RéSUMÉ: Reconnaître, évaluer et traiter les démences: conclusions de la Conférence canadienne de consensus sur la démence.

Développer des énoncés consensuels basés sur les données actuelles de la science sur lesquels on puisse construire des lignes directrices cliniques pour les médecins de première ligne pour l'identification, l'évaluation et la prise en charge des patients déments; ii) diffuser et évaluer l'impact de ces énoncés et des lignes directrices basées sur ces énoncés. Options: Une approche structurée pour l'évaluation, incluant les épreuves de laboratoire recommandées, les choix d'examen de neuroimagerie et de référence en spécialité; la prise en charge des complications (spécialement des problèmes de comportement et de dépression) et l'utilisation d'agents qui améliorent la fonction cognitive. Bénéfices potentiels: Des soins améliorés et fiables aux personnes démentes; un contrôle des coûts par une utilisation plus judicieuse des examens de laboratoire, de la neuroimagerie et de la référence en spécialité; une utilisation appropriée des agents qui améliorent la fonction cognitive. Évidence: Les auteurs de chaque article de fond ont reçu le mandat de faire une recherche de la littérature pour ajouter des informations pertinentes incluant les références citées dans ces articles; consulter d'autres experts dans ce domaine et faire une synthèse de l'information. Ces tâches ont été effectuées conformément aux normes de la preuve. Sur la foi de cette évidence, les énoncés consensuels ont été développés par un groupe d'experts, guidé par un comité de direction de huit individus des domaines de la neurologie, de la gériatrie, de la psychiatrie, de la médecine familiale, de la médecine préventive et des systèmes de santé. Valeurs: Des recommandations ont été développées en portant une attention particulière sur le contexte des soins de première ligne et sont destinées à soutenir le développement des experts de la médecine de famille dans l’évaluation et la prise en charge au cours du suivi de leurs patients atteints de démence. Bénéfices, désavantages et coûts: Une amélioration potentielle des soins aux individus atteints de démence. Une diffusion et une stratégie d’évaluation tentera de mesurer l’impact des recommandations. Recommendations: Voir texte. Validation: Quatre autres équipes de experts ont été contactées pour soutenir les énoncés consensuels et/ou de lignes directrices ont été publiés récemment. Ces recommandations sont généralement en accord avec notre énoncé consensuel. Les énoncés consensuels ont été endossés par les autorités compétentes au Canada. Commanditaires: Les fonds proviennent de contributions égales de sept compagnies pharmaceutiques et d’un octroi du Consortium des Centres canadiens pour la recherche clinique cognitive (C5R). Deux universités canadiennes ont contribué (McGill et McMaster). Plusieurs sociétés ont commandité la participation de délégués à la conférence.


From the Department of Medicine (CP), Department of Psychiatry (AG), McMaster University, Hamilton, ON, McGill Centre for Studies in Aging (SG), Division of Geriatric Medicine (HB), McGill University Montreal, QC, Department of Psychiatry, University of Toronto, Toronto, ON (CC), Department of Family Medicine, University of Western Ontario, London, ON (JWF), Department of Medicine (Neurology), University of British Columbia, Vancouver, BC (HF), Division of Geriatric Medicine, University of Calgary, AB (DBH), Canada

Reprint requests to: C. Patterson, Division of Geriatric Medicine, Hamilton Health Sciences Corporation, Chedoke Hospital Campus, Sanatorium Rd., Hamilton, Ontario L8N 3Z5 Canada
At present there are over 250,000 seniors with dementia in Canada. As dementia occurs predominately in seniors, the aging of our society means that these disorders will affect an increasing number of Canadians. By 2031, there will be an estimated 778,000 seniors with dementia in Canada. The present and increasing burden of suffering which dementing disorders impose on individuals, their caregivers and the health care system makes recommendations for the assessment and management of these conditions timely and important.

In 1989, the Canadian Consensus Conference on the Assessment of Dementia (CCCAD) developed guidelines for the evaluation of individuals with suspected dementia. While these have remained relevant, a wealth of new information has increased our understanding of dementing disorders. We now recognize many forms of dementing illnesses, which can usually be distinguished and have different therapies and prognoses. Better ways of treating the complications of dementia, managing caregiver stress and enhancing cognitive function have become available. Many physicians and others are unaware of these new developments. Clear recommendations, if implemented, could improve the care of individuals with dementia in Canada. Given that the majority of medical care for these individuals is provided by primary care physicians, recommendations should support these physicians in the assessment and management of their patients.

The goals of the Canadian Consensus Conference on Dementia (CCCD) were:
1. To develop consensus statements on which to base clinical practice guidelines for primary care physicians for the recognition, assessment and management of dementing disorders.
2. To base these recommendations upon the best available evidence and widely disseminate them to primary care physicians.
3. To evaluate the impact of these recommendations and guidelines based on these statements.

In this paper we intend to explain the methods we used and provide a summary of the consensus statements agreed to.

Consensus development process:

A Steering Committee was formed, (co-chaired by SG and CP) with representatives from the disciplines of Family Medicine, Neurology, Preventive Health Care, Geriatric Medicine and Psychiatry.

The Canadian Medical Association Guidelines for Clinical Practice Guidelines were utilized. Rather than developing detailed guidelines, the Committee chose to develop consensus statements on which guidelines (which are often context specific) could be based. Topics were chosen for their relevance to primary care physicians. For each topic a lead author for a background paper was selected. The authors were responsible for: a) literature search; b) critical review of articles; and c) preparation of a draft background document. These were circulated to the Steering Committee for initial feedback and then to all conference participants with their feedback directed to the authors.

The conference was held on February 27-28, 1998, in Montreal. Thirty-four participants attended. For each topic, the lead authors provided a brief overview and summary of recommendations. A period of discussion followed, after which the recommendations were either voted upon, or the authors were asked to reformulate recommendations in light of the discussion. This reformulation usually involved rewording or clarification rather than any substantive change. Reformulated recommendations were later voted upon.

Each conference participant (except for the industry observers) voted on the recommendations. The question posed was “does the evidence support the recommendation?” Abstentions were counted as votes against the recommendation. Consensus was defined as greater than 80% of conference participants voting for the recommendation; partial consensus if between 60 and 80%; and, no consensus if less than 60%.

In preparing background papers, authors were instructed to use the rules of evidence developed by the Canadian Task Force on the Periodic Health Examination. The following categories were utilized to grade the levels of evidence.

