

Alzheimer's Disease and Dementia

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Alzheimer's disease

- **Alzheimer's disease (AD)** – not normal aging, not senility
 - **Normal aging:** age- associated memory impairment, declines in speed of processing, fluid ability
 - Individual differences are very important!
 - **Dementia** = gradual loss of function relative to some baseline time point or event (e.g., a stroke, a loss, a life transition)
 - **AD- The most common form of dementia-** 5.4 million persons are diagnosed with AD in the U.S.; 1 in 8 older persons are affected; by 2030 , 7.7 million will be affected, 25 million world-wide. AD deaths up 71% since 2000 (versus declines for cancer)
 - Discovered by Alois Alzheimer in 1906

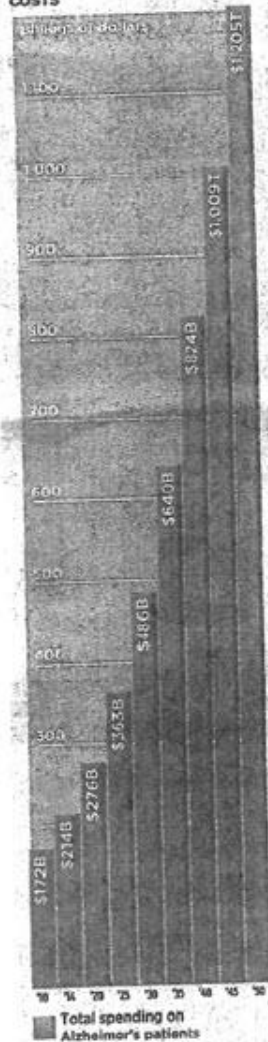
Alzheimer's disease

- **6th leading cause of death overall**; 5th cause of death for persons aged 65 and older, \$183 billion in costs, every **69 seconds**, someone is diagnosed with AD; 15 million family caregivers. **Incidence of Dx of AD increases after age 85.**
- **3 victims- the person suffering with AD** (anger, frustration, stigma, depression, suicidal thoughts-"Fraying at the Edges"), **the family** (shock of Dx for family), **and society** (this suggests that a proactive program of education is in order- hence, the Alzheimer's Association and Related Disorders).
- **Small % of AD is heritable** (a variation of the APOE protein (APOE4-the more copies you have, your odds increase- 1 = 4X, 2 = 12X), early onset (before age 30) - 2% of cases (Columbia NIH study))
- **AD often co-occurs with other forms of dementia and/or with depression.** One can precede the other- e.g. a person who is depressed develops dementia, **or** depression can be a reaction to a Dx of dementia. **Differential Dx important** (and **early Dx critical**-most difficult early on vs. normal aging, and later on-most dementias present similarly)

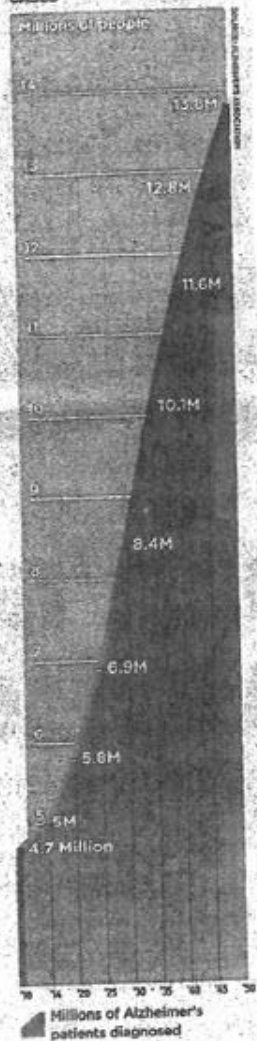
Alzheimer's Costs & Cases Expected to Soar

