# Early-onset dementia

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There is limited information about the types of neurological disorders found in rural Australian populations and data on the frequency of the dementias, especially in younger adults, are even more limited. This creates difficulties for rural practitioners when faced with a patient who may have a dementing illness.

The problems are amplified when the patient is young (under 65) and when there may be limited access to basic neuroimaging and neuropsychometry to help establish a diagnosis and eliminate other pathologies.

The diagnosis of dementia in a younger adult is often difficult, even for practitioners in the city with access to full diagnostic procedures such as MRI, PET scanning and neuropsychometry.

Early-onset dementia may manifest with a wide range of symptoms but memory loss is the most common.

This type of loss involves short-term memory, in particular episodic memory – the ability to recall events from the previous day. Other symptoms may include speech disturbance, behavioural changes and poor concentration – alone or in combination. Often family or work colleagues voice concern about these changes.

The most common primary types of dementia in younger adults are frontotemporal dementia (FTD) and Alzheimer's disease (AD) (see table, above right). These two types occur about equally, each accounting for about one in five young adults with symptoms of dementia. Psychiatric diagnoses, other pathologies such as tumours, neurological disorders such as Parkinson's disease and healthy people (the worried well), make up the remainder.

Early-onset dementia... a difficult diagnosis.

**Primary diagnoses in early-onset dementia**

- frontotemporal lobar degeneration
- Alzheimer's disease
- mild cognitive impairment
- alcohol-induced dementia
- vascular dementia
- prion diseases
- head injury
- posterior cortical atrophy syndrome
- diffuse Lewy body disease

AD is characterised by atrophy occurring mostly in the mesial temporal lobes, showing neuritic plaques and neurofibrillary tangles. FTD is characterised by atrophy in the frontal lobes, the temporal lobes or both (see next page). The progression of these two conditions is variable. The diagnosis of either will reduce the lifespan of the patient and greatly reduce their quality of life.

Treatment with cholinesterase inhibitors or the glutamate antagonist memantine (Ebixa, Memanxa) can benefit patients with AD, but there are no specific treatments for patients with FTD.

In early-onset dementia, cases of FTD and AD are usually sporadic. Occasionally, cases originate from families affected by genetic mutations and multiple members are affected.

The discovery of a genetic cause of a dementing syndrome has implications for future generations and requires input from genetic services in terms of diagnostic and predictive gene testing.

Non-neurological causes presenting as possible dementia in younger adults include obstructive sleep apnoea, HIV encephalopathy, hypoglycaemia, post-coronary bypass grafting and carbon monoxide poisoning.

## CASE HISTORY

Emily, a 57-year-old psychologist from the mid west of WA, attends because of cognitive and behavioural changes reported by her family. When asked why she is seeing you, she says, "I don't really know", and on direct questioning denies any memory problems.

Emily smokes and has a history of hypertension. Her father developed dementia in his late 70s. She has no past history of psychological or psychiatric problems.

Emily's husband and sister-in-law say there has been a progressive decline in her short-term memory over the past five years. She is repetitive and often unable to describe what she did the previous day. She forgets information within a few minutes and becomes increasingly confused and vague.

Emily is still able to perform acts of daily living, but has difficulty handling money. Her driving has deteriorated and she is no longer able to work. Her only regular medications are antihypertensives. How will you manage Emily?

*Case outcome, page 16*

**HOME TRUTH**

- A normal Mini Mental State Examination (MMSE) does not exclude a dementing illness such as FTD – behavioural changes are often the clue to the correct diagnosis even when the MMSE is normal.

# Secondary causes

Dementia can be secondary to various neurological conditions, including Parkinson's disease, Down syndrome, multiple system atrophy, normal pressure hydrocephalus, cerebral autosomal dominant arteriopathy subcortical infarcts and leukoencephalopathy (CADASIL), multiple sclerosis and vascular disease.