I) Evidence obtained from at least one properly randomized controlled trial (RCT).
II) i) Evidence obtained from well-designed controlled trials without randomization.
   ii) Evidence obtained from well-designed cohort or case control analytic studies preferably from more than one centre or research group.
   iii) Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments are included in this category.
III) Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

Each background paper concluded with recommendations which were graded as follows:
A. There is good evidence to support this manoeuvre.
B. There is fair evidence to support this manoeuvre.
C. There is insufficient evidence to recommend for or against this manoeuvre but recommendations may be made on other grounds.
D. There is fair evidence to recommend against this procedure.
E. There is good evidence to recommend against this procedure. Ideally, A or E recommendations are supported by level I evidence. The paucity of level I evidence in the field of dementia resulted in recommendations frequently being based upon less rigorous evidence. A “C” recommendation does not imply that the manoeuvre is useless or harmful: there is simply insufficient evidence to make a stronger recommendation. For each recommendation the grading and strength of supporting evidence is given.

Conference participants were chosen on the basis of:
1. Expertise in dementia or a related area.
2. Reputation for being able to deliver high quality work in a timely manner.
3. Reputation as opinion leaders in the field.
4. Willingness to consider alternative perspectives with an open yet critical mind.

In order to deal with any potential conflict of interest the following procedures were adopted:
1. The process for formulating recommendations was outlined in detail before the conference.
2. The entire process was transparent, with each vote counted by two individuals and recorded.
3. Each conference participant completed a questionnaire outlining previous involvement with pharmaceutical companies, using the form developed by the National Auxiliary Publications Service (NAPS).7

Following the conference, recommendations were collated and circulated to conference participants to ensure that the final recommendations reflected the evidence and conference discussion. Only minor changes to wording, solely to clarify recommendations, were allowed at this point. Endorsement was requested from sponsoring societies through their designated representatives.

**DIAGNOSIS AND NATURAL HISTORY OF DEMENTIA**

Dementia is diagnosed when acquired cognitive deficits are sufficient to interfere with social or occupational functioning in an individual without depression or clouding of consciousness (condensed from American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders8). This syndrome is usually progressive when due to neurodegenerative (primary) or vascular causes but is occasionally reversible.

Once dementia has been diagnosed, the specific cause can often be recognized by the following clinical profiles of the common dementing disorders:

- **Alzheimer’s disease (AD)** is characterized by a gradual onset, continuing decline of memory and at least one additional cognitive domain, not explained by other neurologic or systemic disorders.9 The most common cause of dementia in Canada, AD accounts for about 60% of cases.1
- **Vascular dementia (VaD)** exists as a number of syndromes typically associated with cerebrovascular disease. These are generally characterized by abrupt onset, stepwise decline, impaired executive function, gait disorder and emotional lability, with clinical or neuroimaging evidence of cerebrovascular disease.10 A temporal relationship between a vascular insult and cognitive change should be sought. VaD and AD frequently co-exist – a condition called mixed dementia.11
- **Fronto-temporal dementia (FTD)** is characterized by an insidious onset and slow progression of behavioural changes such as loss of social awareness, disinhibition, mental rigidity, inflexibility, hyperorality, perseverative behaviour, distractibility, loss of insight and declining hygienic standards; prominent language changes frequently occur with reduction in verbal output.12
- **Dementia with Lewy bodies** is a progressive cognitive decline with fluctuating symptoms, recurrent visual hallucinations and spontaneous, extrapyramidal signs. The diagnosis is supported by repeated falls, hypersensitivity to neuroleptics, delusions, non-visual hallucinations and syncope or transient losses of consciousness.13

**1. ASSESSMENT OF DEMENTIA**

While some aspects of cognitive performance (especially timed activities) may deteriorate with advancing age,14 dementia is usually suspected when cognitive losses are associated with declining function in occupational, social or day-to-day functioning. If an individual has only subjective complaints without objective impairments or family confirmation of decline, further investigation for dementia is not warranted. Follow-up studies have shown that depression or anxiety are more likely to be the cause.15,16 If objective evidence of memory loss or decline in other areas of cognition is uncovered by mental status testing, function in terms of daily activities should be assessed. When there is evidence of a decline in function, either from caregivers’ description or objective testing, further investigation and close follow-up are indicated. A structured clinical approach will help to establish the presence of dementia and enable the physician to distinguish underlying causes, including the presence of reversible conditions which may aggravate or even cause cognitive decline.17,18 Substance abuse, adverse drug effects, depression, metabolic disorders and systemic illnesses are among the most common of these.19,20 The history should describe onset, duration and evolution of symptoms and precipitating factors such as stroke. Delirium must be ruled out.21 The presence of depression, delusions, hallucinations, personality changes and other behavioural abnormalities such as apathy or agitation should be sought. A family history of dementing disorders is important. Collateral history from a caregiver is essential. In the physical examination one should look for focal neurological signs. Careful history (including collateral information), physical examination and mental status testing, remain the cornerstone of diagnosis.19 Serial observation at intervals of three to six months may be necessary to confirm the progressive nature of the problem, make a diagnosis of dementia and establish prognosis.22

a) **Dementia is a clinical diagnosis requiring detailed history and physical examination, including office-based psychometric tests (such as the Mini Mental State Examination (MMSE))23,24 as well as scales looking at functional autonomy, particularly for instrumental tasks (such as the Functional Assessment Questionnaire (FAQ)).**25,26 **Serial assessments over time may be necessary to establish and confirm a diagnosis.** (B, III, consensus)27,28

**Basic laboratory tests**

Extensive investigations for potential reversibility are no longer justified unless there are features in the presentation which would suggest an alternative diagnosis such as delirium or a particular reversible cause.3,29-31 Only a few basic tests are suggested for general use (see recommendations). Additional investigations are determined by the results of the history, physical examination and initial investigations. For example, a serum B12 level is indicated if proprioceptive loss, peripheral neuropathy and/or a macrocytic anemia accompany cognitive decline.

b) **For most patients who have a clinical presentation consistent with Alzheimer’s disease with typical cognitive symptoms or presentation, only a basic set of laboratory tests should be ordered:**

- **complete blood count**
- **thyroid stimulating hormone (TSH)**
- **serum electrolytes**
- **serum calcium**
- **serum glucose**

**Neuroimaging in dementia**

Neuroimaging (most commonly computerized axial
tomography (CT, CAT) scanning) has a role in detecting certain causes of dementia such as VaD, tumor, normal pressure hydrocephalus or subdural hematoma. It is currently less effective in distinguishing AD or other cortical dementias from normal aging. Exaggerated cerebral atrophy may be present in advanced AD. Patchy white matter lucencies occur in up to 12% of cognitively intact older individuals and are of uncertain significance.\textsuperscript{32} In primary care settings, some have stated that CT scanning could be limited to atypical cases\textsuperscript{3,29,31} but others have recommended routine scanning.\textsuperscript{28} A recent retrospective study examined the utility of the CCCAD criteria in 200 consecutive memory clinic patients. Application of these criteria would have reduced the number of scans done by nearly two thirds, without changing clinical outcomes.\textsuperscript{2,4} Our recommendation therefore limits CT scanning to individuals who meet the criteria listed. Magnetic resonance imaging (MRI) currently offers no advantage over CT scanning in most cases of dementia.

