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DEMENTIA: A REVIEW

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Abstract:-

Dementia is any decline in cognition that is significant enough to interfere with independent, daily functioning. The aim of this review is to summarize the current findings in the field and address the important contributions of cerebrovascular, physiologic, and cellular alterations to cognitive impairment in these human dementias. Dementia is best characterized as a syndrome rather than as one particular disease. The causes of dementia constitute two broad categories of disease: those that are"neurodegenerative"(originally called "irreversible")and non-neurodegenerative (potentially "reversible"). Lastly. The treatment modalities of these dementias and their management is discussed.

Keywords: *Dementia; Clinical Care; Cognitive Impairment; Alzheimer's Disease*

INTRODUCTION

Dementia is any disorder where significant decline from one's previous level of cognition causes interference in occupational, domestic, or social functioning. Generally, dementia should be considered to be an acquired *syndrome*, with multiple possible causes, rather than a specific *disease* itself. For example, the dementia *syndrome* of progressive decline in language can be caused by various *diseases*, such as Alzheimer disease, a tumor in the language cortex, or frontotemporal lobar degeneration.

Global estimates of dementia prevalence are up to 7% of individuals above the age of 65, with a slightly higher prevalence (8-10%) in developed countries due to longer life spans. [1] Advancing age, genetic profile, and systemic vascular disease are major risk factors for developing dementia. [2]

REVIEW

The Two Broad Categories

A classic way to conceptualize dementia is to consider two broad categories of disease: those that are "neurodegenerative" (originally called "irreversible") and non-neurodegenerative (potentially "reversible"). This dichotomy is a helpful heuristic but is limited by simplicity. For example, patients with dementia can, and often do, have multiple diseases which can be neurodegenerative (e.g., dementia with Lewy bodies) and non-neurodegenerative (e.g., cerebrovascular disease), which cumulatively account for the impairment. [3] Diseases can also impair cognition without leading to a decline in daily functioning, either at diagnosis or subsequently. Mild neurocognitive disorder (from DSM-V) and Mild Cognitive Impairment are used variously to characterize these states. [4-5]

The Neuropathology & Cerebrovascular Mechanisms of Dementia

The prevalence of dementia is increasing in our aging population at an alarming rate. Because of the heterogeneity of clinical presentation and complexity of disease neuropathology, dementia classifications remain controversial. Recently, the National Plan to address Alzheimer's Disease prioritized Alzheimer's disease-related dementias to include: Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, vascular dementia, and mixed dementias. While each of these dementing conditions has their unique pathologic signature, one common etiology shared among all these conditions is cerebrovascular dysfunction at some point during the disease process. [6]

Cerebrovascular changes are common neuropathologic findings in aged subjects with dementia. [7] Vascular remodeling and pathologic changes to the macro- and microvasculature may disrupt blood vessel integrity. Notably, such remodeling leads to vascular disease and cerebral hypoperfusion associated with neuronal injury, structural and functional brain damage. [8] More specifically, neuroimaging findings indicate white matter hyperintensities, cerebrovascular lesions, and cerebral amyloid angiopathy (CAA). [9] Other ultrastructural abnormalities to the microvasculature associated with small-vessel disease, and exacerbated by aging, include capillary wall deterioration and the accumulation of erythrocytes, [10] basement membrane thickening, and pericyte degeneration, [11] resulting in blood–brain barrier (BBB) permeability [12] and vascular cognitive impairment (VCI). Vascular cognitive impairment is a broad term that encompasses cognitive deficits associated with vascular disease, ranging from mild-to-severe cognitive impairment including VaD. [13] A new and all-inclusive term was recently coined referred to as VCID (vascular contributions to cognitive impairment and dementia).