Projections through 2050

COSTS



CASES



Types of Dementia

- **Types of dementia** (a decline in functioning - not senility) (mixed dementia – AD/vascular dementia co-occurring is possible)
- **AD**- gradual onset and decline, a **Dx of exclusion- Dx is termed possible, probable, definite (at autopsy)** (recent work suggests AD may be detected microscopically via PET scans 15-20 years before symptoms even appear)
 - **beta amyloid proteins** form from outside neuron, **tau proteins** (creating tangles) form inside neuron- they collect in **hippocampus** (memory) and **frontal lobe** (judgement)
 - the decline/death of neuron could reflect overproduction of amyloid or brain's inability to clear it out- this cell death accounts for AD brain's smaller size
- **Vascular (multi-infarct)**- mini-strokes, sudden onset, associated with hypertension, declines are sporadic (**scalloping**)- second most common form of organic dementia (dementia with a physical cause leading to the death of neurons)
- **Lewy Body dementia**- microscopic deposits of alpha- synnuclein protein producing Lewy Bodies- age of onset is about 50, memory loss, visual hallucinations, sleep problems, movement difficulties – postmortem exam confirms it (Robin Williams)

Types of Dementia

- **Parkinson's disease**- characteristic symptoms of shaking, 20-30% of persons with PD develop dementia, preceded by behavioral, then cognitive declines- sometimes seen as a Lewy Body Dx- 2 varieties (cognitive, behavioral)
- **Frontotemporal dementia** (behavioral type sometimes referred to as Picks disease in UK) – most common among persons younger than 65. judgment, social skills, personality affected, expressive language affected- occurs earlier in life (50s, 60s) than AD (70+)- often associated with head injury-difficult to care for (CBS 60 Minutes special)- personality/behavior, language/aphasia, motor decline (eye movements-apraxia, walking, balance types- several genetic mutations may predispose persons to behavioral FTD- always fatal
- **Jacob-Creutzfeldt disease**- infectious in nature (variant is Mad Cow)- prions –normal protein found on surface of brain cells/neurons become abnormal and cluster on neuron-rapid onset of dementia
- **Depression**- affective (emotional) with cognitive symptoms
- **AIDS dementia, Normal pressure hydrocephalus (CSF cannot be absorbed), pugilistic dementia/repeated head trauma (Mohammed Ali) , Alcoholic dementia, hyperthyroidism**

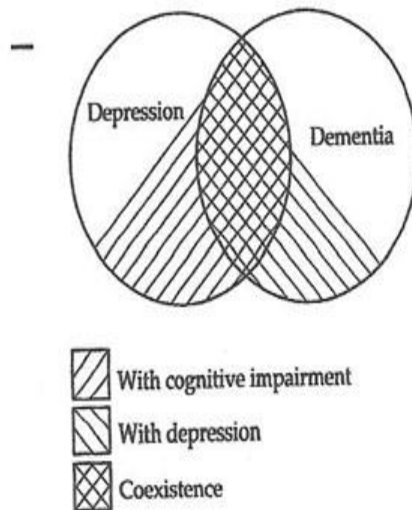


Figure 10.4 Illustration of diagnostic categorization of dementia and depression with coexistence. *Source:* Teri & Reifer (1987).

