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A REVIEW ON ALZHEIMER'S DISEASE

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ABSTRACT

Alzheimer's disease is a growing concern amongst clinicians and researchers, particularly because of the increase in referrals to hospitals and clinics. Longevity brings with it an increase in people with both organic and psychogenic disorders. The link between Down's syndrome and Alzheimer's disease helps our understanding of the disease but also presents us with complexity in terms of assessment and service provision. Our understanding of the aetiology Alzheimer's disease has advanced; in is timely to consider how clinical assessment may also be improved.

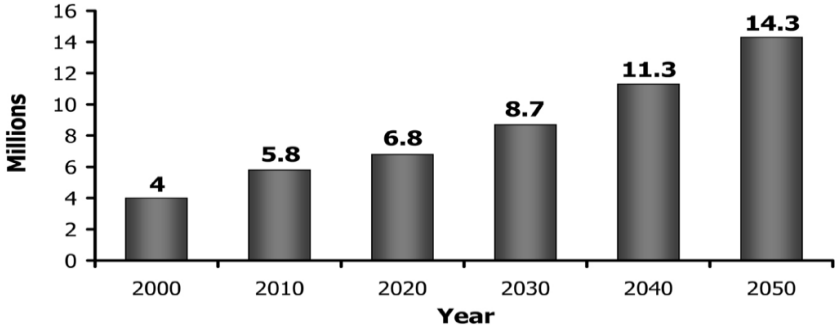
KEY WORDS

Down's syndrome, Alzheimer's disease

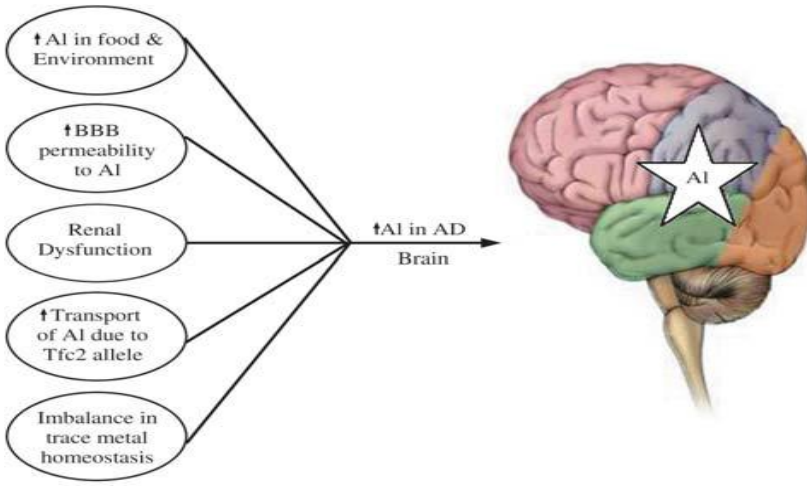
INTRODUCTION

PREVALENCE OF AD

A number of factors, many of them related to differential diagnosis and lack of consensus regarding the pathophysiologic correlates of AD, make determining the prevalence of AD difficult. Although AD is the most prevalent cause of progressive cognitive impairment in the elderly, there are other potential causes of demented behavior that can be mistaken for AD in the clinic. These include, but are not limited to, vascular dementia, Lewy body dementia, Parkinson's disease, Creutzfeldt-Jakob disease, frontal lobe dementia, and progressive supranuclear palsy. In addition, delirium and depression can produce symptoms and signs resembling those of AD



Increasing longevity, especially of people with a learning disability, has brought with it a seemingly ever-increasing demand on health and social services which in turn has seen an increase in research activity (e.g. Thompson, 2000). In particular, clinical psychology services in the United Kingdom (UK) have seen an increasing number of referrals for assessing older clients who have poor cognitive functioning, particularly Alzheimer's disease, and for providing advice for cares about clients who have declining memory ability (Thompson, 1993a). Supportive consultation with staff and clients alike is important and has increased the demands on all services as the size of the older population has grown.



