INTRODUCTION

Dementia with Lewy bodies (DLB) is increasingly recognized clinically as the second most common type of degenerative dementia after Alzheimer disease (AD). In addition to dementia, distinctive clinical features include: visual hallucinations, parkinsonism, cognitive fluctuations, dysautonomia, sleep disorders, and antipsychotic sensitivity.

First described in the 1960s, DLB has a varied clinical presentation that shares features with other degenerative dementias. It was often overlooked pathologically because of the difficulty in identifying cortical Lewy bodies. With the advent of immunohistochemical stains for constituents of Lewy bodies, the prevalence of this disorder began to be recognized. However, challenges remain in defining this as a distinct entity from other degenerative dementias.

There is some clinical imperative to diagnose DLB, as optimal treatment choices (for best efficacy and limitation of significant side effects) are specific to DLB. However, DLB continues to be underrecognized, and the clinical diagnostic criteria continue to be refined to improve specificity and sensitivity.

This article will describe the prognosis and treatment of DLB. The epidemiology, neuropathology, pathogenesis, clinical features, and diagnosis are discussed separately. (See "Epidemiology, pathology, and pathogenesis of dementia with Lewy bodies" and "Clinical features and diagnosis of dementia with Lewy bodies".)

The treatment of other dementia syndromes and the treatment of dementia in general are discussed separately. (See "Cholinesterase inhibitors in the treatment of Alzheimer disease" and "Treatment of
**PROGNOSIS**

As with all of the degenerative dementias, cognitive decline in DLB progresses inexorably to death. Psychotic symptoms, particularly visual hallucinations, tend to persist in patients with DLB [1]. Parkinsonism also worsens over time, especially in patients for whom this is an early feature [2]. In one retrospective series, individuals with impairment of visuospatial skill on baseline neuropsychologic testing had a faster rate of clinical decline compared with those who did not [3].

While some have reported that the rates of cognitive decline are similar for Alzheimer disease (AD) and DLB [4-7], others report a more stable course for DLB [8], and others have found a faster rate of cognitive decline in DLB [9,10]. In one series, patients with DLB lost an average of 5.8 points per year on Mini-Mental State Examination (MMSE) compared with 4.1 points for AD [9]. In this study, survival time in DLB was also shorter than in AD: 7.7 versus 9.3 years since onset of cognitive symptoms, a finding corroborated in another cohort of patients with AD and DLB [11].

The degree of motor parkinsonism and psychiatric symptoms appears to contribute to earlier institutionalization compared with AD [12], and possibly shorter survival [13]. Increased hippocampal atrophy on magnetic resonance imaging (MRI) has also been associated with significantly shorter survival time [14].

**TREATMENT**

Treatment of DLB is symptomatic, targeted toward specific disease manifestations, and based upon somewhat limited evidence. There are no treatments with evidence of disease-modifying effects.

**General strategies** — Because medications may be poorly tolerated in DLB, nonpharmacologic, behavioral strategies aimed at modifying stressors in the environment should be employed whenever possible (see "Management of neuropsychiatric symptoms of dementia", section on 'Nonpharmacologic therapies'). Physical therapy and mobility aids may help in the management of parkinsonism. (See "Nonpharmacologic management of Parkinson disease").

Patient and caregiver education regarding risks, benefits, and limitations of treatments is important. In many cases, treatment choices represent a trade-off between parkinsonism and psychosis, and the relative preferences of the patient and caregiver will be decisive.
Cognition and neuropsychiatric disturbances

**Cholinesterase inhibitors** — Cholinesterase inhibitors may represent a first-line pharmacologic treatment in DLB, although the evidence is as yet somewhat limited [15-17]. While cholinesterase inhibitors were initially developed for Alzheimer disease (AD), the evidence suggests that cholinergic deficits are even greater in DLB.

Multiple anecdotal reports [18,19], open-label studies [20-23], and a limited number of randomized, controlled trials [24-26] suggest that cholinesterase inhibitors are efficacious in DLB, with reported benefit not only in cognition, but also for fluctuations, psychotic symptoms, and parkinsonian symptoms. In some instances, the response has been dramatic, but temporary. The effect size has been reported to be larger than that in patients with AD [27].

- **Rivastigmine** – A multicenter study randomly assigned 120 patients with DLB to rivastigmine (6 to 12 mg per day) or placebo for 20 weeks [24]. Patients on rivastigmine showed significantly reduced anxiety, delusions, and hallucinations (particularly visual), and had significantly better performance on a computerized battery of neuropsychologic tests, especially tasks requiring sustained attention. The differences between rivastigmine and placebo disappeared after drug discontinuation. The expected gastrointestinal side effects as well as hypersalivation, lacrimation, and urinary frequency were seen with a higher frequency in the rivastigmine group, but the drug was well tolerated overall.

  **Rivastigmine** can also be administered by transdermal patch, titrated up to 9.5 mg per day with the option to advance to a 13.3 mg per day patch as the illness progresses.

