory, attention and other cognitive functions).

C. General Exam: Check for cervical bruits; look for signs of systemic disease (COPD, liver failure, etc.)

D. Neuro exam:

Inconsistent: focal signs suggesting strokes, subdural fluid collections, tumors, etc.; signs suggesting Parkinson's (rigidity, tremor, etc.), PSP (no downgaze) or other neurodegenerative disease. (Note: some patients have both PD and AD.)

Supportive (early): none

Supportive (mid to late): Brisk reflexes, extensor plantars, snout, grasp, palmomental reflexes. (These are, however, not sensitive or specific.)

E. Cognitive exam:

Use one simple global cognitive exam to evaluate cognitive function.

Use the MMSE—but copyrights held by Psychological Assessments Resources.

Use the Montreal Cognitive Assessment (MoCA)—my new favorite—test & instructions below.

Useful for:

- Establishing the pattern of deficits
- Evaluation of drug effects (typical increases of 2-3 points are seen on both MoCA & MMSE)
- Annual comparisons (typical yearly decline of 2-3 points/year are seen on both MoCA & MMSE).

Pattern of deficits on the MoCA:

Delayed Recall tests new learning which is always impaired in early AD and MCI due to AD.

Orientation tests recent memory, which is generally impaired in early AD, particularly the date.

Other tests, including Visuospatial/Executive, Naming, Attention, Language, & Abstraction typically become more impaired as patients progress from early to moderate AD. These tests should be more or less intact in patients with MCI due to AD.

Other tests. Useful if the pattern from the MoCA is unclear:

Word Fluency: Intact individuals generate more words to categories (animals, vegetables, fruits; 12-15 or > for each), than letters (F, A, S; 10-12 or > for each); early AD patients show opposite pattern, i.e. can generate more words to letters than categories. (This is the only test that uses the patient as their own control.)

Instructions: "Tell me all the words that you can think of in 1 minute that begin with a certain letter. You cannot use names or different forms of the same words. For example, if the letter was 'R' you could not say Richard or Roger or Rochester, because those are names. You could say 'run' but then you could not say 'runs,' 'running,' or 'ran' because those are different forms of the same word. The first letter is F…." Prompt patients if they do not give any words for any 15 second block. For efficiency, only do as many letters as needed to establish pattern or normality. For categories: "Now we're going to do the same thing only different. I want you to tell me all the words you can think of that are all in the same category (which I will give you). The words can begin with any letters. You can say both big subcategories, as well as small individual items. For example, if the category was 'furniture,' you could not only say 'tables,' 'desks,' and 'chairs,' but also 'armchair,' 'high chair,' 'rocker,' 'recliner,' etc. The first category is 'animals'…." Again, prompt patients after no response for 15 seconds, and only do as many categories as necessary to either establish a pattern or normality.

Attention: *Simple* (always intact in early AD): Digit span forwards, 1 to 20, months forwards, registration (remembering words etc. w/o distraction for 30-60 seconds).

Attention: *Complex* (may be impaired in early AD): Digit span backwards, 20 to 1, months backwards, calculations.

Memory (always impaired in early AD): (note: registration must be intact) drilled word span (= to 1 less than digit span forwards), story "Bill and Tom went fishing…", others. If they don't get the words on free recall, check cued recall and recognition.

Remote Memory (often intact in early AD): Presidents, personal information.

Language (usually intact early, except for naming): naming high and low frequency objects (watch & band, pencil & point), writing sentence, comprehension, repetition, (empty speech late).

Visuospatial (may be impaired in early AD): copy figure

F. Laboratory tests: TSH, B12, Vit D. Also screen for encephalopathy / delirium: CBC, lytes, BUN, Cr, glucose, LFTs, Ca, alb. If clinically indicated: RPR, Lyme titre.

G. Imaging: MR is better for judging atrophy (esp. hippocampal), better for small vessel disease, better for evaluating for unusual conditions. CT is adequate, and better for agitated patients. (Everyone deserves at least one image in the course of their disease. E.g. a subdural on top of AD may explain the patient's current presentation—AD patients don't remember their falls!)

H. Additional w/u:

Behavioral Neurology Evaluation: (1.5-2 hrs over 1-2 visits with neurologist who has additional training in dementias.) Review history, imaging, interviews with patient & caregiver, general and neurological examinations, 20-30 minute cognitive exam. Especially important for complicated patients or those seeking second opinion of specialist. (Will follow patient if you desire.)

Neuropsychological Evaluation: (1-1.5 hrs with neuropsychologist (Ph.D.) + 3-6 hrs with technician for cognitive testing, over 1-3 visits.) Helpful if after your own thorough w/u including 15-20 min cognitive exam it is necessary to better characterize the existing deficit to make a diagnosis. E.g. to help determine the contributions of depression to a memory disorder, or to help evaluate someone who has an above average IQ and educational background such that although they perform normally on your office tests, you still suspect they are impaired. [Caution: all neuropsychologists are NOT equal when it comes to diagnosing dementia; only refer your patients to ones with experience in dementias.]

