Alzheimer’s Disease — Evaluation and Management

Practical Approaches and Considerations for Optimizing Care in the Assisted Living Environment

Analysis and Guidance from the Alzheimer’s Disease, Assisted Living (AD-AL) Expert Consensus Panel—The PROCLAIM Approach to Optimizing Assessment and Intervention in Individuals with Dementia

INTRODUCTION

The financial and social costs of Alzheimer’s disease (AD) are staggering. In the United States, the disease accounts for about $100 billion per year in medical and custodial expenses, with the average patient requiring an average expenditure of about $27,000 per year for medical and nursing care. In addition, 80% of family caregivers report stress, and about 50% manifest symptoms of depression.1,2 Clearly, the monetary, social, medical, and familial burden of caring for individuals suffering from AD and related dementias has emerged as one of the most important public health policy issues of our times.

The American Alzheimer’s Association estimates that about 4.5 million individuals currently suffer from this condition in the United States, and many of those afflicted, in varying stages of their dementia, reside in assisted living environments. Epidemiologists estimate that there may be as many as 14 million individuals in the United States by the year 2050. Perhaps, more than any other environment, this setting, with thousands of locations and networks nationwide, has become the most important source of care, maintenance, and life enrichment for this growing population.

In fact, the critical role and public health dimension of assisted living communities for those suffering from AD and related dementias have become especially important, in part, because residence in such settings frequently provides the last opportunity for individuals to maintain self-care for activities of daily living, enjoy meaningful relationships with friends and family, and ensure that appropriate, proactive treatment has been implemented, before progression of illness leads to inexorable decline. As a result, caregivers in this environment can play a linchpin role in ensuring that optimal care, attention, and interventions are provided during a very delicate and transitional phase in the disease and life process.3 The importance of addressing these human costs cannot be over-emphasized.

As the world’s population grows older, the prevalence of AD is expected to increase to up to 16 million in the United States by the middle of the 21st century.4 Other countries are facing a similar challenge. In an Italian epidemiological survey of AD and other types of dementia, the prevalence of the disease was 3.1% in the population older than age 65, with considerable variation according to the decade of life: 0.6% in individuals ages 60-69 years; 2.0% in those between the ages of 70 and 79; and 10.2% in individuals ages 80-89.5

Although a definitive cause for AD has not yet been precisely delineated, several causes have been proposed.6 Although genetic factors appear to be significant in the development of AD, mutations cur- (Continued on Page 3)
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rently account for approximately 5% of all cases. The accumulation of beta-amyloid in brain tissues contributes to cell death, disruption of cell membranes, inflammatory response, and neurofibrillary tangles, which appear to significantly reduce brain cholinergic activity and increase the risk of AD. Most AD cases occur with advancing age, although family history remains a predisposing factor.

Management of AD is becoming increasingly complex, especially in the assisted living (AL) environment, where both cognitive and behavioral problems must be addressed by a wide range of multidisciplinary healthcare providers (HCPs) including nurses, nurse practitioners, nurse assistants, pharmacists, physicians, physical therapists, and related healthcare providers. Communication among HCPs is critical to successful care, as is establishing realistic goals for patients, caregivers, and their families.

Initiating, monitoring, and ensuring compliance with drug therapy for AD patients can be a critical component of successful care. Three principal cholinesterase inhibitors (rivastigmine, donepezil, and galantamine) and one N-methyl-D-aspartate (NMDA) receptor antagonist (memantine) comprise the core therapeutic arsenal for patients with AD. Caregivers should be knowledgeable about how these medications work, what their side effects are, and what should be expected in the way of a clinical response. Equally important is managing expectations for patients and family members, a key component of compassionate and comprehensive care.

Behavior problems, which accompany AD in its advanced stages, frequently can be managed using environmental modification and alterations in care giving. These approaches are recommended as initial and ongoing strategies, especially as we learn about the potential adverse consequences of antipsychotic medications. However, in cases of advanced disease, especially when disruptive and/or aggressive behaviors predominate and patients may pose harm to themselves, other residents, or caregivers, the use of antipsychotic, anticonvulsant, and/or anxiolytic medications may be necessary. A thorough evaluation should rule out potential contributing factors so that these potent medications are used judiciously.

As a general rule, optimizing quality of care for persons with dementia in the AL setting, especially during the early and middle phases of the illness, requires identifying triggers for medical treatment, implementing a systematic approach to therapy using cholinesterase inhibitors and/or an NMDA receptor antagonist, monitoring patient response, and managing patient and caregiver expectations.

During the late stages of AD, other considerations become increasingly important. Those working in AL environments may be called upon to implement advance directives. Moreover, communicating well with the family will become increasingly important, and likely, more stressful, especially as the patient deteriorates. Individualizing care, providing medication-based control of disturbed behaviors, and attending to patient comfort and the stressors of cognitive and behavioral decline will become primary objectives of compassionate care.

Until recently, the approach to persons with dementia primarily consisted of helping family members cope with the burden of care giving and providing information about services available in AL settings. Over the past decade, however, research and innovations have increased the effectiveness of environmental approaches and pharmacologic options available to HCPs who care for demented patients and their families.

While no dramatic breakthroughs have occurred, the overall management of dementia has become increasingly sophisticated, relying on a combination of drug-based therapy, environmental strategies, and behavioral techniques that maximize life quality for individuals while minimizing risks from medications and other hazards. It is likely that therapeutic strategies will evolve rapidly over the next several years.

Optimizing evaluation, care, and interactions with persons suffering from dementia is the focus of intense study and controversy. The purpose of this consensus report, which has been generated by a multidisciplinary group of healthcare providers—among them, nurses, nurse practitioners, and physicians—caring for AD residents in the AL setting, is to provide a practical and evidence-based guidance for managing patients with AD residing in AL environments.

**MISSION STATEMENT**

The purpose of the AD-AL Consensus Panel, which is supported through an unrestricted educational grant from Brookdale Senior Living and implemented by Pharmatecture, LLC, is to assemble a small, uniquely informed, multidisciplinary, and collegial group of national leaders with expertise in caring for individuals in the assisted living setting. Then,
upon review of clinical trials, expert opinion, and national guidelines, the Panel would generate an evidence-based document outlining approaches to caring for persons with dementia in the AL setting.

The goal was to produce a CME-certified resource that would address the needs of front-line providers in the AL setting. Practical guidance that would be of use to licensed practical nurses (LPNs) and RNs, family members, physicians, nurse practitioners, social service staff, as well as AL program directors and executives would be emphasized.

As a result, this expert-based Clinical Consensus Update is divided into two parts. Because caring for individuals with AD is a team effort, employing various skill sets among many different care providers, the AD-AL Panel felt that this Clinical Consensus Update should attempt to address the needs of multiple provider groups and caregivers who participate, as a team, in the AL setting.

To achieve this goal, Part I focuses on the PROCLAIM strategy for managing AD residents in the AL setting. This section outlines general principles and action plans that can be employed by a wide range of care providers including nurses, nurse assistants, physician assistants, licensed practical nurses, social service providers, pharmacists, and related healthcare providers. Part II provides advanced information and analysis related to patient assessment and drug-based therapy that will be most useful for nurses, nurse practitioners, and consulting pharmacists.

The AD-AL Panel members hope that the PROCLAIM care strategy and action plan for healthcare providers caring for individuals with AD who reside in the AL environment will prove to be useful for improving care and the quality of life in this expanding population.

THE PROCLAIM PARADIGM FOR DEMENTIA CARE IN THE AL SETTING

One of the principal goals of the AD-AL Consensus Panel and this Update is to propose a compassionate, rational, outcome-optimizing, and practical model for healthcare personnel caring for individuals with dementia in the AL setting. To achieve this goal, the AD-AL Consensus Panel has developed a strategy that is based on the PROCLAIM clinical action plan for individuals with dementia who are residing in AL communities (Please see Table 1, The PROCLAIM Strategy for Residents with Dementia Residing in the Assisted Living Setting).

The PROCLAIM guidelines for AD care can be viewed as an awareness and action tool that AL caregivers can use to “proclaim” their commitment to providing compassionate, effective, and optimal care for residents with Alzheimer’s dementia. The approach is designed to account for the complex psychological, medical, financial, and emotional needs of persons with dementia and their families; and, in the process, define milestone interventions and tasks that will improve quality of resident care. The AD-AL Consensus Panel has created the PROCLAIM acronym to suggest an approach that identifies the most important dimensions of care for residents with AD, and that serves as an outline for comprehensive, multidisciplinary care of individuals residing in the AL environment.

