Dementia with Lewy bodies

a common disorder easily missed

Dementia with Lewy bodies, a recently recognised and often partially remediable disorder, may be responsible for 15 to 25% of dementia presentations.

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Because the nature and clinical features of dementia with Lewy bodies (DLB) have relatively recently been understood and delineated, many general practitioners may have difficulty recognising the condition. Yet it is probably the cause of 15 to 25% of dementia presentations, particularly those associated with challenging behaviour, visual hallucinations, delirium, psychosis or any combination of these. DLB may respond, sometimes dramatically, to the cholinesterase inhibitor drugs that were originally developed as a treatment for Alzheimer's disease. When patients who have DLB are given antipsychotic drugs, particularly the older 'typical' antipsychotic drugs, they are at high risk of developing severe parkinsonian and other extrapyramidal effects as well as confusion and agitation. These effects can contribute to increased mortality.[1] If use of antipsychotic drugs cannot be avoided, an 'atypical' drug is preferred.

This article outlines the clinical features of DLB and provides some practical advice about diagnosis and management of the disorder as well as a general diagnostic approach to hallucinations, illusions, delusions, psychosis and delirium affecting an older person. An historical note and information about the underlying pathology of DLB are also provided.

Recognition and diagnosis

Features of DLB (listed in the box on page 20) are based on the criteria developed by an international consensus group, and published in 2005.[2] The criteria represent those that might be used for research. A clinical diagnosis of DLB may allow more liberal criteria, at least in terms of a category of 'suspected DLB'. Considering the potential response to cholinesterase inhibitors, and also the potential adverse response to antipsychotic drugs, use of a clinical category of 'suspected DLB' with an even lower threshold to diagnosis can, in my opinion, be justified.

There are of course many other causes of

IN SUMMARY

- **Dementia with Lewy bodies (DLB) is a relatively common disorder that may present as mild cognitive impairment, established dementia, visual hallucinations, delirium, psychosis or combinations of these.**
- **Symptoms of the disorder may respond, sometimes dramatically, to the cholinesterase inhibitors donepezil, galantamine or rivastigmine.**
- **Antipsychotic drugs may produce severe parkinsonian and other adverse effects in patients with DLB. Risks are lower but still present when the 'atypical' antipsychotic drugs are used.**
- **Clinical features of DLB, relatively recently delineated, are not widely known or recognised.**

functional decline in an older person apart from DLB or other forms of dementia. When an older person presents with possible functional decline a careful history, appropriate examination and investigations should be carried out, looking for other conditions including depression, anaemia, infections, neoplasms, organ failure, hyper- or hypocalcaemia, hyper- or hypothyroidism, thiamine, folate or vitamin B_{12} deficiency, and delirium from any cause.

Common clinical features

Dementia

As community awareness of disorders that cause dementia increases, patients often present with various forms of mild cognitive impairment, the impairment often being insufficient to justify a diagnosis of dementia.

In addition, many definitions of dementia include the requirement that memory impairment (impaired ability to learn new information or to recall previously learned information) be present.[3] In DLB memory is often relatively preserved early in the course of the illness. The DLB Consortium defines dementia in general terms as a 'progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function'. This allows for a diagnosis of DLB even without major evidence of memory impairment.

In assessing for possible dementia, it is useful to pay particular attention to the history from patients and their family or friends. A history of a deterioration in function, particularly if this has been over a period of a year or more, may suggest one of the 'dementias'. The anecdotes told by the patient, family and friends often provide more reliable indications of the type of cognitive problems associated with DLB than does formal cognitive function testing. When testing a patient with DLB, the relative retention of memory functions can mislead clinicians. The patient often has deficits on tests of attention, executive functions and visuospatial ability and may be described as, and observed to be, muddled or confused rather than forgetful.

The term 'executive functions' refers to various brain functions particularly associated with the prefrontal cerebral cortex and its connections – the 'frontal networks'. The term 'executive' is used in the sense of the ability to 'execute' or carry out complex functions, particularly those that are novel and require an integration of thought with experience, emotion and motivation. One author states that damage to prefrontal networks 'impairs mental flexibility, reasoning, hypothesis formation, abstract thinking, foresight, judgment, the online (attentive) holding of information and the ability to inhibit inappropriate responses'.[4]

The widely used Folstein or Standardised Mini-Mental State Examination (MMSE or SMMSE) is insensitive to the abnormalities associated with DLB. I usually use both the 'serial sevens' item and the 'world backwards' items in the MMSE and record the higher of these scores in the total score. The serial sevens item is more sensitive to impairment of executive functions, particularly if it is extended beyond the obligatory five numbers. I usually add a clock drawing test and also ask the patient to copy a drawing of a cube (see the case

Dementia with Lewy bodies

Visual hallucinations in dementia with Lewy bodies are usually recurrent, vivid, often of humans or creatures, and sometimes of repetitive patterns or series of objects that may also include people or creatures. The humans or creatures may be small ('Lilliputian'). Patients are seldom frightened but usually disinterested, amused or entertained by these extraordinary experiences.