Brain FDG PET or ^{99}Tc SPECT: Nuclear medicine tests. Useful for confirming diagnosis of atypical dementia, or AD in a young patient (< age 65). In AD Expect temporal and parietal hypoperfusion. Moderate sensitivity and specificity. In correct clinical setting, areas of medial temporal, temporal, or parietal hypoperfusion suggests AD *regardless of the official interpretation*. PET and SPECT scans (unlike MRI) will often show significant changes from one year to the next, making them a useful follow-up test in the setting of previous negative work-up. In frontotemporal dementia, PET and SPECT shows abnormalities in frontal lobes; in corticobasal degeneration there are abnormalities in parietal lobes; in Lewy body disease there are abnormalities similar to AD but also in occipital lobes; in primary progressive aphasia abnormalities are in left perisylvian areas. Some pathologies yield multifocal patterns: e.g., Lyme disease, cerebral vasculitis.

Florbetapir (Amyvid), flutemetamol (Vizamyl), or florbetaben (Neuraceq) PET: Nuclear medicine tests. Useful for confirming diagnosis of AD in a young

patient (< age 70) or at any age when being sure that the patient has AD would significantly alter prognosis or treatment. Above 95% sensitivity and specificity.

CSF Aβ & tau: laboratory study. Useful for confirming diagnosis of AD in a young patient (< age 70) or at any age when being sure that the patient has AD would significantly alter prognosis or treatment. About 85% sensitivity and specificity.

I. Apply new criteria for AD and MCI due to AD (in slides)

III. Treatment For additional information see Section III of Budson & Solomon, *Memory Loss, Alzheimer's Disease, and Dementia: A Practical Guide for Clinicians*, Philadelphia: Elsevier Inc., 2016.

A. D/c or change anticholinergic agents, sedatives, etc.

B. To enhance cognition:

1. donepezil (generic & as Aricept). Cholinesterase inhibitor. Main side effects are: anorexia, nausea, & diarrhea (occur infrequently, <1 out of 10), also vivid dreams. (Additionally, need to use non-cholinergic paralytic agent for anesthesia; i.e. no succinyl choline) Start with 5mg QD, increase to 10 mg after 4-6 weeks if tolerated. 23 mg tablet available for moderate to severe AD; data suggests it may improve cognition but side-effects (anorexia, nausea, vomiting, diarrhea) also more common. Low income assistance program available. Produces a noticeable improvement in most patients. FDA approved for mild, moderate, and severe AD.
2. rivastigmine (Exelon). Cholinesterase inhibitor. Side-effects are more than donepezil in capsule form, but rivastigmine is now available in a QD patch which has comparable efficacy and fewer side-effects than any drug in this class. Start 4.6 mg/24 hr patch; can increase to 9.5 mg/24 hr patch after one month, and 13.3 mg/24 hr patch after that. Note: 13.3 mg/24 hr patch has more side-effects than 9.5 mg/24 hr patch; most patients do best with the 9.5 mg/24 hr patch. The rivastigmine patch is FDA approved for mild to moderate AD and mild to moderate dementia associated with Parkinson's disease (Lewy Body Dementia).
3. galantamine (now generic, formerly Razadyne, formerly Reminyl). Cholinesterase inhibitor. Similar to Donepezil. Immediate release (IR) and extended release (ER) formulations available; ER is both easier to use and has fewer side-effects (due to lower serum peak levels). ER: Start with 8 mg QD and increase after 4 weeks to 16 mg QD. Can also go to 24 mg QD. IR: 4 mg bid and increase after 4 weeks to 8 mg bid. Can also go to 12 mg bid.

References for cholinesterase inhibitors:

