UNIT NO. 1

OVERVIEW OF DEMENTIA AND DIAGNOSIS OF DEMENTIA

Dr Nagaendran Kandiah

ABSTRACT

Dementia is a syndrome characterised by cognitive, behavioural and neurological deficits. Both neurodegenerative and non-neurodegenerative conditions can result in dementia. Neurodegenerative diseases include diseases such as Alzheimer's disease, Frontotemporal Dementia and Dementia with Lewy body, while non-neurodegenerative conditions include conditions such as vascular dementia and normal pressure hydrocephalus. The prevalence of dementia is on a rising trend with the rapidly ageing population in Singapore. Early diagnosis of dementia is important to allow timely pharmacological and non-pharmacological interventions. A thorough history, cognitive evaluation along with suitable investigational studies is necessary for early diagnosis. The ability to diagnose dementia at the earliest stages has been greatly improved with the use of biomarkers such as medial temporal atrophy on MR imaging and cerebrospinal fluid beta amyloid levels. A 4-step approach to dementia evaluation, incorporating local data, where possible can be used: The first step requires the exclusion of delirium as the cause of the forgetfulness or confusion; the second step involves establishing the diagnosis of dementia; the third step assesses for the behavioural, functional and social problems associated with dementia; and the final step, with the use of a focused history, physical examination, investigations and selected use of neuroimaging, attempts to establish the aetiological diagnosis of the dementia. The management of dementia requires a multidisciplinary approach. While acetyl cholinesterase inhibitors and NMDA antagonist can slow cognitive deterioration, research for newer disease modifying drugs which target the underlying pathology is ongoing. Research into non-pharmacological interventions such as cognitive training is also on-going.

Keywords: Integrated care; Elderly; Chronic conditions

SFP2013; 39(2) Supplement: 8-14

INTRODUCTION

Dementia is a brain disorder that affects millions of people, mostly older adults. Dementia should be viewed as a "late stage" in the continuum of cognitive difficulties. To be able to manage dementia effectively, clinicians should aim to identify the earliest stages of dementia.

NAGAENDRAN KANDIAH, Consultant, Department of Neurology, National Neuroscience Institute; Asst Prof, Duke-NUS Graduate Medical School Singapore

With the rising trend in the prevalence of dementia, especially with Singapore's rapidly greying population, this is an area of intense research in the area of therapeutics as well as the diagnosis of dementia in the earlier stages, even in the preclinical dementia state as with early diagnosis, because the affected patients are then more amendable to benefit from treatment advances.

Dementia is now included as a disease in the chronic disease management programme where Medisave can be used to pay primary care visits.

The diagnosis of dementia requires the presence of dysfunction in memory and other cognitive domains which are progressive, resulting in a decreased level of function[1]. At the stage of dementia the pathological changes in the brain are often well established and profound. Alzheimer's disease (AD) is the most common cause of dementia and the pathological hallmarks of AD include beta-amyloid plaques and neurofibrillary tangles. The second commonest cause of dementia is Vascular Dementia (VaD). In the majority of elderly patients, AD and VaD co-exist and this is termed as Mixed Dementia.

There is evidence to show that these pathological changes begin many years prior to the onset of dementia[2]. The challenge for physicians would be to identify subtle changes in cognition when the pathological changes are only beginning to develop. These earlier stages of disease have been described using several terminologies including mild cognitive impairment (MCI) and cognitively impaired not demented (CIND)[3-4]. It is crucial that clinicians are able to identify these earliest stages of cognitive impairment as intervention is most likely to be effective when initiated at this early stage.

EPIDEMIOLOGY

In Singapore the prevalence of dementia and cognitive disorders is likely to increase rapidly over the coming years. We have the fastest ageing population in the Asia-Pacific region with 15-20% of the total population being above the age of 65 by the year 2030. At the present time it is estimated that we have about 25 thousand patients with dementia and this number is set to increase to 53 thousand by 2020[5-7]. The prevalence of MCI is presently unclear but based on western prevalence rates of 18.5% at age 50-60 and 35-38% at age greater than 60, it is estimated that we currently have 75-100 thousand subjects with MCI[8-9].

ETIOLOGY AND RISK FACTORS

Dementias are largely neurodegenerative conditions including Alzheimer's disease[10], Parkinson's Disease Dementia[11], Lewy Body dementia, Frontotemporal dementia[12], and Creutzfeldt-Jakob disease. However reversible causes such as normal pressure

hydrocephalus, neurosyphilis, B12 deficiency, folate deficiency and Hashimoto's encephalopathy need to be considered and excluded. AD represents the most common cause of dementia followed by vascular dementia.

