



module 257

Mild cognitive impairment and dementia

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Mild cognitive impairment and dementia

GOALS AND LEARNING OBJECTIVES

This module will help you understand the changing healthcare and pharmacological needs of individuals diagnosed with mild cognitive impairment, which then leads to a formal diagnosis of dementia.

You will be able to describe the difference between cognitive impairment in normal ageing and that in dementia, name the different types of dementia likely to be encountered in primary care and understand the pharmacological and non-pharmacological treatment options for dementia.

KEY FACTS

850,000 people in the UK live with dementia, which is projected to rise to over 1 million by 2025

62 per cent of people with dementia are female, probably because life expectancy is higher in women and age is the biggest known risk factor for the disease

There is no cure for any form of dementia, except for the pseudodementias, which may respond to treatment

Risk reduction for dementia includes lowering modifiable cardio and cerebrovascular risk factors

Early interventions include planning for the future in terms of advocacy and end-of-life care options

Pharmacological treatment is multifactorial including pharmacological support of cognitive function and maintaining physical and mental health by inclusion in socially and mentally stimulating activities

Acetylcholinesterase inhibitors and memantine improve cognitive function

Future therapies will include monoclonal antibodies and small molecule treatments

Introduction & module overview

This module introduces the concept of mild cognitive impairment (MCI), which may or may not be related to an individual having the underlying pathophysiology of Alzheimer's disease (AD). For example, people can experience mild cognitive impairment as part of normal ageing, and as a result of a head injury (trauma, infection, surgery or stroke), misuse or inappropriate use of substances including medicines and alcohol, or metabolic disturbances involving glucose, calcium or sodium.

The differential diagnostic process is an important part of establishing the cause of the MCI and then signposting appropriately for treatment or symptom control.

Dementia prevention is now a public health issue that all healthcare professionals need to be aware of to best support their patients and local community.

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Cognitive impairment

Cognitive function is not just about memory, but includes language, visuospatial and perceptual ability, thinking and problem-solving, and personality. This means that any impairment may manifest as memory problems, but also problems in reading or speaking, difficulty in managing financial affairs or loss of interest in attending social activities, through to exhibiting signs of delusion or paranoia, or becoming agitated, anxious or angry.

In normal ageing there are changes in our cognitive functioning: thinking and planning take longer; people may need to make lists to remember their daily activities or use diaries or planners; they may have trouble with word finding; for example, forgetting the names of actors in a film or a famous person (but remembering them later) or forgetting a particular word in the middle of a conversation. These are normal signs. It is only when they become sufficiently severe to interfere with a person's ability to complete their usual daily activities that there is cause for concern.

Mild cognitive impairment due to Alzheimer's disease

A diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) is made according to consensus guidelines. There are two main forms: amnesic and non-amnesic MCI. People with the former diagnosis mainly exhibit problems with their episodic memory (they cannot learn or retain new information) on initial diagnosis and 50 per cent will progress to a formal diagnosis of AD. Currently, there is no ability to predict those most likely to progress to this stage and no pharmacological treatments to halt this process.

This impairment of episodic memory is not normal for age and is generally associated with other symptoms of cognitive impairment sufficient to interfere with normal daily activities and personal relationships. It is important to note that there are other possible causes of cognitive impairment, including head trauma, substance misuse (including alcohol and medication) and metabolic disturbance.

Dementia

Dementia has been defined as "a syndrome consisting of progressive impairment in two or more areas of cognition, sufficient to interfere with work, social function or relationships".

In 2015, there were an estimated 856,700 people with dementia in the UK. Established prevalence rates link the risk of dementia with increasing age, rising from one in 688 people under 65 years, to one in 14 people over 65 years, one in six over 80 years and one in three over 90 years.

Recent research suggests the proportion of people living with dementia has decreased by 20 per cent over the past two decades, linked mainly to reduction in male smoking, leading healthier lives and a reduction of cardiovascular risks.

General symptoms

Dementia is neurodegenerative, so there is gradual onset, often noticed at times of stress or change (e.g. when admitted to hospital with an infection or when there is a change in environment). The presentation of symptoms is influenced by pre-morbid personality. Early symptoms include:



Reflection exercise 1

Would you be able to create a list of referral or signposting links that are local to you for people with dementia and their families?
 • The Alzheimer's Society website (alzheimers.org.uk) or Dementia Action Alliance (dementiaaction.org.uk/resources) provide useful resources for healthcare professionals and the public.



