Alzheimer's disease and dementia

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1. **Alzheimer's disease (AD)** – not normal aging, not senility

    a. **Normal aging**: age- associated memory impairment, declines in speed of processing, fluid ability

        i. Individual differences are very important!

    b. **Dementia** = loss of function relative to some baseline time point or event

    c. **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)

    d. Discovered by Alois Alzheimer in 1906

    e. 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.

    f. **3 victims**- the person suffering with AD (anger, frustration, depression, suicidal thoughts), 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).

    g. 10-20% of AD is heritable (5 variations on the APO genes), early onset (before age 30) - 2% of cases (Columbia NIH study)

    h. See 2019 report of the Alzheimer's Association and Related Disorders for details

2. AD often co-occurs with vascular (multi-infarct) 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)

3. **Types of dementia** (a decline in functioning - not senility) (mixed dementia possible)

    a. **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)

        i. **beta amyloid proteins** form from outside neuron, **tau proteins** (creating tangles) form inside neuron- they collect in hippocampus (memory) and frontal lobe (judgement)

        ii. the decline/death of neuron could reflect overproduction of amyloid or brain's inability to clear it out

    b. **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)

    c. **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

    d. **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

    e. **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

    f. **Jacob-Creutzfeldt disease**- infectious in nature (Mad Cow)- prions –normal protein found on surface of brain cells/neurons become abnormal and cluster on neuron-rapid onset of dementia

    g. **Depression**- affective (emotional) with cognitive symptoms

    h. AIDS dementia, Normal pressure hydrocephalus (CSF cannot be absorbed), pugilistic dementia/repeated head trauma, Alcoholic dementia, hyperthyroidism

    i. **Many causes of dementia are *treatable* (e.g., delirium, depression, drug effects, vitamin B12 deficiency)- this is different from being *reversible***

4. **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. Genetics accounts for 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.

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-Creutzfelt (mad cow – viral) disease, normal Pressure hydrocephalus, vitamin B deficiency, medication effects (antidepressants, sedatives, antihypertensives, older antihistamine drugs, antipsychotic/anticonvulsants).

5. **Some of these forms of dementia are treatable and some of which are not.** CT/PET scans, MRIs are helpful in this respect. AD can only **conclusively** be established via post-mortem examination of brain tissue- senile plaques/neurofillibrary tangles. Persons with AD often live for 10-15 years, and often die of other causes (e.g. cancer, congestive heart failure, stroke).

6. **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.

7. **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.

8. **Major symptoms** (vary across persons): impaired judgment, short term memory loss, problems in thinking abstractly, language use, orientation. These symptoms usually interfere with work or social activity, and are progressive, leading to total dependence on others for care. Often accompanied by inappropriate sexual behavior, paranoia, aggression, ADL/IADL deficits, disturbed sleeping, incontinence. withdrawal, mood/personality- 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)

9. **Stages of AD** (AA specifies 7) are probably an oversimplication (persons vary in degree of decline), loss of explicit to implicit associations, first in, last out - but the disease does progress from normal aging to:

    a. memory difficulties (forgetting names, finding the right words, difficulty with everyday tasks (especially those one did well earlier)
    b. memory for details key to one's own life, everyday task difficulties that were not formerly present, personality (moodiness, paranoia, depression, withdrawal, obsessive behavior), disorientation to time/place, changes in sleep, bowel control, wandering, anger/aggression, lessened awareness of such losses, lack of self care/appearance (counting backwards from 100 by 7s, clock test)
    c. Inability to care for oneself/live independently, flat affect, impaired communication, ADLs/IADLS, difficulty in speaking/understanding speech, increased difficulty in walking, sitting, swallowing,vulnerability fo infections/pneumonia

The above symptoms are frequently accompanied by denial, anxiety, depression, often shared by family members unable or unwilling to face a Dx of AD. Persons and families often operate out of fear of dementia (losing one's skills, becoming dependent on others, lessened quality of life. Dr. Kevorkian's first patient was a 48-year-old woman Dx with AD.