The main pathological hallmarks of AD are the beta-amyloid plaques and neurofibrillary tangles. The risk factors for the development of this pathology include advanced age, family history, vascular risk factors and APOE4 genotype[13-14]. It is also increasingly evident that AD and vascular pathology often coexist and manifests as mixed dementia. Optimisation of vascular risk factors such as diabetes mellitus and hypertension is believed to slow the amyloid cascade resulting in stabilisation of cognitive function among patients with vascular cognitive impairment.

MILD COGNITIVE IMPAIRMENT

Cognitive changes in the elderly occur over a continuum, ranging from normal ageing at one end of the spectrum to dementia at the other end. There has been intense interest in the intermediate stage between normal ageing and dementia. Of the various classification systems, the Mayo Clinic's mild cognitive impairment (MCI) has received the most attention. Its pathological validity is supported by conversion rates to dementia of approximately 12% annually and 80% at six years of follow-up. Originally, MCI diagnosis required the presence of memory complaint (preferably corroborated by an informant), objective memory impairment for age, essentially preserved general cognitive function, normal functional activities and no dementia[15].

The heterogeneity within MCI has led to the proposal of a new classification system, based predominantly on neuropsychological profiles and includes amnestic or single memory MCI, multiple-domain MCI and single non-memory MCI[16-17]. However, the existing clinical criteria for diagnosis of MCI are subjective, variable in operationalisation, and highly dependent on clinical judgment. They are also unable to reliably predict who amongst those with MCI would progress to dementia. Thus, the differentiation between normal cognitive aging and MCI (especially the early stages of MCI) would be extremely challenging using only clinical methods. This has prompted research into the use of more objective neuroimaging (structural and functional), cerebrospinal fluid (CSF), genetic and molecular biomarkers which reflect AD pathogenesis, to complement clinical approaches towards an early and accurate diagnosis of AD. Initial drug trials have not shown clinical benefit, likely related to the heterogeneity of this MCI entity.

Clinical research in accurate characterisation of MCI is of paramount importance in tandem with the concurrent development of disease-modifying therapies to identify those MCI subjects who would stand to gain most from early intervention. These issues currently render MCI to be mainly a research entity at this moment and preclude their current use in routine clinical practice. As such, the discussion below will focus mainly on established dementia.

ASSESSMENT

The evaluation of dementia should be targeted at individuals in whom there is some suspicion of cognitive impairment. This includes subjects with memory or other cognitive complaints, this could either be self-reported or noticed by family members or caregivers; subjects in whom the physician has suspicion of cognitive impairment during the consultation despite the absence of memory or cognitive complaints; subjects who are at increased risk for dementia, such as those with strong family history of dementia and elderly subjects who need to make an important decision (such as making a will, sale of flat, handling complicated financial matters) and in whom mental competency is in question. It is important to note that forgetfulness is not a part of normal aging, while normal older persons might take a longer time to recall, they should still be able to function independently and maintain social functioning should they be given more time to do so.

The evaluation of cognitive impairment should been done via a multifaceted approach, focusing not only on the cognitive complaints, but also on the functional and social consequences of these cognitive changes. This would help the clinician diagnose dementia early, assess for the complications of dementia and establish the aetiology of the dementia and manage accordingly.

With a patient presenting with forgetfulness or confusion, we can use a 4-step assessment to evaluate the cognitive complaint:

(i) Is the forgetfulness or confusion acute or chronic?
(ii) If the forgetfulness or confusion is chronic, is it dementia?
(iii) If it is dementia, what are the complications?
(iv) If it is dementia, what is the aetiology?

(i) Is the forgetfulness or confusion acute or chronic?

If the cognitive complaints is of an acute nature, with a rapid onset and short duration (lasting from few hours to days), it would be important to exclude delirium.

Delirium is defined by the Diagnostic and Statistical Manual of Mental Disorders – fourth edition (DSM-IV); however, this may be difficult to apply in clinical practice. The Confusion Assessment Method (CAM) is a brief and structured assessment commonly used in clinical setting to diagnose delirium. It requires the presence of 3 of the following 4 features: presence of acute change in mental status, fluctuating course with inattention, coupled with either the presence of disorganised thinking or altered level of consciousness. CAM has been shown to have 94-100% sensitivity and 90-100% specificity in the identification of delirium with good inter-observer reliability (kappa test 0.81-1.0). If the cognitive complaints are assessed to be secondary to delirium, the underlying precipitating factors (such as sepsis, stroke disease or drug causes) should be looked out for and the patient would require hospitalisation to manage the delirium and the underlying medical illness.