TOMEK SIKORA/STONE/GETTY IMAGES

continued

Dementia with Lewy bodies (DLB)*

1. Central features

(Essential for a diagnosis of **possible** or **probable DLB**)

- Dementia (see article for discussion of definition)
- Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression
- Deficits on tests of attention, executive function, and visuospatial ability may be especially prominent

2. Core features

(Two core features are sufficient for a diagnosis of **probable DLB**, one for **possible DLB**)

- Fluctuating cognition with pronounced variations in attention and alertness
- Recurrent visual hallucinations that are typically well formed and detailed
- Spontaneous features of parkinsonism

3. Suggestive features

(If one or more of these is present in the presence of one or more core features, a diagnosis of **probable DLB** can be made. In the absence of any core features, one or more suggestive features is sufficient for **possible DLB**. Probable DLB should not be diagnosed on the basis of suggestive features alone)

- REM sleep behaviour disorder
- Severe antipsychotic (neuroleptic) sensitivity
- Low dopamine transporter uptake in basal ganglia (SPECT or PET)

4. Supportive features

(Commonly present with DLB but not proven to have diagnostic specificity)

- Repeated falls and syncope
- Transient, unexplained loss of consciousness
- Severe autonomic dysfunction (e.g. orthostatic hypotension, urinary incontinence)
- Hallucinations in other modalities
- Systematised delusions
- Depression
- Relative preservation of medial temporal lobe structures on CT/MRI
- Generalised low uptake on SPECT/PET perfusion scan with reduced occipital activity
- Abnormal (low uptake) MIBG myocardial scintigraphy
- Prominent slow wave activity on EEG with temporal lobe transient sharp waves

5. A diagnosis of DLB is *less likely*

- In the presence of cerebrovascular disease evident as focal neurological signs or on brain imaging
- In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
- If parkinsonism only appears for the first time at a stage of severe dementia

6. Temporal sequence of symptoms

- When dementia precedes (by 12 months or less) or occurs concurrently with parkinsonism, then consider diagnosis of DLB
- Dementia occurring in well-established Parkinson's disease leads to a diagnosis of Parkinson's disease dementia (PDD)
- Generic terms such as 'Lewy body disease' are useful clinically for either DLB or Parkinson's disease dementia

* Based on the Dementia in Lewy Bodies (DLB) Consortium's revised criteria for the clinical diagnosis of dementia with Lewy bodies (McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB consortium. Neurology 2005; 65: 1863-1872).[2]

study on page 23), as these are more likely than the standard MMSE to pick up problems in attention, executive functions and visuospatial ability. For the clock drawing test I provide a large circle to the patient. Most versions of the test require the patient to draw his or her own circle. Since many patients (particularly those with micrographia associated with DLB) draw a small circle, it is then difficult to assess their placement of figures on the resultant clock face. Other 'bedside' tests are available.[5]

Fluctuations in functional ability

Characteristic variations in attention and alertness in DLB are often associated with marked fluctuation in functional ability. This can contribute to a great variation in opinions about cognitive impairment among family members, professional carers and health professionals, including doctors. The fluctuations in arousal and attention may be so marked that the patient becomes stuporose or unconscious at times, leading to differential diagnoses of epilepsy, syncope or transient ischaemic attacks. Late afternoon spiking of symptoms ('sundowning') is probably more often seen in DLB than in other causes of dementia, and is probably related to the same vulnerability to fluctuating attention and arousal.

Visual hallucinations

In DLB, visual hallucinations are recurrent, vivid and realistic perceptions, seldom frightening, often of humans (particularly children) and creatures (including insects and other animals), and sometimes of repetitive patterns or series of objects that may again include people or animals. The entities usually do not speak or make a sound and usually disappear when approached. Although usually disinterested, amused or entertained by the hallucinations, some patients can be distressed by them. Often the distinction between an hallucination and an illusion may not be clear. Both occur in DLB.

Similar hallucinations and illusions can occur in association with the following.

- Dopaminergic drugs in Parkinson's disease. Their presence may predict later Parkinson's disease dementia.
- Vascular pathology.[6] However, the diagnosis of DLB should not be dismissed too easily because of the presence of vascular disease (see the case study on this page). The combination of Lewy body pathology in the limbic system and other pathology (sometimes vascular) in the 'ventral visual stream' from the occipital cortex may be the key to the visual hallucinations in patients with DLB.[7]
- Visual impairment – the Charles Bonnet syndrome. In 1760 Charles Bonnet described vivid, complex visual hallucinations associated with visual impairment but no mental illness. However, a dual diagnosis of Charles Bonnet syndrome and DLB does occur.[8]
- Delirium.