10. Early Dx and treatment is key! Thorough Dx by separate clinicians (over time), thorough medical workup, drug history are very important. Olfactory difficulties may be diagnostic

Treatments (versus reversing the structural basis for the disease):

    a. **drug therapy** (e.g. aricept, memantine- singly/in combination), Exelon, Reminyl - inhibit breakdown of neurotransmitter acetylcholine) –new drug has shown some promise in randomized clinical trials (**aducanumab** manufactured by Biogen-higher doses removed amyloid plaques with few side effects vs. loser doses and placebos) (TIME, Nov. 11, 2019)
    b. **cognitive** (spaced retrieval) training, engaged lifestyles (e.g. Nun Study)
    c. **validation therapy, treatment of anxiety, depression**, agitation/wandering (sundowning)
    d. **environmental changes** to provide structure and predictability- dementia care units.
        i. group psychotherapy for mildly impaired persons
    e. **immunotherapy** (NIH study-Columbia-focus on chromosome #14- remove plaque, preventative))
    f. Create a cognitive reserve, exercise, brain training

11. **Prevention**? **Nun Study (Snowden)**, avoiding head injury, diabetes, depression, head injury, not smoking, Mediterranean diet (low fat, high fiber), remaining physically active, not having surgery, getting enough sleep (may allow brain to prevent accumulation of amyloid proteins/"clean up").

12. **Grief**: 3 victims (AD sufferer, family, public)-the long goodbye- we "lose" people with AD gradually

    a. **Anticipatory** (you and that person) - fear of dementia and the losses it entails

    b. **Disenfranchised** (you and that person) - AD as a source of dread/shame

    c. **Loss is ambiguous** - no definitive end or course of the disease

    d. Eventuates in the lack of recognition of self and loved ones

        i. Anger and sorrow in having to provide care (physically present, but mentally absent)

        ii. How can you express this to a loved one and expect to be understood?

        iii. A thankless job, guilt over a desired death and over one's feelings

        iv. Learning to let go of the person this person used to be

        v. Concerns over a loved one's safety, guilt that you are not ill

        vi. You do not have to be the perfect caregiver-master the art of forgiving

        vii. **Persons may live for 10-15 years; they "die" in stages: What will change and when, what are the consequences for you and them?**

        viii. 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

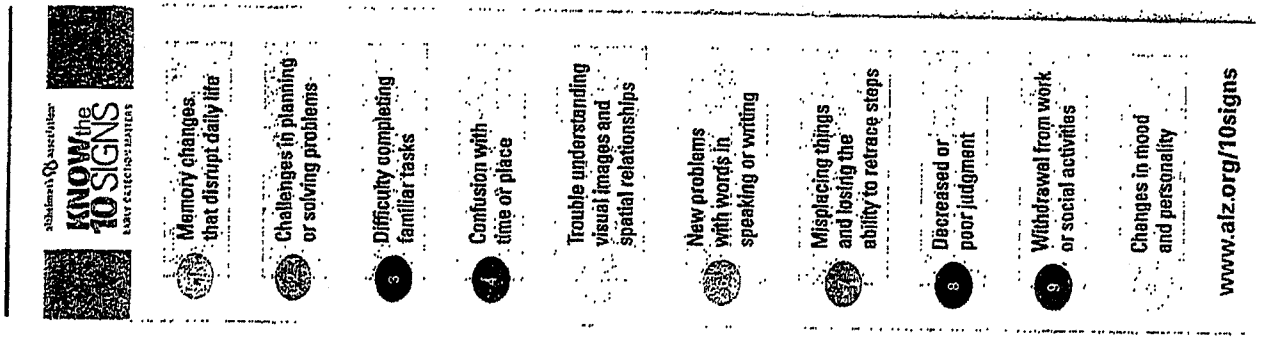
        ix. Caregiver respite- Day Stay; Join a support group- AA sponsored

        x. Keep a journal, seek online support (AD discussion forum)

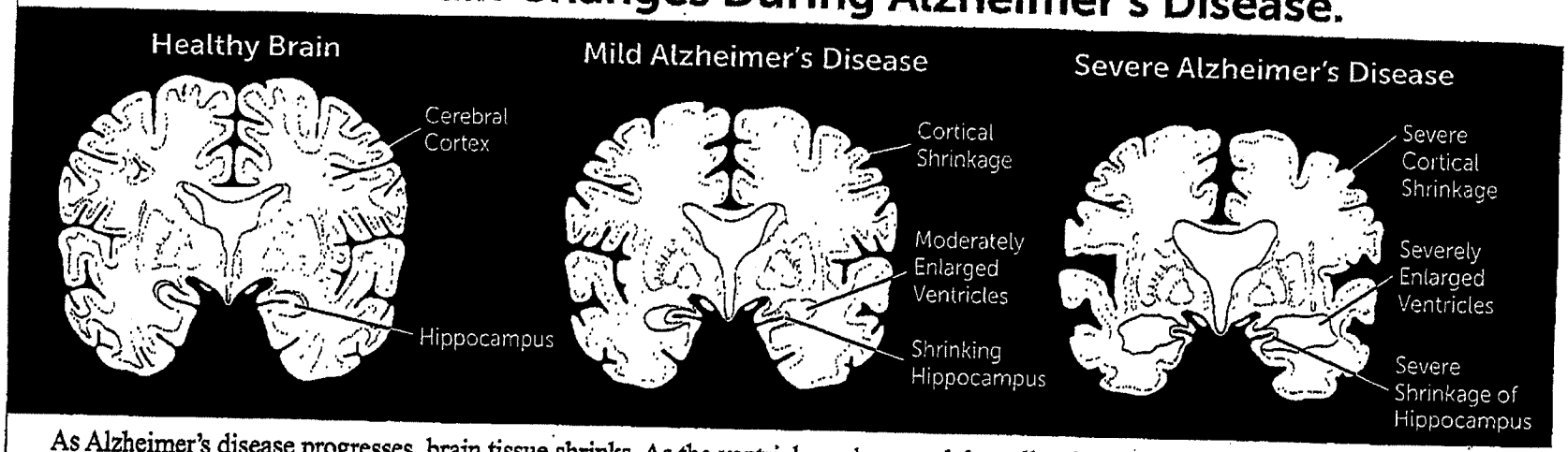
        xi. Seek professional help for isolation from others, self-destructive thoughts, unbridled anger at person or depression