One must also be mindful that acute confusional state can sometimes be superimposed on chronic confusion. If the forgetfulness or confusion is of a subacute nature, developing over a period of week to few months, conditions such as stroke disease, space-occupying lesion, Creutzfeld-Jakob disease and hydrocephalus have to be excluded.

(ii) Is it dementia?

If the cognitive complaints are of a chronic nature, it is first important to exclude depression and late-onset psychiatry disorders. The diagnosis of dementia is then assessed via a clinical approach, either subjectively (looking for features of cognitive decline in the subject) or objectively (testing the subject's cognitive abilities using validated performance-based assessments).

Subjective approach

The DSM-IV criteria for dementia are often used as the gold standard for clinical diagnosis of dementia. It requires the presence of memory impairment, together with deficits in one other cognitive domain (aphasia, apraxia, agnosia and executive dysfunctioning). Examples of practical questions to be asked to the patient's informants with regards to these cognitive domains are shown in Table 1.

The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is a 26-item test that enquires about the subject's memory, cognition and language ability of the last 10 years. The strength of this instrument is its assessment of cognitive changes over a period of time, instead of a single point in time and also it is independent of the subject's premorbid ability or past educational attainments. This has also been validated locally among elderly Chinese subjects with an optimal cut-off score of 3.3/3.4 with 94.3% sensitivity and 94% specificity.

Objective approach

This is an observer-based approach using either performance-based instruments, such as mental status test (brief screening instruments), or a more detailed neuropsychological tests, which is usually administered by clinical psychologists.

There are several mental status tests, some of which have been validated locally. These include the Elderly Cognitive Assessment Questionnaire (ECAQ), Abbreviated Mental Test (AMT), the Mini Mental State Examination[18] the Chinese Mini Mental Status Examination (CMMSE), the Montreal Cognitive Assessment (MOCA), the AD8 questionnaire[19], clock drawing test (CLOX) and Brief Informant Screening test.

The ECAQ (Table 2) is a 10-item cognitive test which assesses memory and information-orientation. Using a cut-off score of 5/6, it has 85.3% sensitivity with 91.5% specificity for identifying cognitive impairment. The 10-item AMT (Table 2) and 28-item CMMSE has also been validated locally. For mild cognitive impairment, AMT's cut-off score is 7/8 (81% sensitivity with 89% specificity) and CMMSE cut-off score of 20/21 (sensitivity 83%, specificity 94%). The CMMSE is more useful in those with higher educational attainment as the AMT has a ceiling effect on these individuals.

The MOCA is a 30-item questionnaire and includes evaluation of memory, executive function, visuospatial function, language and orientation[20]. It has been locally validated for the diagnosis of mild cognitive impairment and mild dementia. It has a higher sensitivity for the diagnosis of early dementia[21].

It is important to keep in mind that these cut-off scores serve as a screening instrument for dementia; where some subjects may score low on cognitive screening test and have no dementia, while others may score very well but have dementia. Language barriers, advanced age and low education may confound the results and provide false-positive scores. We recommend a combined subjective and objective approach and acknowledge the challenges in diagnosing dementia in a certain group of patients.

Neuropsychological testing is useful in detecting subtle cognitive difficulties which is not picked up by the brief screening instruments. They should be performed on subjects who have

TABLE 1. DSM-IV CLINICAL CRITERIA FOR DIAGNOSIS OF DEMENTIA

Cognitive domain	Questions
Amnesia	Any forgetfulness? Did it start gradually or suddenly? Is it progressively worse? And if so, is it smoothly declining or showing a step-wise/ fluctuating decline? Is it over short-term or long-term matters?
AND declines in one of the following domains:	
Aphasia	Any word-finding difficulty or other difficulties with communication?
Apraxia	Any problems with buttoning or dressing? Any difficulties with using utensils during mealtimes?
Agnosia	Any problems recognising familiar faces or familiar items?
Executive dysfunctioning	Any problems handling money (loose change)? Any change in general problem-solving abilities? Is one's work getting to be more disorganised?
OF sufficient severity to cause significant impairment in social or occupational functioning	As a result of the above, is he becoming less independent in the - community? - home-care? - self-care level?