c) A cranial CT scan is recommended if one or more of the following criteria are present:

- age less than 60 years
- rapid (e.g. over one to two months) unexplained decline in cognition or function
- “short” duration of dementia (less than 2 years)
- recent/significant head trauma
- unexplained neurologic symptoms (e.g. new onset of severe headache or seizures)
- history of cancer (especially in sites and types that metastasize to the brain)
- use of anticoagulants or history of a bleeding disorder
- history of urinary incontinence and gait disorder early in the course of dementia (as may be found in normal pressure hydrocephalus)
- any new localizing sign (e.g. hemiparesis or a Babinski reflex)
- unusual or atypical cognitive symptoms or presentation (e.g. progressive aphasia)
- gait disturbance
  (B, II-ii, consensus)\textsuperscript{3,29,31}

Ancillary tests

Many ancillary tests are being investigated for their utility in diagnosing specific dementias, distinguishing subtypes within major categories, determining likelihood of responding to therapy and/or assessing the risk for an individual to develop a dementing disorder. These investigations, (see footnote), are not appropriate for the primary care setting until more evidence of clinical utility is available.

d) A growing number of ancillary tests are available as tertiary care clinical investigations or experimental studies. There is insufficient evidence to suggest that family physicians should use these tests routinely. (see footnote)

(C, III, consensus)

Footnote: Examples of Ancillary Tests for the Diagnosis of Dementia: Brain imaging: MRI hippocampal volumes; functional imaging (PET, SPECT, MRI); Cognitive assessments: reaction time measures; semantic priming; computerized algorithms. Neurophysiological tests: EEG with power spectral analysis; sleep EEG; cognitive evoked potentials (P300). Genetic/neurochemical tests: blood apolipoprotein E (ApoE) genotyping; CSF tau and beta-amyloid fragments.

2. REFERRAL OF PATIENTS WITH DEMENTIA

The initial clinical assessment of memory complaints usually takes place in the primary care setting. Given the difficulties in allocating sufficient time for an informant interview and cognitive assessment of the patient, the use of nonmedical personnel or multiple office visits may be necessary. In some cases, it will be desired or necessary to refer the patient. Identification of “typical” AD has become less a diagnosis of exclusion and more based upon its characteristic features. (i.e. insidious onset, progressive decline over seven to ten years, gradual loss of cognitive and functional abilities). Cases which do not follow this “typical” pattern (e.g. those who manifest early behaviour changes or delusions, fluctuating course, early motor changes) may be considered for referral. Guidelines for referral established at the CCCAD remain appropriate.\textsuperscript{3} The choice of consultant will depend upon the specific reason for referral, availability and preference. In addition to physicians (neurologists, geriatricians, psychiatrists), referral to support organizations (e.g. the Alzheimer Society of Canada) and health care professionals with expertise in cognitive and functional assessment (e.g. occupational therapists, clinical psychologists) may be necessary. Referral may be made to community-based (e.g. home care) and institution-based (e.g. day programs, long-term care facilities) continuing care agencies. Referral to a social worker can be helpful for caregiver support, advice for available services and future planning. Multidisciplinary dementia clinics, where available, provide a valuable local source of expertise.\textsuperscript{33}

Most patients with dementia can be assessed and managed adequately by their primary care physicians. However, there are several reasons to consider a referral to a geriatrician, geriatric psychiatrist, neurologist, or other professional:

- continuing uncertainty about the diagnosis after initial assessment and follow-up
- request by the patient or the family for another opinion
- the presence of significant depression, especially if it does not respond to treatment
- treatment problems or failure with new specific medications for Alzheimer’s disease
- the need for additional help in patient management (eg behavioural problems) or caregiver support
- the need to involve other health care professionals, voluntary agencies such as the Alzheimer Society, or other local service providers
- when genetic counseling is indicated
- when research studies into diagnosis or treatment are being carried out.

(B, III, consensus)\textsuperscript{3}

3. SCREENING AND CASE FINDING

Screening and case finding are appropriate when a condition is common and carries a high burden of suffering: both criteria are present for dementia. In order to be effective, there must be evidence that early identification changes the natural history in a beneficial way without negative effects such as labeling. Resources for screening and case finding should not detract from those allocated to other beneficial manoeuvres.\textsuperscript{34}

Individuals who demonstrate acquired cognitive deficits that do not meet criteria for a diagnosis of dementia have been
described as having “cognitive impairment, not demented” (CIND). Many etiologies exist for CIND, eg. depression, delirium, effects of substance abuse. Recent evidence suggests that after five years, nearly 50% of those with CIND will have deceased and of the survivors 45% will have developed dementia. A simple equation (100 minus MMSE/30 x 100) + (.25 x age) + 10 (if memory problems were reported by an informant) predict the approximate percentage of individuals with CIND who will progress to dementia after five years with a sensitivity of 73% and specificity of 68%. Mild cognitive impairment (MCI) is a more homogeneous condition characterized by memory complaint, normal activities of daily living, normal general cognitive function but abnormal memory for age and without evidence of dementia. While not all authorities agree with this definition, individuals with MCI progress to AD at a rate of 10-15% per year.

Relatives and caregivers can accurately identify cognitive decline and their concerns must always be taken seriously. Individuals who see their primary care physicians frequently are more likely to have their cognitive deficits identified. Short mental status questionnaires are insufficiently sensitive or specific for use in screening. For example, the Folstein’s MMSE, the most commonly used short test of cognitive function, has an average sensitivity 83% and an average specificity of 82% for detecting dementia. If this test were applied to a population of 65- to 74-year-old people, the false positive rate (ie. risk of falsely labeling an individual as demented) would be 93%. Asking about function, especially in instrumental activities of daily living (eg. managing finances, use of telephone, driving) is particularly useful in assessment of patients with signs of possible dementia.