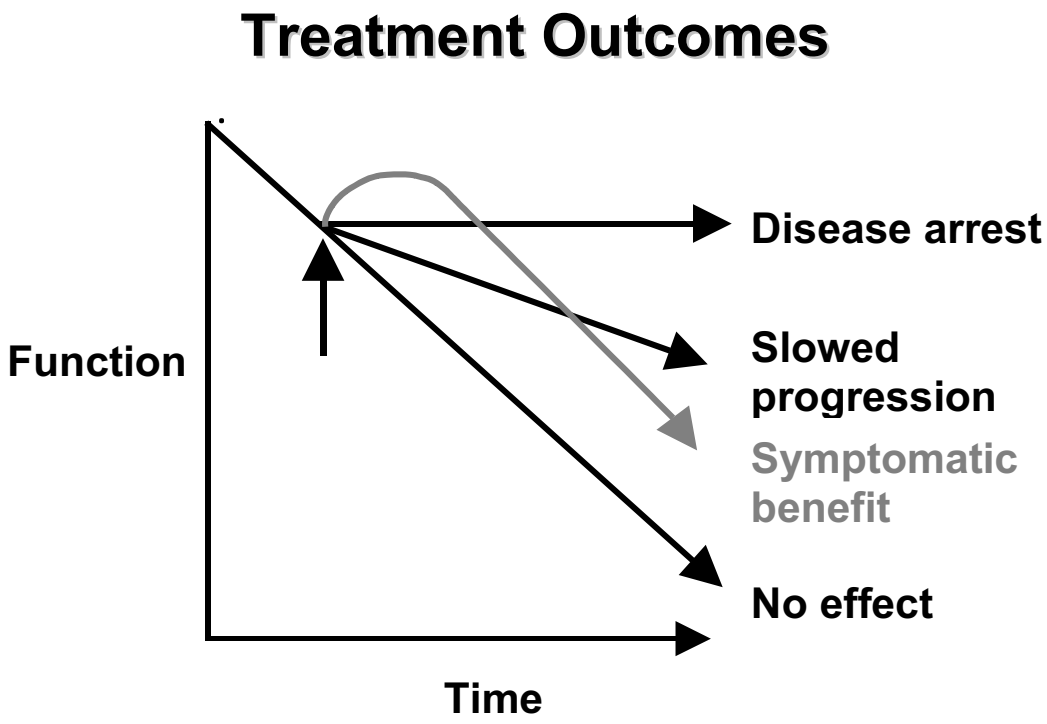
- Improves cognition, participation in activities of daily living, & global function in mild to moderate patients with AD:
  - Donepezil: Neurology 1998;50:136
  - Rivastigmine: BMJ 1999;318:633
  - Rivastigmine patch: Int J Geriatr Psychiatry 2007;22:456
  - Galantamine: Neurology 2000;54:2261

- Improves cognition & behavior in mild to moderate and moderate to severe patients with AD
  - Donepezil: Neurology 2001;57:613 & Lancet 2006;367:1057
  - Donepezil 23 mg: Clin Ther. 2010 Jul;32(7):1234-51.
  - Galantamine: Neurology 2000;54:2269
- Delay to nursing home placement by up to 2 years:
  - Donepezil: J Am Ger Soc 2003;51:937
- Reduces healthcare expenditures because treatment costs are offset by reductions in other healthcare expenditures.
  - Galantamine: Neurology 2000;57:972
  - Donepezil: Dementia and Geriatric Cognitive Disorders 2003;15:44
- Reduces caregiver time by over 1 hour per day
  - Galantamine: Int J Geriatr Psychiatry 2003;18:942
- Mild Cognitive Impairment
  - Donepezil: Neurology 2004;63:651 & NEJM 2005;352:23
- Vascular Dementia
  - Galantamine: Lancet 2002;359:1283
  - Donepezil: Neurology 2003;61:479
- Lewy Body Dementia
  - Rivastigmine: Lancet 2000;356:2031
- Neuropsychiatric inventory meta-analysis
  - JAMA 2003;289:210
- Responders and non-responders
  - 25-30% show an improvement equivalent to a 1 year reversal of symptoms
  - 50-60% show an improvement equivalent to a 6-month reversal of symptoms
  - 10-15% show either less than a 6-month reversal of symptoms or no significant improvement
  - NEJM 2004;351:56.
- How long to use them?
  - Studies suggest at least 4 to 5 years (CNS Drugs 2004;18:757)
  - Recommend: continue as long as there is quality of life to preserve.
  - In patients with moderate or severe Alzheimer's disease, continued treatment with donepezil was associated with cognitive benefits that exceeded the minimum clinically important difference and with significant functional benefits over the course of 12 months. (NEJM 2012; 366: 893-903)

See Figure below for Treatment outcomes curves.

<u>Treatment expectations for cholinesterase inhibitors:</u>
•Small but noticeable improvements:
–Less time spent looking for keys, glasses, etc.
–Repeats self less often
–Dwells in past less

–Easier time keeping track of conversation
–More engaged, outgoing
•Will decline over time even if the cholinesterase is working.



Treatment side effects:
•Gastrointestinal effects
–anorexia
–nausea/vomiting
–diarrhea
•Vivid dreams
–take in AM or earlier PM dose
•Other cholinergic symptoms
–rarely slows heart rate
-muscle cramps
-increased salivation
-rhinorrhea
-can exacerbate existing ulcers (but not known to cause them)

4. huperzine A (Cerebra). Available w/o prescription as a nutritional product. Cholinesterase inhibitor. Similar (perhaps fewer) side effects. 100 mcg of huperzine A BID is equivalent to 5 mg donepezil QHS. Effects are somewhat less impressive. (Obviously, this drug should not be used with other cholinesterase inhibitors.) http://www.nutrapharm.com/