- **Donepezil** – One randomized study found that 12 weeks of therapy with either 5 or 10 mg of donepezil was associated with significant improvements in cognitive and behavioral measures, as well as caregiver burden when compared with placebo [25]. Results of a second randomized trial in 142 patients with DLB were more modest, however, and only the 10-mg dose was associated with an improvement in cognition compared with placebo [26]. Neither 5 nor 10 mg of donepezil led to significant improvements in neuropsychiatric symptoms.

While not reported in the randomized studies as significant risks, there have been case reports of worsening cognitive function, rapid eye movement (REM) sleep behavior disorder, or parkinsonism with cholinesterase inhibitors [28,29]; patients should be monitored carefully while using these drugs. Weight loss is a recognized side effect of cholinesterase inhibitors but in most cases the degree of weight loss is modest [30]. Cholinesterase inhibitors also have demonstrated mild to moderate benefits in Parkinson disease dementia. (See "Cognitive impairment and dementia in Parkinson disease", section on 'Cholinesterase inhibitors'.)
Memantine — Memantine has reported efficacy in moderate to severe AD and vascular dementia, but data in DLB are mixed. Beneficial effects of small magnitude have been demonstrated for global impression scores but not cognition or neuropsychiatric symptoms [16,17].

- A randomized controlled trial of 72 patients with either DLB or Parkinson disease dementia found that patients treated with memantine for 24 weeks performed better on the primary outcome assessment measure, the clinical global impression of change, but not on most of the other secondary outcome measures [31].

- In a subsequent 24-week trial that compared memantine with placebo in 199 patients with either DLB or Parkinson disease dementia, the subset of 75 patients with DLB (but not Parkinson disease dementia or the group overall) demonstrated improved outcome on the same primary outcome measure, but again not on most secondary outcome measures [32].

In most studies, memantine has been well tolerated [31,32]; however, other studies have noted that worsening of delusions and hallucinations with memantine may be particularly problematic in patients with DLB [33,34]. Although one trial in patients with DLB or Parkinson disease dementia reported a potential survival advantage with memantine, data were drawn from a subset of patients with long-term follow-up and confirmatory data are needed [35].

Antipsychotic drugs — The potential for severe sensitivity reactions, including exacerbation of parkinsonism, confusion, or autonomic dysfunction, limits the usefulness of antipsychotic medications in DLB. (See "Clinical features and diagnosis of dementia with Lewy bodies", section on 'Antipsychotic sensitivity'.)

If a patient experiences severe, disabling psychosis, a trial of a cholinesterase inhibitor and/or lowering the dose of antiparkinson medication should be considered first. Randomized, placebo-controlled studies suggest that antipsychotic agents have limited efficacy in patients with dementia in general and in DLB in particular [36]. (See "Management of neuropsychiatric symptoms of dementia".)

When antipsychotic therapy is required, patients and caregivers should be warned about the possibility of severe side effects. In addition to the sensitivity reactions more specific to DLB, these drugs are associated with an increased risk of death when used in older adult patients with dementia. (See "Management of neuropsychiatric symptoms of dementia", section on 'Excess mortality' and "Second-generation antipsychotic medications: Pharmacology, administration, and side effects", section on 'Adverse effects'.)

If antipsychotic therapy is required in patients with DLB, only atypical antipsychotic drugs, such as olanzapine, quetiapine, pimavanserin, ziprasidone, aripiprazole, paliperidone, or clozapine, should be
used in very small doses in order to reduce the risk of severe reaction [37-41]. The older, conventional antipsychotics should be avoided entirely [4].

If the desired clinical response is not seen from one agent, it should be discontinued and another agent tried, rather than escalating the dose of the first agent. If clozapine is used, frequent blood counts must be obtained to monitor for agranulocytosis. Management of severe agitation in the setting of dementia is discussed in detail separately. (See "Management of neuropsychiatric symptoms of dementia", section on 'Agitation or aggression'.)

**Other psychotropic medications** — There have been no systematic studies of the use of antidepressants, anxiolytics, benzodiazepines, or anticonvulsants in the treatment of the behavioral and psychiatric symptoms in DLB [4]. Selective serotonin reuptake inhibitors are commonly used in the treatment of depression. Benzodiazepines are generally avoided (except for REM sleep disorder), especially for long-term use, because of the potential for worsening confusion, gait disorder, and paradoxic agitation. Tricyclic agents are avoided because of their anticholinergic properties. Electroconvulsive therapy has been successfully employed in depressed patients with DLB [42]. (See "Management of neuropsychiatric symptoms of dementia".)

**REM sleep behavior disorder** — REM sleep behavior disorder often responds to low doses of melatonin (3 to 15 mg) or clonazepam (0.25 to 1.5 mg) given at bedtime [43-45]. Melatonin is preferred as initial therapy in the setting of cognitive impairment due to lower risk of side effects. Establishing a safe sleeping environment and counseling patients and bed partners about injury prevention is also important. The treatment of REM sleep behavior disorder is discussed in more detail separately. (See "Rapid eye movement sleep behavior disorder", section on 'Treatment'.)

**Parkinsonian symptoms** — Treatment of parkinsonian symptoms in DLB is similar to that for Parkinson disease, if somewhat less successful [46-48]. (See "Initial pharmacologic treatment of Parkinson disease".)

