

Managing Alzheimer's disease the role of the GP

The GP is in a unique position to follow and support patients with Alzheimer's disease and their families from diagnosis to the end stages of the disease, as illustrated by the following case.

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Pre-stage or early dementia

Florence, aged 81 years, is brought in by her daughter, Sue. Since she was widowed two years ago, Florence has lived in a retirement village. Sue reports that Florence has been having increasing trouble over the last six months or more with names of family members, relaying events and recalling places where she has been. Florence can't understand 'what the fuss is about'.

Sue notes an exaggeration of certain personality traits rather than any distinct personality changes. She describes her mother as reasonably bright and 'no more depressed than usual'. Florence denies sleep disturbance. As part of her care package, the retirement village provides Florence with cleaning and her main meals of the day, and her daughter arranges for her shopping

to be delivered. Florence does her own laundry and minor meal preparation and is independent in basic activities of daily living such as attendance to personal hygiene.

Her medical history includes thyroid ablation, caesarean sections, removal of an ovarian cyst, asthma, osteoporosis and falls. Her medications are thyroxine, salmeterol/fluticasone propionate and alendronate. She is a social drinker only. The physical examination is unremarkable. Her Mini Mental State Examination (MMSE) score is 26/30, scoring 1/3 for short term memory and making a mistake on the date and on serial sevens.

Most likely diagnosis

Florence is most likely to be suffering from either a pre-stage of dementia, otherwise known as

IN SUMMARY

- Regular follow up of patients with suspected Alzheimer's disease is advisable because early diagnosis has many advantages.
- In studies, cholinesterase inhibitors have shown modest benefits in cognitive, functional and behavioural domains for patients with Alzheimer's disease and reduced caregiver time and distress.
- A community Aged Care Assessment Team (ACAT) or community dementia nurse can provide many support services to assist the patient and carer.
- In patients with severe dementia, behavioural disorders can respond well to psychosocial approaches such as behaviour modification, music therapy, aromatherapy, exercise and activity programs.
- The best ally in the continuing care of the person with dementia is the family. Remember to attend also to the carer's physical, psychological and social health needs.

mild cognitive impairment and which is characterised by mild memory loss but no functional impairment, or early Alzheimer's disease, the most common cause of dementia. Of those with mild cognitive impairment, 10 to 15% convert to Alzheimer's disease per year, compared with 1 to 2% of normal controls.^{1,2}

Diagnoses to exclude

Systemic and central nervous system conditions known to cause cognitive decline, such as vitamin B₁₂ and folate deficiency, hypercalcaemia, syphilis, hypothyroidism and subdural haematoma, should be excluded. As well as a basic physical examination, the following investigations should be undertaken:

- a full blood count
- an erythrocyte sedimentation rate
- serum electrolyte, urea, creatinine and glucose levels
- liver function tests
- thyroid function tests
- vitamin B₁₂ and folate levels
- a brain CT scan.

Consultation with a geriatrician would help to address the cause and management of the falls and other comorbidities. Psychiatric disorders such as depression must also be excluded because symptoms such as memory loss, apathy, poor concentration and reduced interest or abandonment of activities may mimic dementia. It is also important to note that depression may complicate dementia, particularly in the early stages when there may be insight into the illness and the prospects of future decline.³

What to do at this stage

Mild cognitive impairment is a useful concept to help patients who present with memory loss in the absence of a full dementia syndrome understand their symptoms and attend to risk factors. However, this diagnosis does not have official nosological status and its validity is controversial because some patients improve, some remain stable and only a proportion go on to develop dementia.

Regular follow up of patients with mild cognitive impairment or suspected Alzheimer's disease is advisable because of the advantages of early diagnosis of Alzheimer's disease for both the patient and family, including:

Managing Alzheimer's disease

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In the early stages of dementia the patient needs support and counselling about the diagnosis and advice on how to compensate for deficits and plan for the future.