There is currently insufficient evidence to recommend for or against identification of CIND or MCI until the natural history and better screening instruments are more clearly defined.

a) There is insufficient evidence to recommend for or against screening for cognitive impairment in the absence of symptoms of dementia.
   (C, II-ii consensus)
b) There is insufficient evidence for or against screening or case-finding for dementia with short mental status questionnaires in unselected older people.
   (C, II-ii, consensus)
c) Given the burden of dementia for older people and their caregivers, it is important for family physicians to maintain a high index of suspicion for dementia and to follow up concerns about and observations of functional decline and memory loss.
   (B, II-ii, consensus)
d) Memory complaints should be evaluated and the individual followed to assess progression.
   (B, II-ii, consensus)
e) When caregivers or informants describe cognitive decline in an individual, these observations should be taken very seriously: cognitive assessment and careful follow-up are indicated.
   (A, II-ii, consensus)

4. GENETICS OF DEMENTIA

First degree relatives of AD patients have a two- to four-fold increase in their personal risk for the disease. In a small number of families there is autosomal dominant transmission for AD manifesting in middle age. Almost all Down syndrome patients over the age of 40 have neuropathological changes typical of Alzheimer’s disease. The ApoE gene on chromosome 19 has three alleles – 2, 3, 4. In the general population, the presence of ApoE4 genotype is associated with an increased risk of AD. For example, a population-based prospective study of individuals over age 75, revealed a relative risk for developing AD of 3.24 (95% CI, 1.67-6.25) in those possessing ApoE4. However, the sensitivity (approximately 50%) and specificity (approximately 75%) for the presence of the ApoE4 genotype in diagnosing AD is insufficiently high to guide diagnosis or accurately quantify genetic risk. The place of genetic testing and genetic risk assessment remains unclear at present. Resources that are available for advice include genetic clinics and the Alzheimer Society of Canada. The consequences of genetic testing must be carefully considered as significant harm can result from inadequate counseling.

a) Screening asymptomatic individuals for genetic risk factors such as ApoE4 is not recommended at this time. (D, III, consensus)
b) There is insufficient evidence at this time to suggest that family physicians should use ancillary tests such as ApoE genotyping for the diagnosis of dementia in symptomatic individuals. (C, III, consensus)
c) Attention should be paid to changes in functional abilities in middle-aged individuals with Down’s syndrome (trisomy 21) because they are at a high risk for Alzheimer’s disease. (B, II-ii, consensus)
d) Asymptomatic individuals presenting to the family physician with concerns regarding inheritance of Alzheimer’s disease can be referred to a genetic clinic if the family history is suggestive of autosomal dominant inheritance. If the family history is not supportive of such inheritance, indeterminate or negative, the family physician should refer to community resources such as the Alzheimer Society or a genetic clinic only if the physician and/or the asymptomatic individual require further reassurance and/or assistance. (B, III, consensus)
e) If a person diagnosed with Alzheimer’s disease presents to the family physician with concerns about family members, these relatives should be encouraged to consult with their own family physicians. (B, III, consensus)
f) Consider collecting a blood sample for provincial DNA banking (where available) in persons diagnosed with Alzheimer’s disease starting before age 60. Consider encouraging an advance directive indicating their willingness to agree to brain banking. (B, III, consensus)

5. PREVENTION OF DEMENTIA

As the etiological factors for dementing disorders become more clearly identified, prevention may become a reality. If the onset of dementia could be delayed by five years, the population prevalence could be reduced by one-half. If delayed by 10 years,
prevalence could decline by 75%.\textsuperscript{55} For VaD, prevention is already potentially possible by treatment of stroke risk factors, by the use of antihypertensives,\textsuperscript{56} HMGCoA reductase inhibitors,\textsuperscript{57,58} and anticoagulants for atrial fibrillation.\textsuperscript{59} Reducing the incidence of stroke may decrease the incidence of VaD,\textsuperscript{60} a recent European randomized controlled trial (RCT) revealed that treatment of systolic hypertension reduced the subsequent incidence of dementia (AD and VaD) by one half.\textsuperscript{61}

The timely correction of metabolic disturbances which can be associated with dementia (eg. vitamin B\textsubscript{12} deficiency, alcohol abuse), can be reasonably expected to reduce the incidence of subsequent dementia. While there is evidence from case control and cohort studies that postmenopausal hormone replacement therapy may reduce the incidence of AD,\textsuperscript{62} a recent RCT of estrogen replacement in established AD failed to demonstrate cognitive improvement or slowing of the dementing process.\textsuperscript{63} Therefore, it is premature to recommend estrogens solely for the purpose of preventing AD. As hormone replacement therapy may be recommended for other reasons, all potential risks and benefits including the potential prevention of AD should be discussed with postmenopausal women.\textsuperscript{64} Similarly, while case control and cohort evidence suggests that nonsteroidal anti-inflammatory drugs (NSAIDs) may be associated with a reduced incidence of AD, it is premature to recommend them for this purpose.\textsuperscript{65} Large prospective RCTs of estrogens, anti-oxidants and NSAIDs are currently underway or are being planned.

Epidemiological studies have shown an association between AD and having fewer years of formal education.\textsuperscript{66} Improved basic education can be viewed as having a potential role in reducing the incidence of AD in addition to other societal benefits. Head injuries have been suggested to increase the subsequent incidence of AD.\textsuperscript{56,67} Encouraging the use of seatbelts and bicycle helmets could have a role in the primary prevention of dementia.

\textbf{a) When clinical conditions that can lead to cognitive impairment are uncovered by clinical and laboratory assessment, appropriate corrective treatment should be instituted.} (eg thyroid or B12 replacement, alcohol abstinence programs, etc.)

By effectively treating other vascular risk factors such as hypertension, cholesterol, diabetes, smoking cessation and prophylactic anticoagulation for chronic atrial fibrillation to prevent stroke, the risk of vascular and Alzheimer’s dementias may also be reduced.

The decision to treat transient ischemic attacks (TIAs) and stroke by secondary prevention measures as above and by use of anticoagulants, antiplatelets and carotid endarterectomy as appropriate, may likewise lower the risk of vascular dementia.\textsuperscript{(B, III, consensus)}\textsuperscript{57,60}

\textbf{b) Physicians should be aware of genetic risks factors for Alzheimer’s disease and follow recommendations under genetic screening.} Evidence suggesting that substandard education (< six years) and that head trauma may increase the risk of Alzheimer’s disease, would lend support to advocacy programs for minimum standards of education and for head injury prevention (such as the use of seatbelts when driving and helmets for cycling or other sports).\textsuperscript{(B, III, consensus)}\textsuperscript{66,67}

\textbf{c) The use of NSAIDs cannot be recommended for the treatment or prevention of Alzheimer’s disease on the basis of available evidence but, if required for arthritis or other conditions, it may afford some protection against the development of Alzheimer’s disease.} \textsuperscript{(C, II-ii, consensus)}\textsuperscript{65}

d) Physicians should provide counseling on the risks and benefits of estrogen therapy in peri- or postmenopausal women. Although current evidence does not support the use of estrogen specifically for the prevention of Alzheimer’s disease, the reduced risk associated with long term estrogen use in epidemiological studies may provide an additional potential benefit to consider when weighing the pros and cons of estrogen therapy. \textsuperscript{(B, II, consensus)}\textsuperscript{62,64}