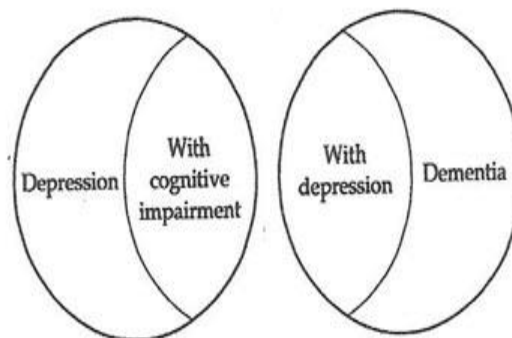
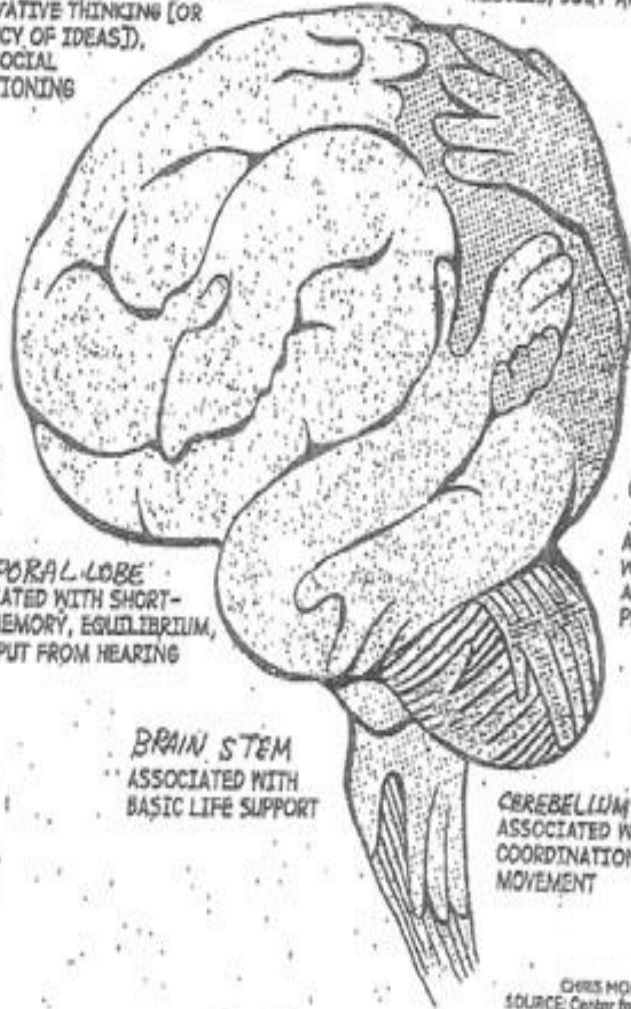


Figure 10.5 Illustration of diagnostic categorization of depression and dementia as mutually exclusive disorders. *Source:* Teri & Reifer (1987).

FRONTAL LOBE
ASSOCIATED WITH HIGHER MENTAL
FUNCTIONS (SUCH AS STRATEGIC
ATTENTION, REASONING, AND
INNOVATIVE THINKING [OR
FLUENCY OF IDEAS]),
AND SOCIAL
FUNCTIONING

PARIETAL LOBE
ASSOCIATED WITH SENSORY
INPUT FROM THE SKIN AND
MUSCLES, BODY AWARENESS



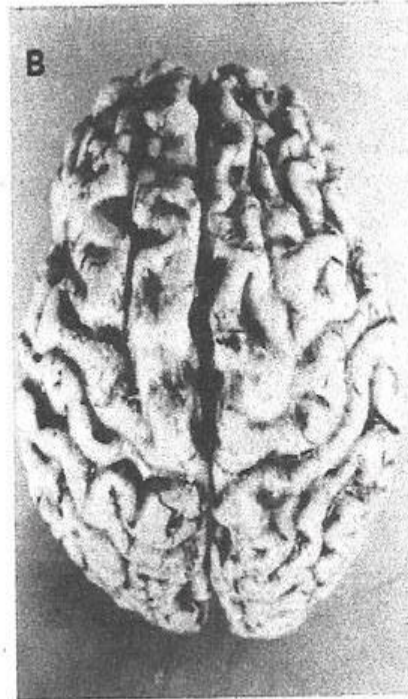
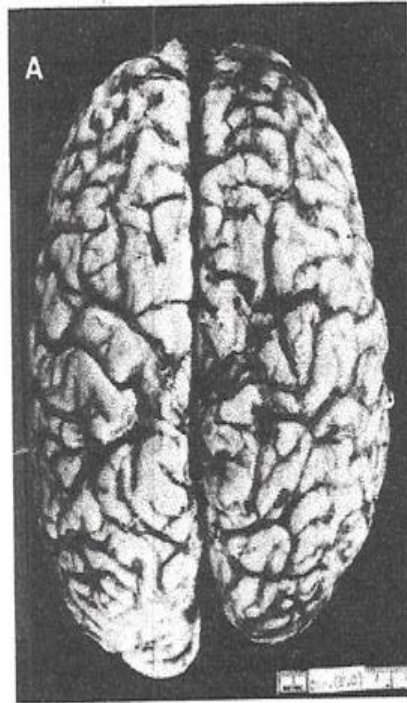
TEMPORAL LOBE
ASSOCIATED WITH SHORT-
TERM MEMORY, EQUILIBRIUM,
AND INPUT FROM HEARING