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- giving the patient time to make informed lifestyle and legal decisions such as enduring power of attorney and enduring guardianship
- allowing early initiation of treatment with acetyl cholinesterase inhibitors (if Alzheimer's disease is diagnosed)
- providing answers to explain symptoms or odd behaviour to families
- warning the patient and family that they should monitor driving and important

continued

Table 1. DSM-IV diagnostic criteria for Alzheimer's disease

A diagnosis of Alzheimer's disease requires memory impairment plus one (or more) of the following cognitive disturbances:

- Aphasia: language disturbance
- Apraxia: impaired ability to carry out motor activities or translate ideas into actions
- Agnosia: failure to recognise or identify objects
- Disturbance in executive functioning: impaired planning, organising, sequencing, abstracting

decision making (e.g. about finances).

Secondary prevention strategies that may be useful in subjects with memory complaints and mild cognitive impairment include attention to cerebrovascular risk factors such as hypertension, diabetes, smoking and hyperlipidaemia. The following general health measures may also reduce the risk of Alzheimer's disease:⁴

- eating more fish
- doing regular physical exercise
- engaging in cognitively stimulating activities
- taking antioxidants such as vitamins E (500 IU per day) and C (500 mg per day)
- taking folate (0.5 mg per day) – this is particularly important if the patient's fasting homocysteine level is high.

The evidence that vitamins E and C reduce the risk of Alzheimer's disease is limited but these vitamins appear to be safe and are relatively cheap. There is one study showing benefit of vitamin E at 1000 IU twice a day for moderate to moderately severe Alzheimer's disease,⁵ and most of the large number of cohort studies indicate that use of vitamins E and C are associated with a lower risk of

Alzheimer's disease. The evidence for the use of *Ginkgo biloba* is also limited.

Mild dementia

About eight months later, Sue reports that Florence seems a little worse. She is getting more lost and forgetful, having more difficulty finding words and recalling the names of things, and is withdrawing socially. She often forgets to do her own laundry, and even when she does do her laundry she becomes confused as to how to use the machine. Sue is now doing her mother's laundry. Florence's MMSE is now 24/30. The previous screening tests were all negative.

Making the diagnosis

The issue of crossing the threshold for the diagnosis of dementia is important because the prescription of disease modifying therapy is contingent upon this. Most of the standardised diagnostic systems used to define dementia rely on the presence of impairment in at least two cognitive domains, accompanied by functional impairment. For example, using DSM-IV criteria,⁶ Florence has now crossed the threshold for diagnosis of Alzheimer's disease (Table 1). Further, these cognitive deficits are now causing significant impairment in social and occupational functioning and represent a significant decline from her previous level of functioning.

The MMSE score is not a diagnosis; it is merely a guide. A MMSE score of 18 to 24 suggests mild dementia, 10 to 17 moderate dementia, and less than 10 severe dementia. These thresholds are very loose as scores on the MMSE vary according to the patient's education and language ability, how it is administered and how the patient feels on the day.

Cholinesterase inhibitors

Florence is eligible for treatment with acetyl cholinesterase inhibitors, three of which are available and subsidised on the Pharmaceutical Benefits Scheme (PBS) in

Australia – donepezil (Aricept), rivastigmine (Exelon) and galantamine (Reminyl) – see Table 2). Numerous clinical trials and independent reviews, including a Cochrane meta-analysis, support the use of cholinesterase inhibitors and show modest benefits for patients in cognitive, functional and behavioural domains and reduced caregiver time and distress.^{7,8} However, the practical efficacy of these drugs remains controversial.

The recent AD2000 donepezil trial confirmed that donepezil produces small improvements in cognition and activities of daily living,⁹ but contrary to a previous open-label study,¹⁰ it did not find any delay in time to nursing home admission. However, there have been methodological criticisms of the AD2000 study.¹¹

A recent meta-analysis examining the efficacy and safety of cholinesterase inhibitors found a modest but significant therapeutic effect (an average of 9% more responders than with placebo) and modestly but significantly higher rates of adverse events (8% in excess of placebo) and discontinuation of treatment.¹²

To be eligible for treatment with cholinesterase inhibitors, Florence's diagnosis must be confirmed by a specialist physician or psychiatrist and she must have a MMSE score of 10 or more. If her score is over 24 she must also have an assessment using the Alzheimer's Disease Assessment Scale (ADAS-COG).

