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About This Supplement

The American Osteopathic Association is partnering with the Alzheimer's Association in a campaign to increase physician and public awareness of the warning signs of Alzheimer disease, the importance of early detection and diagnosis of this disease, and the value of participating in clinical trials.

As part of that partnership, this supplement is being supported by an independent educational grant from the Alzheimer's Association.

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Editors' Message

Alzheimer Disease: The Crisis Is Upon Us

James W. Simpkins, PhD
Brian E. Wood, DO
Brian J. Balin, PhD

This supplement on Alzheimer disease is a collaboration between JAOA—*The Journal of the American Osteopathic Association* and the Alzheimer's Association, the largest private organization devoted to elimination of Alzheimer disease, care for patients with Alzheimer disease, and educational services for caregivers. Alzheimer disease is a condition that robs individuals of their minds, places excessive burdens on caregivers, and threatens the vitality of the US healthcare system. This JAOA supplement is timely because the Alzheimer disease crisis is upon us. This crisis was also highlighted on September 21, 2010—"World Alzheimer's Day," when the Alzheimer's Association and other organizations sought to raise public awareness about Alzheimer disease and its impact on families and communities around the world.¹

To effectively respond to the Alzheimer disease crisis, osteopathic physicians need to be knowledgeable about the basic pathologic mechanisms, diagnostic methods, and treatment options for this disease. Osteopathic physicians should also be familiar with subject recruitment into clinical intervention trials and other studies about Alzheimer disease. Most individuals with Alzheimer disease are seen initially by primary care physicians. In most of these cases, rapid referral of a patient to a specialist for definitive diagnosis is needed to begin treatment with currently available medications, as well as for potential recruitment into clinical trials designed to investigate new disease-modifying medications. Despite the need for specialists, primary care physicians continue to play crucial roles in the care of patients with Alzheimer disease.

As highlighted by recently released figures from the Alzheimer's Association,^{2,3} Alzheimer disease poses an enormous public health problem and an incredible burden on families of patients in terms of care, lost wages, and caregiver distress. This burden is expected to expand exponentially in our lifetimes and those of our children. More than 5 million people in the United States have Alzheimer disease, making this condition the most common form of age-related dementia.^{2,3}

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The number of people in the United States with Alzheimer disease is projected to reach 7.7 million by 2030.^{2,3} Alzheimer disease is the fifth leading cause of death for individuals older than 65 years.^{2,3} Yet, the majority of people in the US elderly population lack access to specialty clinics at large medical centers. Because of this lack of access, Alzheimer disease may go undiagnosed in these people, or their diagnosis may be delayed, resulting in less effective treatment.

Supplement Articles

To address the Alzheimer disease crisis, we need additional research into the basic science behind this devastating neurodegenerative disease—research that will allow us to discover and develop disease-modifying medications for treatment and prevention by better targeting the cause of the disease. This need is highlighted in the present supplement by Xiaoning Bi, PhD, who presents evidence supporting the current focus on drugs that modify the processing of amyloid precursor protein, particularly through the endocytic, autophagic, and lysosomal pathways, which are affected by known Alzheimer disease mutations.

As noted by Robert C. Barber, PhD, crucial to the treatment of patients with Alzheimer disease are biomarkers that can be readily sampled and inexpensively assayed (eg, from patients' blood or urine)—without requiring specialty clinics for sample ascertainment or quantification. Results of such assays could be used to predict disease risk or rate of progression of Alzheimer disease and to differentiate Alzheimer disease from other neurologic conditions. As discussed by Dr Barber, several research groups are making meaningful progress in the development of cerebrospinal fluid biomarkers and blood biomarkers for Alzheimer disease.

Current Alzheimer disease therapies available to healthcare providers are reviewed by Gerald G. Osborn, DO, MPhil, and Amanda Vaughn Saunders, OMS III. Their article covers the use of US Food and Drug Administration–approved medications for relief of cognitive decline and neuropsychiatric symptoms associated with Alzheimer disease, including aggression, agitation, depression, and psychosis. The authors also discuss controversial “off-label” uses of drugs that have been approved for