More specifically, the PROCLAIM strategy emphasizes the importance of PROactive and PROfessional care for residents and their families, in which the needs of those with dementia can be anticipated and managed in the most professional manner possible. The “C” is an important reminder that caregivers should seek consultation from healthcare professionals as required, and that communication is the key to understanding and responding appropriately to the needs of AL residents and their families.

The “C” in PROCLAIM stresses the importance of Life enrichment as a primary goal in the AL setting; and, it emphasizes that Living activities should be maintained to the fullest extent possible. The “A” serves as a reminder that, because disease symptoms change over time, ongoing Assessment of individuals must be a dynamic process, and that the evolving needs of residents with AD are best addressed when mental status, mood, activities of daily living, pain, and the overall well-being of individuals are assessed on a regular basis, through ongoing assessment and re-evaluation.

The “I” in PROCLAIM stresses that Intervention, whether it be environmental, medical, nutritional, psychosocial, or financial, can improve the cognitive, behavioral, social, and/or emotional status of individuals; and, that such interventions should be made when appropriate, with consultation and communication with appropriate individuals. Finally, the “M” in PROCLAIM emphasizes that Medical Management and Monitoring are essential components to overall success, and while there are no ideal solutions to the inevitable decline seen in persons with AD, appropriate use of medications and monitoring clinical effects are critical to success. The overall strategy can be summarized in the PROCLAMATION below:

<table>
<thead>
<tr>
<th>Table 1. The PROCLAIM Strategy for AL Residents With Dementia and Related Conditions</th>
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</thead>
<tbody>
<tr>
<td><strong>PRO</strong> - PROfessional, PROactive, PROtect, PROvide, PROlong</td>
</tr>
<tr>
<td><strong>C</strong> - Commitment, Compassion, Consultation, Communication</td>
</tr>
<tr>
<td><strong>L</strong> - Life enhancement, Life activities</td>
</tr>
<tr>
<td><strong>A</strong> - Attentiveness, Assessment, Action</td>
</tr>
<tr>
<td><strong>I</strong> - Interventions, Improvement, Identification</td>
</tr>
<tr>
<td><strong>M</strong> - Medical Management, Medications, Monitoring</td>
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A PROCLAMATION FOR OPTIMIZING CARE OF INDIVIDUALS WITH ALZHEIMER’S DISEASE RESIDING IN THE ASSISTED LIVING SETTING

We, as healthcare providers, PROCLAIM our commitment to PROvide PROfessional and PROactive care for all residents in our assisted living community, and to focus our team efforts on PROtecting individuals with AD from harm and unnecessary suffering; and, on PROlonging their quality of life, cognitive function, and comfort. We PROCLAIM our Commitment to delivering care that is Compassionate and Courteous and that addresses the Comprehensive medical, psychological, emotional, and financial needs of a Complex and Chronic disease process.

We recognize the importance of Consultation with appropriate sources of medical, nursing, and social service care, and that Communication with providers, residents, and families is key to providing optimal care persons within AL communities. Moreover, we acknowledge the importance of multidisciplinary efforts devoted to Life enrichment and Life activities as primary goals for our residents. In addition, it is clear that ongoing Assessment, Attentiveness, and Action are critical processes for Identifying appropriate Interventions that can Improve overall health and well being of these residents.

Finally, we highlight and stress the importance of Medical Management, appropriate Medications, and vigilant Monitoring as critical components of the PROCLAIM strategy for optimizing life quality and multidisciplinary care for AL residents suffering from dementia and related conditions.

ASSISTED LIVING—A BACKBONE OF COMPASSIONATE HEALTHCARE AND LIFE ENRICHMENT FOR INDIVIDUALS WITH DEMENTIA

More and more, AL residences are providing an increasingly important service for an aging population, and play an increasingly important role in helping individuals with dementia and their families adapt to the challenges of their chronic condition. By definition, assisted living is a residence that provides some assistance with activities of daily living while still promoting and enabling independence for its residents.

Demographics. Currently, it is estimated that there are more than 1.5 million residents in the AL environment which, in the United States, is comprised of about 23,000 facilities, 90% of which have fewer than 15 residents. Recently, however, there has been a significant growth in larger facilities which, in the future, it is predicted will house the majority of individuals seeking assisted living options.

Among those individuals residing in the AL setting, it is estimated that at least 50% have some form of dementia. Approximately 30% of AL communities have a special unit and/or services devoted to dementia or memory disorders. Compared to persons with dementia residing at home, those inhabiting AL communities are older, have more severe cognitive impairment, and are more likely to exhibit wandering, delusions, or aggression.

Unfortunately, AD is often undiagnosed and unrecognized, both by families and clinicians; sometimes even in patients with moderate stage disease and profound symptoms. This resulting “failure to treat” syndrome, therefore, can compromise the PROCLAIM objectives of employing Medications to optimize Life quality and PROlong normal function. In fact, families fail to recognize AD in about 97% of their family members with mild disease, and in almost 50% of those with moderate dementia. Caregivers can play an invaluable role by implementing PROCLAIM-based Assessment and Communication techniques to enhance recognition of AD in its earliest stages, when Medical Management is most beneficial.

Admission and Discharge Characteristics of Residents with AD. Among individuals residing in AL communities who ultimately are cared for in a special dementia or memory care unit, about 37% arrive from a home environment and 30% from a retirement community. An additional 17% are transferred from an AL setting, 11% from an acute care hospital, and about 5% from a chronic, skilled care facility. Discharges from special dementia units in AL facilities also reflect various patient needs but, above all, indicate the progressive nature of AD.

About 77% of AL residents who require specialized care in a dementia unit ultimately will be discharged to a skilled nursing facility, and about 12% will be transferred to another AL facility. Only 7% of these residents are discharged back to a home setting, while about 4% are directed to an acute care hospital. The average duration of stay in an AL facility for patients with documented AD is about 11 months, and 73% of AL discharges or transfers were for greater care needs.

Resident Characteristics and Patient Profiles. Individuals with AD who reside in AL settings tend to require an intermediate or greater level of care, as compared to those residing at home. In addition, persons living at home with AD tend to be younger, less impaired, and require less assistance with activities of daily living. In contrast, nursing home residents tend to be older, more impaired, have more physical needs, and have greater comorbidity as compared to individuals residing in AL settings.

Factors that lead to more complex care for this population include admission from a nursing home, behavioral problems such as depression, aggression, and psychosis, and a history of falling.
While it is generally true that residents in whom the diagnosis of Alzheimer’s dementia has been confirmed (or strongly suspected) should be treated as early in the course of their disease as possible, it is also important to apply the PROCLAIM mandates of Assessment, Identification, and Communication to ensure that the individual who is being cared for actually has AD, and not some other condition with similar symptoms. Caregivers should be sure that cognitive, memory, or behavioral problems they observe are not due to alcoholism, medication-related side effects, stroke, or other conditions (Please see Table 2, Medical Conditions and Drug-Related Side Effects to be Excluded in Patients with Alzheimer’s Disease).

Table 2. Medical Conditions and Drug-Related Adverse Effects to be Excluded in Patients Suspected of Alzheimer’s Dementia

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>Drug-Related Effect</th>
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<tbody>
<tr>
<td>Depression</td>
<td>Metabolic organic failure (liver or kidney disease)</td>
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<tr>
<td>Medication-related</td>
<td>Aphasias</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>Stroke</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>Psychosis</td>
</tr>
<tr>
<td>Infection</td>
<td>Thyroid disorders</td>
</tr>
<tr>
<td>Structural CNS conditions</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>History of head trauma</td>
<td>Anemia</td>
</tr>
<tr>
<td>Sensory impairments</td>
<td>Delirium</td>
</tr>
<tr>
<td>Nutritional deficiencies</td>
<td>Other</td>
</tr>
<tr>
<td>Drug-induced delirium</td>
<td>Other</td>
</tr>
</tbody>
</table>

**AL Caregivers and Their Responsibilities.** Among the multiple caregivers working in the AL setting, advanced practice nurses are an ideal group for providing ongoing assessment, monitoring, consultation, and referral strategies when required. Nurse practitioners, especially those specializing in geriatric care and management of individuals with dementia, should serve as initial consultation points when developing action plans for residents with AL. Advanced practice nurses have played an important role in developing memory centers, protocols, and environmental modifications in the AL setting that support quality care for individuals suffering from AD.