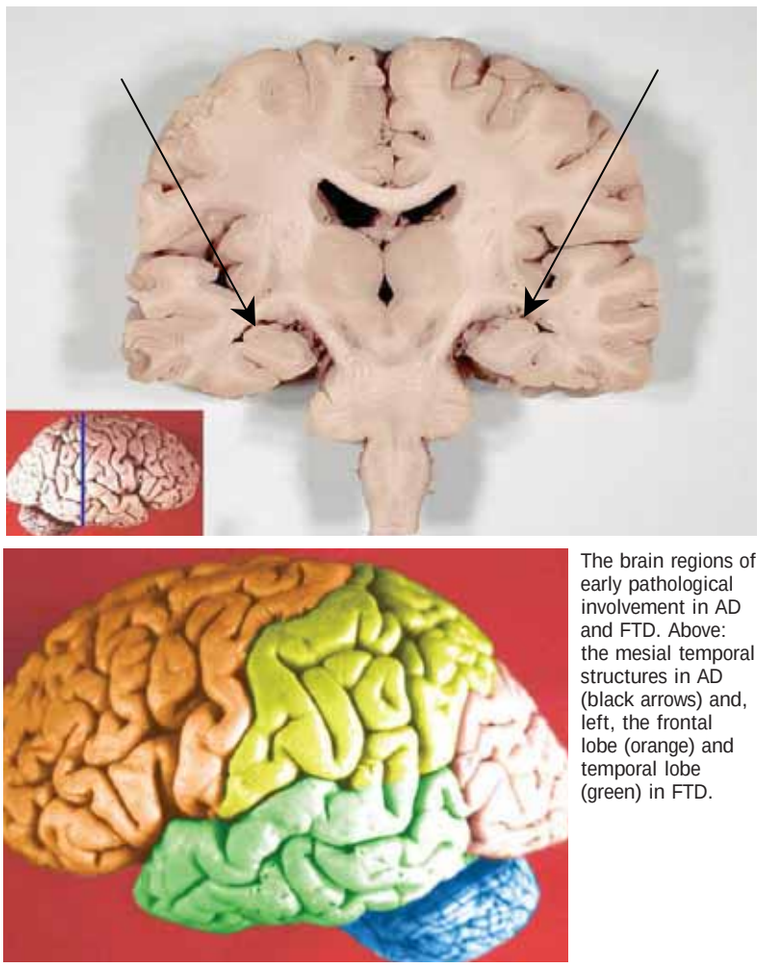
In our experience, diffuse Lewy body disease, which is a combination of Parkinsonian features with dementia, is uncommon under the age of 65. Other factors to consider include the potential effects of alcohol, prion diseases and head injury.

Making the diagnosis in a young adult is made more difficult by the high frequency of psychiatric symptoms and illnesses prompting consideration of a causative dementing illness. For example, patients have been referred to us with severe refractory depression associated with severe memory loss, thought to be caused by co-existent dementia. However, investigations have shown the depression to be a symptom of the dementia, not the cause.

Depression and psychosis can be part of the presentation of early-onset dementia in both AD and FTD. If depression is severe and refractory to treatment, an underlying cause, such as emerging dementia, should be considered.

The absence of a past history of severe depression and an inconsistent premorbid personality for depression further raise the possibility of a pathological cause. In some cases a trial of antidepressant therapy may be reasonable.

A further complication occurs in patients who have been treated with long-term lithium or who have had ECT. They may have atrophy in the frontotemporal regions secondary to treatment and can develop an associated dementing disorder. Other psychiatric disorders to consider are anxiety and post-traumatic stress disorder, both of which may present with memory loss.



The brain regions of early pathological involvement in AD and FTD. Above: the mesial temporal structures in AD (black arrows) and, left, the frontal lobe (orange) and temporal lobe (green) in FTD.

Another factor that contributes to diagnostic difficulty is the false assumption that a normal MMSE excludes dementia. This test has a sensitivity of 52% and a specificity of 96% in the detection of early-onset dementia. The MMSE examination may be normal in a patient with FTD and the diagnosis made through the features of the behavioural syndrome; for example, stereotypic pacing behaviour, frequent standing and sitting, apathy, staring and paucity of speech.