5. Memantine (Namenda). Two mechanisms: 1. Uncompetitive antagonist at the NMDA glutamate receptor. 2. Dopamine agonist. Approved for use in moderate to severe patients (MMSE 15/Blessed 15 or worse). Works well with cholinesterase inhibitors—both are better than either one alone. Improves both cognition and behavior—particularly agitation. Side-effects uncommon, < 1 out of 10. Main side-effect is drowsiness, confusion, and dizziness which is dose related, often transient, and worse in milder patients. A few patients have experienced changes in blood pressure. Old pills are 10 mg. Start at half a pill, then increase weekly by half a pill: ½ qd, then ½ bid, then ½ in AM and 1 in PM, then 1 bid. Can prescribe memantine "titration pack" disp #1 sig. Use as directed, followed by memantine 10 mg BID disp #60. New pills are 7 mg extended release. Start 7 mg QAM, then increase by 7 mg QAM weekly until 28 mg QAM. Latest retrospective data analysis suggest that combination therapy, memantine plus a cholinesterase inhibitor, is superior to either medication alone.
   - References for memantine:
     - N Engl J Med 2003; 348:1333
     - Int J Geriatr Psychiatry 1999;14:135
     - JAMA 2004; 291:317
     - Alzheimer Dis Assoc Disord. 2008 Jul-Sep;22(3):209-21
6. Gingko Biloba. Doesn't work: JAMA 2002;288:835.
7. Ritalin. A useful stimulant when attention or encoding deficits are prominent, or when fatigue, somnolence, and poor energy are issues. Also great when there is a problem with napping during the day and consequent wandering at night—much better to use a stimulant in the morning than a sleeper at night. I use the 20 mg of the sustained release formulation. Can also use Concerta 18 mg or modafinil 100 mg.
8. On-going clinical trials.

C. To slow down disease progression:
   1. Lower homocysteine: Folate, B6, B12 (NEJM 2002;346:476) Can use Folgard (Folate 0.8 mg, B6 10 mg, B12 115 mcg)
   2. Statins
   3. Clinical trials.

E. Managing Agitation. For additional information see Section IV of Budson & Solomon, *Memory Loss, Alzheimer's Disease, and Dementia: A Practical Guide for Clinicians*, Philadelphia: Elsevier Inc., 2016. Try to determine the underlying cause of agitation:
   1. Use non-pharmacologic approaches first!!!
      i. Educate Caregiver.
      ii. Teach 3Rs: Reassure, Reconsider, Redirect
   2. Agitation is often due to anxiety
      i. Start with sertraline (Zoloft) 50 to 100 mg or citalopram (Celexa) 10 to 20 mg [but watch for increased QTc] (others not as good.)
   3. Manage sleep cycle disturbances
      i. Limit naps

ii. Methylphenidate (Ritalin) SR 20 mg or modafanil (Provigil) in AM if needed.

4. Daytime agitation
   i. Risperidone (Risperdal) start 0.25 mg QD
5. Nighttime agitation
   i. Trazodone start 50 mg QHS
   ii. Quetiapine (Seroquel) start 25 mg QHS
6. Studies underway to evaluate prazosin & carbamazepine. (Corbett A, Smith J, Creese B, Ballard C. Treatment of behavioral and psychological symptoms of Alzheimer's disease. Curr Treat Options Neurol. 2012 Apr;14(2):113-25.)
7. Consider 20 mg Dextromethorphan HBr / 10 mg Quinidine sulfate (Nuedexta)
   i. Cummings et al., JAMA. 2015;314:1242-54
   ii. Dosage: Weeks 1: 20/10 QD, 2-3: 20/10 BID, 4+: 30/10 BID
   iii. Need more dextromethorphan? Add 10 mg/5 ml BID to Nuedexta BID
   iv. Common adverse reactions: falls, diarrhea, UTI, dizziness, cough, vomiting, asthenia, peripheral edema, influenza, ⇧GGT, & flatulence
8. Consider pimavanserin (Nuplazid) 40 mg QD. FDA approved to treat hallucinations and delusions associated with psychosis of Parkinson's disease. Clinical trials of AD on-going now. (Cummings et al., Lancet. 2014 383(9916):533-40)
9. Inform families of cardiovascular risk of neuroleptics along with side-effects of drowsiness and Parkinsonism.
10. Refer to psychiatry if needed.

F. Pseudobulbar Affect
   1. What it is: Crying, laughing, or showing other strong emotions for little or no reason. Crying out of proportion to mood is particularly common in AD and vascular dementia.
   2. New Medication FDA approved to treat pseudobulbar affect:
      i. 20 mg Dextromethorphan HBr / 10 mg Quinidine sulfate (Nuedexta)
      ii. 1 capsule daily x 7 days, then 1 capsule Q12H
      iii. Common adverse reactions: diarrhea, dizziness, cough, vomiting, asthenia, peripheral edema, UTI, influenza, ⇧GGT, & flatulence
      iv. Serious side-effects & contraindications mainly related to quinidine

F. Social Work referral often helpful for helping patients and families deal with diagnosis, day programs, nursing home and other long term care placement.

G. Early on, Cognitive Occupational Therapy can be especially helpful for those with a bit of insight, to provide alternative strategies.

H. Driving. For additional information see Section V of Budson & Solomon, *Memory Loss, Alzheimer's Disease, and Dementia: A Practical Guide for Clinicians*, Philadelphia: Elsevier Inc., 2016.
   1. Patients with very mild AD have accident rates similar to 16 to 19 year old drivers (Neurology 2000;54:2205)
   2. Have family members ride as passengers; when they feel uncomfortable patient is not safe to drive. Adult children are best. (Am J OT 2015;69: 6903270030)

3. Rehabilitation hospitals have driving evaluations ($250 to $500), much less expensive than a single accident. Some state registry of motor vehicles do as well.