The PROCLAIM strategy for AD care in the AL environment stresses Compassionate care and Consultation, which requires caregivers to be aware of local and regional consultants that can provide expert care for individuals with AD. Accordingly, it may be helpful for AL communities to generate referral strategies and maintain databases and contact information for centers of excellence for AD.

These databases might include geropsychiatry consultants, Alzheimer’s Disease Assessment and Intervention Centers, and other community resources that can positively impact care of these individuals. Establishing contacts with AD support groups, with social service agencies, and key individuals at the local chapter of the Alzheimer’s Disease Association will expedite the ability of an AL community to meet the comprehensive needs of their residents.

The PROCLAIM emphasis on Attentiveness means recognizing unmet resident needs. These may consist of emotional needs (need for touching, companionship, and attention), physical needs (pain management, hygiene), environmental needs (maintaining a dignified domestic setting), sleep needs (addressing wandering and altered sleep patterns), medication needs (ensuring medication compliance and assessing drug-related side effects), psychological needs (reducing anxiety, confusion, boredom, depression, delusions, hallucinations, and agitation) and behavioral needs (minimizing aggression and problematic behaviors).

Identifying appropriate and safe interventions to address the complex and changing needs of individuals with AD requires, per the PROCLAIM action plan, that caregivers perform structured Assessment and Monitoring of the resident, and learn to document resident behaviors and needs, so that baselines can be established, and subsequent deviations—whether it be improvement or deterioration—from baseline can be appreciated by staff and family members.

Coordination of life activities is a fundamental responsibility of the caregiver and falls into the PROCLAIM categories of Life enhancement, Life quality, and Compassionate care. This requires performing an assessment that is tailored to the specific needs of the resident. It is important to become curious about the needs, limitations, goals, and emotional needs of individuals with AD, and how the objectives of quality of life can best be achieved by pressing into service the Attention of family members, consultants, and other resources.

Ideally, communities should maintain structured assessment and service plans that would permit documentation of the following: (1) Resident memory function and cognitive status; (2) Behavioral problems; (2) Pain; (3) Activities of daily living (ADL); (4) Sleep patterns; (5) Social behaviors with other residents, caregivers, and family; (6) Need for escort to bathroom, dining room, clinic, or other services; (7) Grooming; (8) Medication list and reports of medication-related side effects, if any; (9) Nutrition and food intake and preferences; and (10) Status of other medical conditions.

Documentation of such information is essential so that caregivers can Monitor, Assess, and, when required, introduce Interventions that optimize the resident’s normal life functions and sense of well-being.

As the PROCLAIM action plan stresses, knowing when to call for Consultation and refer residents to specialized resources are primary responsibilities of AL caregivers. The need for consultation frequently focuses on issues surrounding drug therapy, i.e., the need to start medications in an individual who is beginning to show signs of memory impairment and/or dementia, the need to increase the dose...
of a medication, the need to add an additional medication, or the need to decrease the dose or discontinue an agent due to side effects or lack of response.

In summary, the responsibilities of caregivers in the AL environment can be characterized as follows:

- Monitoring residents with AD in the AL setting
- Assessing functional status—including improvements and deterioration—of individuals with AD living in the AL environment
- Recognizing the need for initiating patient referrals to neurologic, psychiatric, or geriatric specialists for further evaluation
- Working with AD caregivers to improve monitoring of behavioral and cognitive function
- Recognizing the need for additional or more intensive therapy in individuals with AD
- Optimizing functional capacity and adaptive behaviors in AD patients living in the AL environment
- Assessing global, behavioral, and ADL function in individuals with AD
- Collecting and documenting information and observational data that AL providers need to communicate to physicians and nurses caring for AD residents in AL setting
- Recognize triggers for involvement of additional caregiver resources in the AL setting for residents with AD

Identifying the AL Resident with Dementia. To ensure that residents of AL communities are PROvided with the PROfessional and PROactive care outlined in the PROCLAIM AL doctrine, it is important that caregivers understand how to recognize and identify individuals who may be suffering from Alzheimer’s Dementia. There are no absolutely definitive diagnostic tests for AD—although MRI scans and PET scans are becoming better at confirming the diagnosis—so caregivers should be aware of current definitions that medical and nursing personnel use to identify persons with dementia.

The Diagnostic and Statistical Manual (DSM-IV) used by physicians and nurses characterizes the symptoms and signs of AD as an illness with slowly progressive, impaired memory and global function in an older individual in whom a medical illness has been excluded. These findings should reflect a decline from the individual’s usual, baseline functional status.

Other experts have tried to further simplify this diagnostic scheme—and more specifically, to identify symptoms that justify starting Medical Management, Medications, and Monitoring as recommended in the PROCLAIM AL care scheme. For example, the Alzheimer’s Disease Management Council (ADMC) proposed in their consensus document that in the absence of a precipitating medical illness or drug-related phenomena, the presence of objective, documented, progressive, and clearly worsening deficits in new learning and memory in an elderly patient, accompanied by signs of functional impairment, are highly suggestive of the diagnosis of AD.

Moreover, it was recommended that even in the absence of overt cognitive dysfunction, unexpected changes in personality or other behaviors should prompt more intensive and detailed investigation of cognitive status. The diagnosis can be confirmed only when medical conditions and drug-related adverse effects that can cause alterations in mentation have been excluded as causative factors. Caregivers should make note of personality changes and initiate consultation and referral to determine whether these changes represent early manifestations of a slowly evolving dementia.

To increase the care provider’s suspicion for AD, and to assist in confirmation of the diagnosis, it is important to distinguish between neuropsychiatric changes that are consistent with the aging process from those that may suggest abnormalities in cognition, behavior, or global functioning. In this regard, while occasional naming or word finding—or annoying, but benign, retrieval impairments that benefit from prompting—may be seen in elderly individuals, such deficits as impaired new learning, social withdrawal, and impairment in activities of daily living (ADLs) should prompt caregivers to seek consultation to determine whether the resident may be showing early signs of dementia. (Please see Table 3, Neuropsychiatric Changes Associated with Aging).

Even when early symptoms of AD are recognized and drug therapy is initiated, it is important to dispel misconceptions or unrealistic hopes about drug therapy, while managing caregiver expectations related to the clinical benefits of medication-based treatment. (Please see Table 4, Goals of Therapy for Alzheimer’s Disease). Goals of drug therapy may include symptomatic stabilization, preservation and/or slowing of inevitable decline in cognition, abating functional impairment, delaying onset of disturbed behaviors, and conservation of ADLs. Delaying institutionalization and requirements for antipsychotic use are other benefits that have been reported.

Caregivers should be aware that while not all practitioners agree about the value of drug therapy in AD, clinical trials clearly support a number of benefits that have been claimed and consistently documented for cholinesterase inhibitors and/or NMDA receptor antagonists (memantine) in AD. Benefits of drug therapy that have been reported include: 1) Improvement or delay in decline of cognition; 2) improvement in global impressions; 3) improvement in functional ability; and 4) delay in nursing home placement.

**TREATMENT GOALS FOR RESIDENTS WITH AD IN ASSISTED LIVING SETTING**

The overarching care and maintenance objectives for individuals with dementia residing in the AL setting are...
summarized in the PROCLAIM directive: (1) Providing PROfessional services and care that PROlong quality of life and comfort, and; (2) a Commitment to delivering care that is Compassionate and courteous and that addresses the

Comprehensive medical, psychological, emotional, and financial needs of a complex, progressive, and chronic disease process. Against this backdrop, one of the most important goals—if not, the most important—is to delay progression and the need for placement in a nursing home.

To achieve these objectives, care providers in the AL setting will need to address five major areas of concern to AD residents, caregivers, and medical staff. They include: (1) cognitive Impairment; (2) behaviors; (3) resident mobility; (4) maintaining activities of daily living (ADLs); and (5) managing incontinence.

Strategies that can help delay the need for nursing home placement include early recognition of Alzheimer’s dementia (or other causes of dementia), followed by early pharmacologic intervention with medications shown to be safe and effective for dementia, depression, and behavioral disturbances (Please see Table 5, Medications for Alzheimer’s Disease). Care providers will prolong quality of life and protect residents by ongoing assessment and modification of the physical environment, with a focus on habilitation safety. Adaptive devices should be used to support independence of ADL. When incontinence develops, it is critical to promptly assess the resident to determine the underlying cause and intervene so the resident is kept comfortable and in as dignified a state as possible.