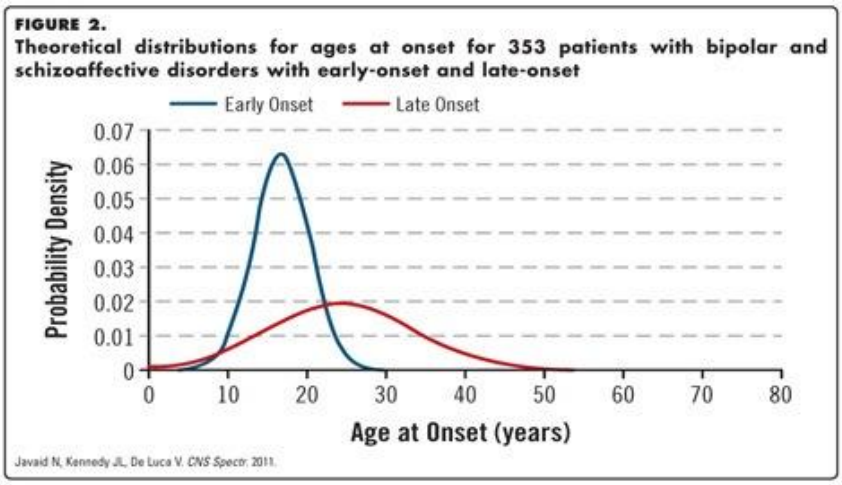
Types of Alzheimer's

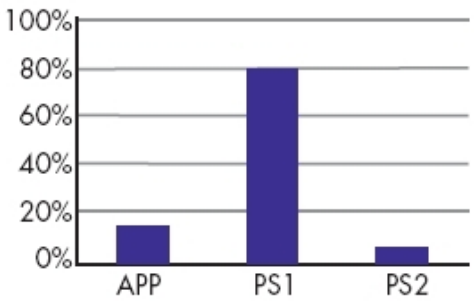
Growing up in the 60's the word "Alzheimer's" didn't exist. Older people were just considered "senile" while younger people were listed as "crazy." Sometimes "it-just-runs-in-that-family" was the entire explanation for someone who suddenly seemed to lose his or her faculties. Today, we know that Alzheimer's disease is real and it isn't a joke. Instead of consigning patients to an institution, more treatments are becoming available as research progresses. There are three known types of Alzheimer's disease to date, and each has its own set of symptoms and treatments. This list is to give a general overview of each type, and is not a medical diagnostic tool or suggestive of any specific treatment. If you or someone you know has or might have this condition, a doctor's diagnosis is necessary.

Early Onset of Alzheimer's disease

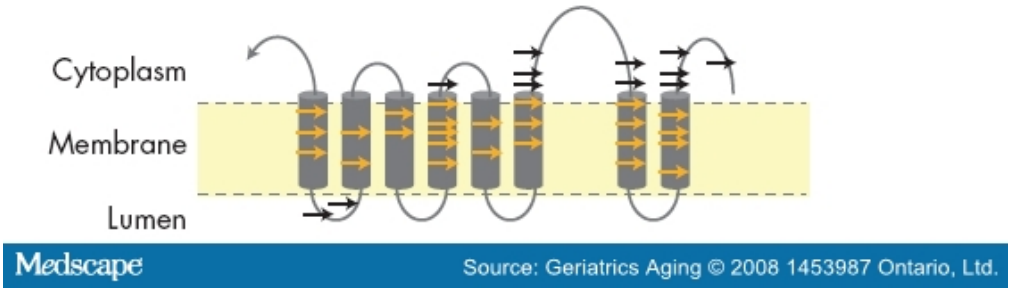
This rare form affects people under 65 years of age. The symptoms appear in the 40-50 age groups. This accounts for less than 10% of all Alzheimer's patients. People with Down's syndrome, who experience premature aging, seem more prone to develop the disease.

So far, research has found abnormalities with chromosome 14 in early onset patients. Late onset patients don't possess the abnormality.