Table 1: Ten warning signs for Alzheimer's disease

Warning sign of Alzheimer's disease	Signs of normal ageing
Memory loss that disrupts daily life Forgetting recently learned or unable to learn new information. Repeatedly asking for the same information	Sometimes forgetting names or appointments but remembering them later
Challenges in planning or problem solving Find it a challenge to manage finance, follow a plan and take longer to do things	Making occasional errors when balancing a cheque book or household accounts
Difficulty completing familiar tasks at home, work or leisure Getting lost driving to familiar places, struggles with project management at work or remembering the rules of a favourite game	Occasionally needing help with settings on microwave or television
Confusion with time or place Losing track of dates, seasons or passage of time. May forget where they are or how they got there	Getting confused about the day of the week but working it out later
Trouble understanding visual images and spatial relationships This is an early sign and includes trouble reading, judging distance and determining colour or contrast. This may also present as hallucinations. In terms of perception, a sufferer may pass a mirror and think someone else is in the room	Vision changes related to cataracts
New problems with communication Difficulty following or maintaining conversation; problems finding or using the correct word	Sometimes having trouble finding the right word
Misplacing items May put items in unusual places (spectacles in the fridge) and may accuse people of stealing them. Cannot retrace steps to find the item	Occasionally misplacing things like spectacles or TV remote control
Impaired or reduced judgement Make poor decisions often involving money or large donations to telemarketers, for example. Less attention to personal grooming	Making a bad decision occasionally
Withdrawal from work or social activities May have trouble keeping up with favourite activities or remembering how to do them. May withdraw socially because of these changes	Sometimes feeling weary of work, family and social obligations
Changes in mood or personality May become confused, suspicious, depressed, fearful, anxious or even delusional. May be upset easily doing routine tasks when out of their comfort zone	Developing a specific way of doing things and being irritable when a routine is disrupted

Adapted from Alzheimer's Association, 2009 alz.org/alzheimers_disease_10_signs_of_alzheimers.asp

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- Memory loss, especially for recent events
- Difficulties with learning and/or retaining new information
- Being more repetitive or misplacing objects (e.g. car keys or spectacles)
- Having trouble with complex tasks such as cooking, driving or dealing with finances
- Reduced ability to reason and problem-solve
- Impairment of spatial and visuospatial awareness (e.g. bumping into objects; getting lost in a familiar place)
- Language problems: inability to find the right word or difficulty following conversations
- Behavioural changes: more irritable, passive, withdrawn or suspicious.

Diagnosis

There is no definitive laboratory or tissue marker for the diagnosis of any dementia, so diagnosis is one of exclusion requiring a full medical history and multi-faceted assessment to exclude pseudodementias (which account for about 1 per cent of all dementias) as these are the only potentially reversible types of the disease.

Diagnostic assessments include laboratory screening of blood indices and imaging techniques such as computed tomography (CT) scans to exclude space occupying lesions, and magnetic resonance imaging (MRI) and positron emission tomography (PET) scans to establish where brain loss is occurring and its severity.

Psychological scales assess disease severity, cognitive functioning, activities of daily living and problem-solving. A practical toolkit for healthcare professionals for assessing cognitive impairment is available at alzheimers.org.uk/site/scripts/documents_info.php?documentID=2159.

Dependent on findings from imaging, blood markers and, where appropriate, genetic testing, a probable diagnosis can be made. In the United Kingdom, AD accounts for 62 per cent of all cases, vascular dementia (VaD) 17 per cent, mixed AD & VaD 10 per cent, dementia with Lewy bodies 4 per cent and frontotemporal dementia 2 per cent. Rarer dementias (including Parkinson's disease dementia, prion disease and alcohol-related dementia) account for 5 per cent.

Signs and symptoms

Disease progression varies considerably, but broadly falls into four stages:

Early stage: This is often misattributed to stress, bereavement or normal ageing. Signs and symptoms include:

- Mood changes
- Loss of short-term memory
- Confusion, poor judgement, unwillingness to make decisions
- Anxiety, agitation or distress over perceived changes
- Inability to manage everyday tasks.