**Medications.** Care providers will need to become familiar with a number of treatment alternatives that are used to manage AD residents in AL communities. For the most part, these medications are used to slow progression of the disease, maintain cognitive function as long as possible, and delay onset of behaviors and nursing home placement. Medications should be used in combination with non-pharmacologic approaches—environmental modifications, physical or social therapy—as part of a comprehensive plan to minimize progression of cognitive and behavioral deterioration.

Appropriately timed drug therapy can produce important medical and financial benefits. For example, prevention of even a small decline in cognition for patients with moderate AD would save about $3700 per patient annually, and relatively small improvements in patients with moderate AD would save approximately $7100 per patient annually.38-40

As outlined in the introduction, two classes of agents are approved for use as first-line therapy for AD (Please See Table 6, First Line Agents Approved for Alzheimer’s Disease, where brand and generic names of commonly used medications are provided).5,11 The cholinesterase receptor inhibitors (ChEIs) galantamine and rivastigmine are approved for treatment of AD patients with mild-to-moderate disease; in addition, rivastigmine also has an indication for treating the dementia associated with Parkinson’s Disease, and is now available as a once-daily skin patch. Donepezil is approved for mild, moderate, and severe AD. The NMDA receptor antagonist, memantine, is approved for moderate and severe stages of AD. More and more, medications from

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**Table 3. Neuropsychiatric Changes Associated with Aging: Distinguishing Among and Identifying Changes in Cognition, Behavior, and Global Functioning That Are Consistent and Inconsistent with Growing Old**

<table>
<thead>
<tr>
<th>Common Changes of Aging</th>
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<tbody>
<tr>
<td>- Occasional naming or word finding difficulty that benefits from prompting</td>
</tr>
<tr>
<td>- General preservation of activities of daily living (ADLs)</td>
</tr>
<tr>
<td>- Reaction time decreased</td>
</tr>
<tr>
<td>- Takes longer time to learn</td>
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</tbody>
</table>

<table>
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<tr>
<th>Inconsistent with Normal Aging*</th>
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</thead>
<tbody>
<tr>
<td>These Changes Should Prompt Further Evaluation</td>
</tr>
<tr>
<td>- Limitations in new learning</td>
</tr>
<tr>
<td>- Impairment in activities of daily living (ADLs)</td>
</tr>
<tr>
<td>- Disinterest or agitation</td>
</tr>
<tr>
<td>- Behavioral disturbances</td>
</tr>
<tr>
<td>- Loss of initiative</td>
</tr>
<tr>
<td>- Social withdrawal</td>
</tr>
<tr>
<td>- Significant change in normal patterns of cognition, memory, or behavior</td>
</tr>
<tr>
<td>- Withdrawal from social patterns</td>
</tr>
<tr>
<td>- Slowly progressive decline from usual/baseline functioning†</td>
</tr>
<tr>
<td>- Unable to initiate tasks</td>
</tr>
</tbody>
</table>

*Some minor disturbances in this list may be consistent with aging, especially in response to situational events
†Consider fronto-temporal dementia, which occurs in younger individuals (< 60 years of age) and is characterized by prominent disordered social conduct in the setting of personality change, without memory change. May also indicate AD.

**Table 4. Goals of Medications Used for Treatment of Alzheimer’s Disease**

| - Stabilize symptoms |
| - Preserve normal function and behavior |
| - Slow inevitable decline in memory and thinking as long as possible |
| - Slow appearance and severity of behavioral symptoms |
| - Slow onset and rate of functional impairment |
| - Preserve activities of daily living (ADLs) |
| - Delay nursing home placement |
| - Delay requirements for antipsychotic use |
| - Optimize caregiving |

Residents will vary in the degree of response in each domain. Medications may be used in other forms of dementia.
Table 5. Medications for Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Generic name (Brand name) Dosage Forms</th>
<th>Initial Dose, mg/day [Usual Dose Range, mg/day]</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cholinesterase Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Donepezil (Aricept) Tablet, orally disintegrating tablet</td>
<td>5 [5-10]</td>
<td>Y/N</td>
<td>Nausea, Dizziness, Diarrhea, Headache, Muscle cramps</td>
</tr>
<tr>
<td>Galantamine (Razadyne ER) Liquid, extended-release capsule</td>
<td>8 mg/day (ER) [16-24] Liquid (4 mg/mL)</td>
<td>Y</td>
<td>Nausea, Vomiting, Dizziness, Diarrhea, Anorexia</td>
</tr>
<tr>
<td>Rivastigmine (Exelon) 1) Capsule, liquid 2) Skin Patch (Patches better tolerated than oral formulation)</td>
<td>1) 1.5 (twice daily) [6-12] 2) –One Exelon Patch, 4.6 mg/24 hours once daily (starting dose) –One Exelon Patch, 9.5 mg/24 hours once daily (maintenance)</td>
<td>Y</td>
<td>Nausea, Vomiting, Dizziness, Diarrhea, Headache</td>
</tr>
<tr>
<td><strong>NMDA-receptor Antagonist</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memantine (Namenda) Tablet</td>
<td>5 [20]</td>
<td>Y/N</td>
<td>Confusion, Headache, Constipation, Hypertension</td>
</tr>
<tr>
<td><strong>Antidepressants: Tricyclic Antidepressants (TCAs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic name (Brand name) Dosage Forms</td>
<td>Usual Dosing in Geriatric Patients</td>
<td>Administer With Food (Y/N)</td>
<td>Common Adverse Events (ADEs)*</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-----------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Amitriptyline (Vanatrip, various) Tablet</td>
<td>10-25 [25-100; therapeutic plasma level 100-250 ng/mL]</td>
<td>Y/N</td>
<td>Orthostatic hypotension Ataxia Extrapyramidal symptoms Sedation Urinary retention Dry mouth</td>
</tr>
<tr>
<td>Clomipramine (Anafranil, various) Capsule</td>
<td>25 [50-150]</td>
<td>Y</td>
<td>Dry mouth Dizziness, ataxia Sleep problems Stomachache Tremor</td>
</tr>
</tbody>
</table>

*Adverse events reported in clinical trials in at least 2% of patients receiving drug and at a higher frequency than placebo-treated patients.
### Table 5. Continued

**Antidepressants: Tricyclic Antidepressants (TCAs) — Continued**

<table>
<thead>
<tr>
<th>Generic name (Brand name) Dosage Forms</th>
<th>Usual Dosing in Geriatric Patients</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Desipramine</strong>&lt;br&gt;(Norpramin, various)&lt;br&gt;Tablet</td>
<td>10&lt;br&gt;[25-100; therapeutic plasma level, 125-300 ng/mL]</td>
<td>N</td>
<td>Dry mouth&lt;br&gt;Urinary retention&lt;br&gt;Light headedness&lt;br&gt;Drowsiness&lt;br&gt;Insomnia&lt;br&gt;Mild tremors</td>
</tr>
<tr>
<td><strong>Doxepin</strong>*&lt;br&gt;(Sinequan)&lt;br&gt;Capsule, liquid</td>
<td>10&lt;br&gt;[10-75; therapeutic plasma level, 110-250 ng/mL]</td>
<td>Y (for oral solution, mix with milk or juice)</td>
<td>Drowsiness (most common reported ADE)&lt;br&gt;hypotension&lt;br&gt;Dizziness&lt;br&gt;Nausea and vomiting</td>
</tr>
<tr>
<td><strong>Imipramine</strong>&lt;br&gt;(Tofranil)&lt;br&gt;Capsule, tablet</td>
<td>10&lt;br&gt;(25-100; therapeutic plasma level, 125-250 ng/mL)</td>
<td>N</td>
<td>Orthostatic hypotension&lt;br&gt;Confusion&lt;br&gt;Anxiety&lt;br&gt;Ataxia&lt;br&gt;Dry mouth</td>
</tr>
<tr>
<td><strong>Nortriptyline</strong>&lt;br&gt;(Pamelor)&lt;br&gt;Capsule, liquid</td>
<td>10&lt;br&gt;(10-50; therapeutic plasma level, 50-150 ng/mL)</td>
<td>Y/N</td>
<td>Urinary retention&lt;br&gt;Anorexia&lt;br&gt;Hypotension&lt;br&gt;Confusion&lt;br&gt;Ataxia&lt;br&gt;Insomnia&lt;br&gt;Dry mouth&lt;br&gt;Urinary retention</td>
</tr>
</tbody>
</table>

* Not recommended for treatment of geriatric depression.
## Table 5. Continued
### Antidepressants: Selective Serotonin Reuptake Inhibition (SSRIs)