6. Ethical issues in dementia

Loss of insight, declining capacity to make reasonable decisions and risk to others must be carefully balanced against preservation of autonomy. Recognizing the scope of relevant ethical issues, the conference participants chose to focus on two areas; disclosure of diagnosis and driving. Other important issues which were not dealt with include:

- Participation in research
- Decision-making: respecting individual choice
- Quality of life
- Behaviour control
- Use of restraints
- Advance directives
- End-of-life decisions

Several publications have looked at these difficult issues. The interested reader is directed to “Tough Issues”\textsuperscript{68} and recent reviews by Fisk et al\textsuperscript{69} and Cohen et al.\textsuperscript{70}

7. Disclosure of diagnosis

The case for informing an individual of the diagnosis rests upon the patients’ right to know (principle of autonomy). Knowledge of the diagnosis can allow for future planning (eg. advance directives, power of attorney and planning for future living arrangements). Disclosure allows for consent to treatment and participation in research. It facilitates the dialogue between patient and caregiver, avoiding the conspiracy of silence that might otherwise exist. Arguments against disclosure include the risk of depression and, in rare instances, of suicide, concern about diagnostic uncertainty and the lack of effective disease modifying treatments. Most seniors and caregivers of AD state that they would wish to be told the diagnosis.\textsuperscript{71} While taking each individual case on its own merits, it is considered ethically preferable to inform persons with dementia of their diagnosis.\textsuperscript{71}

While each case should be considered individually, in general the diagnosis of a dementing condition should be disclosed to the patient and family.

This process should include a discussion of prognosis, diagnostic uncertainty, advance planning, treatment options, support groups and future plans.

Exceptions to disclosure to the patient could be severe dementia where understanding of diagnosis is unlikely, phobia about the diagnosis and severe depression.

\textsuperscript{(B, III, consensus)}\textsuperscript{71}
8. DRIVING AND DEMENTIA

The risk of motor vehicle collisions and fatal injury increases with the duration and severity of dementia.72 Reporting concerns about driving to provincial Ministries of Transport is mandatory in many but not all provinces. Physicians’ assessment of driving safety in the office setting is inaccurate.73 The exception is where the patient is so severely demented that an increased driving risk is obvious. Performance-based evaluations of driving are preferable for accurate assessment especially in uncertain cases.73,74 The physician should ask about driving problems, accidents or infractions and look for significant deficits in visuospatial abilities, attention and judgement. Lesser degrees of impairment in combination may be equally hazardous. Other conditions that may affect the patient’s level of consciousness or abilities (eg. syncope, hypoglycemia, seizures, transient ischemic attacks) as well as medications that can affect cognition should also be considered. Long half-life benzodiazepines substantially increase the risk of motor vehicle collision in older individuals.73 Descriptions of how patients actually drive should be sought from observers. Asking about behaviour (eg. anger) and abilities in daily function (eg. getting lost) are potentially useful for assessing driving risk. Even if the risk is currently considered acceptable, review at periodic intervals (to be determined by the patient’s rate of decline or onset of new symptoms) is recommended. Physicians who have concerns regarding a patient’s capacity to drive, should communicate their concern to the patient and caregiver and suggest an evaluation of driving competency.

a) While caring for patients with cognitive impairment, physicians should consider risks associated with driving. Focused medical assessments (including specific details in the medical history and physical examination) are recommended in addition to the general medical evaluation.

(B, III, consensus)73

b) Physicians should be aware that driving difficulties may indicate other cognitive/functional problems that need to be addressed.

(B, III, consensus)73

c) Physicians should encourage patients with Alzheimer’s disease and their caregivers to plan early for eventual cessation of driving privileges and provide continuing support for those who lose their capacity to drive.

(B, III, consensus)73

d) Primary care physicians should notify licensing bodies of concern regarding incompetence to drive even in those provinces that have not legislated mandatory reporting by physicians, unless the patient gives up driving voluntarily.

(A, III, consensus)73

e) Physicians should advocate strongly for the establishment and access to affordable validated performance-based driving assessments.

(B, III, consensus)79

9. CAREGIVING IN DEMENTIA

Caregivers have multiple roles in caring for individuals with dementia. Their reports are often as reliable as objective measures of cognitive decline and may alert health care professionals to the presence of dementia.76 Caregivers play a vital role in providing direct care for dementia patients. Physicians rely on caregivers to monitor changing status and symptoms and need to include them in treatment plans. Absence of caregivers is a major predictor of earlier institutionalization of individuals with dementia. Higher perceived caregiver burden also leads to earlier institutionalization.

Up to 50% of caregivers experience significant psychiatric symptoms during the course of their caregiving.77 Despite these negative consequences, many caregivers also report a sense of satisfaction with their role, particularly a sense of accomplishment in keeping their loved ones at home. Support for caregivers is offered by agencies such as the Alzheimer Society of Canada, specialized dementia services, support groups and community services providing education and case management. Programs comprising several of these elements have been shown to delay institutional admission.78 Partnerships between primary care physicians and caregivers are strongly recommended to help families cope with the care of individuals with dementia. The family physicians’ role includes: establishing and conveying the diagnosis; management of behavioural disorders related to dementia; assistance with advance planning; assessing and treating caregivers for depression and other illnesses; and, facilitating referral to appropriate services for additional assistance.

a) Acknowledge the important role played by the caregiver in dementia care; work with caregivers and families on an ongoing basis from the time of diagnosis of dementia until the death of the patient; schedule regular appointments for patients and caregivers together and alone.

b) Educate patients and families about the disease and how to cope with its manifestations. This includes appropriate modifications to the home environment and learning to communicate and interact with the dementia patient.

c) Evaluate caregiver coping strategies and encourage caregivers to care for themselves, using health promotion and stress reduction strategies.

d) Assess the caregiver’s social support system and help caregivers rally support for themselves from appropriate family members and friends.

e) Enquire about caregiver-burden, psychiatric and health problems by regular meetings with caregivers, asking specific questions about their health and caregiver strain; offer treatment for these problems (individual psychotherapy or medications as indicated) or refer to appropriate specialists or services.

f) Refer caregivers to appropriate community services for dementia care (eg day care, respite, local Alzheimer Society) realizing that it may take encouragement and time for these services to be used; if available, refer patients to specialized dementia services that offer comprehensive treatment programs.

g) Discuss legal and financial issues and obtain appropriate help for caregivers and families if required.

