

A 100-Year Update on Alzheimer's Disease and Related Disorders

This month marks the 100th anniversary of the scientific presentation in which Dr. Alois Alzheimer described the clinical and neuropathologic features of the disease that now bears his name.^{1,2} In this issue of *The Journal of Clinical Psychiatry*, our "Focus on Alzheimer's Disease and Related Disorders" section commemorates this historic event with the publication of a review article on Alzheimer's disease. Richard Caselli, Thomas Beach, Roy Yaari, and I consider the clinical and neuropathologic features, evaluation, and management of Alzheimer's disease; known genetic risk factors and suggested pathogenic mechanisms; and some of the promising disease-slowing and prevention strategies that remain to be rigorously tested. The article also considers the still evolving concept of mild cognitive impairment, the amnesic subtype of which is characterized by a nondisabling impairment in memory, is frequently associated with the histopathologic features of Alzheimer's disease in expired patients, and is associated with increased rates of subsequent conversion to dementia.³

On November 3, 1906, Alzheimer described his original patient to colleagues at the 37th Conference of Southwest German Psychiatrists in Tübingen, Germany.^{1,2} Auguste D (Figure 1) was a 51-year-old woman who was admitted to the Frankfurt hospital with disabling impairments in memory and language, auditory hallucinations, paranoid delusions, and aggressive behaviors. She continued to decline, became bedridden, and died from decubitus ulcer-induced septicemia 5 years later. At postmortem examination, the patient's brain was characterized by cerebral atrophy and at least some atherosclerosis. Using staining methods developed by his colleague Franz Nissl, Alzheimer discovered the characteristic histopathologic features of this disorder, currently known as neuritic plaques and neurofibrillary tangles. In 1907, Alzheimer published his lecture, and similar cases were soon reported by Alzheimer and other physicians in older persons.² In 1910, Alzheimer's mentor Emil Kraepelin referred to these presenile and senile dementias as "Alzheimer's disease."⁴ Indeed, Alzheimer's disease was used to support Kraepelin's groundbreaking and still influential thesis that psychiatric diagnoses should be predicated on reliable symptom clusters, supported by their ability to predict a person's prognosis and clinical course, and ultimately validated and clarified on the basis of their pathobiological and etiologic features.

At the time of Auguste D's illness, the average life expectancy at birth in the United States was about 47 years. A century later, the average life expectancy at birth in the United States is about 78 years. The average life expectancy in several other countries is even greater, and the number of persons living past the age of 85 years around the world continues to soar. Even now, those older than 85 years have an almost 50% chance of being afflicted by Alzheimer's disease, and those with a loved one older than that age have an almost 50% chance of being a family caregiver. For these and other reasons, there is an urgency to do far more for those currently afflicted and those of us at future risk for this disorder. Here are just a few suggestions for physicians who see patients with cognitive impairment: (1) properly evaluate the problem, (2) identify potentially reversible and aggravating causes, (3) distinguish between Alzheimer's disease and the non-Alzheimer dementias, and (4) consider the full range of medication and nonmedication management resources and strategies to treat both the cognitive and the highly prevalent and morbid noncognitive behavioral symptoms, or (5) refer patients to a dementia specialist who can provide these services.

A new standard of care is needed to more fully address the range of medical and nonmedical needs that patients and families are likely to face during the course of the

Figure 1. Auguste D: Alois Alzheimer's Original Patient^a



^aReprinted with permission from Maurer et al.²

illness. Treating physicians and their colleagues should be trained to help patients and families understand the range of medical, caregiving, financial, legal, daycare, assisted living, and family caregiver challenges that may come their way. Physicians should help patients and families provide the local resources needed to best address these problems, and they should be reimbursed by third-party payers to make this critical effort even remotely possible.

The identification of effective palliative, disease-slowing, and prevention therapies must become an urgent priority. While there is a diversified and growing portfolio of promising disease-slowing treatments, there is a tightening bottleneck in the availability of patients for clinical trials. Moreover, while there is a diversified and growing portfolio of promising primary prevention therapies, it would take millions of dollars, thousands of healthy volunteers, and many years to determine whether or when the healthy volunteers in a clinical trial develop symptoms, making it almost impossible to rigorously assess these treatments. Since an even modestly effective prevention therapy would have an enor-

mous public health benefit, the identification of an effective prevention therapy could help avert a financially overwhelming health care problem. The 5-year, \$60 million "Alzheimer's Disease Neuroimaging Initiative" is intended to demonstrate how brain-imaging methods and other biomarker assays may be used as "therapeutic surrogates" to help in the cost-effective and rigorous evaluation of promising disease-slowing treatments.⁵ Meantime, my colleagues and I have been interested in the use of brain-imaging measurements in cognitively normal carriers of a common Alzheimer's susceptibility gene, with the eventual goal of testing primary prevention therapies without having to study thousands of healthy volunteers or wait many years to determine whether or when persons in a primary prevention study develop symptoms.⁶

A century ago, Alois Alzheimer and his colleagues articulated the problem. Let us find a way to halt the progression and prevent the onset of Alzheimer's disease without allowing another century to go by. Indeed, let's do everything we can to end the disorder that bears Alzheimer's name without losing a generation. If you have suggestions or comments regarding "Focus on Alzheimer's Disease and Related Disorders," please feel free to contact me at Eric.Reiman@bannerhealth.com.

Eric M. Reiman, M.D.
Deputy Editor

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