<table>
<thead>
<tr>
<th>Generic name (Brand name)</th>
<th>Dosage Forms</th>
<th>Usual Dosing in Geriatric Patients</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa, various)</td>
<td>Liquid, tablet</td>
<td>10-20 [20-40]</td>
<td>Y/N</td>
<td>Nausea, Dry mouth, Somnolence, Insomnia, Sweating increased</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>Liquid/tablet</td>
<td>5-10 [10]</td>
<td>Y/N</td>
<td>Nausea, Ejaculation disorder, Insomnia, Diarrhea, Somnolence</td>
</tr>
<tr>
<td>Fluoxetine (Prozac/Prozac Weekly, various)</td>
<td>Capsule, liquid, tablet</td>
<td>10 [20-40]</td>
<td>Y/N</td>
<td>Nausea, Headache, Insomnia, Nervousness, Anxiety</td>
</tr>
<tr>
<td>Fluvoxamine (Various)</td>
<td>Tablet</td>
<td>25-50 [50-200]</td>
<td>Y/N</td>
<td>Nausea, Headache, Somnolence, Insomnia, Asthenia</td>
</tr>
<tr>
<td>Paroxetine (Paxil/Paxil CR, various)</td>
<td>Liquid, tablet, controlled-release tablet</td>
<td>10-20 [20-40]</td>
<td>Y/N</td>
<td>Nausea, Somnolence, Headache, Dry mouth, Asthenia</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>Liquid, tablet</td>
<td>25-50 [50-200]</td>
<td>Y/N; food increases extent of absorption</td>
<td>PI; frequency in adults, 50-200 mg/d</td>
</tr>
</tbody>
</table>

* Not recommended for treatment of geriatric depression.
<table>
<thead>
<tr>
<th>Generic name (Brand name) Dosage Forms</th>
<th>Usual Dosing in Geriatric Patients</th>
<th>Initial Dose, mg/day</th>
<th>Dose Range, mg/day</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buproprion (Wellbutrin/Wellbutrin SR, GlaxoSmithKline; various) Tablet, sustained-release tablet</td>
<td>75</td>
<td>[100-300]</td>
<td>N</td>
<td>Headache</td>
<td>Dry mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Constipation</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta, Lilly) Delayed-release capsule</td>
<td>40 (20 mg BID)</td>
<td>[40-60]</td>
<td>Y/N</td>
<td>Nausea</td>
<td>Dry mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Constipation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dizziness</td>
</tr>
<tr>
<td>Mirtazapine (Remeron/Remeron SolTab, Organon, various) Tablet, disintegrating tablet</td>
<td>7.5-15</td>
<td>[15-45]</td>
<td>Y/N</td>
<td>Somnolence</td>
<td>Dry mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increased appetite</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Constipation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Weight gain</td>
</tr>
<tr>
<td>Nefazodone (Various) Tablet</td>
<td>50-100</td>
<td>[150-500]</td>
<td>Y/N</td>
<td>Xerostomia</td>
<td>Drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Constipation</td>
</tr>
<tr>
<td>Trazodone (Desyrel, Sandoz; various) Tablet</td>
<td>50</td>
<td>[50-300]</td>
<td>Y</td>
<td>Dizziness</td>
<td>Dry mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Parkinsonian gait</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tremor</td>
</tr>
<tr>
<td>Venlafaxine (Effexor/Effexor XR, Wyeth) Tablet, extended-release capsule</td>
<td>25-37.5</td>
<td>[75-300]</td>
<td>Y</td>
<td>Nausea</td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Somnolence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abnormal ejaculation</td>
</tr>
</tbody>
</table>
### Table 5. Continued

#### Traditional Antipsychotics

<table>
<thead>
<tr>
<th>Generic name (Brand name) Dosage Forms</th>
<th>Usual Dosing in Geriatric Patients</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chlorpromazine</strong> <em>(Thorazine, various)</em> Tablet, oral concentrate, suppositories, injection</td>
<td>20-75 [20-200]</td>
<td>Y</td>
<td>Hypotension Sedation Anticholinergic effects Extrapyramidal symptoms</td>
</tr>
<tr>
<td><strong>Haloperidol</strong> <em>(Haldol, various)</em> Tablet, oral concentrate, injection</td>
<td>0.25-1 [1.5-2]</td>
<td>Y</td>
<td>Fatigue Rigidity Bradykinesia Drowsiness Tremor</td>
</tr>
<tr>
<td><strong>Thioridazine</strong> <em>(Mellaril, various)</em> Tablet, oral concentrate</td>
<td>20 [20-75]</td>
<td>Y</td>
<td>Drowsiness Dry mouth Extrapyramidal symptoms Dose-related prolongation of the QT interval</td>
</tr>
</tbody>
</table>

#### Atypical Antipsychotics

<table>
<thead>
<tr>
<th>Generic name (Brand name) Dosage Forms</th>
<th>Usual Dosing in Geriatric Patients</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Olanzapine</strong> <em>(Zyprexa/Zyprexa Zydis/ Zyprexa IntraMuscular)</em> Tablet, disintegrating tablet, injection</td>
<td>2.5-5 [5-10]</td>
<td>N</td>
<td>Accidental injury Somnolence Pain Abnormal gait Fever</td>
</tr>
<tr>
<td><strong>Risperidone</strong> <em>(Risperdal)</em> Tablet, oral solution</td>
<td>0.5 mg BID [1-2]</td>
<td>N</td>
<td>Injury Somnolence Falls EPS-related events UTI</td>
</tr>
</tbody>
</table>
**Paliperidone**
(Invega®)  
3 mg - 12 mg once daily  
Recommended dose:  
6 mg once daily  
Maximum does in renal  
impairment: 3 mg/day

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Dosage Forms</th>
<th>Usual Dosing in Geriatric Patients</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)*</th>
</tr>
</thead>
</table>
| Ziprasidone (Geodon) | Capsule, powder for injection | 40-80 [80-160] (ND) | Y | Somnolence  
EPs  
Headache  
Dizziness  
Akathisia |

* No published geriatric data.

**Benzodiazepines & Sedative Hypnotics**

<table>
<thead>
<tr>
<th>Generic name (Brand name) Dosage Forms</th>
<th>Usual Dosing Initial Dose, mg/day [Dose Range, mg/day] (**OBRA Maximum Recommended Dose, mg/d)</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)</th>
</tr>
</thead>
</table>
| Estazolam (ProSom, various) Tablet | 0.5-1 [1-2] (0.5) | N | Somnolence  
Asthenia  
Dizziness  
Coordination abnormal  
Lower extremity pain |
| Flurazepam (Dalmane, various) Capsule | 15 [15-30] (15) | N | Drowsiness  
Dizziness  
Depression  
Nausea, vomiting  
Difficulty urinating  
Headache  
Dry mouth |
| Quazepam (Doral) Tablet | 15 [7.5] (7.5) | N | Excessive drowsiness  
Incoordination  
Cognitive deficits  
Confusion |
| Temazepam (Restoril, various) Capsule | 7.5 [7.5-15] (15) | N | Drowsiness  
Headache  
Fatigue  
Nervousness  
Lethargy |
| Alprazolam (Xanax) Tablet | 0.25 mg BID or TID [2 mg total dose] | Y/N | Drowsiness  
Light-headedness  
Fatigue |

**OBRA: Omnibus Budget Reconciliation Act**
Table 5. Continued

### Benzodiazepines & Sedative Hypnotics — Continued

<table>
<thead>
<tr>
<th>Generic name (Brand name)</th>
<th>Dosage Forms</th>
<th>Usual Dosing</th>
<th>Administer With Food (Y/N)</th>
<th>Common Adverse Events (ADEs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial Dose, mg/day [Dose Range, mg/day] (**OBRA Maximum Recommended Dose, mg/d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triazolam (Halcion, various)</td>
<td>Tablet</td>
<td>0.125 [0.125-0.25] (1)</td>
<td>N*</td>
<td>Drowsiness, Headache, Dizziness, Nervousness, Light-headedness</td>
</tr>
<tr>
<td>Eszopiclone (Lunesta)</td>
<td>Tablets</td>
<td>1 [1-2] (ND)</td>
<td>N*</td>
<td>Unpleasant taste, Dizziness, Dry mouth, Diarrhea, Pain</td>
</tr>
<tr>
<td>Zolpidem (Ambien, various)</td>
<td>Tablets</td>
<td>5 [5-10] (ND)</td>
<td>N</td>
<td>Headache, Abdominal pain, Asthenia, Somnolence, Dysmenorrhea</td>
</tr>
<tr>
<td>Clonazepam (Klonopin, various)</td>
<td>Tablets, orally disintegrating tablets</td>
<td>0.5-1 [1] (1.5)</td>
<td>Y/N</td>
<td>Somnolence, Upper respiratory infection, Depression, Fatigue, Memory disturbance</td>
</tr>
<tr>
<td>Diazepam (Valium, Diastat, various)</td>
<td>Tablets, oral solution, injection</td>
<td>2 [2-5] (5)</td>
<td>Y</td>
<td>Somnolence, Headache, Diarrhea, Euphoria, Rash</td>
</tr>
<tr>
<td>Lorazepam (Ativan, various)</td>
<td>Tablets, injection, oral solution</td>
<td>0.5-1.5 [1.5-2] (2)</td>
<td>N*</td>
<td>Somnolence, Accidental injury, Hypertension, Headache, Vasodilation</td>
</tr>
<tr>
<td>Oxazepam (Serax, various)</td>
<td>Tablets, capsules</td>
<td>30 [30-45] (30)</td>
<td>N</td>
<td>Excessive drowsiness, Incoordination, Cognitive deficits, Confusion</td>
</tr>
</tbody>
</table>