Patients with mild cognitive impairment report memory loss without the loss of other cognitive functions and this may raise the possibility of a dementia. To make a formal diagnosis of this condition, neuropsychometric assessment of memory testing must show an abnormality at least 1.5 SD below normal. Some patients in this category progress to dementia while others remain stable, so long-term follow-up is essential. In situations where a definite diagnosis is difficult, the most powerful diagnostic tool can be the passage of time.

GPs in a rural setting face a challenge when assessing younger adults with the possibility of a dementing illness. In some cases, patients with symptoms of early-onset dementia have been mistakenly told by doctors that dementia does not occur in young adults and diagnosis has been delayed.

If there is any uncertainty, the GP must consider specialty referral to a neurologist with a special interest in the diagnosis of dementia in young adults and with full access to diagnostic imaging and neuro-psychometry.

# Common dementia symptoms

Memory loss is the most common presenting symptom of both AD and FTD. In patients with AD, memory loss is typically episodic. In those with FTD, the loss is short term and non-specific, and probably relates to impaired or reduced attention or concentration.

Patients with FTD often have associated characteristic behavioural disturbances that help make the diagnosis.

For example, they may have a behavioural syndrome characterised by loss of insight, disinhibition, impulsiveness, tactlessness, impaired social judgement, hyperorality (dietary compulsions or consuming inedible products) and hypersexual behaviour, or there may be apathy, depression and obsessive compulsive phenomena. Some patients develop Parkinson's disease-like syndrome and motor neurone disease.

Letting it all go ... people with FTD may have a behavioural syndrome that can include disinhibition and impulsiveness.

Others develop a linguistic disorder known as primary progressive aphasia, which is associated with lobar atrophy in the dominant temporal lobe.

They may have non-fluency of speech or difficulty retrieving single words, with impaired repetition or a variant semantic dementia in which they experience impaired confrontational naming (the inability to correctly name presented objects) with decreased single word comprehension.

Some may have features of progressive supranuclear palsy (supranuclear gaze paresis, with Parkinsonian-like symptoms and frontal lobe dysfunction) or cortico-basal degeneration (alien limb phenomena, apraxia with extrapyramidal features and frontal lobe dysfunction).

Patients with AD can also present with a linguistic disorder characterised by non-fluency of speech and aphasia.

A more unusual presentation in those with posterior cortical atrophy syndrome (a variant of AD) is difficulty with visuospatial function characterised by an inability to recognise objects, or groups of objects, visually.

Sometimes AD patients have a frontal lobe syndrome if the pathology extends into the frontal regions.

# Investigations

Ideally patients presenting with memory loss, behavioural changes or speech disturbance should have a CT scan to exclude brain tumours and cerebrovascular pathology: mesial temporal lobe and frontal lobe atrophy excessive for age supports a diagnosis of dementia.

An MMSE may be useful, but the GP should not be misled by a normal result in the context of behaviour and other changes that may indicate dementia.

An FBE, ESR, CRP, $B_{12}$, red cell folate, thyroid function tests and, if appropriate, VDRL should be arranged. If results are negative but the GP is still concerned by spouse, carer and family reports of cognitive deterioration, the patient should be referred to a neurologist with access to MRI and functional imaging PET scans, which may enhance diagnostic sensitivity and specificity. Neuropsychiatric assessment can help in the diagnosis of dementia and aid in the distinction of mood disturbance and depression from dementia.

If initial tests are negative, but families and carers are still concerned, refer the patient to a neurologist with access to MRI.

# Treatments improve memory

There are no curative treatments for diseases such as FTD and AD.

Memory loss of mild to moderate severity in AD, but not FTD, can be treated with cholinesterase inhibitors, such as donepezil (Aricept), rivastigmine (Exelon) and galantamine (Reminyl) if the patient has an MMSE of >10 and <25.

Generally these drugs improve memory function over a 6-12 month period but do not influence progression of the disease. Treatment should continue if there is a two-point improvement after six months, or if not, another cholinesterase inhibitor should be tried.

