It's All in the Genes

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Over the past 10 years, we have witnessed improvement in diagnostic criteria for Alzheimer's disease (AD) and related conditions, including vascular dementia and dementia with Lewy bodies. The advances have facilitated research on the natural history of these disorders, on genetic and acquired risk factors, and on symptomatic therapies. Increasing central nervous system cholinergic activity using cholinesterase inhibitors has been found to alleviate some of the cognitive and behavioural symptoms and stabilize some of the functional decline. The availability of such symptomatic treatment has increased patient and caregiver interest in early diagnosis. The use of cholinesterase inhibitors is now a component of the usual management of AD, mixed AD/vascular dementia, and dementia with Lewy bodies.

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In the near future, there will be clarification of diagnostic criteria for Parkinson-associated dementia and we will see the results of randomized clinical studies aimed at delaying conversion from amnestic mild cognitive impairment to diagnosable dementia (predominantly AD). Positive results will bring a large number of baby boomers to consult their general practitioners for assessment of their memory complaints. There is a pressing need to define clearly who among those with mild cognitive impairment is at risk of progression towards dementia. Results of large-scale epidemiologic studies, such as the Canadian Study of Health and Aging, and ongoing genetic studies, such as GenADA (comparing persons with AD versus carefully matched controls) are likely to determine a number of risk markers. These markers

could be applied to individuals, allowing a definition of minimal, age-associated risk to moderate or high risk of progression. At the very least, the diagnosis of AD may become possible at an earlier stage than is currently possible.

A number of etiologic hypotheses related to AD are being tested in people with mild to moderate AD, with the aim of disease stabilization. For example, medications with neurotrophic, antioxidant or anti-amyloid actions may stop or slow down the rate of cell loss and modify disease progression. The trial design to confirm such a disease-modification effect is a comparison of the decline in cognition and global functioning over one year in persons on standard treatment plus the new medication to those taking placebo. These clinical measures are supplemented by a volumetric magnetic resonance imaging. Researchers are hoping for a reduction in the rate of brain atrophy.

If successful, these disease-modification treatments could be used in patients with mild cognitive impairment, but also in asymptomatic individuals with high genetic risk. Children of persons with AD would be able to receive individual risk assessment, which will likely include genetic testing in a general practitioner's office or in local laboratory facilities. For most, minimal age-associated risks will be found and lifestyle protective factors, such as leisure activities and good nutrition (including red wine) will be the proper advice, along with treatment of vascular risk factors, such as systolic hypertension. At that point, AD, and possibly some of its related disorders, will be amenable to primary prevention in the same way cardiovascular diseases are currently very well managed by general practitioners. Dx

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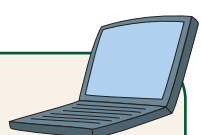

1. The Alzheimer Society of Canada: *www.alzheimer.ca*
2. Society for Neuroscience: *http://apu.sfn.org*