**Sedative—MT1 MT2 AGENT**

| Ramelteon (Rozerem) | Tablets | 8 mg [8 mg] | Y/N (Not with high-fat meal) | Somnolence, Dizziness, Fatigue |
the Chel class and memantine are being used in combination to achieve better results in terms of delaying progression of cognitive impairment.

For more advanced disease, especially when depression, aggression, hallucinations, and/or behavioral problems develop, some combination of antidepressants, neuroleptics, traditional antipsychotics, atypical antipsychotics, and/or anticonvulsants may be required. For more specific information, please see Table 5, Medications for Alzheimer’s Disease, which includes individual sections, organized by drug class, specifying dosing, relation to food intake, and common side effects for antidepressants, antipsychotics, neuroleptics, and sedative hypnotics.

**Monitoring Effects of Medications.** The PROCLAIM mandate for managing AD residents in the AL setting stresses the importance of Communicating important information to residents and families, and the value of Monitoring the effects—both good and, occasionally, negative—of Medications. Healthcare providers should have realistic expectations about the effects of medications in AD, and be prepared to communicate this information to residents, when appropriate, but especially to family members (Please see Table 4, Goals for Medications Used for Treatment of Alzheimer’s Disease).

In general, Alzheimer’s medications are able to slow the progression of cognitive dysfunction (memory and related capabilities) based on tests (ADAS-COG, MMSE) used to monitor patients. In some cases, behavior problems can be improved and medications may delay placement in nursing homes, but these benefits tend to be selective rather than uniform.

While not yet supported by research, some consideration should be given to the potentially unfavorable consequences of not treating individuals with AD. These consequences may include the following: (1) earlier nursing home placements; (2) increased likelihood of aggressive behaviors; (3) increased caregiver and family stress; (3) earlier decline in memory; (4) behavioral disturbances that are more frequent and/or severe; (5) earlier decline in ADLs; and (6) possible increased need for additional medications to manage behav-

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### Table 6. First-Line Agents Approved for Alzheimer’s Disease: Starting Dose, Minimum and Maximum Therapeutic Dose, Cost*, and Titration Strategies

<table>
<thead>
<tr>
<th>Cholinesterase Inhibitors</th>
<th>NMDA Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donepezil (Aricept®):</strong></td>
<td><strong>Memantine (Namenda®):</strong></td>
</tr>
<tr>
<td>Initiate oral therapy at 5 mg once daily, at bedtime; after 6 weeks, increase dose by 5-10 mg once daily. The minimum therapeutic dose for donepezil is 5 mg once daily. Cost range: $135-$145.</td>
<td>The recommended starting dose for memantine is 5 mg once daily with or without food. The recommended target dose is 20 mg/d. The dose should be titrated in 5 mg increments to 10 mg/d (5 mg twice daily), 15 mg/d (5 mg and 10 mg as separate doses), and 20 mg/d (10 mg/d twice daily). The minimum recommended interval between dose increases is one week. Cost range $130-$140. Also available as oral solution.</td>
</tr>
<tr>
<td><strong>Rivastigmine (Exelon®):</strong></td>
<td></td>
</tr>
<tr>
<td>Initiate oral therapy at 1.5 mg twice daily, taken at the end of a full meal. At 4-week intervals, increase (ExelonAE) each dose by 1.5 mg, up to a maximally effective, tolerated therapeutic dose. The maximum dose is 6 mg twice daily. The minimum therapeutic dose for rivastigmine is 3 mg twice daily. Cost range $130-$144. Rivastigmine has been shown to be both an acetylcholinesterase inhibitor and a butyryl cholinesterase inhibitor. The minimum recommended interval between dose increases is 4 weeks. A skin patch, 10 cm2 (9.5 mg/24 h) rivastigmine, is now available, and is associated with a better tolerability profile than oral medication. Starting dose of patch is 4.6 mg/24 h.</td>
<td>*Estimated cost to the pharmacist for one month of therapy at the target dose based on average wholesale prices in Red Book, Montvale, NJ. Cost to patient will be higher depending upon prescription filling fee and other factors.</td>
</tr>
<tr>
<td><strong>Galantamine (Razadyne®):</strong></td>
<td></td>
</tr>
<tr>
<td>Initiate oral therapy at 4 mg twice daily, with food. At 4-week intervals, increase each dose by 4 mg up to a maximally effective, tolerated therapeutic dose. The maximum dose is 12 mg twice daily; the minimum therapeutic dose for galantamine is 8 mg twice daily. Cost range: $125-$135. Galantamine has been shown to be both a cholinesterase inhibitor and to have nicotinic receptor actions.</td>
<td>1. Aricept [package insert]. Teaneck, NJ: Eisai Inc; 2000.</td>
</tr>
<tr>
<td></td>
<td>2. Exelon [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2001; and ADMC panel opinion statement.</td>
</tr>
</tbody>
</table>
ior problems (Please see Table 7, Possible Consequences of Not Treating Patients with Alzheimer’s Disease).

Table 7. Possible Consequences of Not Treating Persons With Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Possible Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earlier nursing home placements</td>
</tr>
<tr>
<td>Aggression</td>
</tr>
<tr>
<td>Caregiver and family stress</td>
</tr>
<tr>
<td>Earlier decline in memory</td>
</tr>
<tr>
<td>Behavioral disturbances</td>
</tr>
<tr>
<td>Impaired activities of daily living (ADLs)</td>
</tr>
<tr>
<td>Possible increased need for additional medications to manage behavior problems</td>
</tr>
</tbody>
</table>

As a general rule, it is best to initiate drug therapy as early as possible in persons with AD, including those with mild and moderate disease, where the impact of treatment and delayed progression can be considerable. Any interruptions in therapy should be as brief as possible, and patience is required when titrating medications until the best-tolerated therapeutic dose is achieved. The optimal duration of therapy is uncertain, and as emphasized, it has become increasingly common to combine an NMDA receptor antagonist such as memantine with one of the cholinesterase receptor inhibitors.

Finally, a number of evaluation instruments, scales, and monitoring tools are used to assess the status and severity of the disease and, especially, to determine whether patients are responding to medications (Please see Table 8, Scales and Evaluation Instruments Used to Monitor Patients with Alzheimer’s Disease and Response to Pharmacological Therapy).14-21 Many of these are used in research settings, whereas others may be used by the resident’s physician or nurse practitioner to monitor progression or stabilization of their dementia symptoms.

Cessation of Drug Therapy. One of the most important questions that arises when caring for individuals with dementia is when it might be appropriate to discontinue medications that are being used to treat the cognitive symptoms of this condition. Definitive answers are difficult to come by and the issue is somewhat complex for a number of reasons. First, it should be stressed that most clinical trials evaluating ChEIs and NMDA receptor antagonists have been conducted for periods ranging from 3 to 12 months. Therefore, the long-term effects of drugs on stabilization are somewhat uncertain. Second, medication therapy carries a financial burden, and therefore, if therapeutic results, as gauged by resident, caregivers, and clinicians are not favorable, there is no reason to incur unnecessary costs of drug therapy.