        xii. Self-care is very important- physically, socially, cognitively, spiritually

        xiii. Avoiding isolation/stigma, treating depression, learning new ways of communicating, having ongoing support from others, dealing with legal implications of victim's declining competence (power of attorney), educating oneself regarding available services,



How the Brain Changes During Alzheimer's Disease.



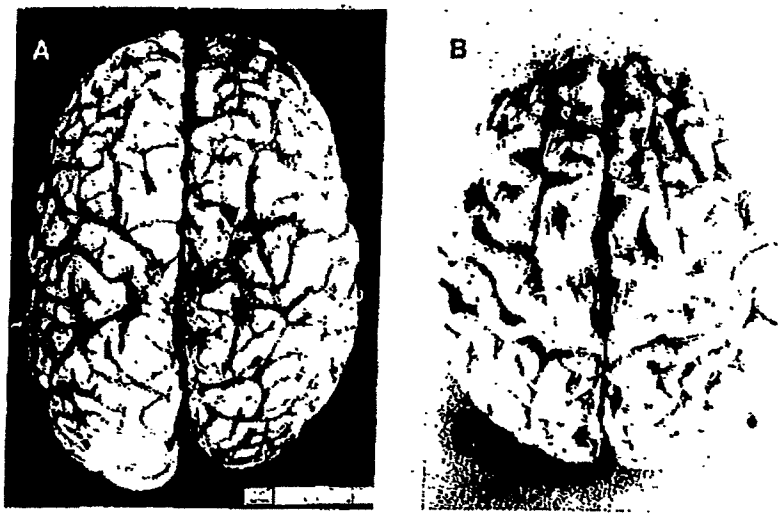
As Alzheimer's disease progresses, brain tissue shrinks. As the ventricles enlarge and the cells of the shrinking hippocampus degenerate, memory declines. When the disease spreads throughout the cerebral cortex, language, judgment, behavior, and bodily functions decline along with memory until death,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

TABLE 10.1

ALZHEIMER'S DISEASE—TYPICAL COURSE AND RANGE OF SYMPTOMS

Age of onset:	45 years of age or older
Premorbid history:	Usually unremarkable for emotional and physical health
Initial symptoms:	Psychiatric: depression, anxiety, agitation, withdrawal, hallucinations, paranoia, jealousy Memory: forgetfulness, i.e., "losing things," forgetting names, commitments; disorientation in new surroundings, i.e., getting "lost" in a store, or while driving
Middle stage symptoms:	Language: difficulty finding words in conversation or in naming objects; loss of verbal and behavioral spontaneity Withdrawal, i.e., no longer wants to go out or be with people (including friends and family) Purposeless overactivity, i.e., cleaning and re-cleaning the house Inability to handle professional and financial responsibilities Poor judgment and insight Social indiscretions; i.e., making loud demands in a restaurant or store, inappropriate verbalizations in public Lack of concern for the future
Late stage symptoms:	Decreased language skills; significant word finding problems; poor verbal comprehension; decreased reading, writing, and math skills Difficulty performing simple gestures Inability to use common objects such as stove, washing machine Gross disorientation in time and place, i.e., may become lost easily even in own home
Very advanced symptoms:	Total dependency on caretaker for simple tasks, i.e., dressing, eating, toilet functions Inability to comprehend or communicate with people No awareness of past or future
Death usually occurs 5–10 years after diagnosis of disease	

Source: Ware & Carper (1982).



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.