(B, III, consensus)

10. CULTURAL ISSUES IN DEMENTIA

In a multicultural society such as Canada, physicians need to be aware that the concept of dementia is essentially a Western one. In many cultures this diagnostic label does not even exist.79 In making diagnoses, cultural sensitivity must be observed. One
must avoid over-reliance on mental status instruments that may not be valid in other cultural groups. Standard cognitive testing measures frequently contain items which are biased for educational attainments or ethnicity. It can be extremely difficult to assess individuals whose language of communication is different from the examiner. Different cultural or ethnic groups may have different proportions of the various causes of dementia. For example, VaD is the most common type in Japan but when Japanese men migrate to Hawaii they appear to be more susceptible to the development of AD. Decisions about management may be affected by cultural differences in, for example, willingness to seek institutional care.

a) Family physicians need to be aware of the cultural impact on families' recognition and acceptance of dementia in a family member and that more in-depth questioning about symptoms and the meaning of aging may be required.

(b, III, consensus)

b) Physicians should recognize that measures of cognitive abilities (eg MMSE) will often overestimate cognitive impairment in many cultural and/or linguistic groups.

(b, III, consensus)

c) The care and management of patients from specific cultural groups should take into account the risk of isolation, the importance of culturally appropriate services and special issues that arise in providing caregiver support.

(b, III, consensus)

II. Depression and dementia

Depressive symptoms occur frequently in individuals with AD; one study found at least one depressive symptom was present in 63% of individuals. Prevalence estimates for major depressive disorder vary between 6% and 20%. It has been suggested that major depressive disorders become less common as dementia advances and insight is lost, although this is controversial. Other depressive syndromes that occur in dementia include chronic dysthymia, grieving and bipolar affective disorders. It may be difficult to distinguish depression from personality changes such as apathy and passivity which are commonly found in AD and FTD; or emotional lability, which is most commonly associated with VaD. Much has been written about distinguishing dementia from depression but these syndromes often co-exist. Many symptoms such as sleep disturbance, anorexia, irritable behaviour, anergia and social withdrawal may occur in both dementia and depression. When symptoms suggesting depression occur, a trial of antidepressants can be considered. Response to antidepressant therapy is less predictable in dementia. Unfortunately there is a paucity of RCTs to guide the prescribing physician. Anticholinergic side effects from many antidepressants (particularly the tricyclic drugs) limit their usefulness in AD, as cognitive deficits may worsen on these medications.

Moclobemide, selective serotonin reuptake inhibitors (SSRIs), trazodone, nefazodone and venlafaxine are considered reasonable choices since they have minimal anticholinergic effects. Trazodone may cause hypotension in high doses. If tricyclics are to be used, nortriptyline is preferred if sedation is required and desipramine if no sedation is desired. An antidepressant trial should last at least two to three months and be continued if the patient has responded. Continued use of medication must be regularly re-evaluated. Depressive illness coincident with dementia should be treated before starting a cognitive enhancer.

a) As depressive syndromes are frequent in patients with dementia, physicians should consider diagnosing depression when presented with the subacute (eg weeks, rather than months or years) development of symptoms characteristic of depression such as: behavioural, weight and sleep changes, sadness, crying, suicidal statements, or excessive guilt.

(b, III, consensus)

b) Depressive illness should be treated and, when refractory, the patient should be referred to a specialist.

(b, III, consensus)

c) Depressive symptoms which are not part of a major affective disorder, severe dysthymia or severe emotional lability should initially be treated nonpharmacologically.

(b, III, consensus)

d) In patients with disturbing emotional lability or pathological laughing and crying, consider a trial of an antidepressant or mood stabilizer.

(b, III, consensus)

12. MANAGEMENT OF BEHAVIOURAL DISTURBANCES IN DEMENTIA

Behavioural and psychological signs and symptoms of dementia are common, serious problems that impair the quality of life for both patient and caregiver. At some point during the course of the illness, 90% of patients have behavioural problems. They are particularly common in long-term care institutions. While behavioural manifestations tend to occur later in AD and VaD, they occur more frequently and earlier in the course of FTD and Lewy body dementias. Assessment should include a review of potential triggers (eg, pain, intercurrent illness, medications). Behaviours should be carefully documented. It is important to look for precipitants such as physical treatments, bathing, mealtimes, company, or loneliness. Consequences of the behaviours should also be recorded. The act of observing and documenting these behavioural symptoms and signs can in itself reduce the number of incidents by learning to recognize, anticipate and avoid provocation. Non-pharmacological interventions are generally tried first and may involve environmental modifications, therapy with light, music, pets or activity and specific behavioural techniques. Until recently there was little RCT evidence that psychotropic medications are effective in demented individuals. Traditional neuroleptic agents appear modestly effective but have a high incidence of extrapyramidal side effects including parkinsonism and tardive dyskinesia.

Recent RCTs of atypical neuroleptics have established the value of these agents for treating the behavioural and psychological symptoms of dementia. Risperidone, at a dose of 1-2 mg per day is superior to placebo and haloperidol. Similar benefit has been demonstrated for olanzapine and it is likely that quetiapine may also be beneficial. The atypical agents exhibit a much lower incidence of extrapyramidal side effects than traditional antipsychotic drugs and may be more efficacious.
Neuroleptics with marked anticholinergic effects, such as chlorpromazine and thioridazine should be avoided. Several antidepressants such as trazodone\textsuperscript{100-102} and the SSRI s have been recommended but trials are generally small or inconclusive. Benzodiazepines should be used cautiously, in low doses and on an “as required” basis. No medication will control wandering, which is best managed with behavioural and environmental modifications. In view of the sensitivity of demented individuals to psychotropics, the old adage “start low and go slow” should be observed. After instituting or changing a medication, an appropriate period of observation should ensue before changing the therapeutic approach again. This period will usually be of several weeks duration.

a) Serious behavioural and psychological disturbances are commonly found in persons with dementia. Family doctors should ask caregivers about such disturbances and regularly evaluate their patients. An evaluation to rule out treatable or contributory causes should be done with a new onset of agitation, aggression, psychotic behaviour, sleep disturbance, or wandering.