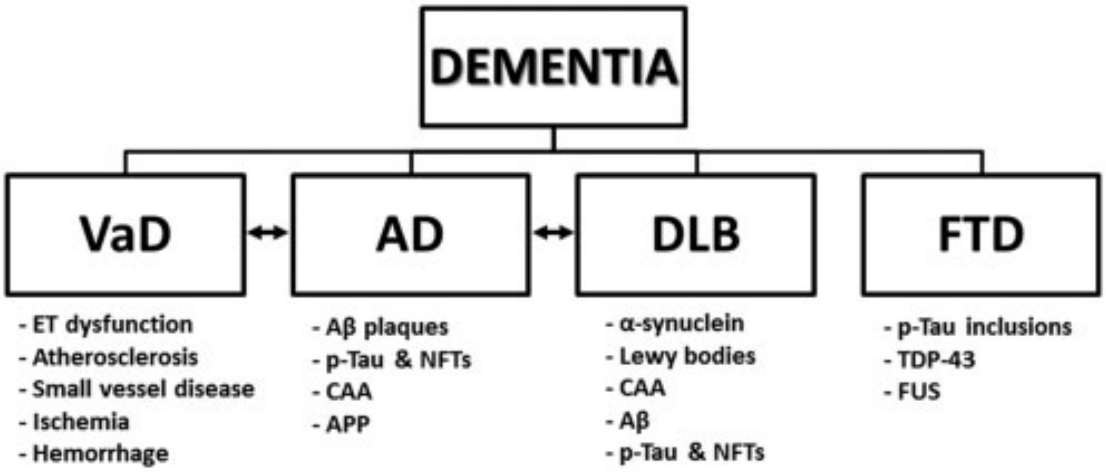

Fig. 1 Classifications of dementia subtypes & associated neuropathologic features. A hierarchy listing the four major categories of dementia

The Treatment of Dementia

Treatment of dementias represents an important but relatively neglected part of neurological care of the elderly population. Individual therapeutic interventions may make only small changes to the quality of life of individuals afflicted with dementia, but when used in combination these interventions synergize and can make a significant difference. Additionally, given the societal scale of the problem of dementia care, the overall impact, in economic and sociological terms, of such therapies is of consequence. Presently there are no disease-modifying treatments for any of the neurodegenerative dementias. Instead, the clinician has several therapeutic tools to mitigate cognitive and behavioral consequences of dementias. There are also strategies to minimize harm to patients with dementia. [14-16]

A Framework for Classifications of Treatments of DEMENTIA

Before going on to the types of interventions presently recommended for dementias and the evidence for their efficacy, it may be helpful to sketch out a theoretical framework, which we may use to place the various approaches into context. [17] For the purposes of this paper, we classify therapeutic interventions in dementias (both current and future therapies) in the following way:

• **Disease-modifying interventions:** These may:

A. Retard the progression of disease. Rationale: slowing the chronic decline due to disease will maintain function for a longer period of time.
B. Stop progression of disease—this would constitute a cure.
C. Reverse damage already done to the brain.

Interventions may be:

Pharmacological interventions—via varied mechanisms such as:

A. Reducing the rate of production of amyloid or tau.
B. Increasing clearance of amyloid or tau.
C. Reducing toxicity of amyloid or tau.
D. Reducing neuroinflammation.
E. Reducing neurodegeneration via another mechanism.

Nonpharmacological interventions—these are multimodal lifestyle interventions which may prevent or reduce the rate of progression in the early course of the disease.

• **Symptom modification:**

A. Pharmacological amelioration of cognitive symptoms such as deficits in memory, concentration, speed of mentation, and others.
B. Pharmacological management of neuropsychiatric symptoms (anxiety, depression, apathy, and agitation).
C. Nonpharmacological interventions to ameliorate cognitive and neuropsychiatric symptoms.

• **Harm minimization:** A dementia patient is vulnerable to deliberate and accidental harm. One goal of treatment is to protect the patients against potential harms. For example, by:

A. Modifying the living environment to best suit the diminished capacities of the individual.
B. Guarding against abuse, including exploitation, isolation, loneliness, and violence.
C. Restricting patient activities which may harm the individual. The best example of this is driving. [18]

CONCLUSION

Cognitive impairment and dementia continue to be major contributors to the global burden of disease. In this brief review, we highlight selected dementia syndromes from among dozens of different diseases. Efforts to preserve daily functioning abilities and quality of life should be the driving aim of dementia management across the lifespan. Dementias are chronic diseases that require longitudinal care, ongoing counseling, and psychosocial support for patients and families by dedicated

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