Spontaneous parkinsonism

Lewy body pathology is common to Parkinson's disease and DLB, the difference being mainly in the areas of the brain that are most affected and when these areas are affected in the course of the illnesses. Parkinsonian features (parkinsonism) are often, but not always, present in DLB. Tremor at rest is not a common feature of parkinsonism in DLB, whereas postural instability, gait difficulty and facial immobility are more likely. Treatment with dopaminergic drugs may be less effective in DLB than in Parkinson's disease and may trigger delirium, hallucinations and deterioration in function.

Contrary to many clinicians' beliefs, spontaneous parkinsonism is not required for a diagnosis of DLB. In the 2005 consensus statement (see the box on page 20), one of the three core features of DLB is 'spontaneous (not antipsychotic drug-induced) features of parkinsonism'. The 2005 consensus criteria, by allowing several 'suggestive features' to have greater diagnostic weight than in the earlier (1996) statement, give less relative diagnostic weight to spontaneous parkinsonism.

Case study. Mr LB

Mr LB had evidence of a fluctuating but progressive cognitive deterioration, relatively preserved memory function (2/3 on recall item, MMSE 20/30), vascular cerebral pathology previously thought to be the only cause of his problems, previous postoperative delirium and recurrent visual hallucinations. He described seeing 'little gremlins...more like a stick or insect...they literally took the next door house apart, then brushed it with a feather and put it together again...they wrecked my flower garden then put it back the next day...I hit one with a half-brick but then there was nothing there...they can go into the ground and disappear...sometimes 1 inch high jellyfish follow me around the house and yard'. He had dug up pavers and thrown half bricks to eradicate the creatures.

A previous trial of 1.25 mg olanzapine daily had resulted in drowsiness and little positive response. There was also little response to 8 mg galantamine daily, but with 16 mg/day the hallucinations ceased and function improved (MMSE 27/30). Two years later Mr LB moved from home to residential care.

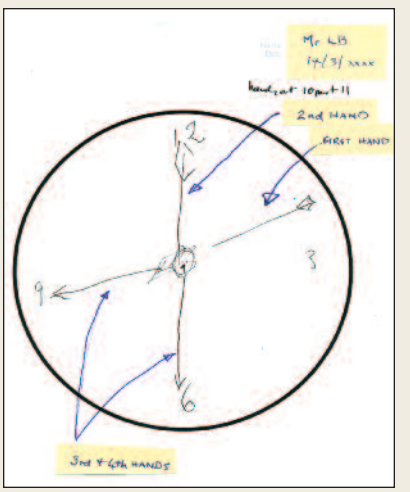


Figure A. Mr LB was asked to draw a clock. He placed the 12, 3, 6 and 9 well and when asked to place the hands at '10 past 11' correctly placed the minute hand but then, possibly distracted by the other figures, drew three more hands. This suggests perseveration – the tendency to continue with a particular action or thought despite it being inappropriate to the context, which in turn suggests poor executive function.

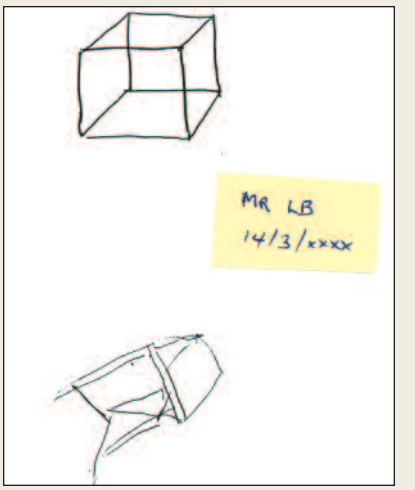


Figure B. Mr LB was asked to copy the drawing of the cube (Mr LB's attempt is the lower drawing). His drawing of the cube is disorganised and he has drawn double lines unnecessarily (perseveration?). His difficulties may be the result of impairment of visuospatial or executive functions.

Rapid eye movement (REM) sleep behaviour disorder

REM sleep behaviour disorder is due to incomplete motor inhibition during REM sleep and is associated with agitated, sometimes violent behaviour during sleep –

acting out of dreams. The disorder can be confirmed by a sleep study, although a patient with DLB may not be able to tolerate such a study. The patient, after an episode of REM sleep behaviour disorder, may recall a vivid dream and may have difficulty distinguishing this from reality. General sleep disturbances, common in DLB, and sometimes REM sleep behaviour disorder, may respond to the cholinesterase inhibitors. If this fails, a small dose of clonazepam (Paxam, Rivotril), if not otherwise contraindicated, can be effective.

Other psychotic phenomena, anxiety and depression

Although hallucinations are usually visual in DLB, hallucinations in other modalities can occur. Delusions can also occur, often secondary to the visual hallucinations or REM sleep behaviour disorder. Depression and anxiety can occur in association with any cause of dementia including DLB. Even when other diagnoses such as paraphrenia (late onset schizophrenia, schizophrenia-like psychosis, delusional disorder) or psychotic depression appear to be primary, consideration can be given to the possibility of underlying DLB.

