

Canadian Consensus Conference on Dementia: Two Years Later

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It is now three years since the Canadian Consensus Conference convened in Montreal to review evidence, reach consensus and make recommendations on a wide variety of diagnostic and management strategies for dementia. The dizzying pace of progress in the whole field of dementia has continued, and our approaches to management, in particular, have continued to evolve.

In recent years the interest in mild cognitive impairment (MCI) has escalated. MCI is the border state between normality and dementia. Many attempts have been made to define this prodromal stage of Alzheimer's disease (AD), and considerable controversy has been generated concerning its exact definition.^{1,2} As consensus slowly emerges, it is evident that MCI, characterized by memory loss but with preservation of other domains of cognition, progresses at a predictable annual rate of 5-15% to AD.¹ There is intense interest in the condition, and currently therapeutic trials, which aim to delay progression to dementia, are underway with agents such as estrogens, cholinesterase inhibitors, COX-II inhibitors, and Vitamin E.

Alzheimer's disease has a multifactorial etiology. Genetic factors include predisposing genes (especially the apoE-4 allelic genotype) and rare deterministic genes on chromosomes 1,14,21.³ There appears to be a complex interplay among factors such as ischemia, inflammation and excessive beta amyloid production and deposition. A recent review describes these interacting factors.⁴

There have been several advances in therapeutics. A second acetylcholinesterase inhibitor, rivastigmine, has been approved for use in Canada for mild to moderate stages of AD,^{5,6} and a third, galantamine, will be available in the near future.^{7,8} These agents have generally similar properties to donepezil. The results of a multi-centre clinical trial of donepezil in moderate to severe AD have been presented.⁹ This study revealed that donepezil has positive effects on behaviour, performance of daily activities and reduction of caregiver stress well into the later stages of AD. These results were not entirely anticipated, as many would have predicted from the cholinergic hypothesis that such agents would have less, and not more, benefits in later disease, as further degeneration of cholinergic neurons occurred. This study paves the way for broader indications for cholinesterase inhibitors, and we may see these agents used for apathy and other behavioural problems in more advanced cases of dementia.

Published case series have suggested that donepezil is helpful in managing the hallucinations, delusions, cognitive and behavioural symptoms in dementia with Lewy bodies.¹⁰ Subsequently, a large randomized placebo controlled trial of rivastigmine in dementia with Lewy bodies has confirmed the benefit of cholinesterase inhibitors in this disorder. These findings were presented in abstract at the World Congress of

Alzheimer's Disease in July 2000 and are currently also in press.

There have been advances too in the management of difficult behaviours (behavioural and psychological symptoms of dementia – BPSD). Two large randomized controlled trials have demonstrated the efficacy of risperidone, an atypical neuroleptic agent, in the management of aggression and other behavioural problems in dementia.^{11,12} Furthermore, in one of these studies¹¹ risperidone was clearly superior to haloperidol, a frequently prescribed traditional neuroleptic agent. A clinical trial of olanzapine has revealed that this agent is also beneficial and safe in BPSD¹³ and it is probable that quetiapine, another atypical neuroleptic agent will also prove efficacious in this setting. Despite their cost, the significantly lower risk of extrapyramidal side effects, particularly parkinsonism and tardive dyskinesia, together with their proven efficacy are leading to their emergence as first line agents in BPSD.

Regardless of these advances in therapy, the diagnosis of dementia still depends heavily upon a careful history and gathering of information from corroborative sources. History, together with physical, neurological and cognitive examinations, a limited number of laboratory investigations and selective neuroimaging continue to constitute the mainstay of appropriate diagnosis. Support of the caregiver, recruitment of community supports and enrollment in advocacy organizations such as the Alzheimer's Society will always be the cornerstone of therapy. While Alzheimer's and other dementias continue to be terrifying diseases, they are far less so than in the past, as the exponential growth of knowledge leads us to better understanding and constantly improving therapies.

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