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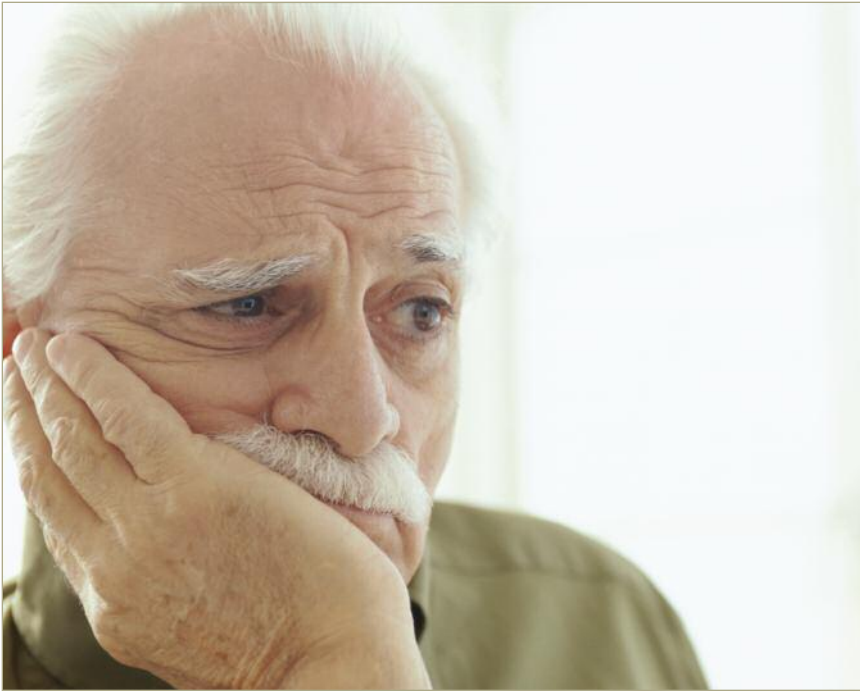
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other indications.

New investigative drugs in clinical trials for Alzheimer disease are described by Pamela E. Potter, PhD. Her review addresses current efforts in the development of improved cholinergic agonists, of drugs that decrease β -amyloid levels, and of drugs that decrease tau phosphorylation. Dr Potter also addresses anti-inflammatory drugs, drugs that increase nitric oxide and cyclic guanosine monophosphate levels, and drugs that decrease neuronal death or promote neuronal regeneration. Although results of clinical trials on such medications have been disappointing to date, the introduction of useful biomarkers and the enrollment of subjects who are in the earliest stages of Alzheimer disease or who have mild cognitive impairment may be helpful in research efforts.

Much more effort is needed to better train healthcare providers—including osteopathic physicians and osteopathic medical students, residents, and fellows—regarding the unique needs of patients with Alzheimer disease and their families. The latest in current and emerging treatments for these patients is described by Katherine E. Galluzzi, DO; Denah Appelt, PhD; and Brian Balin, PhD, who review evidence for multiple stages of disease progression from mild

cognitive impairment through Alzheimer disease. These authors explain the need for screening tests that are both sensitive to staging of Alzheimer disease and useful in primary care practices. They also describe the association between depression and Alzheimer disease.

Finally, Janice A. Knebl, DO, and Deepti Patki, MS, address an issue of vital importance to advancing our knowledge of potential treatments—the recruitment of subjects into clinical trials of medications for Alzheimer disease. The authors discuss the many barriers to participation in clinical drug trials in general as well as the particular challenges of recruitment of patients with Alzheimer disease into trials. Interestingly, Dr Knebl and Mr Patki clearly describe the need for consent and participation of caregivers, as well as of the patients themselves. This need makes the recruitment process for Alzheimer disease drug trials more challenging than it is for most other clinical drug trials. Nevertheless, the authors document an appealing approach to successful recruitment into Alzheimer disease trials.

Understanding Alzheimer Disease

To best understand Alzheimer disease, we must remember the principles of mind, body, and spirit enunciated many

years ago by the founder of the osteopathic medical profession, Andrew Taylor Still, MD, DO. We must make the most of our roles as providers of care for patients affected by this devastating disease and for the family members and friends of these patients. Furthermore, we must strive to include all of our knowledge in the education of new generations of osteopathic physicians, who will care for patients in the future. We are excited and pleased that one member of this new generation (Ms Saunders) is included in the authorship of an article in the present *JAOA* supplement. It is only with awareness of all of our traditional principles that we as osteopathic physicians can remain at the forefront of healthcare delivery for the many people affected by Alzheimer disease who are in need of our support and services.

In summary, Alzheimer disease is one of the greatest challenges to our healthcare system today, and the impact of this disorder will predictably increase with the aging of our population. Knowledge of disease mechanisms, screening, and diagnosis are essential to our attempts to manage this devastating disease. Current and future treatments, modern care for patients, and recruitment into clinical drug trials are vital to primary care physicians, who remain important links in successful treatment of patients with Alzheimer disease. The present *JAOA* supplement is a valuable resource in efforts to meet the needs of primary care physicians and, thereby, to improve the lives of patients with Alzheimer disease and their loved ones.

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