Moderate stage: This is associated with needing more support for tasks of everyday living, including reminders to eat, wash, dress and use the lavatory. People are increasingly forgetful and may fail to recognise others. Distress, aggression and anger are common, perhaps due to frustration. Risks include wandering and getting lost, leaving taps running or the gas on, inappropriate behaviour, dressing incorrectly, loss of day-night cycle and hallucinations.

Late stage: This includes an inability to recognise familiar objects, surroundings or people – although there can be some flashes of recognition. Increasing physical

frailty means people may start to shuffle or walk unsteadily, eventually becoming confined to bed or a chair. Difficulty eating and sometimes swallowing, weight loss, double incontinence and gradual loss of speech all occur in this late stage.

End-of-life stage: Requires good palliative care services.

Alzheimer's disease

Diagnosis is by clinical and neuropsychological examination and the presence of deficits in at least two areas of cognition with progressive worsening of memory. There is no disturbance of consciousness and an absence of other disorders to account for dementia. Pathophysiological features include neurofibrillary tangles and amyloid plaque deposition.

AD is most likely the sum of external factors (an environmental trigger) plus inherent host factors (genetic predisposition). However, genetic predisposition only accounts for about 5 per cent of all cases and influences, whether AD occurs as early onset (<55 years) or late onset (>65 years). Increasingly, evidence suggests that AD is related to lifestyle choices.

Associated risk and protective factors include:

Increasing age: Age reflects the passage of time, so there is more time for genes to express themselves. This leads to an increasing inability to repair cell damage and/or more time to be exposed to environmental agents that may be involved in the onset of AD

Gender: Studies suggest a slightly higher incidence in women than men, but this may be because women live longer

Genetic predisposition: Specific genes link age at onset, duration and disease severity. Genetic risk is an autosomal dominant inheritance. Each person with an affected gene had one parent with the gene, and the offspring of a person with an affected gene has a 50:50 chance of inheriting the gene. It does not skip generations and men and women are equally affected

Head injury: Deposition of amyloid plaques triggering neurodegeneration

Other risk factors: Epilepsy, herpes zoster/simplex virus, alcohol, smoking, cardiovascular and cerebrovascular disease, older maternal age.

Protective factors include:

Education: Maintaining intellectual functioning and exercise – a healthy cardiovascular system equates to a healthy cerebrovascular system.

Vascular dementia

Vascular dementia (VaD) refers to a group of syndromes where dementia is precipitated by ischaemia or haemorrhage secondary to cerebrovascular disease. VaD usually has sudden onset and then follows a step-wise process (periods of stability followed by sudden decline) as the result of cerebral ischaemic events. There are focal neurological signs and symptoms, and relative preservation of personality. Often there is nocturnal confusion, the presence of depression and patchy cognitive impairment.

VaD is potentially preventable by improving cerebral perfusion and preventing ischaemia by the use of antiplatelets, warfarin or novel anticoagulants, and by controlling underlying hypertension, cardiovascular disease and/or diabetes. Statins have a role in lipid regulation, which may contribute to the pathogenesis of dementia – so they may have a role in reducing incidence of VaD.

Dementia with Lewy bodies

Dementia with Lewy bodies (DLB) typically follows a progressive, fluctuating course and is delirium-like, with fluctuating periods of confusion and variations in attention and alertness. Visual hallucinations are common, as are Parkinsonian features such as rigidity and bradykinesia with repeated falls. Pathophysiological features include Lewy bodies and the widespread reduction of choline acetyltransferase in the neocortex and dopamine in the caudate nucleus.

Reflection exercise 2

How could you support the carer of a person with dementia to ensure medication is being given appropriately? Would you recommend any memory aides and, if so, which ones and why?



Next month's CPD module...