There is concern that these medications may exacerbate psychotic symptoms in DLB, but our clinical experience and small case series suggest that by using a conservative approach (small doses and slow upward titration), these agents are generally effective and well tolerated [29,49]. Worsening of psychotic symptoms and REM sleep disorder may require addition of a small dose of an atypical antipsychotic [49,50].

Levodopa seems to be more effective than dopamine agonists and produces fewer side effects [51]. A suggested initial dose is one-half tablet of carbidopa-levodopa (Sinemet) 25/100 mg three times daily, titrated upward over several weeks as tolerated and according to the clinical response. Anticholinergic agents are generally avoided in DLB because they may worsen cognitive function.
Orthostatic hypotension — Medical therapy can improve symptoms of orthostatic hypotension in most DLB patients [52,53]. We have used fludrocortisone, midodrine, and a combination of the two successfully in several of our patients. Anticholinergic agents for the treatment of urinary incontinence should probably be avoided in DLB patients who have orthostatic hypotension. (See "Treatment of orthostatic and postprandial hypotension".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Cognitive impairment and dementia".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Dementia with Lewy bodies (The Basics)"
- Beyond the Basics topic (see "Patient education: Dementia (including Alzheimer disease) (Beyond the Basics)"

SUMMARY AND RECOMMENDATIONS

Dementia with Lewy bodies (DLB) is the second most common form of degenerative dementia after Alzheimer disease (AD).

- DLB is characterized clinically by deficits in attention and visuospatial function, fluctuating cognition, recurrent visual hallucinations, and spontaneous motor features of parkinsonism.
Other associated symptoms include repeated falls, syncope, autonomic dysfunction, antipsychotic sensitivity, delusions, hallucinations in other modalities, sleep disorders, and depression. (See "Clinical features and diagnosis of dementia with Lewy bodies").

- Nonpharmacologic, behavioral therapies, when appropriate, are preferred over medications, which have a high rate of adverse effects. (See "Management of neuropsychiatric symptoms of dementia", section on 'Nonpharmacologic therapies'.)

- We suggest a treatment trial with a cholinesterase inhibitor to ameliorate cognitive and behavioral symptoms in patients with DLB (Grade 2C). (See 'Cholinesterase inhibitors' above.)

- If disabling psychotic symptoms persist after initiating treatment with cholinesterase inhibitors, we suggest cautious addition of a very low-dose atypical antipsychotic agent (eg, quetiapine 12.5 mg per day) after informing patients and caregivers of the risks, including the development of severe antipsychotic sensitivity reactions (Grade 2C). (See 'Antipsychotic drugs' above.)

- We suggest starting levodopa for treatment of disabling parkinsonism (Grade 2C). Low doses and slow upward titration with monitoring for increased psychosis is advised (eg, one-half tablet of Sinemet 25/100 mg three times daily, titrated upward over several weeks as tolerated and according to the response). (See 'Parkinsonian symptoms' above.)

- For patients with rapid eye movement (REM) sleep behavior disorder, we suggest melatonin as initial therapy rather than clonazepam (Grade 2C). Patients and bed partners should also be counseled on ways to alter the sleeping environment to prevent injury. (See 'REM sleep behavior disorder' above.)

ACKNOWLEDGMENT

The editorial staff at UpToDate would like to acknowledge Ann Marie Hake, MD, who contributed to an earlier version of this topic review.

Use of UpToDate is subject to the Subscription and License Agreement.

REFERENCES


Contributor Disclosures

**Martin R Farlow, MD** Grant/Research Support: AbbVie; Accera; ADCS Posiphen; Biogen; Eisai; Eli Lilly; Genentech; Novartis; Suven Life Sciences [Alzheimer disease]; vTv Therapeutics [Alzheimer disease (TTP488 azeliragon)]. Consultant/Advisory Boards: Avanir; AZTherapies; Cerecin; Cognition Therapeutics; Cortexyme; Eli Lilly & Company; Longeveron; MedAvante; Merck; Otsuka Pharmaceutical; Proclara; Neurotrope Bioscience; Swing Therapeutics; Takeda; vTv Therapeutics; Zhejiang Hisun Pharmaceuticals [Alzheimer disease]; Allergan [Alzheimer disease (Memantine)]; Biogen MA [Alzheimer disease (Neurodiem Global Scientific Committee)]; Danone [Alzheimer disease (Drink mixture of long-chain omega-3 fatty acids, uridine, choline, B vitamins, vitamin C, vitamin E, and selenium)]; Eisai [Alzheimer disease (BAN2401)]; Green Valley [Alzheimer disease (Sodium oligo-mannurarate GV-971)]; Samumed [Alzheimer disease (SMO7883)]. Patent Holder: Elan [Alzheimer disease (Transgenic mouse model)]. **Steven T DeKosky, MD, FAAN, FACP, FANA** Consultant/Advisory Boards: Biogen; Cognition Therapeutics [Alzheimer disease]; Amgen [Neuroscience]. **Janet L Wilterdink, MD** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

**Conflict of interest policy**