The choice of cholinesterase inhibitor should be dictated by personal experience and patient preference. There are no strong data to show that one has greater efficacy than any other. Donepezil is the only cholinesterase inhibitor with a long enough half-life to be administered once daily and might have some advantages for patients living alone. A once daily dose of galantamine will soon be available.

Contraindications and side effects

Relative contraindications to the use of cholinesterase inhibitors are active peptic

ulceration, bradycardia, bradyarrhythmias such as heart block, left bundle branch block, sick sinus syndrome and asthma. These are not absolute as peptic ulcer can be treated with proton pump inhibitors beforehand. It may be prudent for patients to have a cardiological review before commencing a cholinesterase inhibitor if there is a bradyarrhythmia. Asthma, as in Florence's case, should be monitored.

The most common side effects of these drugs are gastrointestinal, including nausea, anorexia, diarrhoea, vomiting and abdominal pain. Other nonspecific side effects include agitation, headache, muscle cramps, insomnia, incontinence or frequency of urination and defaecation, and vivid nightmares. Most of these side effects are transient and seen in the first week or so of treatment.

Assessing response

The patient's response to treatment is best assessed at around three months when a repeat MMSE must demonstrate a two-point improvement (or four-point decrease on the ADAS-COG) for continued subsidised supply of a cholinesterase inhibitor. If treatment is discontinued due to lack of tolerability or response, a trial of another cholinesterase inhibitor is worthwhile.

Memantine

In 2003, memantine (Ebixa) became the first drug to be approved for the treatment of moderately severe to severe Alzheimer's disease. Its mechanism of action is quite different to the cholinesterase inhibitors: it is an N-methyl-D-aspartate (NMDA) receptor partial antagonist that acts by blocking glutamate

and preventing excitotoxicity, which is a feature of Alzheimer's disease. It is not listed on the PBS. It is generally well tolerated and adverse effects are uncommon. They include agitation, gastrointestinal upset, insomnia, dizziness and headache. It can be given in conjunction with a cholinesterase inhibitor.¹³

Psychosocial issues

Support

The patient needs support and counselling about the diagnosis and advice on how to compensate for deficits and plan for the future. The needs of the carer will alter according to the stage of disease and the nature of the carer's relationship with the patient. Early on, education and information are useful and can be provided by the GP and/or Alzheimer's Australia (see the box on

Table 2. Medications for Alzheimer's disease*

	Donepezil (Aricept)	Rivastigmine (Exelon)	Galantamine (Reminyl)	Memantine (Ebixa)
Mechanism of action	Specific and reversible inhibitor of acetyl cholinesterase	Pseudoirreversible inhibitor of acetyl cholinesterase and butyryl cholinesterase	Reversible inhibitor of acetyl cholinesterase and a modulator of nicotinic receptors	NMDA receptor antagonist
Half-life	70 hours	2 hours in plasma (with a duration of action of 10 hours)	5-6 hours	60-100 hours
Elimination	Renal and hepatic	Renal	Renal and hepatic	Renal
Potential for drug interactions	Low	Low	Low	Low
Presentation	Tablet	Capsule or liquid	Tablet	Tablet or liquid
Dosing frequency and precaution	Once daily	Twice daily, capsule to be taken with food or liquid to reduce gastrointestinal intolerance	Twice daily, to be taken with food to reduce gastrointestinal intolerance	Twice daily, to be taken with a little liquid, with or without food
Starting dose	5 mg daily	1.5 mg twice daily	4 mg twice daily	5 mg in the morning for one week
Titration	Increase after four to six weeks to 10 mg daily	Flexible dose increases at intervals of at least four weeks to 3 mg twice daily, then 4.5 mg twice daily, to a maximum of 6 mg twice daily	Flexible dose increases at intervals of four weeks to 8 mg twice daily, up to a maximum of 12 mg twice daily	Increase by 5 mg weekly to 10 mg twice daily

* Adapted from reference 7.