memory complaints but do not yet satisfy criteria for dementia; depressed subjects who present with memory complaints to help in determining whether the memory complaints is due solely to the depression or whether they have concomitant dementia; and subjects in whom decision-making capacity is being assessed. Psychometric testing can be a useful adjunct in the latter scenario. In addition, neuropsychological testing may be helpful in dementia aetiological differentiation[22]. Neuropsychometric batteries have been validated locally in the elderly Chinese and the Vascular Dementia Battery test has also been validated in the Singapore population.

Neuropsychological tests are also useful in individuals in whom the diagnosis of dementia is inconclusive (such as those subjects with performance below 1SD or 1.5SD below age and education adjusted norms) and serial monitoring for performance decline over time is useful in establishing the diagnosis.

TABLE 2. LOCALLY VALIDATED BEDSIDE SCREENING INSTRUMENTS FOR DEMENTIA

Elderly Cognitive Assessment Questionnaire (ECAQ)

Items	Score
Memory	
1. I want you to remember this number. Can you repeat after me (4517). I shall test you again in 15 mins.	1
2. How old are you?	1
3. When is your birthday? OR in what year were you born?	1
Orientation and information	
4. What is the year?	1
5. Date?	1
6. Day?	1
7. Month?	1
8. What is this place called? Hospital/Clinic	1
9. What is his/her job? (e.g. nurse/doctor)	1
Memory Recall	
10. Can you recall the number again?	1
Total score	

Abbreviated Mental Test (AMT)

Items	Score
What is the year?	1
What is the time? (within 1 hour)	1
What is your age?	1
What is your date of birth?	1
What is your home address?	1
Where are we now?	1
Who is our country's Prime Minister?	1
What is his/her job? (show picture)	1
Memory phrase "37 Bukit Timah Road"	
Count backwards from 20 to 1	1
Recall memory phrase	1
Total score	

(iii) What are the Dementia complications?

The complications of dementia can be broadly divided into behavioural and psychological symptoms, functional problems and social problems (discussed in subsequent chapters). These should be evaluated in all patients with dementia as these issues are the major cause of stress on the caregiver and assessment would enable the clinician to target subsequent management effectively.

Functional difficulties can be assessed at 3 levels: community functioning, home functioning and self-care. They are generally affected with the progression of dementia in a descending order and also allow these functional deficits to serve as markers of dementia severity. It is important when asking for functional deficits to ask for a change in the level of function, i.e. whether the patient is functioning at the same level as before and whether the patient is as independent as before. It is also important to make sure that these difficulties result from cognitive difficulties and not physical disabilities.

The severity of dementia can be staged using the Diagnostic and Statistical Manual of Mental Disorders-3rd revised edition (DSM-III-R) criteria where mild dementia is defined as impairment for work and social activities with the capacity for independent living remaining largely intact. Moderate dementia takes place when independent living is hazardous and would require some degree of supervision. Severe dementia is characterised by impaired activities of daily living such that continual supervision is required. Other formal functional assessment scales include Clinical Dementia Rating Scale (CDR), Functional Assessment Staging (FAST), Barthel Index and Blessed Dementia Scale (BDS).

(iv) What is the Dementia aetiology?

Having determined the cognitive impairment to be chronic and having met clinical criteria for dementia, as well as assessing for the complications of dementia, the final step of the clinical evaluation involves determining the dementia aetiology.

The types of dementia can be broadly divided into 2 categories – irreversible and reversible causes (Table 3). The aim of determining dementia aetiology is to rule out potentially reversible causes of dementia and selecting appropriate treatment strategies for the irreversible dementias. This is done via clinical history and physical examination, followed by laboratory investigations and neuroimaging. There are guidelines and practice parameters developed for evaluating of dementia etiology and also more specific criteria for diagnosis of the more common Alzheimer's disease (AD) and vascular dementia (VD).

In the history, it is important to ask for the nature of the cognitive decline (sudden or gradual), progression – either gradually progressive (more suggestive of AD) or stepwise/fluctuating course (suggestive of VD). A history of significant alcohol ingestion and medication use (such as antipsychotics, antidepressants, anticholinergic agents and sedative-hypnotic agents) and history of medical, neurological and psychiatric illness is important.

