

# How to manage your patient's dementia by discontinuing medications

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Mrs. J, age 75, has moderate Alzheimer's dementia and lives at home with her husband. Since her Alzheimer's disease (AD) diagnosis 2 years ago, Mrs. J generally has been cooperative and not physically aggressive, but has experienced occasional depressive symptoms. However, Mr. J reports that recently his wife is becoming increasingly confused and agitated and wanders the house at night. His efforts to calm and coax her back to bed often lead to increased agitation and yelling. On 1 occasion Mrs. J pushed her husband. Mr. J is concerned that if these behaviors continue he may not be able to care for her at home. Mr. J read online that antipsychotics might reduce aggressive behavior, but is concerned about the increased risk of mortality and stroke with these medications.

Mrs. J receives donepezil, 10 mg/d, sertraline, 50 mg/d, and extended-release oxybutynin, 10 mg/d. Her over-the-counter (OTC) medications include acetaminophen, 650 mg as needed for pain, ranitidine, 150 mg/d, and docusate sodium, 100 mg/d. Several nights last week, Mr. J gave his wife an unknown OTC sleep medication, hoping it would stop her nighttime wandering, but it did not help. Physical examination, laboratory testing, and urine culture are all normal.

Most dementia patients experience neuropsychiatric disturbances, especially at later stages, that often lead to caregiver distress and nursing home placement. Although these symptoms may signal progressing

dementia, environmental factors, medical conditions, and medications may worsen functioning and should be considered in the assessment.<sup>1</sup>

Mrs. J has no medical problems that were identified as possible triggers for her behavior. Mr. J's interference with his wife's wandering could have increased her agitation, but he is gentle toward her and she has become agitated with no apparent trigger. "Sundowning" and poor sleep also may be involved, as sleep deprivation can lead to delirium and worsen cognitive deficits and behavioral problems.<sup>1</sup> Depression also should be considered.<sup>1</sup> Finally, Mrs. J is taking several medications with anticholinergic prop-

## Practice Points

- During the initial evaluation of cognitive complaints, **look to discontinue medications** that may cause cognitive impairment, including anticholinergics.
- In addition to worsening cognitive impairment, **anticholinergic medications may contribute to behavioral disturbances**, psychosis, and delirium in patients with dementia.
- **Side effects of acetylcholinesterase inhibitors can prompt anticholinergic use**, which is likely to negate the beneficial effects of the acetylcholinesterase inhibitor.
- Nonpsychiatric medications, including over-the-counter drugs, can have anticholinergic properties. **Consult with nonpsychiatric clinicians** to discontinue inessential medications that may be harmful for dementia patients.

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## Table

## Drugs with clinically significant anticholinergic effects\*

Drug class	Medication(s)
Anticonvulsants	Carbamazepine
Antidepressants	Amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, paroxetine, protriptyline, trimipramine
Antihistamines	Azelastine nasal spray, brompheniramine, carbinoxamine, chlorpheniramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, diphenhydramine, hydroxyzine, mepyramine olopatadine nasal spray, phenyltoloxamine, promethazine, triprolidine
Antiparkinsonian agents	Benzotropine, procyclidine, trihexyphenidyl
Antipsychotics	Chlorpromazine, clozapine, loxapine, molindone, olanzapine, pimozide, promethazine, quetiapine, thioridazine
Asthma and chronic obstructive pulmonary disease medication	Glycopyrrolate, ipratropium, <sup>†</sup> tiotropium <sup>†</sup>
Bladder antispasmodics	Darifenacin, flavoxate, oxybutynin, solifenacin, tolterodine, trospium
Gastrointestinal antispasmodics	Atropine, belladonna alkaloids, clidinium, dicyclomine, hyoscyamine, methscopolamine, propantheline
Insomnia medications	Diphenhydramine, doxylamine
Motion sickness/dizziness/nausea medications	Dimenhydrinate, meclizine, prochlorperazine, promethazine, scopolamine, trimethobenzamide
Muscle relaxants and pain medications	Cyclobenzaprine, meperidine, orphenadrine, phenyltoloxamine
Ulcer and acid reflux agents	Cimetidine, glycopyrrolate, ranitidine

\*Not a comprehensive list  
<sup>†</sup>Unknown whether CNS effects are important  
**Source:** Reference 5

erties—oxybutynin, ranitidine, and an unknown OTC sleep medication, which likely contains diphenhydramine or doxylamine—that might contribute to her agitation.

Patients with dementia are highly sensitive to the cognitive and psychiatric adverse effects of anticholinergic medications. In studies of patients with mild or moderate Alzheimer's dementia who received the potent anticholinergic scopolamine, adverse effects included:

- memory impairment
- restlessness
- disjointed speech
- motor incoordination
- drowsiness
- euphoria
- agitation
- hallucinations
- hostility.

Many of these effects worsened with increasing doses.<sup>2,3</sup> Age-matched controls experienced less severe memory impairment and no behavioral symptoms, which

suggests that dementia-related damage to the cholinergic system leads to increased sensitivity to anticholinergics.