**OCCIPITAL
LOBE**
ASSOCIATED
WITH SIGHT
AND IMAGE
PROCESSING

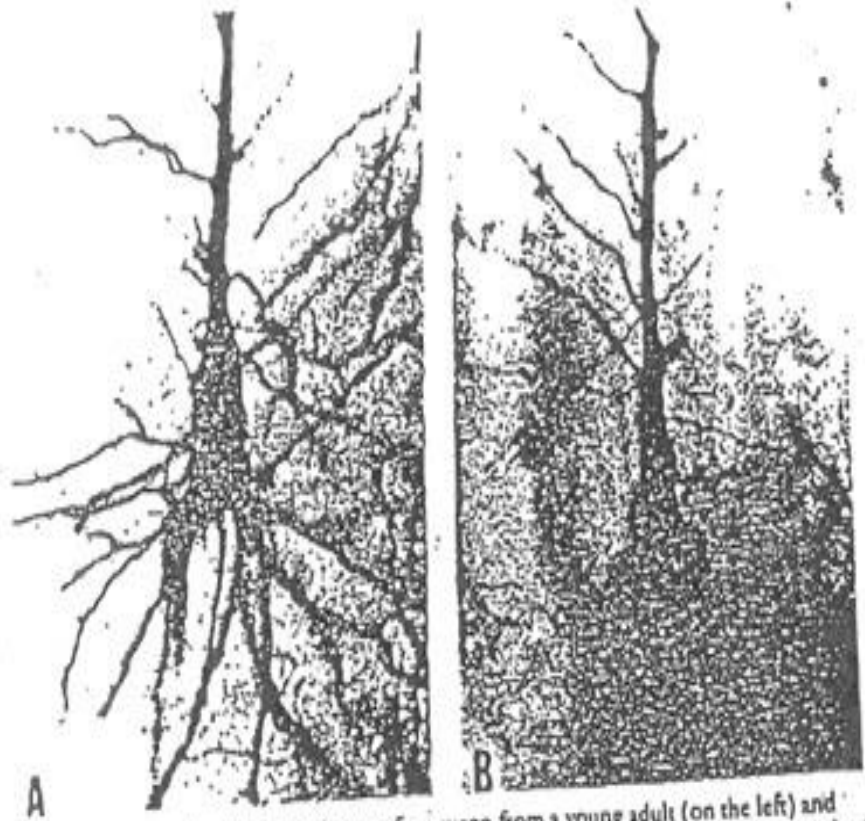
BRAIN STEM
ASSOCIATED WITH
BASIC LIFE SUPPORT

CEREBELLUM
ASSOCIATED WITH
COORDINATION AND
MOVEMENT

CHRIS MORRIS, Special Contributor
SOURCE: Center for BrainHealth at UT Dallas

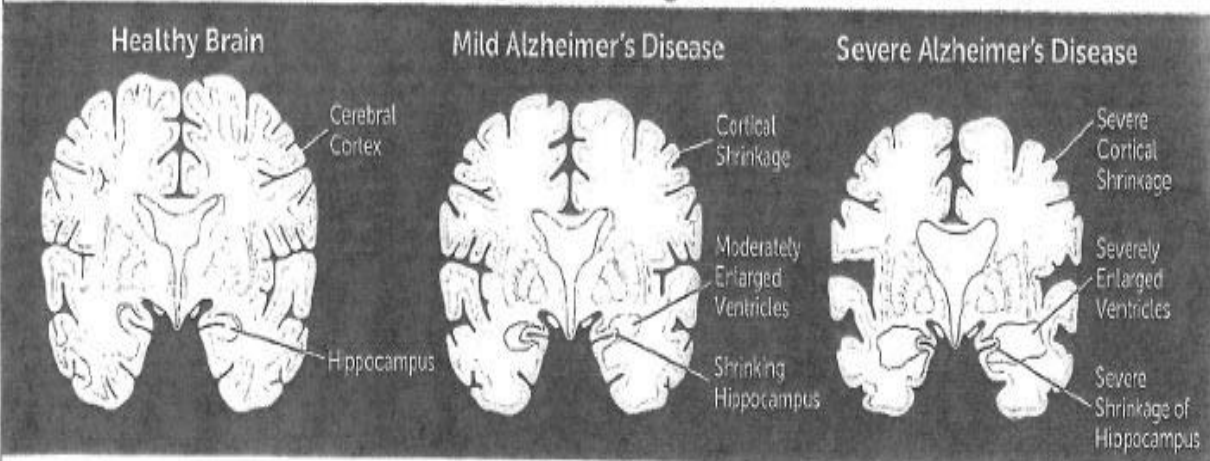


Relative to a normal aged brain (A), the brains of people suffering from Alzheimer's disease (B) are disproportionately small, and have alterations in both the fissures and sulci of the cerebral cortex.



■ FIGURE 4.6 These photos of a neuron from a young adult (on the left) and another from an 80-year-old (on the right) show the change in dendritic density very clearly. (Source: Scheibel, 1992, Figure 5, p. 160. Reprinted by permission of Academic Press, Orlando, FL, and author.)

How the Brain Changes During Alzheimer's Disease.



As Alzheimer's disease progresses, brain tissue shrinks. As the ventricles enlarge and the cells of the shrinking hippocampus degenerate, memory declines. When the disease spreads throughout the cerebral cortex, language, judgment, behavior, and bodily functions decline along with memory until death, usually 8 to 10 years after diagnosis. *Research is our only hope. Please give generously today.*

- 1 Memory changes that disrupt daily life
- 2 Challenges in planning or solving problems
- 3 Difficulty completing familiar tasks
- 4 Confusion with time or place
- 5 Trouble understanding visual images and spatial relationships
- 6 New problems with words in speaking or writing
- 7 Misplacing things and losing the ability to retrace steps
- 8 Decreased or poor judgment
- 9 Withdrawal from work or social activities
- 10 Changes in mood and personality