TABLE 3. TYPES OF DEMENTIA

Irreversible causes
- Degenerative causes – Alzheimer's disease (AD), frontotemporal dementia, diffuse Lewy body dementia.
- Cerebrovascular disease – vascular dementia (VD).
- Prion-associated disorders (Creutzfeld-Jakob disease).
- Neurogenetic disorders.

Potentially reversible causes
- Infectious disorders – meningitis, encephalitis.
- Toxic or metabolic causes – hypothyroidism, vitamin B12 deficiency, alcohol-related syndromes.
- Autoimmune Dementia-Hashimoto's Encephalopathy, VGKC associated dementia
- Neoplastic causes.
- Hydrocephalus – obstructive or normal pressure hydrocephalus.

A targeted physical examination should be performed, looking for focal neurological deficits (such as visual field defects, hemiparesis, hemisensory loss, asymmetric deep tendon reflexes or unilateral extensor plantar responses). It is also important to examine for extrapyramidal signs such as rigidity and bradykinesia, movement disorders and gait abnormalities as these may point to certain aetiological diagnosis.

Dementias which are related to metabolic abnormalities are thought to be reversible. The most commonly recommended haematological tests are: full blood count, urea and electrolytes, serum calcium, serum glucose, thyroid function tests and vitamin B12 levels. We do not advise routine testing for neurosyphilis given the problems in interpreting the results of testing. Serum Venereal Disease Research Laboratory (VDRL) testing detects only 75% of tertiary syphilis and CSF VDRL may be negative in 30-70% of cases and neurosyphilis. Thus we recommend testing only when patients exhibit clinical features of neurosyphilis.

Other biomarkers which can help in establishing dementia diagnosis include apolipoprotein-E e4 allele, CSF-tau and β -amyloid for AD, CSF 14-3-3, neuron-specific enolase and electroencephalogram for Creutzfeld-Jakob disease. However, these are not performed routinely.

Neuroimaging is useful in the differential diagnosis of dementia and are also necessary in the diagnostic criteria in AD and VD. This may be helpful in justification of aggressive management of vascular risk factors in those patients found to have cerebrovascular disease on neuroimaging. They are also useful in detection of very early dementia as the functional and structural brain changes takes place before clinical manifestation of cognitive deficits. They consist of either structural imaging techniques [computed tomography (CT) scan of head and magnetic resonance imaging (MRI)] or functional neuroimaging techniques (Positron emission tomography and single-photon emission tomography).

Whether all patients with dementia require a structural imaging is an important clinical question, for which there is no consensus. The value of neuroimaging is the identification of cerebral infarcts and clinically important surgical brain lesions (SBLs) such as subdural haematomas, cerebral tumours and normal pressure hydrocephalus. The Canadian Consensus Conference on the Assessment of Dementia (CCCAD) has outlined the criteria for undertaking a CT scan, only if certain conditions are met (Table 4).

We also believe that the functional stage of the dementia is also relevant and important, over and above the duration of cognitive symptoms. In a patient with advanced dementia of long duration (>2 years), we believe that a brain scan is not warranted to detect potentially reversible SBLs. However, if the patient's dementia is still mild and moderate (even after 2 years), a brain scan is indicated.

TABLE 4. CANADIAN CONSENSUS CONFERENCE CRITERIA FOR PERFORMING CRANIAL CT IN PATIENTS WITH DEMENTIA

CT is recommended if one or more of these criteria are present.
- Patients are less than 60 years old.
- Rapid (e.g. over 1-2 months), unexplained decline in cognition or function.
- Dementia of relatively short duration (< 2 y).
- Recent, significant head trauma.
- Unexplained neurologic symptoms (e.g. new onset of severe headache or seizures).
- History of cancer, especially of a type or at a site associated with metastasis to the brain.
- Use of anticoagulants or history of bleeding disorder.
- History of urinary incontinence and gait disturbance early in the course of dementia (suggestive of normal pressure hydrocephalus).
- Presence of any new localising signs on physical examination (hemiparesis, Babinski's sign).
- Unusual or atypical cognitive symptoms or presentation (e.g. progressive aphasia).
- Gait disturbance.

Summary of Approach to Patient with Memory Complaint

- Is the memory complaint acute or chronic?
  Rule out delirium
- If it is chronic, is it dementia?
- If it is dementia, what are the complications?
  Behavioural, functional, social aspects of dementia
- What is the aetiology?
  Clinical evaluation (history, clinical examination, laboratory tests, + neuroimaging)
  To rule out reversible causes.
  If irreversible cause, clinical criteria in the differential diagnosis of dementia aetiology.