A cross-sectional study of 230 patients with AD identified anticholinergic use as a risk factor for psychosis (odds ratio 2.13, 95% confidence interval, 1.03 to 4.43), after adjusting for age and cognition.<sup>4</sup> Among patients receiving 2 or 3 anticholinergics, 69% had psychotic symptoms compared with 48% of those receiving 1 anticholinergic and 32% of those receiving no anticholinergics.<sup>4</sup> Anticholinergic overdoses can cause psychotic symptoms and delirium. A subtle presentation of delirium from prescribed anticholinergics may be confused with worsening dementia.<sup>1</sup>

continued

## Clinical Point

Drugs with anticholinergic effects can contribute to agitation and psychosis in dementia

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## Clinical Point

Consider discontinuing anticholinergics if they are not essential to a patient's health or if safer alternatives are available

## Related Resources

- Cancelli I, Beltrame M, D'Anna L, et al. Drugs with anticholinergic properties: a potential risk factor for psychosis onset in Alzheimer's disease? *Expert Opin Drug Saf*. 2009;8(5):549-557.
- Meeks TW, Jeste DV. Beyond the black box: what is the role for antipsychotics in dementia? *Current Psychiatry*. 2008;7(6): 50-65.
- Centers for Education and Research on Therapeutics. Anticholinergic pocket reference card. [www.chainonline.org/home/content\\_images/Anticholinergic%20Pocket%20Card%20CLR%203\\_12\\_10.pdf](http://www.chainonline.org/home/content_images/Anticholinergic%20Pocket%20Card%20CLR%203_12_10.pdf).

### Drug Brand Names

Amitriptyline • Elavil	Hyoscyamine • Cystospaz, Levbid
Atropine • Sal-Tropine	Imipramine • Tofranil
Azelastine nasal spray	Ipratropium • Atrovent
• Astelin	Loxapine • Loxitane
Belladonna alkaloids	Meclizine • Antivert
• Donnatal	Meperidine • Demerol
Benztropine • Cogentin	Mepyramine • Anthisan
Brompheniramine	Methscopolamine • Pamine
• Dimetane	Molindone • Moban
Carbamazepine • Carbatrol, Tegretol, others	Nortriptyline • Aventyl
Carbinoxamine • Palgic	Olanzapine • Zyprexa
Chlorpheniramine	Olopatadine nasal spray
• Chlor-Trimeton	• Patanase
Chlorpromazine • Thorazine	Orphenadrine • Norflex
Cimetidine • Tagamet	Oxybutynin extended-release • Ditropan XL
Clemastine • Tavist	Paroxetine • Paxil
Cliadinium • Quarzan	Phenyltoloxamine
Clomipramine • Anafranil	• Dologesic, Durayin, others
Clozapine • Clozaril	Pimozide • Orap
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Cyproheptadine • Periactin	• Compazine
Darifenacin • Enablex	Procyclidine • Kemadrin
Desipramine • Norpramin	Promethazine • Phenergan
Dexbrompheniramine	Propanthelin • Pro-Banthine
• Drixoral	Protriptyline • Vivactil
Dexchlorpheniramine	Quetiapine • Seroquel
• Polaramine	Ranitidine • Zantac
Dicyclomine • Bentyl	Scopolamine • Scopace
Dimenhydrinate	Sertraline • Zoloft
• Dramamine	Solifenacin • VESicare
Diphenhydramine	Thioridazine • Mellaril
• Benadryl, Somnex, others	Tiotropium • Spiriva
Docusate Sodium • Colace	Tolterodine • Detrol
Donepezil • Aricept	Trihexyphenidyl • Artane
Doxepin • Adapin	Trimethobenzamide • Tigan
Doxylamine • Aldex, Unisom, others	Trimipramine • Surmontil
Flavoxate • Urispas	Tripolidine • Actifed
Glycopyrrolate • Robinul	Trosipium • Sanctura
Hydroxyzine • Atarax	

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## When to discontinue

When diagnosing dementia it is important to address other potential causes of cognitive impairment, including medications. Approximately one-third of patients with dementia receive anticholinergic drugs, which suggests that providers often do not recognize the potential for harm with these medications.<sup>5</sup> After patients receive acetylcholinesterase inhibitors (AChEIs)—which are used to enhance cognition in dementia patients—increased anticholinergic use may follow, often to treat adverse effects of AChEIs.<sup>5</sup> This may negate the benefits of AChEIs and pose risk of further harm from the anticholinergics.<sup>1,5</sup> Although any time is a good time to discontinue an inessential anticholinergic in a patient with dementia, providers might consider screening for these drugs at the initial diagnosis, after initiating a cholinesterase inhibitor or increasing a dose, or if the patient develops psychotic or behavioral symptoms.

For Mrs. J, ranitidine and oxybutynin likely were used to treat gastrointestinal complaints and urinary frequency, which are known adverse effects of AChEIs. Many OTC preparations for insomnia, respiratory symptoms, and allergies contain older, anticholinergic antihistamines. Advise caregivers of dementia patients about possible adverse effects of OTC medications to prevent anticholinergic exposure. The *Table (page 35)* provides a partial list of medications thought to have clinically significant anticholinergic effects.

'Pharmacologic debridement' refers to tapering and discontinuing medications that are no longer necessary or appropriate. Prescribers often are hesitant to discontinue medications prescribed by other clinicians and may assume that a medication used long term has been tolerated and helpful. However, as patients age—particularly if they develop dementia—their ability to tolerate a medication can change. Patients with dementia also may have difficulty attributing adverse experiences to medications and communicating these effects to providers. Some medical providers may not recognize adverse psychiatric and cognitive effects of the nonpsychiatric medications they pre-

The sum of the evidence suggests that drugs with anticholinergic effects can contribute to agitation and psychosis in dementia.

scribe because they do not have sufficient dementia expertise. Consulting with these providers may help determine the risk-benefit considerations of these medications.

Generally, anticholinergics should be discontinued if they are not essential to a patient's health or if safer non-anticholinergic alternatives are available.<sup>5</sup> Tapering may be necessary to prevent adverse effects from cholinergic rebound if a potent anticholinergic has been used chronically.<sup>5</sup> The first step in addressing Mrs. J's agitation is to discontinue the anticholinergic medications and monitor her symptoms. This pharmacologic debridement may avert the

use of antipsychotics, which carry serious risks for dementia patients.<sup>1</sup>

#### References

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