I. Non-pharmacologic approaches
1. Aerobic exercise has been proven to improve memory in healthy older adults and patients with mild Alzheimer's disease likely related to increased production of growth factors in the brain which stimulates hippocampal stem cells. (PNAS 2011;108(7) 3017-3022)
2. Mediterranean diet is beneficial (JAMA Intern Med. 2015;175(7):1094-1103. doi:10.1001/jamainternmed.2015.1668)
3. Social activities have also been shown to improve cognition in healthy older adults and patients with mild Alzheimer's disease
4. Use of habit can be helpful. Habit learning (procedural memory, learning by doing) is intact in mild Alzheimer's disease and therefore these patients can learn new routines and improve their lives.

J. Alzheimer's Association: www.alz.org, is a great resource for patients and families.

K. Chronic Traumatic Encephalopathy For additional information see Chapter 13 of Budson & Solomon, *Memory Loss, Alzheimer's Disease, and Dementia: A Practical Guide for Clinicians*, Philadelphia: Elsevier Inc., 2016. (summary below.)

L. Resource for patients and families: Budson & O'Connor, *Seven Steps to Managing Your Memory: What's Normal, What's Not, and What to Do About It*, New York: Oxford University Press, 2017.

Definition & etiology	• Chronic traumatic encephalopathy is a progressive neurodegenerative disease associated with repetitive brain trauma.
Cognitive and behavioral symptoms, in order of prevalence at presentation	• Memory impairment • Executive dysfunction • Attention & concentration difficulties • Sadness/depression • Hopelessness • Explosivity • Language impairment • Visuospatial difficulties • "Out of control" • Physically violent • Verbally violent • Impulse control problems • Suicidal ideation/attempts
Summary of diagnostic criteria	**General Criteria for Traumatic Encephalopathy Syndrome:** *All five criteria must be met* 1) History of multiple impacts to the head. 2) No other neurological disorder present that likely accounts for all clinical features 3) Clinical features must be present for a minimum of 12 months 4) At least 1 Core Clinical Features must be present and considered a change

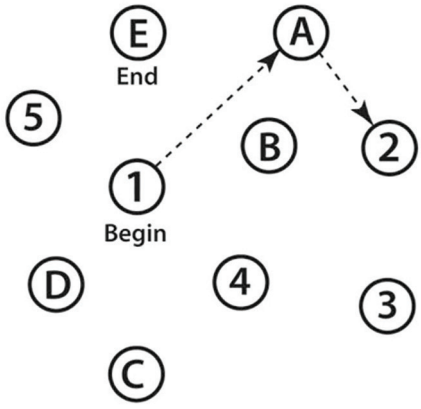
	from baseline 5) At least 2 Supportive Features must be present **Core Clinical Features of Traumatic Encephalopathy Syndrome:** *At least 1 must be met:* 1) *Cognitive*. Difficulties in cognition substantiated by impairment on standardized tests 2) *Behavioral*. Emotionally explosive, physically and/or verbally violent 3) *Mood*. Feeling overly sad, depressed, and/or hopeless **Supportive Features of Traumatic Encephalopathy Syndrome**: *At least 2 must be present:* (1) *Impulsivity*, (2) *Anxiety*, (3) *Apathy,* (4) *Paranoia*, (5) *Suicidality*, (6) *Headache*, (7) *Motor Signs,* including dysarthria & features of parkinsonism, (8) *Documented Decline*, for a minimum of one year, (9) *Delayed Onset*, at least 2 years **Traumatic encephalopathy syndrome diagnostic subtypes:** (1) Behavioral/Mood Variant, (2) Cognitive Variant, (3) Mixed Variant, (4) Dementia.
Imaging findings	• Cavum septum pellucidum is commonly seen on MRI or CT. Atrophy and hypofunction is typically observed in medial temporal and in frontal lobes.
Treatment	• Treatment is supportive. Cholinesterase inhibitors, memantine, and SSRIs can be tried.
Top differential diagnoses	• Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, vascular dementia, progressive supranuclear palsy, corticobasal degeneration, and normal pressure hydrocephalus.