Home medication reviews for vulnerable older people – the pharmacist's role

Learning scenario 1

John Warner is 58 and retired six months ago from his job as a university lecturer. Although you have dispensed prescriptions for his high blood pressure, you have not met him before. He comes into the pharmacy with his wife, who asks for a word in private. Mr Warner seems pleasant and sociable but you notice his shirt is buttoned incorrectly and his socks do not match. He says he feels completely fine, just a little tired and more forgetful than usual. At this, his wife gets rather upset and says that he is not just forgetful anymore, but a danger to himself. He took their two dogs for a walk yesterday to the local park but could not remember his way home. When you ask Mr Warner about this he admits it has been getting worse for some years and was one of the reasons he took early retirement. He had put this down to work-related stress but admits things are getting worse, not better. He wants to know if this is just old age or whether he might have something worse, like dementia. What do you suggest the signs and symptoms that Mr Warner has been displaying are likely to be?

- Early onset dementia
- Worsening memory due to old age
- Mild cognitive impairment
- Early signs of a neuro-degenerative process such as dementia

People with DLB exhibit extreme sensitivity to antipsychotics, leading to a three-fold increase in mortality as they exacerbate both motor and cognitive disability. These medications should be avoided completely if possible. If there is an absolute need to use them, they should be started at one-quarter of the usual dose, monitored carefully and withdrawn as soon as possible.

Lewy bodies are also found in the brains of people with Parkinson's disease (PD). Eighty per cent of people with PD will develop PD dementia over time and exhibit the same sensitivity to antipsychotics.

Behavioural and psychological symptoms of dementia

Behaviour changes are in response to disease progression and are associated with the death of brain cells, as well as the frustration at not being able to communicate or remember effectively.

Behavioural and psychological symptoms of dementia (BPSD) occur in 95 per cent of people with dementia and include the expression of delusions, hallucinations, agitation or aggression, depression, anxiety, elation or euphoria, apathy or indifference, disinhibition, irritation or lability, aberrant motor behaviour (wandering), night-time behaviour (sundowning), or a change in eating habits.

Symptom management

People who receive a diagnosis of mild cognitive impairment due to AD (sometimes known as amnesic MCI) will need early support and signposting to information resources for dementia care and also legal guidance; for example, in terms of setting up advance directives and power of attorney.

Evidence suggests that reducing and/or treating cardiovascular and cerebrovascular risks appropriately, eating healthily, exercising regularly, being involved in mentally and socially stimulating activities, reducing stress and getting sufficient sleep, all reduce the risk of and/or delay the onset of dementia. Evidence-based activities include singing,



Learning scenario 2

Mr Barnett rings you one morning in a bit of a state. His wife has fallen again, hit her head and it has been bleeding. After ensuring that Mrs Barnett is conscious and not confused, you ask him to tell you what has happened over the past week or so that may have been causing the falls. You remember that Mrs Barnett was started on donepezil 5mg about two months ago and was also taking digoxin and aspirin for atrial fibrillation. Mr Barnett says that nothing in their routine had really changed, except last week the specialist increased the donepezil dose to 10mg. Mrs Barnett had not fallen before that, he says, but as the medication was still the same, how could it be involved? What would you advise Mr Barnett?

- Continue as normal and see if the falls stop
- If the falls are only happening during the day, change to a night-time dose
- Contact the GP or specialist immediately as the increased dose may be causing a slowed heart rate, which is leading to the falls
- Contact the prescriber and ask that his wife be switched to memantine

 **Answers on page vi**

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learning a new language, dancing, gardening, group exercise (walking, swimming, playing table tennis), completing jigsaws, crosswords, mind exercises and also listening to music.

Therapeutic treatment of the dementias

NICE Technology Appraisal (TA) 217 states that three licensed acetylcholinesterase inhibitors (AChEIs) – donepezil, rivastigmine and galantamine – are recommended for mild and moderate AD, and the NMDA-receptor antagonist memantine for managing moderate or severe AD or for people who cannot tolerate AChEIs.

Acetylcholinesterase inhibitors

These may improve memory significantly but benefits in social relationships, mood, behaviour and activities of daily living outweigh this. Rivastigmine is also licensed for the symptomatic treatment of mild to moderately severe Parkinson's disease dementia. AChEIs are also an option for people with a mixed diagnosis including AD. There are no licensed treatments for any other of the dementias, although HIV-related dementia has been greatly reduced by the use of highly active antiretroviral therapy (HAART).

Side-effects are predominantly cholinergic and include diarrhoea, nausea, possible vomiting and nasal rhinitis. Others include muscle cramps, fatigue, insomnia and dizziness. AChEIs may cause syncope and any falls or faints should be referred immediately.