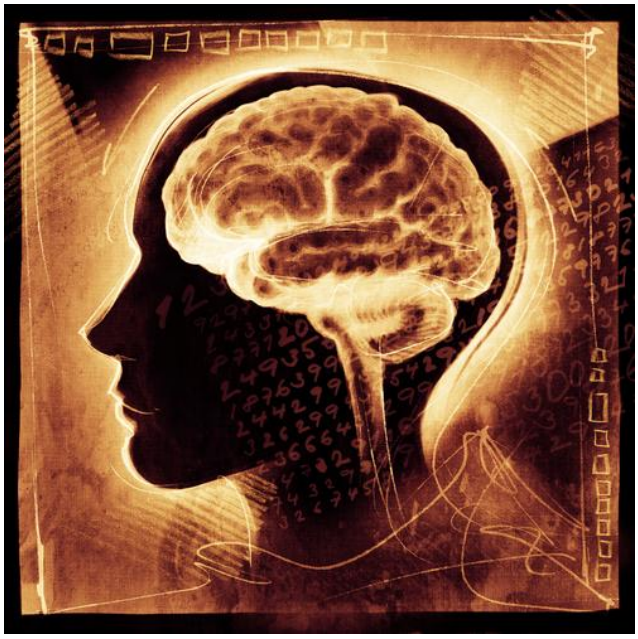




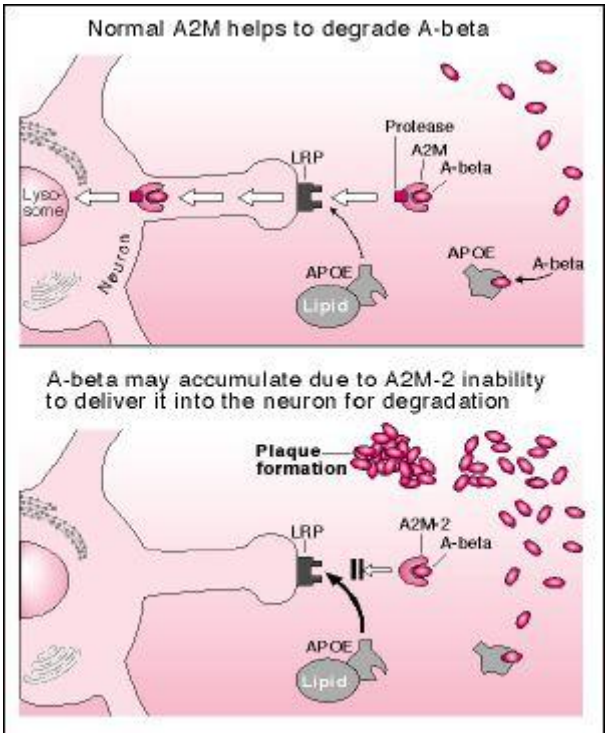
Gene	# Mutations	# Families
APP	30	80
PS1	168	370
PS2	10	18
Total	208	468



Late Onset Alzheimer's disease: This form appears in people 65 and over, making roughly 90% of cases. It strikes roughly half of all people over 85 years of age. So far, heredity hasn't been proven to be a factor.