Environmental (eg changes in light/sound stimulation level) and behavioural modifications should be attempted first, often with advice from the Alzheimer Society and specialists. (B, I, consensus)\textsuperscript{94}

b) If medications are required for the symptomatic control of agitation, aggression or psychotic behaviour, consider low doses of neuroleptics, an SSRI or trazodone. (B, I, partial consensus 77%)\textsuperscript{96,100-103}

c) For sleep disturbances, consider trazodone. (B, II-ii, partial consensus 63%)\textsuperscript{101}

d) After successful control of symptoms with pharmacotherapy, regularly evaluate the need for continuing treatment and consider withdrawal of medication with close monitoring for emerging symptoms. (B, III, consensus)\textsuperscript{98}

### 13. Pharmacological therapy of dementia

Despite the introduction of pharmacological agents for dementia, the mainstay of management continues to be education and support for caregivers and treatment of complications. Cognitive enhancing agents have been primarily developed for AD. While the authors of the background paper reviewed a large number of agents, recommendations are offered only for agents which are currently easily available. In making these recommendations, the goals of anti-dementia therapy were carefully reviewed. Guidelines for initiating and monitoring the effect of anti-dementia drugs are based upon the expert opinion of the London (UK) Alzheimer’s Disease Treatment Working Group.\textsuperscript{104} For individual drugs, a systematic review of English language articles was carried out to identify all RCTs. This included a Medline search from 1986; review of the reference list from articles retrieved from the Medline search and contact with experts in the field of behavioural neurology and cognitive enhancement. Forty-one articles were considered for review, of which 27 were of acceptable methodological quality. Efficacy trials of drugs for dementia typically evaluated had to include at least one measure of cognitive function and at least one global measure. Drugs available for use in Canada in March 1998 were donepezil, vitamin E and ginkgo biloba. Rivastigmine was approved for use in 2000.

Donepezil is approved for the symptomatic treatment of mild to moderate probable AD. In three RCTs, donepezil has shown improvements in both cognitive performance and global functioning when compared to placebo.\textsuperscript{105-107} The benefits are usually modest (an average improvement of two points on the MMSE) and may not be apparent for three months after starting the medication but clinically useful improvement does occur in some individuals. Recent evidence indicates that donepezil has benefits on cognitive, behavioural and functional measures in more advanced stages of Alzheimer’s than previously thought.\textsuperscript{108}

Rivastigmine is the second cholinesterase inhibitor approved in Canada for the treatment of mild-moderate AD. There are two published pivotal RCTs, each showing significant benefit in terms of cognition and global improvement. Benefit continued during the duration of the two six-month trials.\textsuperscript{109,110} Benefit (and side effects) were greatest at a dose of 6-12 mg per day, given in two divided doses, and are supported by a systematic review.\textsuperscript{110a}

Two RCTs of ginkgo biloba have been published in the English language literature.\textsuperscript{111,112} In each of these a standardized ginkgo preparation (EgB761) was used. In one study, 222 outpatients with mild to moderate AD were randomized to receive placebo or 240 mg/day of EgB761.\textsuperscript{111} The primary outcome measure was the therapeutic responder rate, defined as a change in cognitive scale score of at least one standard deviation from the baseline on at least two of the three outcome measures. Twenty-eight percent of the ginkgo group and 10% of the placebo group responded but there was a large (30%) drop out rate. Therapeutic response rate is not a standard way of assessing response in North America. In the second study, 120 mg/day of EgB761 was compared with placebo in 327 individuals with AD or multi-infarct dementia.\textsuperscript{112} Only 50% of the ginkgo group and 38% of the placebo group completed the study. Of those completing 52 weeks of treatment, a modest but statistically significant improvement was recorded in cognitive performance and also in a rating scale provided by relatives. The high drop out rate, lack of availability of EgB761 extract and lack of standardized preparations led the reviewers to conclude that there was insufficient evidence for or against this drug.

While there are theoretical reasons to believe that Vitamin E may be beneficial in AD, only one RCT of Vitamin E has been published.\textsuperscript{113} Vitamin E (2000 units) was compared with selegiline (10 mg) daily in a double-blind, placebo-controlled, randomized, multi-centre trial involving 341 patients with moderate AD.\textsuperscript{113} The duration of treatment was two years and the primary outcome measure was the time to the occurrence of any of the following: death, institutionalization, loss of the ability to perform basic activities of daily living or severe dementia (clinical dementia rating of 3). The primary analysis revealed no difference between either of the treated groups or placebo. However, despite random allocation, the baseline score on the MMSE was higher in the placebo group than in the other three groups and this variable is well-known to be highly predictive of outcome. When the results were reanalyzed to include the baseline MMSE scores as covariate, significant delays in time to the primary outcome were increased (selegiline median time 655 days; vitamin E 670 days; combination therapy 585 days; placebo 440 days). It is unclear why combination therapy...
appear less effective and selegiline itself appears to offer no advantages over the less expensive vitamin E. As such the reviewers dealt only with vitamin E. It was felt that there was insufficient evidence to make a recommendation for or against this agent. A dissenting opinion was written.

While cure would be the ideal goal, currently available agents do not allow this possibility. Monitoring of the response to medications should include the use of standardized instruments such as the MMSE and FAQ at regular intervals. Reasonable treatment goals include:

- halting or slowing the course of the disease with respect to measurable cognitive and functional decline leading to institutionalization
- improvement in memory and other cognitive functions
- maintenance or improvement in self-care abilities
- improvement in behavioural abnormalities, improvement in mood, contentedness and quality of life of the patient and/or caregiver.

### a) Guidelines for anti-dementia drugs

- It is recommended that primary care physicians be instructed through Continuing Medical Education (CME) on the administration and interpretation of measures of functional activities and cognitive abilities.
- After treatment has been started, re-evaluation should occur regularly, such as every three months
- Records should be kept such that stabilization, improvement or persisting deterioration in subjects treated with an anti-dementia drug will be determinable and will indicate whether to continue or discontinue the drug.
- Caregivers should be asked to keep a written record of personal impressions and historical data on the performance of the patient in daily life.
- Where the primary care physician is unable to perform such assessments, referral to a specialist is advised.
- Primary care physicians should be able to communicate appropriate information concerning dementia including realistic treatment expectations to their patients and their families.

(B, III, consensus)

### b) Use of donepezil and rivastigmine

Donepezil and rivastigmine are the only two drugs available in Canada for the treatment of mild to moderate Alzheimer’s disease. Statistically significant differences in favour of each drug were found on cognitive tasks and on the Clinician’s Interview Based Assessment of Change but the long-term clinical benefit remains unclear. At present there is no evidence to support the use of either drug in preventing Alzheimer’s disease.

A trial course of donepezil or rivastigmine can be prescribed to informed and willing patients with mild to moderate dementia due to probable Alzheimer disease, in the absence of contraindications.

(B, I, consensus)

### c) Use of vitamin E (Please see dissenting opinion below)

There is currently (March 1998) insufficient evidence to recommend the use of vitamin E for the treatment or prevention of Alzheimer’s disease. At the doses evaluated in clinical trials there were side-effects in some patients. The benefit of low dose vitamin E has not been evaluated.

(C, I, consensus)

### d) Use of ginkgo biloba

There is currently (March 1998) insufficient evidence to recommend the use of ginkgo biloba for the treatment or prevention of Alzheimer’s disease. There is great variability between different preparations of ginkgo.