Patient and carer support

Alzheimer's Australia

Alzheimer's Australia conducts courses for people with early dementia (defined as having insight into their condition) and their supporters – for example, 'Living with memory loss', a seven-week course of three hours per week. Tollfree helpline: 1800 639 331. Website: www.alzheimers.org.au

The National Dementia Behaviour Advisory Service

The National Dementia Behaviour Advisory Service provides 24-hour telephone assistance to informal and professional caregivers. Tollfree helpline: 1300 366 448.

page 20). Feedback about programs offered by Alzheimer's Australia has been overwhelmingly positive.

Legal issues

Provisions need to be made for:

- a will, if one has not already been made
- enduring power of attorney for future management of financial affairs
- enduring guardianship for future decision making with regards to accommodation, services and healthcare
- advance directives with regards to end of life treatment decisions.

If there is any doubt about capacity to execute any of these documents (each of which have separately defined legal criteria for capacity), assessment by a medical practitioner or psychologist with expertise in this area should be sought.

Driving

Driving is a difficult issue but needs to be discussed at this stage. Some patients will voluntarily relinquish their licence or agree to self-restriction once the effects of Alzheimer's disease on driving are

discussed.⁷ Other patients may need assessment at a specialised driving assessment unit or by an occupational therapist. If patients are still working, consideration should be given to the safety of the patient and others.

Moderate dementia

A few years later, Sue describes Florence to be experiencing intermittent paranoid ideation. Florence believes there is a conspiracy involving various village staff members, that she is under surveillance and that someone is interfering with her belongings. She drew these inferences from various sounds, such as footsteps or knocking, and smells, but hasn't heard any voices. She is often preoccupied with these ideas and has devised ways to 'protect herself' (e.g. banging on the walls at night, or showering at certain times). These symptoms distress her and make her angry. Her MMSE score is now 17/30.

Behavioural and psychological symptoms of dementia (BPSD): psychotic symptoms

Emergence of psychotic symptoms may be a manifestation of the dementia *per se* or due to a superimposed delirium, which must be excluded first with an evaluation of the patient's medical state.¹⁴ Common causes of delirium include urinary tract or chest infection, drug toxicity, pain and severe constipation. It is important to note that dementia is the strongest risk factor for delirium¹⁵ and patients may suffer from both.

Psychotic symptoms are a common manifestation of dementia. About 30% of patients with dementia have delusions and about 20% have hallucinations.³ Antipsychotic medication is most effective in treating these symptoms. However, treatment should be reserved for those patients who are distressed by their symptoms or whose symptoms impact on their functional ability.

If psychotropic medications are to be

used, there must be some consideration of the risk–benefit ratio in each patient and discussion with the patient or substitute decision maker. A determination must be made of the patient's capacity to understand the nature and the effect of the treatment and therefore capacity to give consent. If the patient is unable to give consent, it must be sought from the person responsible or equivalent proxy decision maker.

Local and international consensus favour atypical antipsychotics over traditional antipsychotics for dementia-related psychosis and behavioural disturbances not responding to other measures, mainly because of their lower rate of extrapyramidal side effects.¹⁶ Atypical antipsychotics include risperidone (Risperdal, Risperdal Consta), olanzapine (Zyprexa), quetiapine (Seroquel), amisulpride (Solian) and aripiprazole (Abilify).

Of these drugs, risperidone and olanzapine have been best studied for use in the treatment of psychosis and agitation in dementia, with mixed results supporting olanzapine¹⁷ and stronger support for risperidone.¹⁸ The recommended dose for risperidone is 0.5 to 2 mg per day, with a modal dose of 1 mg per day. It has a very low risk of anticholinergic side effects but can cause postural hypotension and extrapyramidal side effects, although to a lesser extent than haloperidol (Serenace) or other traditional antipsychotics. The recommended dose for olanzapine is 2.5 to 10 mg per day. It has a low risk of extrapyramidal effects, but has been associated with diabetes.