Delirium

The association of delirium with DLB is not listed by the consensus group[2] but has been noted often to be the first sign of DLB.[9] The term 'delirium' has mostly replaced other terms such as 'acute brain syndrome', 'acute confusional state', 'confusional state' and 'acute encephalopathy'. Delirium in association with DLB can be precipitated by minor illnesses and anaesthetics and can be more prolonged and severe than expected, considering the immediate cause. Many older patients presenting with delirium will subsequently be found to have dementia.[10]

The association of delirium with DLB and the dangers of traditional antipsychotic drugs in DLB need to be more widely appreciated, particularly in general hospital settings. On the other hand, antipsychotic drugs are often dramatically effective in delirium and if clinically indicated should not be withheld from old people experiencing this disorder. Much lower dosages than usual and the possibility of using an atypical antipsychotic need to be considered.

Parkinson's disease dementia

Parkinson's disease dementia and DLB are related but different entities. The incidence of dementia in patients with Parkinson's disease may be as high as six times that of age-matched controls, but it usually occurs late in the disorder.[11] The associated pathology is variable, including cortical, limbic and hippocampal Lewy body disease and Alzheimer's disease. If Parkinson's disease precedes dementia this is, by convention, called Parkinson's disease dementia (PDD). However, if dementia precedes Parkinson's disease by more than 12 months, this is called DLB.

Clinical management of Parkinson's disease dementia is often difficult and functional deterioration more rapid than in Parkinson's disease without dementia. The pattern of cognitive deficits is often similar to that of DLB, with prominent fluctuation, relatively retained memory function and impaired executive functions. These features can lead to the clinician missing the diagnosis or its functional significance. Major difficulties may occur with medication compliance and other competence, autonomy and behavioural issues (e.g. driving, management of finances, living alone, hedonistic homeostatic dysregulation[12]). The motor features in Parkinson's disease dementia are often of the 'akinetic/rigid' type with less prominent tremor. Dopaminergic drugs may be less effective in controlling these features and more likely to produce adverse effects.

Hallucinations, illusions, delusions affecting an older person

As mentioned earlier, a number of conditions apart from DLB can cause hallucinations, illusions or delusions in an older person. These other conditions include delirium, late onset schizophrenia, schizophrenia-like psychosis, psychotic depression, manic psychosis and Charles Bonnet syndrome. Each of these conditions can benefit from treatment and management in its own right. Some of these conditions can be secondary to DLB and this may be apparent after treatment for the presenting condition and/or on the basis of the history. The flowchart on page 25 may assist in conceptualising the diagnostic process in such a clinical situation.