MONTREAL COGNITIVE ASSESSMENT (MOCA®)

Version 8.1 English

Name:
Education: Date of birth:
Sex: DATE:

VISUOSPATIAL / EXECUTIVE



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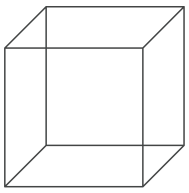


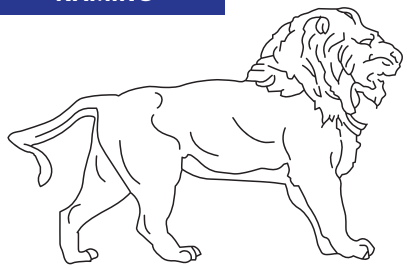
Copy cube

Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS __/5

NAMING



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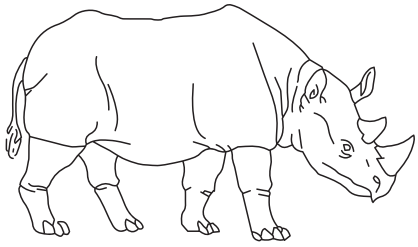

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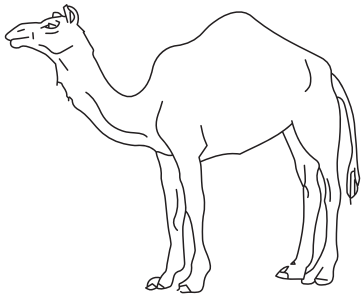

[ ]

__/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1ST TRIAL					
2ND TRIAL					

NO POINTS

ATTENTION

Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order. [ ] 2 1 8 5 4

Subject has to repeat them in the backward order. [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0**

__/3

LANGUAGE

Repeat: I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency: Name maximum number of words in one minute that begin with the letter F. [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler

__/2

DELAYED RECALL

Memory Index Score (MIS)

(MIS)	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
X3		[ ]	[ ]	[ ]	[ ]	[ ]	
X2	Category cue						MIS = ____ /15
X1	Multiple choice cue						

__/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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www.mocatest.org

Administered by: _____

Training and Certification are required to ensure accuracy

MIS: /15
(Normal ≥ 26/30)
Add 1 point if ≤ 12 yr edu

TOTAL __/30

Montreal Cognitive Assessment (MoCA)
Version 8.1

Administration and Scoring Instructions

The Montreal Cognitive Assessment (MoCA) was designed as a rapid screening instrument for mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The MoCA may be administered by anyone who understands and follows the instructions, however, only a health professional with expertise in the cognitive field may interpret the results. Time to administer the MoCA is approximately 10 minutes. The total possible score is 30 points; a score of 26 or above is considered normal.

All instructions may be repeated once.

1. Alternating Trail Making:

Administration: The examiner instructs the subject: *"Please draw a line going from a number to a letter in ascending order. Begin here* [point to (1)] *and draw a line from 1 then to A then to 2 and so on. End here* [point to (E)]."

Scoring: One point is allocated if the subject successfully draws the following pattern: 1- A- 2- B- 3- C- 4- D- 5- E, without drawing any lines that cross. Any error that is not immediately self-corrected (meaning corrected before moving on to the Cube task) earns a score of 0. A point is not allocated if the subject draws a line to connect the end (E) to the beginning (1).

2. Visuoconstructional Skills (Cube):

Administration: The examiner gives the following instructions, pointing to the cube: "*Copy this drawing as accurately as you can."*

Scoring: One point is allocated for a correctly executed drawing.

- Drawing must be three-dimensional.
- All lines are drawn.
- All lines meet with little or no space.
- No line is added.
- Lines are relatively parallel and their length is similar (rectangular prisms are accepted).
- The cube's orientation in space must be preserved.

A point is not assigned if any of the above criteria is not met.

3. Visuoconstructional Skills (Clock):

Administration: The examiner must ensure that the subject does not look at his/her watch while performing the task and that no clocks are in sight. The examiner indicates the appropriate space and gives the following instructions: *"Draw a clock. Put in all the numbers and set the time to 10 past 11."*

Scoring: One point is allocated for each of the following three criteria:

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• Contour (1 pt.): the clock contour must be drawn (either a circle or a square). Only minor distortions are acceptable (e.g., slight imperfection on closing the circle). If the numbers are arranged in a circular manner but the contour is not drawn the contour is scored as incorrect.
• Numbers (1 pt.): all clock numbers must be present with no additional numbers. Numbers must be in the correct order, upright and placed in the approximate quadrants on the clock face. Roman numerals are acceptable. The numbers must be arranged in a circular manner (even if the contour is a square). All numbers must either be placed inside or outside the clock contour. If the subject places some numbers inside the clock contour and some outside the clock contour, (s)he does not receive a point for Numbers.
• Hands (1 pt.): there must be two hands jointly indicating the correct time. The hour hand must be clearly shorter than the minute hand. Hands must be centered within the clock face with their junction close to the clock center.

4. Naming:

Administration: Beginning on the left, the examiner points to each figure and says: *"Tell me the name of this animal."*

Scoring: One point is given for each of the following responses: (1) lion (2) rhinoceros or rhino (3) camel or dromedary.

5. Memory:

Administration: The examiner reads a list of five words at a rate of one per second, giving the following instructions*: "This is a memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn't matter in what order you say them."* The examiner marks a check in the allocated space for each word the subject produces on this first trial. The examiner may not correct the subject if (s)he recalls a deformed word or a word that sounds like the target word. When the subject indicates that (s)he has finished (has recalled all words), or can recall no more words, the examiner reads the list a second time with the following instructions: *"I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time."* The examiner puts a check in the allocated space for each word the subject recalls on the second trial. At the end of the second trial, the examiner informs the subject that (s)he will be asked to recall these words again by saying: *"I will ask you to recall those words again at the end of the test."*

Scoring: No points are given for Trials One and Two.