■ **FIGURE 5.5** This neuron is from a patient diagnosed from autopsy as having suffered from Alzheimer's disease. You can see how tangled and fragmented the dendrites have become. (Source: Scheibel, 1992, from Figure 6, p. 162. Reprinted by permission of Academic Press, Orlando, FL, and author.)

Symptoms of Depression

- **Emotional- dysphoria**- dejected mood, sadness, loss of interest, sense of failure, irritability, worry, helplessness, hopelessness
- **Cognitive**-pessimism, rumination, poor memory, memory complaints, difficulty in concentrating, delusions, hallucinations, suicidal thoughts, self-blame
- **Physical/somatic**-loss of appetite, fatigue, sleep disturbances, weight loss
- **Appearance**-stooped posture, sad face, withdrawal, suspiciousness, hostility, confusion, unkempt, weight loss, constipation
- **Psychomotor**-slowed speech and movements, shuffling slow gait
- **Psychomotor agitation**-continued motor activity, wringing of hands, picking of skin, pacing, restless sleep, grasping at others

SEPARATING DEMENTIA AND DEPRESSION

Characteristics	Depressed	Dementia
Depression	++++	++
Sleep and appetite disturbance	+++	++
Suicidal thoughts	++	±
Emotional lability	+	+++
Anxiety	+++	++
Hostility-irritability	++	+++
Confusion	++	++++
Disorientation	+	++++
Impaired recent memory	+	++++
Decreased mental alertness	++	++++
Unsociability	++	++++
Uncooperativeness	++	++++

Note: Plus sign refers to positive indicator for the disorder; Minus sign refers to negative indicator (contra-indicative) for the disorder. More pluses, for example, indicate that greater weight needs to be given characteristic defining either dementia or depression.

Adapted from C. Salzman & R. Shader. (1979). Clinical evaluation of depression in the elderly. In A. Raskin & L. Jarvik (Eds.), *Psychiatric symptoms and cognitive loss in the elderly* (p. 50). New York: Hemisphere Publishing.