In several pooled studies of elderly subjects with cerebrovascular risk factors, risperidone has been associated with adverse cerebrovascular events such as transient ischaemic attack and stroke in 3.4% of patients, compared with 1.2% of patients taking placebo. Similarly, olanzapine has been associated with such events in 1.3% of patients, compared with 0.4% of patients taking placebo.¹⁹ Traditional antipsychotics may also be associated

with an increased risk of cerebrovascular events or death but these have not been investigated in such detail.

Risperidone is the only atypical antipsychotic that has an approved indication for behavioural disturbances in dementia, even though it is not approved on the PBS. All the atypical antipsychotics are listed on the PBS only for schizophrenia; none of them has a PBS authority listing for the treatment of behavioural disturbance or even for dementia-related psychosis.

A placebo-controlled study with haloperidol – which does not require authority – over six weeks showed significant benefit for psychosis and psychomotor agitation at higher doses of 2 to 3 mg per day but not at lower doses of 0.5 to 0.75 mg per day.²⁰ However, a subgroup of patients on the higher dose developed significant extrapyramidal side effects. We recommend a dose range for haloperidol of 0.25 to 2 mg daily (rarely to 3 mg).

Support services

At this point it would be helpful to refer Florence and Sue to the community Aged Care Assessment Team (ACAT) or community dementia nurse who can provide support services – for example, home help, medication monitoring, day centre attendance and community transport.

Carer support

Six months later Sue returns alone and is extremely distressed. Her mother is becoming increasingly difficult to handle and Sue has borne the brunt of both the care and her mother's constant abuse.

Although there have been many calls for GPs to be more proactive in addressing the support needs of carers,²¹ it is often not easy. A continuing supportive relationship with carers can make it easier for them to discuss their distress. Even GPs committed to working with carers can face considerable barriers such as the patient's refusal to allow carer involvement in

consultations and the carer's denial or reluctance to discuss such issues. This is especially the case if the patient is present or the carer perceives the GP to be too busy or very medically focused.²¹

Carers have identified ways in which GPs might ease their burden. These include discussion and, where appropriate, assessment of the carer's own physical, psychological and social health needs, and provision of information and relevant referrals.²¹ It is important to work out what the carer needs: information, practical support (e.g. community nurse visits), emotional support, respite or more involvement from her siblings in sharing care responsibilities (see the box on this page). ACAT approval will be required if respite care is to be considered.

Severe dementia

Florence has deteriorated significantly over the last year or so. Her MMSE score is now 7/30. You have organised respite care in a nursing home. A week into the respite stay you get a call from the nursing home to say Florence attacked a male agency staff member, and the home doubt it can keep her. A behaviour monitoring chart over the last five or six days shows occasional resistance to care, otherwise she has had quite warm interactions with staff, particularly with those with whom she is familiar. She very much likes staff company and enjoys an occasional cup of tea with one particular staff member. Her room in the nursing home is barren and devoid of personal effects.

Troubleshooting family problems

Carers have difficulty understanding the disease

- Use psychoeducational approaches – e.g. information from the GP, literature or Alzheimer's Australia.
- Refer to Alzheimer's Australia.

Carers feel burden and strain

- Provide practical assistance (e.g. local Aged Care Assessment Team input) and respite.
- Provide psychoeducation as above and counselling from GP or Alzheimer's Australia (offers face-to-face or telephone counselling on an individual or group basis).

One member of the family bears an unequal share of caring

- When this is driven by guilt and the carer's past relationship with the patient, individual therapy for the carer may be warranted.
- When this is a manifestation of longstanding family dynamics, family meetings or formal family therapy may be warranted to promote understanding between family members and encourage more even distribution of care.
- 'The weekend cure', which involves each member of the family caring for the patient for 48 hours, can be very useful.