Table 8. Scales and Evaluation Instruments Used To Monitor Natural History of Alzheimer’s Disease And Patient Response To Pharmacological Therapy

<table>
<thead>
<tr>
<th>Mini-mental State Examination</th>
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</thead>
<tbody>
<tr>
<td>Measures cognition</td>
</tr>
<tr>
<td>Assesses orientation, registration, recall, language, and attention</td>
</tr>
<tr>
<td>Uses a 30-point scale</td>
</tr>
<tr>
<td>Requires approximately 5-10 minutes to complete</td>
</tr>
<tr>
<td>Minimal training needed to administer in outpatient setting</td>
</tr>
<tr>
<td>Administered by and useful for primary care practitioners and nurses</td>
</tr>
<tr>
<td>On average, score decreases about 2-4 points per year in patients with Alzheimer’s disease</td>
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<thead>
<tr>
<th>Function Activities Questionnaire</th>
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<tbody>
<tr>
<td>Intended to quantify level of disability</td>
</tr>
<tr>
<td>Scores functional capacity on a scale of 1 (normal) to 7 (severely incapacitated)</td>
</tr>
<tr>
<td>Requires 5-10 minutes to complete</td>
</tr>
<tr>
<td>Easy to administer by caregiver</td>
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<table>
<thead>
<tr>
<th>Physical Self-maintenance Scale and Instrumental Activities of Daily Living (ADLs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluates patient’s ability to perform basic and instrumental tasks</td>
</tr>
<tr>
<td>Assesses eight areas of higher functioning on a scale of 1 to 5, and six basic tasks that are fundamental to daily function</td>
</tr>
<tr>
<td>Requires about 10 minutes to complete scale</td>
</tr>
<tr>
<td>Very useful in clinical practice</td>
</tr>
<tr>
<td>Minimal training required to administer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Examinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini-COG</td>
</tr>
<tr>
<td>Clock Drawing</td>
</tr>
<tr>
<td>University of Washing AD Exam</td>
</tr>
</tbody>
</table>

Continued on Page 18…
Clearly, however, certain parameters and triggers for cessation of drug therapy have been identified by experts and they should be considered by those caring for individuals with AD. One should consider discontinuation of therapy if the patient has failed attempts at monotherapy (use of a single drug) with at least two or more cholinesterase inhibitors, a NMDA inhibitor, or combination therapy with agents from the two aforementioned classes. If the patient demonstrates loss of clinical effect, manifested by accelerated and progressive cognitive deterioration, it may be time to obtain consultation and consider drug cessation.

Clearly, if the resident demonstrates intolerance (due to unmanageable drug-related side effects) to the drug(s), cessation may be necessary. Finally, if an individual deteriorates to the point of having no meaningful social interactions or quality of life benefit as determined by caregivers and health care providers, the financial costs of prolonged drug therapy probably are not justified. Other criteria and recommendations for discontinuing drug therapy have been proposed by national associations, working groups, advisory councils, and consensus panels, and may be employed to assess need for drug cessation.13

Table 8. Continued


ASSESSMENT, EVALUATION, AND MANAGEMENT OF BEHAVIORAL DISTURBANCES

The PROCLAIM strategy emphasizes the importance of ongoing resident assessment and evaluation in order to identify the need for interventions that may improve life quality for residents. Especially when it comes to behavioral problems that frequently accompany dementia, caregivers should attempt to identify the specific problem behavior avoiding generalities (WHAT), characterize its timing and frequency (WHEN), determine what surroundings or specific environment brings on the behavior (WHERE), and whether other residents or specific staff are involved (WITH WHOM). These things should be documented in order to characterize a pattern that potentially can be addressed with behavioral or environmental modification.

It should also be determined just how troubling or dangerous the behaviors may be to the resident, to other residents, or caregivers. One should look for signs of agitation or aggression, delusions, hallucinations, depression, anxiety, and sleep disturbances, and if any of these interfere with ADLs, present harm to the resident or others, or lead to other problems, consultation should be obtained and the problems addressed promptly. When severe and unresponsive to behavioral, social, or environmental modifications and interventions, medication-based treatment may be required (Please see Table 9, Behavioral Symptoms and Medications in Patients with Alzheimer’s Disease).

Experts have attempted to organize such behavioral problems into a symptom cluster, one of which is called Behavioral and Psychological Symptoms in Dementia (BPSD). Based on this categorization, about 20-40% of behavioral problems fall into the depression category, about 30-40% include a component of psychosis, and 50-80% of behavioral problems include a dimension of aggressive or agitation-related symptoms.

Managing AD residents with behavioral problems requires that care providers rule out other causes such as delirium or acute confusional states that can also lead to these symptoms. Medical causes such as infection, metabolic abnormalities, and medication toxicity should be evaluated and ruled out.

Agitation and aggressive behavior in patients with dementia are worrisome symptoms that are most often seen in patients with moderate or severe dementia. These behaviors may be instigated by a number of factors, including: (1) Cognitive, memory, or language deficits, which can cause confusion and misunderstanding; (2) frightening delusions or visual hallucinations; (3) depression; (4) sleep disorders; (5) medication-related side effects; and (6) unrecognized/untreated pain. Caregivers should attempt to systematically identify factors that may be responsible for aggressive behavior and seek consultation so the appropriate interventions can be made.

National associations have weighed in on the value of
nonpharmacologic approaches for controlling aggressive behaviors and agitation. Of special importance are The American Academy of Neurology (AAN) Practice Parameters for managing agitation and behaviors in patients with AD, which were issued in 2001. A Guideline Reaffirmed document was released on Oct. 18, 2003.

Overall, the AAN practice parameters support the use of first-line nonpharmacologic strategies for agitation, especially when identifiable causes such as pain or environmental triggers are responsible. Pain can be a powerful trigger to behavioral and/or memory derangements, and caregivers should make every attempt to communicate with residents and assess patterns that suggest pain as an underlying cause of behavioral problems. The use of a regularly scheduled mild analgesic may reduce some behaviors.

The PROCLAIM approach to AD management in the AL environment stresses Compassionate care, Life enhancement, and maintenance of Life activities. This may require caregivers to use nonmedication-based approaches to patient care. As a rule, while pharmacologic therapy is the first line of treatment for the cognitive and memory disturbances seen in AD, the principles of nonpharmacologic management should be employed as an initial strategy for managing behavioral disturbances.

The AAN Guidelines recommend that educational programs be offered to family caregivers to improve caregiver satisfaction and to delay the time to nursing home placement. In addition, the staff of long-term care facilities should be educated about AD to minimize the unnecessary use of antipsychotic medications. Behavior modification, scheduled toileting, and prompted voiding should be employed to reduce urinary incontinence. Functional ability of AD residents can be increased by graded assistance, skills practice, and positive reinforcement.

When behavioral disturbances become problematic, resident safety is of utmost importance. Usually, this means controlling physical (i.e., driving) and financial risks for the resident, and interventions that address the resident’s intra-facility social patterns and environment. The “3S” acronym (Serenity, Structure, and Support) can be helpful in developing a care plan for residents with behavioral problems. The Serenity component means that one should avoid inducing overt frustration or anger on the part of residents with AD. Structure can be helpful in maintaining resident stability. Therefore attempt to maintain regular schedules and facilitate positive habits as part of the resident’s routine. Support for all stakeholders is key. This means reducing caregiver strain by seeking social support and using respite services.

Behavioral modification is often effective in relieving anxiety or agitation. Wandering, hoarding, withdrawal, social inappropriateness and repetitive questioning may respond more favorably to behavioral modification. It should be stressed that medications do not work optimally alone, nor will they relieve most of the symptoms. Compassionate care based on Communication skills can make a substantial difference in reducing the problems associated with disturbed behaviors. For example, one can attempt to distract individuals with AD with tasks or food. Except in extreme behaviors, one should attempt to compromise with the individual rather than medicate them.

### Table 9. Behavioral Symptoms and Medications in Patients with Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Behavioral Symptoms in Which Medications Should Be Considered</th>
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<tbody>
<tr>
<td>• Aggressive behaviors</td>
</tr>
<tr>
<td>• Psychosis</td>
</tr>
<tr>
<td>• Hallucinations</td>
</tr>
<tr>
<td>• Paranoia</td>
</tr>
<tr>
<td>• Delusions</td>
</tr>
<tr>
<td>• Deliriumt</td>
</tr>
<tr>
<td>• Obsessive-compulsive behaviors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medications Used to Treat Disturbed Behaviors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atypical Antipsychotics</strong></td>
</tr>
<tr>
<td>• Risperidone</td>
</tr>
<tr>
<td>• Olanzapine</td>
</tr>
<tr>
<td>• Quetiapine</td>
</tr>
<tr>
<td>• Ziprasidone</td>
</tr>
<tr>
<td>• Aripiprazole</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Typical Antipsychotics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Haloperidol</td>
</tr>
<tr>
<td>• Thorazine</td>
</tr>
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<table>
<thead>
<tr>
<th><strong>Anticonvulsants</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Valproate/divalproex</td>
</tr>
<tr>
<td>• Carbamazepine</td>
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<table>
<thead>
<tr>
<th><strong>Benzodiazepines (For short-term use at low doses)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clonazepam</td>
</tr>
<tr>
<td>• Others</td>
</tr>
</tbody>
</table>

* † Reversible causes of delirium should be investigated and treated appropriately

Note: Antipsychotics should be used in patients who manifest disturbed behaviors only if medical therapy and non-pharmacologic approaches to AD have been maximized and found not to be effective.
than force a single solution or action; sometimes, it is best
to back off, let the resident relax, and redirect their attention
from a problematic behavior to one that is more positive. The
dictum, “They can’t resist if you don’t insist,” can go a long
way toward diffusing an uncomfortable encounter.