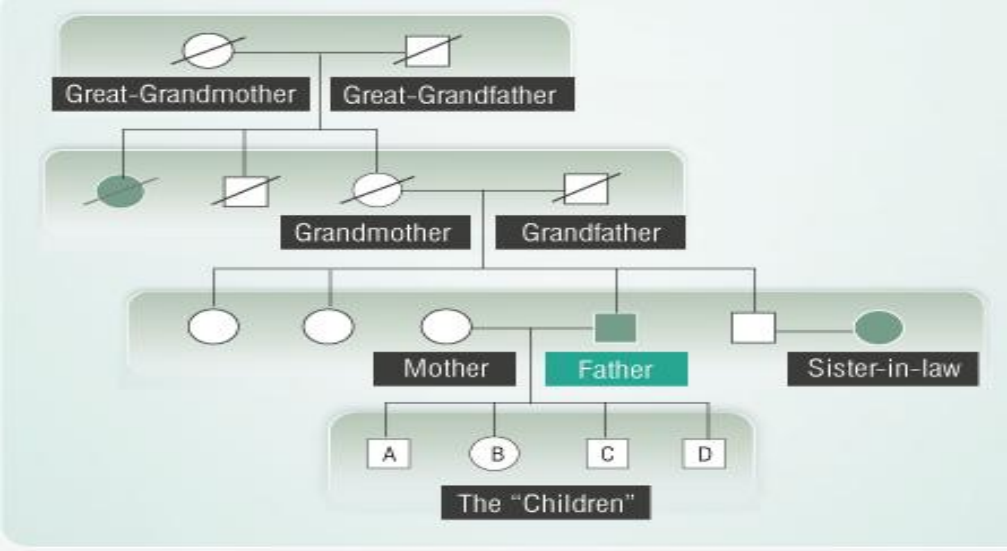


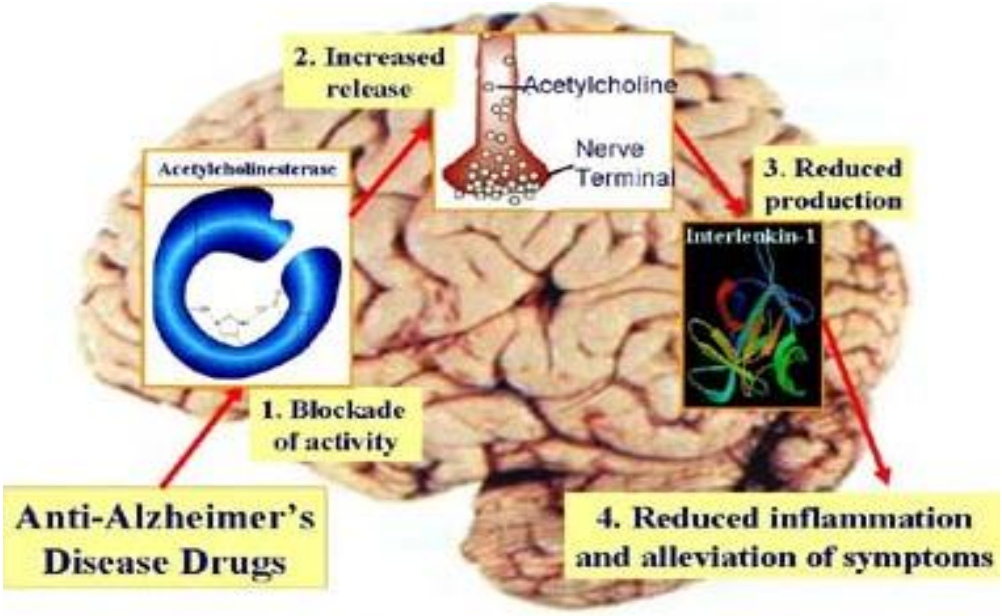
Late-Onset Alzheimer's Gene Suggests Interplay of Genes Determines Timing and Risk of Disease



Familial Alzheimer's disease

This group makes up less than 1% of cases, and is clearly evidenced by multiple patients over 2 or more generations being diagnosed with the disease. The onset seems to show up in the patient's 40's.





SYMPTOMS

These symptoms are common to all forms of Alzheimer's disease. Each symptom alone isn't a true diagnostic tool.

Language: Tripping over one's tongue isn't that big a deal for most people, unless you're the President of the United States with 200 reporters present. Forgetting a name for an object is also common with menopause.

Odd Behavior: Okay, this could apply to all of us. Leaving a cell phone in the refrigerator while getting orange juice, trying to get three kids to the bus, answering the question of where someone's shoes are and trying to get ready for work yourself isn't out of the ordinary.

Personality and mood changes: Stress, menopause, and other life experiences can make us all moody. Sudden outbursts of anger for no reason and changing back just as suddenly is a reason to take notice.

Personal hygiene: This is something that families and friends need to take note of. A fastidious person, who suddenly stops bathing, wears stained or dirty clothing or just seems to stop caring for themselves needs to be addressed quickly.

Memory loss: Just because hubby forgot to bring home milk when you called him 30 minutes ago isn't a reason to suspect Alzheimer's. If, after spending the day with the kids, he suddenly can't seem to remember any details at all and it seems to be happening with increasing frequency, it's time to call a doctor. Not recognizing family members or confusing a family member with someone from the past is also a red flag.