In patients with moderate to severe AD and an MMSE of 10-14, memantine can be prescribed.

Medicare Australia has determined that GPs can prescribe this agent provided the diagnosis is confirmed by a neurologist, specialist physician or psychiatrist and the MMSE recorded on the application.

Any co-morbid psychiatric conditions such as depression and psychosis should be managed appropriately.

Medications may not control certain behaviours in patients with FTD, for example, stereotypical motor behaviours such as frequent pacing. These patients may require care in a dementia facility.

## THE GEMS

- Dementia does occur in adults under 65 years of age – unexplained progressive memory loss, speech and behavioural change merit consideration of a dementing illness.
- AD and FTD are the main causes of early-onset dementia.
- Always consider obstructive sleep apnoea as a possible cause of memory loss in a young adult.
- Beware of unexplained depression as a cause of memory loss – it may indicate an emerging dementia.
- Normal structural imaging, such as CT and MRI, does not exclude a dementing disease – neuropsychometry and functional imaging such as PET scanning may be needed.

# Supportive care

The diagnosis of dementia in a younger adult is particularly tragic. The diagnosis has a profound effect on the spouse, often leading to depression, marital disharmony or separation, and sometimes suicidal thoughts.

In some cases, the memory loss or behavioural change can lead to marital separation even before diagnosis, leaving the patient with few emotional and family supports.

The behavioural disturbances associated with FTD often lead to considerable psychosocial stress and affect family dynamics, resulting in relationship difficulties, especially if there are young children.

Consider, for example, the 50-year-old farmer who develops AD or FTD and is no longer able to work to support his family, drive or care for himself, or the teenager, returning home from school, to witness his incontinent father.

The rural doctor is vital in supporting the patient and their family and often rural communities are very helpful, rallying to provide a supportive care network.

Long-term follow-up is essential to manage speech, communication, bulbar function (including swallowing) and behavioural changes.

Patients may need to be in a dementia facility if their behaviour is not manageable at home.

In Geraldton and the mid-west of WA, for example, patients are fortunate to be supported by community neurological nurse specialists who liaise between the patient, spouse, family, GP and neurologist – in this case myself – to help maintain the patients in the community and enhance their quality of life.

Patients may require placement in an appropriate dementia-specific care facility if the behaviours become unmanageable in a home setting.

This might not be available in a country town and can require the patient to travel to the local regional centre or major city.

Alzheimer's Australia provides support services to people with dementia, their family and carers. The National Dementia Helpline (1800 100 500) is a confidential, nationwide service for information and support. Support services and resources for health professionals, patients, families and carers groups can be found on the Alzheimer's Australia website (www.alzheimers.org.au), which has links to state association websites.

## CASE OUTCOME

*From page 13*

When you examine Emily, she believes she is 65 rather than 57 and she is disinhibited and fatuous. Her neurological examination is otherwise normal and assessment of episodic memory (by self-report of what she has done the previous day) is impaired.

You do an MMSE (28 out of 30) and order a CT scan and screening blood tests, all of which are normal. You refer her to a neurologist. A brain MRI shows mild chronic small vessel disease and some involutional change more pronounced in the mesial temporal structures and with non-specific features.

The specialist also arranges a PET scan, which shows a marked reduction in metabolic activity in both parietal and posterior temporal lobes, more pronounced in the left hemisphere with some mild involvement in the frontal lobes – highly suggestive of AD. The EEG is normal.

Note the poor visuospatial construction with numbers in the wrong location and an inability to correctly put the hands at 10 past 11.

Emily's repeat MMSE is 16 out of 30, she has a grossly impaired clock drawing test (see left) and normal depression scale. Neuropsychometry shows global deterioration in all cognitive domains, compatible with an emerging neurodegenerative dementia.

Emily's husband and sister-in-law are counselled and treatment with donepezil 5mg daily is started, increasing to 10mg after one month. Emily is advised to stop smoking. She and her husband are considering involvement in trials of passive immunisation to the Aß peptide implicated in the pathogenesis of Alzheimer's disease.