INVESTIGATIONS

We are now fortunate to have a wide range of investigational tools including CT brain, MRI brain, PET scans, cerebrospinal fluid (CSF) studies and genotyping. With the availability of such tools which have been demonstrated to have reliable sensitivity and specificity the diagnosis of dementia and MCI should move away from being a "diagnosis of exclusion" to a

"diagnosis of inclusion". Structural brain imaging with MRI is useful to evaluate for hippocampal atrophy which is the hallmark of AD while disproportionate atrophy of the frontal lobes may be indicative of frontotemporal dementia[23]. MRI is also valuable in demonstrating white matter disease and lacunar infarctions which are suggestive of vascular dementia. Special MRI sequences such as the diffusion weighted imaging (DWI) can demonstrate diffusion abnormalities which are highly specific for Creutzfeldt-Jakob disease. These advanced neuroimaging techniques will have increasing importance once MCI is accurately characterised and disease-modifying treatments have been shown to be effective. CSF studies of beta amyloid, total tau and phospho-tau have been demonstrated to have a high specificity for the diagnosis of AD. CSF examination is also valuable in managing reversible conditions such as encephalitis and autoimmune encephalopathies. PET scans also can help distinguish between AD and FTLD based on the pattern of glucose hypometabolism.

MANAGEMENT

Management of cognitive disorders requires a multidisciplinary approach including pharmaceutical and non-pharmaceutical management of the patient, caregiver support and provision of long term nursing care. The mainstay of pharmaceutical management includes acetyl cholinesterase inhibitors[24]. Patients who are initiated on AchEIs should be offered the highest tolerable dose for an adequate length of time. Switching from one AchEI to another or switching from an oral formulation to a patch delivery may need to be considered for patients who develop intolerable side effects.

Memantine, a NMDA receptor antagonist may be useful for patients with moderate to severe AD. In view of the increased risk of cardiovascular and cerebrovascular events with both typical and atypical antipsychotics, these drugs should be reserved for patients with severe behavioural symptoms. Several disease modifying agents are now in phase 3 clinical studies. They target the amyloid cascade or the production of tau and preliminary studies have demonstrated promising results.

CONCLUSIONS

Dementia represents a late stage of disease along the continuum of cognitive impairment. Early diagnosis of dementia is important to allow timely pharmacological and non-pharmacological management. Early diagnosis also allows adequate time for patients and caregivers to cope with the significant emotional and economic costs of the illness. A 4-step clinical approach could be a succinct framework to aid the family physician in evaluating the individual who presents to the clinic with cognitive complaints such as forgetfulness or confusion. Management of cognitive disorders requires a multidisciplinary approach including pharmaceutical and non-pharmaceutical management of the patient, caregiver support and provision of long term nursing care.