Repeating things: As a child, I heard the stories that always seemed to start "...when I was your age..." However, someone with Alzheimer's may repeat the same story two or three times in an hour while forgetting they've just done so. This should be taken as a red flag. Disorientation and "confusion": Someone with Alzheimer's can become lost in a neighborhood they've known for years, or even in their own home. The simplest task, say for example, making a bed may have the patient asking how it's done or becoming frustrated at not being able to do it alone. While there currently is no cure, treatments are available and research is ongoing to halt or even prevent this fatal disease. A licensed doctor who specializes in Alzheimer's disease should be consulted regarding specific treatment for any patient. For more information, help can be found in your phone book under listings for helpful numbers or call The Alzheimer's Association at 800-272-3900.

Alzheimer Disease pathology

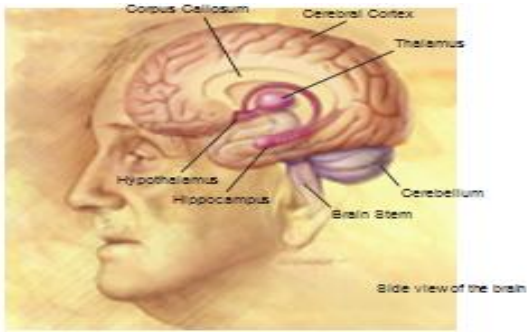
Changes in brain structure

1) Alzheimer's disease pathology can be characterized on a macro level as the progressive loss of brain tissue. As the disease

progresses neurons die in a particular pattern over time. One of the earliest sign of AD is memory loss, particularly short term recall. The brain area involved in memory include the cortex, especially the hippocampus.

2) Pre clinical AD hippocampus the structure responsible for memory formation(short and long term memory) to the cerebral cortex, several studies such as once including magnetic resonance imaging suggest that neuronal loss(measured by atrophy in select regions) may start years before sign of memory loss emerge.

Major Areas of the Brain



As the brain atrophies, cerebrospinal fluid fills in the space previously occupied by brain tissue. In mild to moderate AD, patient experience more prominent memory loss (ex. difficulty recalling well known names and confusion about familiar places), A decline in the ability to process complex thoughts (ex. Difficulty with balancing the check book or preparing a meal), and mood and personality changes.

In the brain, atrophy extends to other areas of the cerebral cortex. At the later stages of AD progression, the cortex has atrophied in areas that control speech, reasoning sensor processing, and conscious thought.

As expected with this degree of brain atrophy, the symptoms of severe AD increasing severity (impaired long term memory, weight loss, and inability to sit up).

Degenerative process in AD

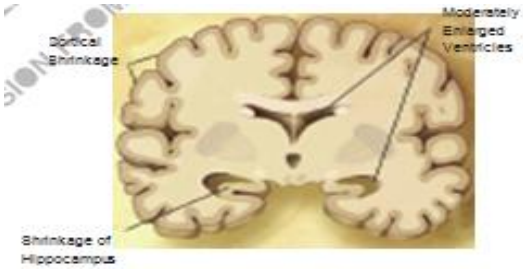
On a micro level AD is characterized by 3 neuropathologic hallmarks extra cellular plaques of β-Amyloid protein (Amyloid plaques), intracellular neurofibrillary tangles (NFTS), and neuronal degeneration.

Plaques and NFTS were 1st discovered by Alois Alzheimer in a 1906 autopsy of a demented patient.

Although they are a defining component of AD, they are not unique to AD. Plaques and NFTS occur with normal aging and in some other neuro regenerative disorders. In AD, Plaques and NFTS are localized to areas in the brain that correspond to clinical symptoms.