6. Attention:

Forward Digit Span: Administration: The examiner gives the following instructions: "*I am going to say some numbers and when I am through, repeat them to me exactly as I said them.*" The examiner reads the five number sequence at a rate of one digit per second.

Backward Digit Span: Administration: The examiner gives the following instructions: "*Now I am going to say some more numbers, but when I am through you must repeat*

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them to me in the backward order." The examiner reads the three number sequence at a rate of one digit per second. If the subject repeats the sequence in the forward order, the examiner may not ask the subject to repeat the sequence in backward order at this point.

Scoring: One point is allocated for each sequence correctly repeated (N.B.: the correct response for the backward trial is 2-4-7).

Vigilance: Administration: The examiner reads the list of letters at a rate of one per second, after giving the following instructions: "*I am going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, do not tap your hand.*"

Scoring: One point is allocated if there is zero to one error (an error is a tap on a wrong letter or a failure to tap on letter A).

Serial 7s: Administration: The examiner gives the following instructions: *"Now, I will ask you to count by subtracting 7 from 100, and then, keep subtracting 7 from your answer until I tell you to stop."* The subject must perform a mental calculation, therefore, (s)he may not use his/her fingers nor a pencil and paper to execute the task. The examiner may not repeat the subject's answers. If the subject asks what her/his last given answer was or what number (s)he must subtract from his/her answer, the examiner responds by repeating the instructions if not already done so.

Scoring: This item is scored out of 3 points. Give no (0) points for no correct subtractions, 1 point for one correct subtraction, 2 points for two or three correct subtractions, and 3 points if the subject successfully makes four or five correct subtractions. Each subtraction is evaluated independently; that is, if the subject responds with an incorrect number but continues to correctly subtract 7 from it, each correct subtraction is counted. For example, a subject may respond "92 – 85 – 78 – 71 – 64" where the "92" is incorrect, but all subsequent numbers are subtracted correctly. This is one error and the task would be given a score of 3.

7. Sentence repetition:

Administration: The examiner gives the following instructions: *"I am going to read you a sentence. Repeat it after me, exactly as I say it* [pause]: ***I only know that John is the one to help today.****"* Following the response, say: *"Now I am going to read you another sentence. Repeat it after me, exactly as I say it* [pause]: ***The cat always hid under the couch when dogs were in the room.****"*

Scoring: One point is allocated for each sentence correctly repeated. Repetitions must be exact. Be alert for omissions (e.g., omitting "only"), substitutions/additions (e.g., substituting "only" for "always"), grammar errors/altering plurals (e.g. "hides" for "hid"), etc.

8. Verbal fluency:

Administration: The examiner gives the following instructions: *"Now, I want you to tell me as many words as you can think of that begin with the letter F. I will tell you to stop after one minute. Proper nouns, numbers, and different forms of a verb are not permitted. Are you ready?* [Pause] [Time for 60 sec.] *Stop."* If the subject names two consecutive

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words that begin with another letter of the alphabet, the examiner repeats the target letter if the instructions have not yet been repeated.

Scoring: One point is allocated if the subject generates 11 words or more in 60 seconds. The examiner records the subject's responses in the margins or on the back of the test sheet.

9. Abstraction:

Administration: The examiner asks the subject to explain what each pair of words has in common, starting with the example: *"I will give you two words and I would like you to tell me to what category they belong to* [pause]: *an orange and a banana.*" If the subject responds correctly the examiner replies: *''Yes, both items are part of the category Fruits.''* If the subject answers in a concrete manner, the examiner gives one additional prompt: *"Tell me another category* to *which these items belong to."* If the subject does not give the appropriate response *(fruits)*, the examiner says: *"Yes, and they also both belong to the category Fruits."* No additional instructions or clarifications are given. After the practice trial, the examiner says: *"Now, a train and a bicycle."* Following the response, the examiner administers the second trial by saying: *"Now, a ruler and a watch."* A prompt (one for the entire abstraction section) may be given if none was used during the example.

Scoring: Only the last two pairs are scored. One point is given for each pair correctly answered. The following responses are acceptable:

- train-bicycle = means of transportation, means of travelling, you take trips in both
- ruler-watch = measuring instruments, used to measure

The following responses are **not** acceptable:

- train-bicycle = they have wheels
- ruler-watch = they have numbers

10. Delayed recall:

Administration: The examiner gives the following instructions: *"I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can remember."* The examiner makes a check mark (√) for each of the words correctly recalled spontaneously without any cues, in the allocated space.

