Reporting from the Second Canadian Colloquium on Dementia

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The idea of a national conference on dementia came from the recognition that, while Canada is disproportionately endowed with internationally acclaimed experts in dementia, there was no national forum that allowed for the exchange of knowledge between these experts and the specialists caring for their patients.

Program Highlights
The second CCD was fortunate to have a large number of internationally renowned speakers from across Canada and the United States. Some of the highlights are as follows:

The Nun Study. One of the keynote presentations of the CCD was by Dr. Suzanne Tyas, a graduate in epidemiology and biostatistics from the University of Western Ontario and an investigator in the Nun Study, headed by Dr. David Snowden at the University of Kentucky. Dr. Tyas spoke on “Early and Late-life Predictors of Alzheimer’s Disease,” based on findings from the Nun Study. She reported findings from the Nun Study suggesting that AD is a consequence of a long chain of events spanning the life experience, including genetics, lifestyle and environment, brain development and reserve, AD severity in the brain, atrophy, other medical diseases, age at symptom onset and severity of symptoms. For example, early-life autobiographies from the convent archives have shown a strong relationship between low linguistic ability in early life and a high risk of AD in late life. Late-life events, such as stroke, can increase the risk as well as the severity of AD. Dr. Tyas also suggested that folate deficiency might be an important risk factor in the development of AD.

In describing a group of cognitively intact nuns referred to as the “Magnificent Seven,” Dr. Tyas showed how the prevalence of AD increases linearly with age, from 65 years until 90 years, after which there appears to be a drop in prevalence.

MCI debate. In the true nature of a Canadian debate, there was more consensus than difference between the two internationally acclaimed debaters on mild cognitive impairment (MCI): Dr. John Morris from the Washington University School of Medicine and Dr. Howard Chertkow from McGill University. The resolution was “MCI is the earliest stage of Alzheimer’s disease,” with Dr. Morris debating in the affirmative and Dr. Chertkow debating in the negative. Dr. Morris emphasized the importance of a reliable informant in detecting dementia. He claimed that change in everyday function due to cognitive impairment predicts the development of dementia and that the quality of clinical information from the informants and the labeling threshold of the clinician determine the diagnosis. While agreeing that not all MCI predicts
AD, he argued that all AD patients go through a MCI stage. In addition, Dr. Morris argued that all patients with plaques and tangles will develop AD if they live long enough.

Dr. Chertkow pointed out that the high degree of variability among definitions of MCI could alter, by up to four-fold, the number of subjects meeting MCI criteria. He also pointed out that the rate of progression of MCI to dementia varies substantially across different centres and referral sources, from 100% in St. Louis, France (tertiary referral) down to 0%-18% in Montpellier, France (population study). In a McGill study, 27 of 90 patients still had MCI after a mean of 11 years of memory complaints. Dr. Chertkow stressed the importance of differentiating between those individuals who progress from MCI to dementia and nonprogressors. It is possible that some of those who do not progress to dementia may have age-related memory loss, unrelated to AD pathology. Dr. Chertkow gave examples of pathological studies where patients with clinically diagnosed AD had no AD pathology, and where patients meeting the pathological definition of AD had no dementia. Dr. Chertkow argued that AD should be regarded as a clinical disease and not as a neuropathology. Because some patients with MCI will not progress to AD, Dr. Chertkow saw a message of hope in the diagnosis of MCI.

From the onset of the debate, there was consensus that not all MCI patients develop AD. At the end of the debate, the audience was left with the impression that, while there is uncertainty about the definition of MCI and the ability to predict its progression to AD, it remains an important diagnostic concept to researchers and clinicians alike.

Vascular dementia. Dr. Vladimir Hachinski of the University of Western Ontario and editor for Stroke, brought his considerable perspective and wisdom to an entertaining appraisal of the role of vascular disease in dementia, entitled “Vascular Dementia: Sorting Through the Confusion.” Although there are criteria of high specificity for dementia of primary vascular origin, Dr. Hachinski explained that sensitivity is poor. This is shown not only by variable vascular pathologies and the highly variable clinical expression of vascular disease, but by more recently recognized interactions of cerebrovascular disease and neurodegenerative pathology, such as AD. Clinically apparent stroke poses a major risk for later dementia. Experimental infarction in mice bearing a familial AD gene left these animals with larger residual lesions than those seen in animals without the AD gene. Although a precise diagnostic definition of the vascular contribution...findings from the Nun Study ... suggest that AD is a consequence of a long chain of events spanning the life experience, including genetics, lifestyle and environment, brain development and reserve, AD severity in the brain, atrophy, other medical diseases, age at symptom onset and severity of symptoms.

Amyloid cascade theory. Dr. Peter St. George-Hyslop, director of the Centre for Neurodegenerative Diseases at the University of Toronto, reviewed the evidence for the “amyloid cascade” theory of AD and the ratio-
nale for therapy with injections of Aβ proteins—the so-called vaccination therapy. The pioneer human trial of Aβ40 injections had been stopped because of the occurrence of a sterile encephalitis. The clinical and pathological data currently available from the human trial suggests a favourable effect on cognitive function and a reduction in amyloid burden in the brain. Transgenic animals developed by Dr. Hyslop and his colleagues at the Centre for Research in Neurodegenerative Diseases are making it possible to pursue a variety of strategies to circumvent the inflammatory reaction observed in the human study. These strategies include modification of the injected Aβ peptide to remove the sequences triggering inflammation and passive immunizations. The vaccination approach remains an exciting research priority.

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and his colleagues at the Mayo Clinic. Dr. Boeve discussed the relationship between rapid-eye-movement (REM) behavioural sleep disorder and Lewy-body disease using graphic video clips of patients undergoing sleep studies who violently enacted their dreams.

Dr. Serge Gauthier discussed the design of clinical trials in AD and Dr. Howard Feldman reviewed the data on current and forthcoming treatments for AD, including the new (to North America) drug, memantine.

Drs. David Conn and Dmytro Rewilak reviewed the pharmacologic and nonpharmacologic approaches to the treatment of behavioural symptoms of dementia.

Dr. Michael Gordon talked about ethical issues in dementia and Dr. Gary Naglie presented his research on the rating of quality of life in individuals with AD.

Dr. Morris Freedman presented on frontotemporal dementia (FTD) while introducing the audience to the Theory of Mind and its potential use in diagnosing FTD.

The use of neuroimaging in the diagnosis of dementia was reviewed by Dr. Piero Antuono from the Medical College of Wisconsin.

Dr. Chris MacKnight discussed the value of case-finding versus screening for dementia in primary care.

While still savouring the success of the second CCD, the organizing committee is already working hard on the program for the third CCD, to be held in Ottawa, Ontario between October 27-29, 2005. We look forward to seeing you there!

**Relationships with Industry**

In this era of increased vigilance over relationships between the pharmaceutical industry and physicians, it was extremely important to the organizers of the second CCD that clear boundaries exist between the pharmaceutical companies providing financial support and the program development. As a result, the pharmaceutical companies sponsoring the second CCD generously provided their support through unrestricted educational grants. These were grants-in-aid that allowed the organizing committee to develop the program independent of any influence from the industry.