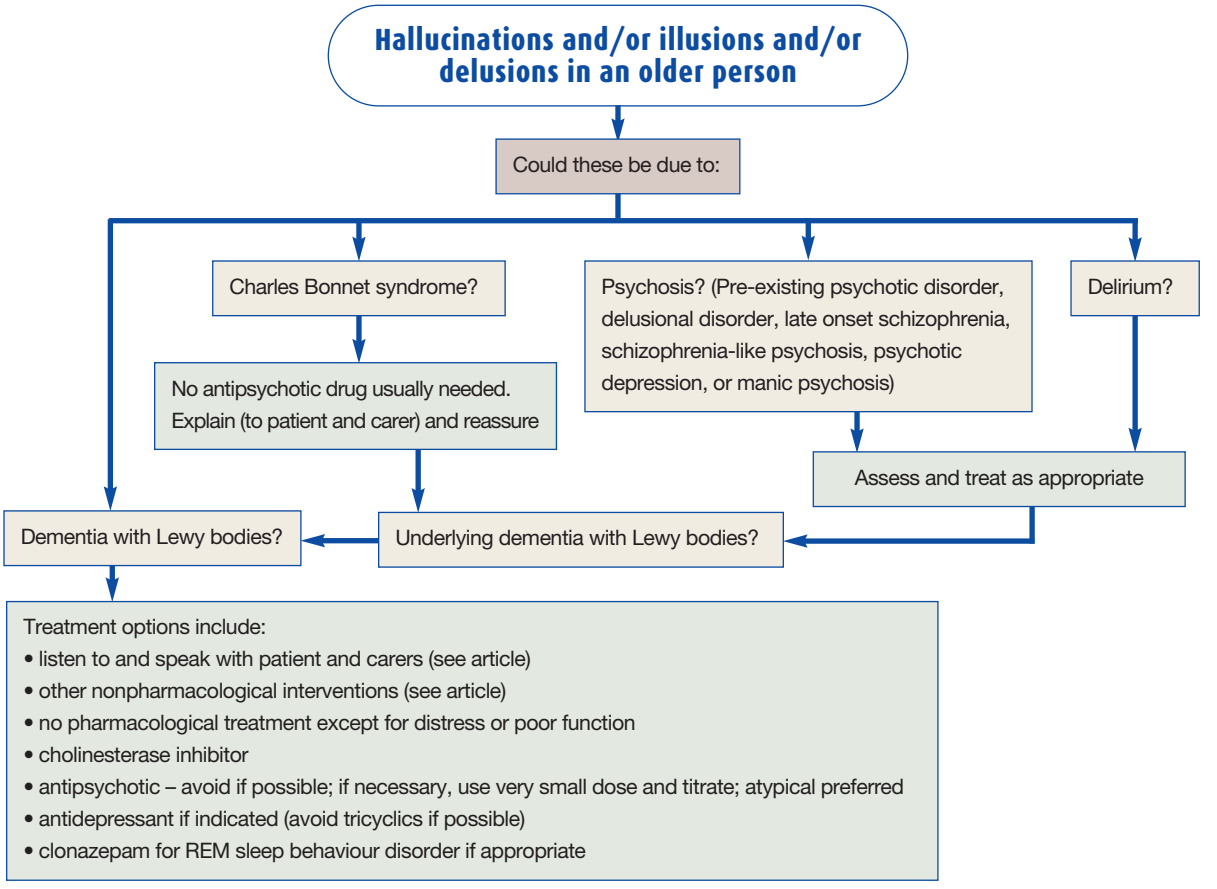
Treatment of DLB

Cholinesterase inhibitors

The cholinesterase inhibitors (ChEI, also called acetylcholinesterase inhibitors – AChEI) donepezil (Aricept), galantamine (Reminyl) and rivastigmine (Exelon) were developed for the treatment of Alzheimer's disease but have been shown in some small studies and case reports often to be beneficial in DLB, more so than in Alzheimer's disease.[13,14] Reviews of recent evidence are available in the 2005 consensus statement[2] and several other reviews.[15,16] When these drugs are given, the patient's carers and sometimes the patient themselves often report significant and encouraging improvement in general function, return to activities previously abandoned, reduction in apathy, reduction in visual hallucinations or their prominence, all with little improvement in forgetfulness (see the case study on page 26). Challenging behaviour associated with hallucinations may also respond to cholinesterase inhibitors. Depression may also be reduced, although it is difficult in practice to separate the effects on depression from improved initiative and increased confidence. However, it must be said that some patients with apparent DLB gain little or no benefit from cholinesterase inhibitors.

As is apparent in the account of Mr LB (see the case study on page 23), improvement of function may not be apparent until the maximum tolerated dose is attained.

A diagnostic approach to hallucinations, illusions, delusions affecting older people



Cholinesterase inhibitors are symptomatic treatments only and there is no convincing evidence of disease-modifying effects. Their use in dementia is essentially palliative, sometimes easing distress and improving or maintaining function for as long as possible before inevitable decline.

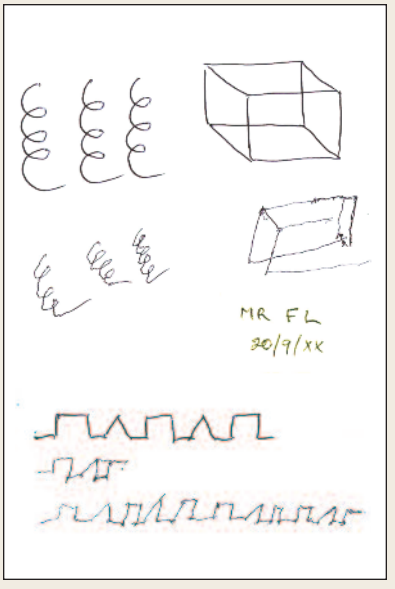
When prescribing cholinesterase inhibitors, it is important to consider the potential adverse effects, which include prominent gastrointestinal effects (e.g. anorexia, nausea, vomiting or diarrhoea).[17] Gastrointestinal effects are less likely to occur if drug dosages are increased at one month intervals rather than more quickly. Other possible adverse effects include agitation, insomnia, vivid dreams, asthma, excess lachrymation, rhinorrhoea, bradyarrhythmias, muscle cramps and dizziness. Cardiac slowing and associated conduction effects can occur. Therefore it is wise to obtain an electrocardiogram before the patient starts taking the drug. The presence of sinoatrial or atrioventricular dysfunction including sick sinus syndrome are relative contraindications to the use of cholinesterase inhibitors. Other medications taken by the patient may contribute additively to bradycardia or conduction defects.

There have been reports of worsening tremor, motor and other functions when cholinesterase inhibitors were given to patients with Parkinson's disease but this is not usual, particularly at lower doses.[2,18] Excess lachrymation, rhinorrhoea and excess salivation triggered or worsened by these drugs is more likely in patients with DLB and Parkinson's disease dementia than in those with other causes of dementia. An increased risk of postural hypotension, falls and syncope in patients with DLB and Parkinson's disease dementia taking cholinesterase inhibitors has also been reported.[19] The risk–benefit case for prescribing these drugs for Parkinson's disease dementia is weaker than for DLB.