Scoring: **One point is allocated for each word recalled freely without any cues.**

Memory index score (MIS):

Administration: Following the delayed free recall trial, the examiner provides a category (semantic) cue for each word the subject was unable to recall. Example: ''*I will give you some hints to see if it helps you remember the words, the first word was a body part*.'' If the subject is unable to recall the word with the category cue, the examiner provides him/her with a multiple choice cue. Example: *"Which of the following words do you think it was, NOSE, FACE, or HAND?"* All non-recalled words are prompted in this manner. The examiner identifies the words the subject was able to recall with the help of a cue (category or multiple-choice) by placing a check mark (√) in the appropriate space. The cues for each word are presented below:

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Target Word	Category Cue	Multiple Choice
FACE	body part	nose, face, hand (shoulder, leg)
VELVET	type of fabric	denim, velvet, cotton (nylon, silk)
CHURCH	type of building	church, school, hospital (library, store)
DAISY	type of flower	rose, daisy, tulip (lily, daffodil)
RED	color	red, blue, green (yellow, purple)

* The words in parentheses are to be used if the subject mentions one or two of the multiple choice responses during the category cuing.

Scoring: To determine the MIS (which is a sub-score), the examiner attributes points according to the type of recall (see table below). The use of cues provides clinical information on the nature of the memory deficits. For memory deficits due to retrieval failures, performance can be improved with a cue. For memory deficits due to encoding failures, performance does not improve with a cue.

MIS scoring				**Total**
Number of words recalled spontaneously	…	multiplied by	3	…
Number of words recalled with a category cue	…	multiplied by	2	…
Number of words recalled with a multiple choice cue	…	multiplied by	1	…
	Total MIS (add all points)			**---/15**

11. Orientation:

Administration: The examiner gives the following instructions: "*Tell me today's date.*" If the subject does not give a complete answer, the examiner prompts accordingly by saying: *"Tell me the [year, month, exact date, and day of the week]."* Then the examiner says: *"Now, tell me the name of this place, and which city it is in."*

Scoring: One point is allocated for each item correctly answered. The date and place (name of hospital, clinic, office) must be exact. No points are allocated if the subject makes an error of one day for the day and date.

TOTAL SCORE: Sum all subscores listed on the right-hand side. Add one point for subject who has 12 years or fewer of formal education, for a possible maximum of 30 points. A final total score of 26 and above is considered normal.

Please refer to the MoCA website at www.mocatest.org for more information on the MoCA.

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AD8 Dementia Screening Interview

Patient ID#:_____
CS ID#:_____
Date:_____

Remember, "Yes, a change" indicates that there has been a change in the last several years caused by cognitive (thinking and memory) problems.	**YES, A change**	**NO, No change**	**N/A, Don't know**
1. Problems with judgment (e.g., problems making decisions, bad financial decisions, problems with thinking)			
2. Less interest in hobbies/activities			
3. Repeats the same things over and over (questions, stories, or statements)			
4. Trouble learning how to use a tool, appliance, or gadget (e.g., VCR, computer, microwave, remote control)			
5. Forgets correct month or year			
6. Trouble handling complicated financial affairs (e.g., balancing checkbook, income taxes, paying bills)			
7. Trouble remembering appointments			
8. **Daily** problems with thinking and/or memory			
TOTAL AD8 SCORE			

Adapted from Galvin JE et al, The AD8, a brief informant interview to detect dementia, Neurology 2005:65:559-564

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The AD8 Administration and Scoring Guidelines

A spontaneous self-correction is allowed for all responses without counting as an error.

The questions are given to the respondent on a clipboard for self–administration or can be read aloud to the respondent either in person or over the phone. It is preferable to administer the AD8 to an informant, if available. If an informant is not available, the AD8 may be administered to the patient.

When administered to an informant, specifically ask the respondent to rate change in the patient.

When administered to the patient, specifically ask the patient to rate changes in his/her ability for each of the items, ***without*** attributing causality.

If read aloud to the respondent, it is important for the clinician to carefully read the phrase as worded and give emphasis to note changes due to cognitive problems (not physical problems). There should be a one second delay between individual items.

No timeframe for change is required.

The final score is a sum of the number items marked "Yes, A change".

Interpretation of the AD8 (Adapted from Galvin JE et al, The AD8, a brief informant interview to detect dementia, Neurology 2005:65:559-564)

A screening test in itself is insufficient to diagnose a dementing disorder. The AD8 is, however, quite sensitive to detecting early cognitive changes associated many common dementing illness including Alzheimer disease, vascular dementia, Lewy body dementia and frontotemporal dementia.

Scores in the impaired range (see below) indicate a need for further assessment. Scores in the "normal" range suggest that a dementing disorder is unlikely, but a very early disease process cannot be ruled out. More advanced assessment may be warranted in cases where other objective evidence of impairment exists.

Based on clinical research findings from 995 individuals included in the development and validation samples, the following cut points are provided:

- 0 – 1: Normal cognition
- 2 or greater: Cognitive impairment is likely to be present

Administered to either the informant (preferable) or the patient, the AD8 has the following properties:

- Sensitiv ity >84%
- Specific ity >80%
- Positive Predictive Value > 85%
- Negative Predictive Value > 70%
- Area under the Curve: 0.908; 95%CI: 0.888-0.925