(C, I, consensus)

### Validation

Four other sets of clinical practice guidelines have been published recently. While all of these guidelines were aimed at an American audience, recommendations were broadly similar. In detail, however, a number of discrepancies were present, originating partly from the different audiences targeted for these documents. The following organizations have received and endorsed the recommendations of this paper: Alzheimer Society of Canada; Canadian Neurological Society; Canadian Society of Geriatric Medicine; College of Family Physicians of Canada; Consortium of Canadian Centres for Clinical Cognitive Research; Société Québécoise de Gériatrie. Conference participants report that slides of the recommendations have been well-received at continuing medical education presentations.

### Discussion

“Guidelines for complex interventions are hard to build.”

Dementia is an extremely complex field. The epidemiology of this syndrome is beginning to be understood. Current agreement on diagnoses, even among experts with specific diagnostic criteria, is far from perfect. There are no treatments which are clearly effective in the majority of cases. Finally, complications of dementic illnesses are legion and difficult to manage.

For these and other reasons, guidelines for dementia care based upon sound evidence are hard to produce. To develop consensus statements we reviewed all the evidence that could be gathered using a comprehensive search strategy. We used a ranking of levels of evidence which is well-established and widely emulated. Wherever possible, we based our recommendations on the best evidence available. Where evidence was lacking, often a “C” recommendation was given: this does not recommend for or against the manoeuvre but simply states that there is insufficient evidence to make a decision on evidence alone. Levels of evidence and strength of recommendations were incorporated into each background paper, although at consensus, the strength of recommendations was modified in some cases.

For those in the field, it was no surprise that there were very few studies which fulfilled criteria for level I evidence. We elected to adopt the best available evidence approach making free use of the conclusions of other consensus groups and the expert opinion of our group to supplement those areas where level I evidence was lacking but where clinical direction appeared important.

The organizing committee also decided to produce consensus statements rather than true clinical practice guidelines. This was primarily in response to concern that primary care in Canada is so diverse that universal guidelines are not practical and would

* Recommendation on rivastigmine added subsequent to the conference (see pg 122)
not be applicable in every setting. It was felt, instead, that groups of physicians could formulate appropriate guidelines from these consensus statements, ones which would be more applicable to their particular setting.

Some of the recommendations are more vague than prescriptive. This resulted from the necessity to reach consensus among a diverse group of professionals that included primary care and specialist physicians, as well as other disciplines. We attempted to distill the available evidence and wisdom into statements helpful to primary care physicians. Indeed, seven out of the 34 participants were primary care physicians and every attempt was made to keep the focus of the recommendations on primary care. Rapid evolution of the field will result in new developments and recommendations: the preceding represents the best available advice at the time of the conference in Feb. 1998.

CONFERENCES PARTICIPANTS

Steering Committee: C. Patterson, Co Chair, McMaster University; S. Gauthier, Co Chair, McGill University; H. Bergman, McGill University; C. Cohen, University of Toronto; J. Feighniter, University of Western Ontario; H. Feldman, University of British Columbia; A. Gree, McMaster University; D. Hogan, University of Calgary; Participants: B.L. Beattie, University of British Columbia; S.E. Black, University of Toronto; R. Bouchard, Université Laval; M.A. Chang, Alzheimer Society of Metropolitan Toronto; H. Chertkow, McGill University; A.M. Clarfield, Ministry of Health, Israel; D. Dastoor, McGill University; D. Gass, Dalhousie University; B. Groulx, McGill University; R. Handfield-Jones, College of Family Physicians of Canada; C. Herbert, University of British Columbia; N. Herrmann, University of Toronto; P. Jennett, University of Calgary; H. Karlinsky, University of British Columbia; A. Kertesz, University of Western Ontario; D. Krulicki, Alzheimer Society of Canada; G. Lacombe, Université Sherbrooke; L. LeDuc, Alzheimer Society of Canada; P. McCracken, University of Alberta; G. Naglie, University of Toronto; D. Pringle, University of Toronto; W. Pryse-Phillips, Memorial University; A. Robillard, Montreal; P. Rochon, University of Toronto; K. Rockwood, Dalhousie University; D. Sadovnik, University of British Columbia; S. Sterberg, University of Toronto; D. Strong, University of Manitoba; H. Strong, Memorial University; L. Thorpe, University of Saskatchewan; S. Wetmore, University of Western Ontario, College of Family Physicians of Canada; C. Wolfson, McGill University; G. Worrall, Newbrook Community Health Centre

SOCIETY REPRESENTATIVES

Alzheimer Society of Canada: Linda LeDuc; Canadian Academy of Geriatric Psychiatry: Carole Cohen; Canadian Neurological Society: Andrew Kertesz; Canadian Society of Geriatric Medicine: Peter McCracken; College of Family Physicians of Canada: Steven Wetmore; Consortium of Canadian Centres for Clinical Cognitive Research: David Hogan; Société Québécoise de Gériatricie: Guy Lacombe.

INVITED SPEAKER: A. M. Clarfield, Division of Geriatrics, Ministry of Health, State of Israel

COORDINATOR: L. Edwards, Canadian Congress of Neurological Sciences, Calgary

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Table: Optional additional tests that may be helpful to diagnose specific causes of dementia (from Clarfield)

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DISSENTING OPINION ON VITAMIN E –
DRS D. B. HOGAN, S.E. BLACK

Recommendation Proposed: There is currently (March 1998) fair evidence to support the use of vitamin E in high doses (2,000 IU/daily) for the treatment of Alzheimer’s disease of moderate severity (level I evidence).

Justification: Agents which protect against oxidative damage may slow the progression of Alzheimer’s disease. A double-blind, placebo-controlled, randomized trial in patients with Alzheimer’s disease of moderate severity showed that alpha-tocopherol (vitamin E, 2000 IU/day) led to a statistically significant delay in the time to one of four primary outcomes (death, institutionalization, loss of ability to perform basic activities of daily living, or progression to severe dementia) if the baseline MMSE score was included as a co-variate.\(^1\) This delay was approximately 230 days (nearly eight months). There was no statistically significant difference in the frequency of adverse effects (as compared to those subjects receiving placebo) in those who received vitamin E after adjustment for multiple comparisons. Vitamin E is safe with few reported cases of toxicity at dosages less than 3000 IU/d.\(^2\) Vitamin E supplementation may also decrease the risk of cancer\(^3,4\) and cardiovascular disease.\(^5,6\) It may improve immune function in the elderly.\(^7\) Vitamin E has been shown to slow the progression of Alzheimer’s disease at a dose which is safe for humans. There is the potential as well for additional health benefits with its use.

References