DLB is not an indication for cholinesterase inhibitors approved by the Australian Therapeutic Goods Administration (TGA). The TGA-approved indication for cholinesterase inhibitors has until recently been 'mild to moderately severe Alzheimer's disease'. Donepezil is now

Case study. Mr FL: cognitive assessment and daughter's letter

Figures A and B (below). Mr FL's cognitive assessment, conducted on 30 September. Mr FL's drawing of a clock shows a slight tendency to bunch the figures together (probably poor planning and regulation). He also drew a single hand when asked to place the hands at '10 past 11'. His attempts to copy drawings of a cube, three spirals and an alternating pattern are also illustrated. Note the intention tremor apparent in the spirals and that one spiral has an extra loop. This suggests perseveration (uncontrollable repetition of a particular response and difficulty changing set). Perseveration is also apparent in the alternating pattern. These abnormalities could be interpreted as being due to visuospatial and/or frontal executive abnormalities.



The letter below from Mr FL's daughter illustrates the dramatic changes that can follow treatment with cholinesterase inhibitors in DLB. Often the patient or relative's account provides better evidence of functional decline (and improvement) than tests such as the MMSE.

9 December, xxxx

Dear Dr Williams,

I would like to have the following personal observations placed on record for my father in relation to the Reminyl that you have prescribed for him.

My father's medical records show that since June this year he has suffered from severe psychotic episodes, depression, paranoia, chronic fatigue and sleepiness, as well as confusion and a range of other symptoms including walking difficulties, tremors and a shuffling gait, indicative of dementia, diagnosed tentatively as a combination of vascular dementia and Lewy Body dementia

Before he started taking Reminyl my father had deteriorated to the point where he was regularly experiencing both auditory and visual hallucinations. He was incapable of going shopping by himself or remembering what he needed to buy. He was also no longer able to cook for himself. He slept almost all day, had great difficulty hearing anyone and anything even though his hearing aid was working well. When I rang him, he would hang up because he could not hear anything and assumed it was a nuisance caller. When I called on him, his house was dark and shuttered even at 1 o'clock in the afternoon, and he would invariably still be lying in bed. The day I visited him to tell him that his ECG results indicated that he could start on the Reminyl, he was severely depressed to the point where I was concerned that he was getting suicidal thoughts.

On 6 October my father started taking 8 mg of Reminyl. Within a week his health turned around completely. His hearing improved. He no longer felt chronically tired and was no longer sleeping all day. The auditory hallucinations (that he calls "messages") stopped and he was able once more to go shopping by himself. He started working in the garden again and started to cook again.

In response to your suggestion that a higher dose of Reminyl might see even greater improvements in his health, my father started taking a 16 mg dose of Reminyl on 10 November. This did not agree with him so well. After about a week he experienced a painful heaviness in his legs, felt tired but agitated and developed quite a severe tremor in his hands.

It is possible that this higher dose was too much for him, given that he had been skipping his daily dose in the two weeks before he started on the higher dose. Alternatively, the problem may have lain in the fact that he was taking the Reminyl at the same time as the Lanoxin. Given that both medications slow down the heart rate, I wonder whether this was a factor in his bad reaction to the higher dose. In response to this bad reaction after trying the 16 mg dosage for a week, I suggested he cut back to 8 mg of Reminyl, and that he take the Lanoxin in the evening so that he wasn't compounding the effects of the Reminyl and Lanoxin.

Since changing to this new regime on 24 November, his condition has stabilised and he has improved in numerous ways. His hearing is much better; the messages have stopped; his memory has improved; he is no longer so tired and depressed that he wants to sleep all day; he is once more active in the kitchen and garden; and is independent enough to go shopping and to the bank by himself. I am amazed at the difference that this medication has made to the quality of my father's life in such a short time, and look forward to ongoing stabilisation and other improvements in his life skills and independence.

Yours sincerely,

xxxxxxxxxxx

TGA approved for severe Alzheimer's disease. Nevertheless, behavioural problems and hallucinations affecting patients with apparent severe dementia may respond to cholinesterase inhibitors.

Similarly, the Pharmaceutical Benefits Scheme (PBS)-approved indication for cholinesterase inhibitors is for mild to moderately severe Alzheimer's disease (MMSE 10/30 or more) not for DLB. However, postmortem studies of patients who have documented clinical Lewy body disease mostly show coexisting Alzheimer's disease pathology.[2] Many patients with probable DLB clinically also fulfil the criteria for a clinical diagnosis of Alzheimer's disease.

An added level of difficulty within the PBS for the GP prescriber is that the diagnosis of mild to moderately severe Alzheimer's disease has to be confirmed by a 'specialist/consultant physician' (e.g. a geriatrician, neurologist or psychiatrist). The PBS Authority protocol is relatively complicated, including the need to demonstrate improvement using specific criteria within the first six months of treatment. The GP prescriber, particularly in rural, regional and outer metropolitan areas, may have limited access to specialists who have experience both with these drugs and with DLB.