REFERENCES

1. American Psychiatric association. Diagnostic and statistical manual of mental disorders (1V-TR), 4th edition-text revision. Washington, DC 2000.
2. Price JL, Morris JC. Tangles and plaques in nondemented aging "preclinical" Alzheimer's disease. Ann Neurol 1999;45:358-68.
3. Petersen RC. Mild cognitive impairment as a diagnostic entity. J Intern Med. 2004;256:183-94.
4. Ebly EM, Hogan DB, Parhad IM. Cognitive impairment in the nondemented elderly. Results from the Canadian Study of Health and Aging. Arch Neurol. 1995;52:612-9.
5. Chiam PC, Ng TP, Tan LL, Ong PS, Ang A, Kua EH. Prevalence of dementia in Singapore--results of the National Mental Health Survey of the Elderly 2003. Ann Acad Med Singapore. 2004; 33:S14-5.
6. Asia Pacific Members of Alzheimer's Disease International. Dementia in the Asia Pacific Region: The epidemic is here. Alzheimer's disease International 2006. Available at: http://www.accesseconomics. com.au/publicationsreports/search.php
7. Inter-Ministerial Committee on Health Care for the Elderly 1999
8. Barker A, Jones R, Jennison C.A prevalence study of age-associated memory impairment. Br J Psychiatry. 1995;167:642-8.
9. Richards M, Touchon J, Ledesert B, Richie K. Cognitive decline in ageing: are AAMI and AACD distinct entities? Int J Geriatr Psychiatry. 1999; 14:534-40.
10. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR, Jr., Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7(3):263-9.
11. Kandiah N, Narasimhalu K, Lau PN, Seah SH, Au WL, Tan LC. Cognitive decline in early Parkinson's disease. Mov Disord. 2009 Mar 15;24(4):605-8.
12. Tan YL, Ng A, Kandiah N .Frontotemporal dementia in Southeast Asia: a comparative study. Dement Geriatr Cogn Dis Extra. 2013 Jan;3(1):1-9.
13. Graff-Radford NR, Green RC, Go RCP, et al. Association between apolipoprotein E genotype and Alzheimer's disease in African American subjects. Arch Neurol 2002; 59:594-600.
14. Casserly I, Topol E. Convergence of atherosclerosis and Alzheimer's disease: inflammation, cholesterol, and misfolded proteins. Lancet 2004; 363:1139-46.
15. Chong MS. Making the diagnosis of dementia. Singapore Family Physician 2008; 35(1):66-72.
16. Feldman HH, Kandiah N. Early identification of Alzheimer's disease: what have we learned from mild cognitive impairment? CNS Spectr. 2008 Mar;13(3 Suppl 3):4-7
17. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7(3):270-9.
18. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12(3):189-98.
19. Chin R, Ng A, Narasimhalu K, Kandiah N. Utility of the AD8 as a Self-Rating Tool for Cognitive Impairment in an Asian Population. Am J Alzheimers Dis Other Demen. 2013 Mar 14

20. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53(4):695-9.
21. Ng A, Chew I, Narasimhalu K, Kandiah N. MOCA is effective for the diagnosis of MCI and Mild Alzheimer's disease in Singapore. Singapore Medical Journal. 2013 (In Press)
22. Kandiah N, Narasimhalu K, Lee J, Chen CL. Differences exist in the cognitive profile of mild Alzheimer's disease and subcortical ischemic vascular dementia. Dement Geriatr Cogn Disord. 2009;27(5):399-403
23. Jack CR Jr, Petersen RC, Xu YC, Waring SC, O'Brien PC, Tangalos EG, Smith GE, Ivnik RJ, Kokmen E.Medial temporal atrophy on MRI in normal aging and very mild Alzheimer's disease. Neurology. 1997 Sep;49(3):786-94.
24. Doody RS, Stevens JC, Beck C, et al. Practice parameter: management of dementia (an evidence-based review).Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001;56:1154-66.

FURTHER READINGS

1. Clinical Practice Guidelines for Dementia (April 2013). <http://www.moh.gov.sg/mohcorp/publications.aspx?id=16970>
2. Chong MS, Sahadevan S. An Evidence-based Clinical Approach to the diagnosis of dementia. Annals Academy of Medicine Singapore 2003;32:740-8.
3. Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N, Small GW, Miller B, Stevens JC. Practice parameter: Diagnosis of dementia (an evidence-based review) Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001; 56:1143-53.
4. Feldman HH, Jacova C, Robillard A, Garcia A et al. Diagnosis and treatment of dementia: 2. Diagnosis. CMAJ 2008; 178(7):825-36.
5. Chertkow H, Massoud F, Nasreddine Z, Belleville S et al. Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia. CMAJ 2008; 178(10) 1273-85.
6. Peterson RC. Conceptual overview. IN: Petersen RC, ed. Mild cognitive impairment: Aging to Alzheimer's disease. New York, NY: Oxford University Press, Inc; 2003:1-14.

LEARNING POINTS

- **Cognitive dysfunction manifests along a continuum ranging from mild cognitive impairment to dementia.**
- **The strongest risk factors for AD are age, family history and APOE genotype.**
- **While dementia is often secondary to a neurodegenerative pathology, other reversible causes such as normal pressure hydrocephalus needs to be excluded.**
- **Investigative tools such as MRI and CSF studies can help establish a diagnosis of mild cognitive impairment and early dementia.**
- **The four-step approach to dementia evaluation consists of:**
  - **Exclusion of delirium as the cause of the forgetfulness or confusion.**
  - **Establishing the diagnosis of dementia.**
  - **Assessing for the behavioural, functional, and social problems associated with dementia.**
  - **Establishing the aetiological diagnosis of dementia.**
- **Management of cognitive disorders requires a multidisciplinary approach including pharmaceutical and non-pharmaceutical management of the patient, caregiver support and provision of long term nursing care.**