Brain Changes in Preclinical Alzheimer's Disease

Brain Changes in Mild to Moderate Alzheimer's Disease



Brain Changes in Severe Alzheimer's Disease

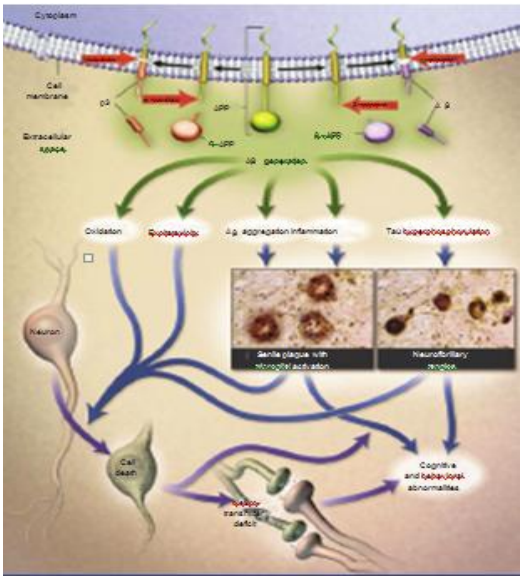
β- Amyloid hypothesis

β- Amyliod plaques are clumps of insoluble peptides that results from the abnormal cleavage of amyliod precursor protein (APP), the exact function of which is

unknown. APP is normally cleaved by 3 enzymes β-secretase, γ-secretase, and α-secretase, cleavage by β-secretase, followed by γ-secretase, yield a soluble 40 Amino acid peptide.

In AD, A variant from of the γ-secretase cleaves APP at an incorrect place, creating 42 Amino acid peptid called A β42 or AB, which is not soluble and aggregates. **α**-secretase actually serves a protective function as it cleaves APP at a site that prevents Aβ formation.

Diagram of the Amyloidal Cascade



Treatment for Alzheimer's

As there is no cure, Alzheimer's treatment is only successful in slowing down the process and by managing some of its symptoms. Medication may be prescribed to help with agitation, hallucinations, anxiety, and depression. Some of the common medications used for treatment are: Amide, Cognac, Aricept, Exelon and Razadyne. These medications can have many side effects such as muscle weakness, upset stomach, loss of appetite, weight loss, or drowsiness. There are many studies currently be conducted vigorously to come up with more Alzheimer's treatment options.

Aging is the biggest risk factor for acquiring Alzheimer's disease. At the age of 65, ten percent of the population will acquire the disease, while those over the age of 85 stand a 50% chance.

DIAGNOSIS OF ALZHEIMER'S

Diagnostic Screens and Tests

The possible evaluations for AD range from asking the subject to draw a clock, to an hours-long battery of neuropsychological tests, to the latest techniques in neuro imaging, but, more often than not, an early diagnosis is made via astute questioning of patient and family members combined with the results of rapid, office-based tests, a sampling of which is provided below.

The Folstein Mini-Mental State Examination (MMSE)

Is the most commonly used test to assess serial cognitive changes in AD. On average, MMSE scores change at a rate of about 4 points per year in patients with AD. Although the MMSE is a useful tool for detecting mild to severe AD, it has been criticized for lack of sensitivity in detecting mild dementia in the absence of reports from a family informant. Even a perfect MMSE score does not exclude MCI or mild AD. Age and education affect performance on the MMSE. Age- and education-adjusted norms have recently been published.

The Clock Drawing Test

Is a rapid test for office based practice? Although some contest its utility as a screen for very mild dementia, it does offer some degree of validity across different cultural backgrounds.

Scores are based on the ability to draw the face of a clock with the hands pointing to the appropriate numbers of a designated time.

The Blessed Information Memory Concentration Test

Is also useful and widely used, but it has been criticized for failing to sample a number of cognitive functions (e.g., language and visuospatial abilities).

DISCUSSION

Alzheimer's disease is unique in that it may be the only late-life disease that has a long "silent" prodromal phase, no validated biological test for diagnosis, and imprecise measures of correlation between progression of phenotype and progression of pathology. Diagnosis during life is based on the clinical phenotype of symptom progression, which is heterogeneous between individuals. Part of the variation in clinical presentation may be due to the presence of other types of neuropath logical changes