Memantine

Memantine (Ebixa), an NMDA receptor antagonist, acts in a very different way from the cholinesterase inhibitors. There is some evidence of effectiveness in moderately severe to severe Alzheimer's disease, such that it has obtained TGA approval for this indication. It has also recently been listed on the PBS (authority required) for the treatment of patients with moderately severe Alzheimer's disease (patients with an (S)MMSE of 10-14) as monotherapy. There is very little evidence of its effectiveness in DLB. Some case reports and small series report improvement in some patients and adverse effects in others.[20] It can be given in combination with the cholinesterase inhibitors.

Useful patient and carer resources for dementia

Alzheimer's Australia

Alzheimer's Australia provides information, services and support for all forms of dementia – not only Alzheimer's disease. Among many other items available on its website (www.alzheimers.org.au/) is a summary for patients and their carers of the features of DLB. Details of Alzheimer's Australia's program for those experiencing mild, early dementia ('Living with Memory Loss') can also be obtained through this website. A 24-hour phone 'Helpline' is also available (1800 100 500).

American Academy of Neurology

An article for patients and carers, 'Not all dementia is Alzheimer: Dementia with Lewy bodies', can be downloaded from the American Academy of Neurology's website (www.neurology.org/cgi/content/full/65/12/E26).

Antipsychotics

Antipsychotic drugs, which act by interfering with the actions of the neurotransmitter dopamine, may be given to patients with behavioural and psychological symptoms of dementia (BPSD), hallucinations, illusions, delusions, delirium and psychosis, any of which may be associated with DLB. Frequent adverse effects of these drugs in any patients are parkinsonism and other extrapyramidal disorders (dyskinesia, akathisia, tardive dystonia).

Most patients with DLB have Lewy body pathology in key dopaminergic brain structures and some may have spontaneous parkinsonism. Even if they do not have parkinsonism they may be especially vulnerable to the adverse dopamine blocking effects of these antipsychotic drugs, particularly the D_2-dopamine blocking effects. Patients with DLB may develop very significant and potentially dangerous parkinsonian or other extrapyramidal adverse effects even on low doses of antipsychotic drugs. Parkinsonism may persist for weeks or months, well after the antipsychotic drug has been stopped. Antipsychotic drugs in patients with DLB may also cause increased agitation and deterioration in cognitive function, including delirium.

It may not be possible to avoid using an antipsychotic drug in DLB if cholinesterase inhibitors are ineffective or if more acute symptom or behaviour control is necessary. In such a situation an atypical antipsychotic drug should be considered, rather than a traditional antipsychotic drug (such as haloperidol). The formulations and usual recommended dosages for the antipsychotic drugs have not usually been developed with older adults in mind, and minimal, sometimes 'homeopathic' doses should be given initially and then slowly titrated against response and adverse effects. The known D_2-receptor site affinity of the various antipsychotic drugs[17] and clinical experience suggest that if an antipsychotic drug is indicated for a patient with DLB or Parkinson's disease, the best choices in terms of limiting parkinsonism risk may be (in descending order) quetiapine [Seroquel], clozapine [Clopine, CloSyn, Clozaril], olanzapine [Zyprexa], ziprasidone [Zeldox], amisulpride [Solian] and risperidone [Risperdal]. The listing of D_2-receptor site affinity quoted in reference 17 does not provide information on several other novel and atypical antipsychotics recently available (aripiprazole [Abilify], paliperidone [Invega]). Among the atypical antipsychotic drugs, only risperidone is approved under the PBS for 'behavioural disturbances characterised by psychotic symptoms and aggression in

patients with dementia where nonpharmacological methods have been unsuccessful'.

Treatment of depression and anxiety

In patients with DLB, cholinesterase inhibitors, presumably by improving function and independence, may reduce depression and anxiety. If an antidepressant is given, it is preferable to prescribe one of the newer serotonin reuptake inhibitors (SSRIs) or moclobemide rather than older tricyclic antidepressants. SSRIs and tricyclic antidepressants may both trigger delirium in association with DLB, but the tricyclics, being anticholinergic, are more likely to do so.