Conflict between multiple family members about what is 'right' or needed for the patient

- Family therapy and 'The weekend cure' are helpful.

Elder abuse or financial exploitation

- Contact the Police or Guardianship Tribunal (or equivalent State tribunal for appointing proxy decision makers).

Consultant's comment

The recent death of as public a figure as the former US President Ronald Reagan from Alzheimer's disease some 10 years after diagnosis highlights the profound significance of dementia for sufferers and their families.

Demographic research reveals that the risk of Alzheimer's disease doubles every 5.1 years after the age of 60 years, with a prevalence rate of 0.7% at 60, rising to 23.6% by the age of 85 and older.

The number of elderly people (older than 65 years) will increase from 2.1 million in 1995 to 5.72 million by 2041 with a projected 254% increase in dementia sufferers from 130,000 to 459,000 during that 45-year period. This rapid increase in the number of people with dementia will pose particular challenges to the Australian community and the medical profession in particular in terms of how best we manage and care for this very disabled sector of our community.

Dementia comes with a very high price tag not only for the sufferers but also the families entrusted with their care. It was estimated in 2002 that dementia resulted in a loss of some 117,000 years of healthy life at a total aggregated cost to the community of \$3.2 billion – a figure that will double by 2010.

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BPSD: aggression

Consider first what is the cause of this aggression. Once a medical illness or delirium is excluded by examination and investigations, consider nonpharmacological approaches to the problem. Despite methodological weaknesses in many studies of psychosocial approaches to behaviour disorders of dementia, there is good evidence to support the efficacy of the following measures:²²

- behaviour modification, which is useful with undesirable behaviours such as aggression and screaming
- music therapy (especially if choice of music is individualised to the person's taste)
- aromatherapy with specific oils – lavender oil (*Lavendula officinalis*) and lemon balm (*Melissa officinalis*)²³
- bright light therapy
- person-centred care, including dementia care mapping
- exercise
- simulated presence (use of a tape recording of a loved one when the

person is agitated)

- changes to the physical environment
- activity programs.

Nonspecific measures are also quite effective: for example, giving the person attention, showing physical affection, structuring social programs and encouraging staff to communicate respectfully. Programs that focus on providing staff with training or support have benefits in reducing levels of agitation in residential settings. Family carers can also be taught techniques to prevent or reduce behavioural disturbances. There is good evidence that family carers can be trained to be therapists for the person with dementia and reduce rates and levels of depression.

In this case, it is likely that Florence is bored and feels isolated in an unfamiliar environment. She may hit out because she is frightened or because she does not understand staff requests for co-operation with activities of daily living. Consider environmental changes such as asking the daughter to bring in personal

effects and photos and create a portfolio of photos and familiar objects that her mother can bring with her on every respite admission. Similarly, an audiotape tape of Florence's preferred music or videotapes prepared by the family, or of Sue talking to her as if on a telephone call (simulated presence) may be helpful during times of agitation.

Try to access diversional therapy while Florence is in respite. If this is not available, consider volunteer companionship to provide activities, stimulation and familiar company during Florence's stay. The clue from the behaviour chart is that she responds to familiar faces. Sometimes it is helpful if one or two staff members with whom the patient is familiar do very brief regular checks or greetings and if possible to show a familiar face at the beginning of any care activity that the patient finds difficult. If possible, ask for an assessment by a behavioural psychologist.

If the aggressive behaviours continue despite nonpharmacological approaches and they present a risk to the patient or others or compromise the patient's care, pharmacological options such as anti-psychotic agents or selective serotonin reuptake inhibitors can be trialled.¹⁴

Conclusion

Dementia is a disease of long duration, lasting an average of 10 years from onset of first symptoms to death. The GP is uniquely placed to provide the continuing support for the long haul in partnership with the patient, the family, other health providers and Alzheimer's Australia. Modestly effective medications are now available, and while these offer hope to patients and family, it is important that everyone realises they are not cures.

The long term management of dementia is a challenge that, when met, can be very rewarding. **MT**

A list of references is available on request to the editorial office.

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