AD Risk factors and Dx

- **AD risk factors: Age (85+), gender (women), traumatic head injury** statistical risk factors, as is the presence of an extra gene on chromosomes 1, 14, 19, and 21. Some suggest genetics (a form of the APO4 gene) to account for up to 10-20% of all cases, and usually is associated with the early onset of AD (younger than age 50).
- The rapidity of progression is greatest for persons with early onset AD.
- Some limited evidence associates Agent Orange exposure and AD
- **AD is properly considered a Dx of exclusion. Eliminate other forms of dementia- this suggests a multidisciplinary, comprehensive assessment-** e.g. vascular dementia, Parkinson's disease, Huntington's chorea, depression, head injury, delirium, alcoholic dementia, AIDS dementia, Jacob-Creutzfeldt disease, normal pressure hydrocephalus, vitamin B-12 deficiency, medication effects (antidepressants, sedatives, antihypertensives, older antihistamine drugs, antipsychotic/anticonvulsants).
- **Persons with AD are coping with the discrepancy between the inner and outer worlds- very important**

Clinical Picture

- **Major symptoms of AD** (vary across persons): impaired judgment, short term memory loss, problems in thinking abstractly, language use, orientation, difficulty with everyday tasks
- These symptoms usually interfere with work or social activity, and are progressive, leading to total dependence on others for care. (**first in-last out-implicit/overlearned associations**)
- costs/benefits of false negative/false positive errors of Dx
- **No one symptom is diagnostic-look for patterns of symptoms**
- **AD** - Often accompanied by inappropriate sexual behavior, paranoia, aggression, agitation, ADL/IADL deficits, disturbed sleeping, incontinence, withdrawal, mood/personality changes
- increased presence of **beta-amyloid protein** in certain areas of the brain and not others (hippocampus, frontal lobe) vs. normal aging (general distribution of beta-amyloid protein).
- Some new work on mice suggests **Tau proteins** may cause production of amyloid proteins between cells, causing them to clump together, undermining function. Damage is localized to **hippocampus** (memory) and **frontal lobe** (judgement, executive function), as opposed to normal aging (generalized in nature re: amyloid protein)
- **Still Alice**-Julianne Moore

Treatability/MCI

- **Some of these forms of dementia are treatable and some are not.** CT/PET scans, MRIs are very helpful in this respect-may ID Alzheimer's prior to symptoms appearing.
- AD can only **conclusively** be established via post-mortem examination of brain tissue- senile plaques/neurofibrillary tangles. Persons with AD often live for 10-15 years, and often die of other causes (e.g. cancer, congestive heart failure, stroke).
- **Treatability** - (e.g., symptoms of delirium, depression, drug effects, vitamin B12 deficiency)- **this is different from being reversible** (undoing the cause of AD)

Mild Clinical Impairment

- **AD is often, but not always preceded (5-7 years) by a period of cognitive decline, termed Mild Cognitive Impairment (MCI),** relating to memory loss, or difficulties with attention/concentration, language, executive functioning (planning, decision-making), problems with relationships between objects in space (e.g. copying a clock, matching blocks to a design, copying designs) and/or personality change (depression, agitation).
- **MCI implies no impairment in social/work functioning, no evidence of dementia at present. “pre-clinical”-structural changes in brain are likely present despite no Dx symptoms**
- **Persons with MCI or undiagnosed persons with AD often can compensate for the gradual loss of their skills.** This often occurs in the early stages of the disease or via the support of for example, a spouse.
- Some persons with **MCI** progress to AD, some do not – **clinically heterogenous**

Differential Dx- AD vs. Normal Aging

Ten Warning Signs of AD vs. Normal Aging

No one warning sign is key-patterns are important, especially those that cannot be explained/out of character are important to recognize and follow-up on-the more areas of difficulty, the more likely AD/dementia is causal

1. **Memory loss that disrupts everyday life** vs. occasional forgetting/remembering later (why did I come in this room? Where is my purse?)
2. **Problem solving difficulties/following a plan** vs. occasional mistakes/recognizing them
3. **Problems in completing familiar everyday tasks (e.g. dressing, driving, playing a game, cooking)** –awareness of these failures is diagnostic as the disease progresses (left vs. right hemisphere losses) vs. occasional needs for help/responds to help/suggestions-