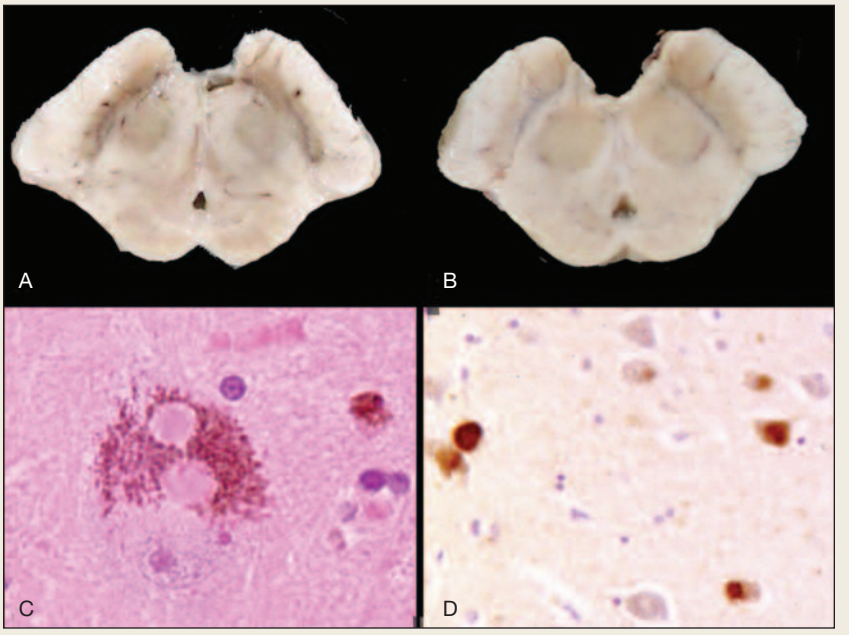
Other therapeutic interventions

There is much that can be done for individuals with dementia and their carers, by providing opportunities for them to:[21]

Lewy body disease: a brief history and underlying pathology

History

1912	Fritz (Friedrich) Heinrich Lewy first described intracellular inclusion bodies, particularly in brain stem neurons associated with Parkinson's disease.
1919	Tretiakoff named these bodies 'Lewy bodies' ('corps de Lewy').
1933	Lewy was dismissed on racial grounds (his father was Jewish) from his position as Director of the Neurological Research Institute and Clinic in Berlin. He moved to England that year, then to the USA where he later changed his name to Frederic Henry Lewey.[22]
1980s and 1990s	Postmortem studies demonstrated the presence of cortical and subcortical Lewy bodies combined with Alzheimer pathology in many patients with dementia.[23] That is, these bodies were present in brain structures not known to be associated with Parkinson's disease.
1992	McKeith and others reported sometimes catastrophic, even fatal, neuroleptic sensitivity in patients with 'senile dementia of Lewy body type' compared with patients with Alzheimer's disease.[1]
1996	First consensus guidelines for the clinical and pathological diagnosis of dementia with Lewy bodies (DLB).[24]
1997	Immunohistochemical stain developed for alpha-synuclein, a key component of the intracellular Lewy bodies. Using this stain, cortical and limbic Lewy bodies were found to be much more common than previously thought and were associated with DLB.
2002	High densities of Lewy bodies in inferomedial temporal lobe structures including the amygdala reported to be associated with visual hallucinations in DLB and Parkinson's disease.[7,25] The Lewy bodies themselves do not appear to cause cell death.
2005	Third report of the DLB Consortium on the diagnosis and management of dementia with Lewy bodies.[2]



Figures A to D. Pathology of Lewy bodies. A (top left). Appearance of the brainstem in someone without Lewy body disease. Note the dark stripes of tissue on either side running at about a 45° angle. This is the 'substantia nigra'. B (top right) Appearance of the brainstem in someone with Lewy body disease. The dark stripes of tissue are pale. C (bottom left). High power microscopic appearance in someone with Lewy body disease of one of the remaining pigmented cells in the brainstem, containing two Lewy bodies (pink rounded structures in amongst the brown pigment). D (bottom right). High power microscopic appearance of Lewy bodies (rounded brown structures) in the cortex of someone with Lewy body dementia stained with special stains that identify cortical Lewy bodies.

PHOTOS COURTESY OF A/PROF JILLIAN KRIL, DEPARTMENT OF PATHOLOGY, UNIVERSITY OF SYDNEY, AND THE AUSTRALIAN BRAIN DONOR PROGRAMS, PART OF THE AUSTRALIAN BRAIN BANK NETWORK.

- communicate their experiences
- deal with their grief and distress
- deal with advance planning (e.g. wills, power of attorney), issues related to competence (e.g. living alone, managing medications, managing finances, driving) and protection against financial and other abuse
- improve their understanding of the disorders causing dementia and of the associated symptoms and behaviours
- gaining access to practical measures of assistance.

General practitioners can refer to Aged Care or Psychogeriatric/Mental Health Services for Older People teams, and usually through these agencies to dementia counsellors in their local area, for assistance with many of these issues. Alzheimer's Australia and programs such as 'Living with Memory Loss' can also provide assistance, sometimes locally.

Much of the management of dementia also involves providing an environment and lifestyle that is as normal as possible while avoiding situations of potential failure or danger. It has also been suggested that optimal levels of stimulation in patients with DLB might assist impaired arousal and attention.[2]

Usually someone in the patient's family, learning of the diagnosis of DLB, will access the internet for more information. The box on page 29 provides some useful website addresses.

Summary

DLB is a frequent cause of dementia. It is characterised by cognitive impairment usually without prominent memory impairment, and often one or several of the following features: pronounced fluctuations in function, recurrent visual hallucinations and parkinsonism. It is also often associated with severe antipsychotic drug sensitivity and REM sleep behaviour disorder. Symptoms of DLB may respond, sometimes dramatically, to cholinesterase inhibitors. MT

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

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Dementia with Lewy bodies
a common disorder easily missed

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