



# Alzheimer's & Other Dementias

Progress in understanding dementia will take us from translation to transformation.

By Jeffrey Cummings, MD, ScD



There has been enormous progress in understanding Alzheimer's disease (AD). Once considered a late-life dementia, AD is now recognized as beginning with amyloid accumulation in the brain, years before symptom onset. Progressing from no cognitive impairment, to mild cognitive impairment/prodromal AD, to dementia over 15 to 20 years, AD dementia is now identified as the severe end of a continuum that begins in midlife. This is a radical reconceptualization creating opportunities for early recognition, risk reduction, clinical trials, and (eventually) approved therapies to defer onset or slow progression of cognitive impairment. In this issue, Dr. Scharre presents this evolving concept of the AD spectrum.

Neuropsychologic testing creates profiles unique to specific dementias and their variants, making neuropsychologic assessment of great value clinically. Drs. Medina and Banks describe the use of neuropsychologic assessment in practice.

Biomarkers provide insight into the earliest symptomatic and presymptomatic phases of AD, and brain imaging is among the most powerful approaches available. Drs. Ayers, Svaldi, and Apostolova present a comprehensive overview of brain imaging for differential diagnosis of dementias. Measures of biomarkers amyloid (A), tau (T), and neurodegeneration (N) have been codified into the ATN Research Framework for AD Diagnosis. Drs. Gauthier and Rosa-Neto comment on strengths of this approach and elements of AD pathology that may be added as knowledge evolves. New biologic tools such as amyloid imaging and genetic testing provide compelling information but must be interpreted with care. Early diagnosis cannot be allowed to produce an early surrender of hope. Dr. Grill discusses the complexities and provides practical guidance for revealing biomarker information.

Neuropsychiatric symptoms are among the most disabling features of AD, decreasing quality of life and increasing the likelihood of residential care. Characterization of and therapy for behavior changes are progressing; new therapies are likely to come soon. Drs. Ismail and Goodarzi describe an approach to diagnosing and treating behavioral symptoms of dementias.

Sleep changes are common in AD and rapid-eye-movement (REM) sleep behavior disorder is a diagnostic feature of dementia with Lewy bodies (DLB). Sleep changes affect cognition, function, and behavior and adversely affect caregivers.

Dr. Pao provides a practical overview of sleep disorders in dementias, their role in diagnosis, and management strategies.

Improved recognition of AD brings better recognition of nonAD dementias, including FTD and DLB. Greater diagnostic accuracy improves management and outcomes and facilitates clinical trials for these less common disorders. Dr. Galvin describes diagnosis and management of DLB, and Drs. Taylor and Finger discuss the subtypes of FTD.

Reducing risk for late-life cognitive decline is a critically important public health goal. Lifestyle choices can decrease AD risk, and more people are concerned about ensuring that lifespan is matched by brainspan. Diet and nutrition, physical and mental fitness, connectedness and sense of purpose, good sleep, stress reduction, and control of vascular risk factors can reduce AD risk. Drs. Saif, Sadek, Bellara, Hristov, and Isaacson describe a brain health program that should be initiated early and maintained throughout life.

Pharmacologic interventions and clinical trials are making marked headway in concert with biomarker reporters on drug effects. Monoclonal antibodies and small molecules with promise for disease modification, cognition enhancement, or reduction of behavior symptoms are in clinical trials. Failures in AD drug development are common, and there have been many disappointments as agents with early-stage promise have not shown superiority over placebo in later stages. Every trial, however, is a learning experience and the field is moving forward. Drs. Cummings and Zhong describe current clinical trials and emerging therapeutics.

These dramatic scientific advances have meaning to the extent that they are integrated into the care of patients. This special issue of *Practical Neurology* is devoted to this translation-to-transformation momentum as we use better science to inform better care. ■

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