AD versus Normal Aging (continued)

4. **Disorientation to time/place** vs. confusion but figuring it out later
5. **Understanding visual images/spatial relationships (lack of self recognition)** vs. visual changes via cataracts
6. **New problems w/words, speaking, writing** vs. occasional problem word finding
7. **Misplacing things/cannot retrace steps** vs. occasional misplacing (e.g. glasses)
8. **Decreased poor judgment/decision-making (e.g. money, personal grooming)** vs. occasional poor decisions
9. **Withdrawal from work/social activity** vs. sometimes weary of work/family duties
10. **Changes in mood/personality (e.g. suspicious, fearful, depressed, angry)** vs. irritation when routine is changed

See AARP Bulletin March 2024!

Dx and Treatment

- **Early Dx/treatment key!** Thorough Dx by separate clinicians (over time), thorough medical/neuro workup, drug history very important. Olfactory difficulties **may** be diagnostic
- **New blood test (PreclivityAD)** may help ID senile plaques/changes in such over time
- **Treatments (versus reversing** the fundamental structural basis for the disease):
 - **drug therapy –older drugs**(e.g. Aricept, Memantine/Namenda- singly/in combination), Exelon, Reminyl - inhibit breakdown of neurotransmitter acetylcholine) –doubious + side effects–
 - **New drug (s)** – some promise in RCTs (**aducanumab/Aduhelm**) manufactured by Biogen-higher doses removed amyloid plaques with few side effects vs. lower doses and placebos) (TIME, 11/11/19)-very costly (\$28K/year/pt.-Medicare) **despite FDA approval, its use is still debated-FDA may have rushed its approval despite dubious clinical trials data (DMNews)-tested on AD patients with mild symptoms/early stages of the disease**
 - **New drug (s) - Leqembi/Lacanemba-** mfd by Eisai-FDA fast track approval pending –results of clinical trials (Jan 2023), not full approval-decreases amyloid protein in early AD pts-injectable, brain bleed/swelling side effects which must be monitored- \$26,500/year
 - **cognitive** (spaced retrieval) training, engaged lifestyles (e.g. Nun Study)
 - **validation therapy (Naomi Feil), treatment of anxiety, depression, agitation/wandering** (sundowning)-disorientation vs. unorientation (**discrepancy between inner and outer world**) ****
 - **environmental changes** provide structure and predictability- dementia care units.
 - Lifestyle changes-exercise, social/cognitive stimulation, group therapy -mildly impaired persons
 - **immunotherapy** (NIH study-Columbia-focus on chromosome #14- remove plaque, preventative)

Prevention

- **Create a cognitive reserve via mental exercise, brain training (Nun Study-Snowden) -** applies both to AD dementia and to normal cognitive aging
- **Prevention? Put the odds in your favor**
 - avoiding head injury-avoid risky activities
 - Diabetes-prevention and management
 - Depression-accurate Dx and treatment (drug treatment, cognitive-behavior therapy)
 - not smoking/quitting
 - Mediterranean diet (low fat, high fiber), antioxidants (dark chocolate, berries, nuts. Apples, spinach, beans-inhibit oxidation which produces free radicals)-this enhances sleep quality, which lowers risk of AD
 - being physically active, mental and social engagement are important
 - not having unnecessary surgery requiring general anesthesia
 - getting enough sleep (sleep may allow brain to prevent accumulation of amyloid proteins/"clean up")

Grief and Dementia

- **Grief:** 3 victims (AD sufferer, family, public)-the long goodbye- we “lose” people with AD gradually-they also become more aware of this
 - **Anticipatory** (you and that person) - fear of dementia and the losses it entails
 - 30% say that upon Dx, they would consider suicide
 - **Disenfranchised** (you and that person) - AD as a source of dread/shame
 - **Loss is ambiguous** - no definitive end or course of the disease-this interferes with the grieving process
 - **Eventuates in the lack of recognition of self and loved ones**
 - Anger and sorrow in receiving a Dx and having to provide care (physically present, but mentally absent)
 - How can you express this to a loved one and expect to be understood?
 - A thankless job, guilt over a desired death and over one’s feelings
 - **Learning to let go of the person this person used to be**
 - Concerns over a loved one’s safety, guilt that you are not ill
 - **You do not have to be the perfect caregiver**-master the art of forgiving
 - **Caregiving (especially in isolation) is stressful**-for every 10 years of such, your life is shortened by 1 year - OSU study estimates caregiving to shorten life by 4-8 years

