Focus on Alzheimer's Disease and Related Disorders

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The Journal of Clinical Psychiatry is committed to informing its readers about the progress now being made in the scientific understanding, diagnosis, treatment, and prevention of Alzheimer's disease. With this commitment in mind, the *Journal* announces its plan to publish from time to time special articles and sections as part of a "Focus on Alzheimer's Disease and Related Disorders" series. To inaugurate the series, this issue includes a report in which Andreas Papassotiropoulos, M.D., and his colleagues implicate a cluster of cholesterol-related genes in the vulnerability to late-onset Alzheimer's disease and propose for subsequent research studies a cholesterol-related genetic risk score to help characterize an individual's vulnerability to this disorder.

A DEVASTATING AND INCREASINGLY COMMON PROBLEM

Alzheimer's disease is the most common form of disabling impairment in memory and thinking.[1] According to one community survey, Alzheimer's disease afflicts about 10% of people older than 65 and almost half of those older than 85 years of age.[2] The disorder is characterized not only by a gradual and relentless decline in memory and other cognitive domains, but also by the frequent occurrence of noncognitive psychiatric symptoms. Indeed, these noncognitive symptoms are a common cause of family caregiver distress and nursing home placement. Alzheimer's disease is a disorder that routinely leaves its mark on the entire family, illustrated by the finding that more than half of patients' primary family caregivers become clinically depressed.[3] As people live to older ages, the prevalence of the disorder is projected to multiply, taking an escalating toll on afflicted persons, their families, and health care financing systems around the world.

Several medications (the cholinesterase inhibitors donepezil, galantamine, and rivastigmine and the *N*-methyl-D-aspartate [NMDA] receptor antagonist memantine) have been approved for use in the United States because of their modest but potentially significant amelioration of cognitive symptoms. Several medications may help alleviate certain noncognitive psychiatric treatments, and other nonpsychiatric medical and nonmedical treatments may also be beneficial. Even so, there remains a need to optimize the evaluation and care of patients, to discover treatments that could attack Alzheimer's disease at its heart, and to introduce these treatments at the earliest possible time. Clinicians must become armed with the information, experience, and skills needed to serve both the medical and nonmedical needs of their patients and families. Researchers must find more effective ways to alleviate the burden on patients and their families and avert a financially overwhelming public health problem. Even a modestly effective prevention therapy would have an enormous impact: delaying the onset of Alzheimer's disease by only 5 years could reduce the number of afflicted patients by half!

SCIENTIFIC PROGRESS

In the face of this devastating and increasingly common disorder, we are encouraged by the remarkable scientific progress that has been made in the understanding of Alzheimer's disease and the discovery of promising disease-slowing and prevention therapies. Researchers have begun to characterize the cascade of molecular events leading to the plaques, tangles, and "dying back" of neurons found in the brains of patients, providing targets against which to aim disease-slowing treatments. They have implicated a number of genetic and nongenetic risk factors for Alzheimer's disease, providing leads for the development of promising prevention strategies and raising the possibility of introducing those treatments at the earliest and most responsive time.

The efficacy and tolerability of proposed disease-slowing and prevention therapies remain to be established. Meantime, researchers have developed promising investigational medications and immunization therapies to slow

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He has received research support from the National Institute of Mental Health (RO1 MH57899), the National Institute on Aging (P30 AG19610), the State of Arizona, the Alzheimer's Association, GlaxoSmithKline, and Banner Health Foundation. He is currently leading a brain imaging study evaluating the cholesterol-related genetic risk score proposed in the article by Papassotiropoulos et al.

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the progression of Alzheimer's disease (for review, see reference 4). Medications, dietary supplements, and healthy lifestyle interventions have been suggested to prevent its onset, and cost-effective ways to determine which of these treatments are effective are being studied. For instance, better animal models of Alzheimer's disease have been developed (e.g., reference 5), providing the opportunity to help identify the best treatments to consider in clinical trials, and the development of brain imaging markers of disease progression[4,6–8] promises to help evaluate those treatments in the most effective way.

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