ABSTRACT
Dementia represents a late stage of disease along the continuum of cognitive impairment. With the prevalence of cognitive dysfunction rapidly rising, there is an urgent need for early diagnosis and intervention. 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. The management of dementia requires a multidisciplinary approach. While acetyl cholinesterase inhibitors can slow cognitive deterioration, newer disease modifying drugs which target the underlying pathology are at advanced levels of testing.


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 and hence clinicians should aim to identify the prodromal stages of dementia. 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. 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.

There is evidence to show that these pathological changes begin many years prior to the onset of dementia. 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). 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.
with most patients having difficulty finding words and may resort to using alternative words which are simpler. Problems with comprehension are often observed in the moderate to severe stages of dementia. Difficulties in executive function manifests with problems in planning, organizing and judgement. Patients may have difficulty with routine tasks such as cooking and driving and are often unable to acquire new skills such as computing. It is always preferable that the cognitive symptoms are corroborated by a family member.

Cognitive evaluation across a range of domains including memory, language, visuospatial function and executive function needs to be performed. Cognitive tests such as the mini mental state examination (MMSE), frontal assessment battery (FAB) and the Montreal cognitive Assessment (MoCA) are valuable in identifying deficits across domains\(^1\)\(^2\)\(^13\). Adequate emphasis on mood and behaviour is also crucial. Screening for depression with standardized questionnaires should be routinely performed.

While clinicians need to be familiar with the typical manifestation of AD, which represents the most important cause of dementia, it is also important to recognize the manifestations of the less common causes of dementia. Patients with frontotemporal dementia for instance may have relatively preserved short term memory but may present with behavioral changes in the form of disinhibited behavior or alternatively they may present with a progressive aphasia. Patients with dementia with Lewy body classically present with vivid visual hallucinations, fluctuating cognition and extrapyramidal features such as tremors or bradykinesia.

**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\(^1\)\(^4\). 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. 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 pharmacological management includes acetyl cholinesterase inhibitors\(^15\). 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 behavioral 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.

**REFERENCES**

7. Inter-Ministerial Committee on Health Care for the Elderly 1999
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 need to be excluded.

• Investigational tools such as MRI and CSF studies can help establish a diagnosis of mild cognitive impairment and early dementia.

• Disease modifying agents are at advanced stages of investigation and have shown promising preliminary findings.

OVERVIEW OF DEMENTIA