in the brain in addition to those typically considered to be AD-related. These characteristics make it difficult not only to accurately diagnose AD but also to identify risk or protective factors for the disease; they also make it challenging to implement interventions efficiently and economically to incorporate or exclude these factors would have relatively less risk (cost) to individuals. Age may also be a central issue in regard to the timing of the exposure. There may be a window of time during which exposures influence risk of Alzheimer's for example, obesity in mid-life may be associated with increased risk of AD, while obesity in late life may be associated with reduced risk of disease. The latter finding may be explained by the weight loss often associated with the disease itself. But the point is clear that different exposures may have effects at different times along the life course or the natural history of AD. Ideally the exposure should be measured in different age groups within the same study to control for inter-study variability in measurement, but this may not be realistic given the long period of follow up necessary when studying exposures in mid-life. Interventions may also have different effects at different points throughout life or the AD process. Although one might assume that interventions or lifestyle modification should be undertaken as early as possible, there may be other windows during which a given intervention may exert its effect. Careful consideration of the complex relation of exposure, age, and disease will likely be key to understanding the factors that alter risk of AD and cognitive decline.

CONCLUSION

The many benefits to the patient, caregiver, and society are the motivating factors for establishing a diagnosis of AD as early in the course of the disease as possible. This goal can be obtained by watching for prodromal AD or MCI, which may occur before clinical AD. Early diagnosis can be facilitated by using validated office-based tests and by paying close attention to reports from family members. Once the diagnosis is made, it is critically important to educate patients and caregivers regarding the reality of the disease and the limitations of available treatments. Nothing will alter the ultimate outcome of AD, but it is nonetheless a treatable disorder in pharmacological and non pharmacological realms. To reinforce this and other key messages, it is imperative to refer family caregivers to the Alzheimer's Association or other local care giving advocacy groups. AChEIs prolong the retention of mental function, and probably quality of life, for patients and caregivers alike.

REFERENCES

1. Weisberg B, Jived A, and Know sky S, Auer SR: Alzheimer's Disease; in Caret sky HR cither EF III, Eisenberg MG (Ends): Medical Aspects of Disability, 3. Network Springer, 2005, pp 79–118.
2. Kit wood T: Dementia Reconsidered: The Person Comes First. Milton Keynes Open University Press, 1997.
3. France EH, Soured LE, Auer SR, Aram I, Know sky S: Evidence and mechanisms of retro genesis in Alzheimer's and other dementias: management and treatment import. Am J Alzheimer's Disusing Other Demon 2002; 17: 202–212.
4. Ferry CP, Prince M, Braine C, Broadly H, Fratiglioni L,Ganglyi M, Hall K, HasegawaK, Hendrie H, Huang Y, Jorm A, Mather C, Menezes PR, Rimmer E, Scazufca M, for Alzheimer's Disease International: Global prevalence of dementia: a Delphi consensus study. Lancet 2005; 366: 2112–2117.
5. Wimo A, Winblad B, Jönsson L: An estimate of the total worldwide societal costs of dementiain 2005. Alzheimer Dementia 2007; 3:81–91.
6. Hendrie HC. Epidemiology of dementia and AD. Am J Geriatr Psychiatry 1998; 6:S3–S18.
7. Shah Y, Tangalos EG, Peterson RC. Mild cognitive impairment: When is it a precursor to AD? Geriatrics 2000; 55:62–68.
8. About Alzheimer's. Available at: www.alz.org/AboutAD/overview.htm Accessed January 29, 2003.
9. Evans DA, Scherr PA, Cook NR et al. Estimated prevalence of AD in the United States. Milbank Q 1990; 68:267–289.
10. Marin DB, Sewell MC, Schlechter AAD. Accurate and early diagnosis in theprimary care setting. Geriatrics 2000; 57:36–40.
11. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th Ed., Text Revision. Washington, DC: American Psychiatric Association, 2000.

12. Lockwood KA, Alexopoulos GS, van Gorp WG. Executive dysfunction in geriatric depression. Am J Psychiatry 2002; 159:1119–1126.
13. Alexopoulos GS, Meyers B, Young RC et al. The course of geriatric depression with 'reversible dementia': A controlled study. Am J Psychiatry 1993; 150:1693–1699.
14. Honig LS, Mayeux R. Natural history of AD. Aging Clin Exp Res; 2001; 13: 171–182.
15. Polvikoski T, Sulkava R, Myllykangas L et al. Prevelance of Alzheimer's disease in very old people: A prospective neuropathological study. Neurology, 2001; 56:1690–1696.

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