It is important to note that an individual may experience relatively severe adverse effects with one agent, but not another. Non-response with one does not mean non-response with all, and an alternative should be tried.

The decision when to stop an AChEI is complex, as even when it seems there is no response, there may be a rapid deterioration in mood and behaviour on discontinuation. In these instances, clinical advice is to restart as soon as possible.

In end-stage care, when the process is one of palliation, all medication should be reviewed and withdrawn as appropriate.

Memantine

Studies demonstrate significant improvement in cognition, activities of daily living and global outcomes, and a reduction in agitation with memantine. Common adverse effects include constipation, hypotension, confusion, dizziness, headache and tiredness. If tiredness is present, evening dosing could be considered to promote sleep.

Other treatments

People with dementia and their families may turn to OTC and herbal supplements to try and prevent and/or delay the onset of dementia. Popular remedies include ginkgo biloba, which increases cerebral blood supply and reduces blood viscosity. Evidence for improvement is inconsistent and it is unknown whether long-term use delays or prevents onset of dementia, but it is safe to use and well-tolerated. There is a theoretical interaction with aspirin or warfarin, and the prescriber should be consulted before use in these circumstances.

Other vitamin or mineral supplements, such as folic acid, vitamin B12 or iron are only effective if there is a deficit. (Deficits are linked to impaired cognition and often referred to as a pseudodementia.) Older people may not eat sufficient fresh green vegetables or dietary protein to sustain normal levels and active transport mechanisms for B12 absorption may be impaired.

Non-pharmacological approaches

Educational programmes for carers (family and support organisations) using behavioural interventions are more effective than most pharmacological treatments in dealing with behavioural and psychological symptoms of dementia.

These include distraction, reality orientation, occupational activities, reminiscence, sensory stimulation, social interaction, as well as exploring any possible underlying causes, such as pain, anxiety, depression, or a recent change or upsetting event.

The management of sundowning (where people can lose a sense of whether it is day or night) is achieved by minimising catnapping during the day (to increase sleep at night), regular exercise, and establishing a day and night routine. Use of bright light (Lux) in the morning can reduce the incidence of agitation in the evening.

Future treatments

Current clinical trials include the re-positioning of licensed medicines, such as antihypertensives (calcium channel blockers) or antidiabetic agents (pioglitazone), as well as exploring the effect of insulin resistance on brain function.

Potential treatments aimed at the prevention and treatment of established dementias include monoclonal antibodies, which aim to reduce cerebral amyloid deposition, and small molecules, which reduce amyloid-beta production, tau aggregation or neuroinflammation.

• *References available from the Editor on request*



Answers: learning scenario 1

- Early onset dementia**
INCORRECT. Early onset dementia is diagnosed in people who are under 55 years of age.
- Worsening memory due to old age**
INCORRECT. Relatively speaking, Mr Warner is still quite young. In addition, in old age, visuospatial awareness (which enables a person to find their way home) is generally intact.
- Mild cognitive impairment**
INCORRECT. There are defects in episodic memory in mild cognitive impairment, but getting lost in familiar places implies more serious cognitive difficulties.
- Early signs of a neurodegenerative process such as dementia**
CORRECT. The behaviour Mr and Mrs Warner describe is related to the short-term memory impairment and changes in visuospatial skills that are seen in the early stages of dementia.



Answers: learning scenario 2

- Continue as normal and see if the falls stop**
INCORRECT. Any fall needs to be investigated as a priority due to the risk of further head trauma or possible fractures.
- If the falls are only happening during the day, change to a night-time dose**
INCORRECT. This is not a solution. Mrs Barnett could still fall if she gets up in the night.
- Contact the GP or specialist immediately as the increased donepezil dose may be causing a slowed heart rate, which is leading to the falls**
CORRECT. Her GP should know about the falls as these may be a result of bradycardia from the donepezil and digoxin causing syncope, which leads to collapse and falls.
- Contact the prescriber and ask that Mrs Barnett is switched to memantine**
INCORRECT. Memantine is not appropriate for mild AD and is only recommended for moderate AD if there is intolerance to all AChEIs.



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