Caregiving and Dementia

- **Persons may live for 10-15 years; they “die” in stages: What will change and when, what are the consequences for you and them?**
- **Hold on to the past, focus on the positive, and live from day to day- stay in the present; review the past with a loved one**
- **Caregiver respite- Day Stay; Join a support group- AA sponsored**
- Keep a journal, seek online support (AD discussion forum)
- Seek professional help for isolation from others, self-destructive thoughts, unbridled anger at person or depression
- **Self-care is very important-** physically, socially, cognitively, spiritually
- Avoiding isolation/stigma, treating depression, learning new ways of communicating with loved one, having ongoing support from others, dealing with legal implications of victim’s declining competence (power of attorney), educating oneself regarding available services (e.g., wife of AD sufferer in Ohio)

Suggestions for communicating with Alzheimer's disease patients:

- 1. Be patient-** it may take some time and repeated requests in order for the person to understand you. Learn to communicate via facial expressions, voice tone, body language, daily behaviors. These are also often the ways AD patients communicate when they cannot verbalize. Being patient also allows the person to decide what he/she needs and/or wants to say. If you do not understand what the person is saying, ask the person to point or gesture.
- 2. Repetition is key-** provide simple reminders, create simple routines.
- 3. Slow down-** AD patients cannot process information quickly- keep your requests simple- one idea or behavior at a time. It may take the person quite awhile to carry out the simplest of tasks.

4. Speak in short, active, sentences. Do not speak in the passive tense (referring to other people). The first word in a sentence will be interpreted as the subject (The man fed the dog vs. the dog was fed by the man).

5. Refer to concrete, real objects.

6. Use redundant sentences. (Pick up the cup vs. pick up the cup on the table, pick up the cup you drank from).

7. Have the person repeat back what you have said. You may have repeat yourself several times.

8. Use visual aids whenever possible.

Supplement this with auditory, tactile, olfactory, and gustatory cues. Your tone of voice and facial expressions count! The more cues, the better.

9. Ask simple questions. (Would you like chicken or pork? vs. Would you like chicken for dinner?; what would you like to drink? vs. are you thirsty?). Ask one question at a time.

10. As the disease progresses, the importance of taking time to understand what the person is thinking or feeling grows. Ask questions!

11. Make eye-to-eye contact. If necessary, approach the person from the front and ID yourself.

12. Treat the person with respect, value his/her humanity. Communicate your love verbally and nonverbally. Never talk about him/her as if he/she was not there. Do not talk down to him/her. **Persons with dementia are not children.**

13. Avoid confrontation, criticizing, correcting, or arguing. Keep calm. Ask for help if you need it.

14. Doing as many of the above as possible will facilitate communication with the person, lessen that person's acting out or emotional outbursts, and lessen your frustration as a caregiver.

15. Dementia patients are struggling to understand what is happening to them and are trying to make sense of everyday life.

Supporting them and letting them know they are still loved and indeed do still count in this respect will give you (and them) much satisfaction.

16. Your learning to communicate can be **calming** to the person with AD; this increases the quality of your interactions with that person

What Alzheimer's Patients Ask of You

Do Not Ask Me to Remember

Do not ask me to remember
Do not try to make me understand
Let me rest and know you are with me
Kiss my cheek and hold my hand
I'm confused beyond your concept
I am sad and sick and lost
All I know is that I need you to be with me at all cost
Do not lose your patience with me
Do not scold or curse my cry
I can't help the way I am acting
Can't be different though I try
Just remember that I need you
That the best of me is gone
Please don't fail to stand beside me
Love me till my life is done