CATIE Studies. The CATIE study indicated that there was no
significant improvement in the Clinical Global Impression
of Change for risperidone, olanzapine, or quetiapine in
comparison with placebo at 12 weeks or in the rates of drug
discontinuation for inefficacy over longer-term follow-up.

These results are consistent with those of three placebo-
controlled withdrawal studies that indicated no worsening of
behavior when long-term administration of neuroleptic drugs
is stopped. There are no long-term treatment studies focusing
specifically on the management of psychosis in AD, leaving
a substantial gap in the evidence base for pharmacotherapy
for these individuals.

The balance of evidence supports the conclusion that
there is an increased risk of cerebrovascular adverse events
in people with dementia who are treated with risperidone or
olanzapine. However, it is unclear whether this is a class effect
or something specific to several drugs. Far less clinical trial
information is available for other atypical antipsychotic drugs.
In general antipsychotic agents must be used with great caution,
and employed only if the benefits outweigh risks.

Psychosis. One of the hallmarks of the PROCLAIM approach
to care of AD residents in the AL setting is to PROtect patients
from harm to themselves or others, and to identify residents
who require Medical Management. Among conditions that
impair life quality, and that may cause disturbances, harm, or
aggression to others, psychosis is among the most important
difficult to recognize and treat.

As a rule, diagnostic criteria for the psychosis of AD
requires, first, excluding schizophrenia and other causes of
psychotic symptoms. Once other conditions are ruled out,
the presence of hallucinations and/or delusions, frequently
lasting for more than a month, should suggest psychosis.
Frequently, these can be disruptive to resident functioning,
and can be associated with agitation, negative symptoms,
and depression.

In general, delusions are more common than hallucinations
and occur in up to 30% of persons with severe AD. Paranoid
delusions are the most distressing, and they may be fleeting
or persistent. PROviding Compassionate care means that
Medication-based Intervention, as outlined in PROCLAIM,
may be required when residents and/or their families are
significantly impacted or disturbed by psychotic symptoms.

Depression. Depression is a common and difficult-to-manage
condition that is encountered frequently in individuals with
AD. One of the PROCLAIM directives is to Identify problems
for which Interventions can produce improvement in overall
well-being and mental health, and in this regard, depression is
among the most important conditions requiring early recogni-
tion and intervention. Depression can lead to heightened pain
sensations, and conversely, unrecognized pain syndromes
can lead to depression and withdrawal, or, in some instances,
agitation, thereby complicating patient management.

First, it should be stressed that depression, in and of itself,
can cause symptoms and signs of cognitive impairment,
so it is not unusual to confuse signs of depression with
other findings in AD. It is common for residents with
dementia to develop apathy, social withdrawal, and sleep
disturbances. These symptoms suggest depression but may be
due to cognitive defects. In addition, persons with dementia,
especially those in the earlier stages, may develop depression
in reaction to deteriorating mental capacity. In line with the
PROCLAIM action plan, which advocates appropriate use of
Medications, Medical Management, and patient Monitoring,
a therapeutic trial of antidepressants may be the only feasible
diagnostic strategy to determine whether symptoms are
caused by underlying depression.

The criteria for depression in the setting of AD include a
number of findings, and recognizing this treatable condition
can be facilitated by attention to the PROCLAIM principles
of Communication, Attention, and Consultation. Care pro-
viders should take note of residents who have a decreased
affect, appetite disruption, or sleep disturbance. In addition,
agitation, irritability, fatigue, and loss of energy can indicate
depression. In extreme cases, depressed individuals may
complain of worthlessness, hopelessness, and thoughts of
death or suicidal ideations. Such extreme complaints should
prompt the care provider to seek immediate Consultation to
determine what Interventions might be necessary, as outlined
in the PROCLAIM strategy.

PART II—Advanced Diagnostic and Treatment
Strategies for Nurse Providers in the Assisted Living
Setting—Guidance for the Geriatric Nurse Practitioner

DIAGNOSIS, INDEX OF SUSPICION, AND
TREATMENT TRIGGERS

Many residents entering AL facilities do so because of
a gradual deterioration in the ability to care for themselves,
or because family members have determined that a more
supervised setting will offer advantages at a particular
stage of life. The point is that while many individuals
entering are pre-identified as suffering from dementia, a
significant percentage develop signs and symptoms of the
disease during their stay in an AL community. Hence, it is
important that caregivers in the AL environment know how
to recognize the manifestations of dementia in their residents,
so that PROCLAIM-mandated actions, including Assessment,
Intervention, Medical Management, and Medications, can be
implemented as soon as possible.

Although there are no available definitive electrophysi-
Diagnostic criteria for dementia require an individual to have 1) memory impairment; 2) at least one of the following: aphasia (language difficulties), apraxia (diminished ability to perform motor activities in the presence of intact motor function), agnosia (inability to recognize or name objects despite intact sensory function), or disturbance in executive function (diminished ability to plan or organize); and 3) impaired social or occupational functions. These impairments must occur in the absence of other disorders that could cause similar signs and symptoms.

The earliest symptom of AD usually is the insidious onset and progression of memory loss. Initially, this memory loss can be difficult to differentiate from the common experience of age-associated benign forgetfulness. However, individuals with the latter are aware of the deficit and their ADLs are minimally or not at all impaired. Some degree of language impairment also is common in AD. Frequently, names of objects may be forgotten and replaced by the word “thing;” characteristically, speech may be littered with errors in naming (i.e., cup for bowl, “spork” for spoon). Problems with spatial orientation are common.

In these cases, patients become lost in familiar locations and are unable to learn new directions. One of the most disturbing features noted by family members is personality change. Patients may become apathetic, agitated, or paranoid and may accuse people of taking things from them. As the dementia progresses, inappropriate behavior and delusional thoughts may intervene. Later stages of AD are characterized by apathy, decreased speech output, failure to recognize family members, and incontinence. Death often results from aspiration pneumonia or infected decubitus ulcers. Life expectancy following a diagnosis of AD varies widely, but the average range is 8-12 years.

MANAGING RESIDENT EXPECTATIONS AND RESPONSE TO THERAPY

It should be emphasized to both residents and caregivers that improvement, stabilization, and/or delay in progression of cognitive and/or behavioral dysfunction are valuable endpoints for monitoring benefits of drug therapy. However, it also may be helpful to adjust family expectations, as well as those of caregivers, by communicating that clinical improvements may not always be observable by caregivers, especially when a delayed decline in relative worsening is the primary benefit likely to be observed in an individual patient.

To enhance cooperation with a treatment plan that commonly is hampered by medication-related side effects and that requires patience during the drug titration period, residents and their families should PROactively be counseled about barriers that may need to be crossed on the journey from drug initiation to achievement of a maximally tolerated therapeutic dose of a given medication. An explanation of possible side effects is advisable, as well as strategies for dealing with bumps in the road when they arise. When
there is reluctance to embark on drug therapy, the ethics and potential adverse consequences (accelerated pace of mental decline) of not treating individuals who are eligible for and amenable to clinical benefits of drug therapy should be explained to the appropriate stakeholders (Please see Table 7, Possible Consequences of Not Treating Patients with Alzheimer’s Disease). The intent should never be to convey a sense of guilt, rather to inform and educate.

With respect to pharmacologic management of individuals with AD residing in AL communities during early stages of the disease, drug therapy aimed toward improvement or stabilization of memory and cognition—with either a cholinesterase or NMDA inhibitor, or a combination (see below)—is a pivotal clinical objective in persons with AD.

Accordingly, a number of factors should be considered when devising an optimal approach for implementation of a drug-based treatment plan for AD, including: 1) Risk- and stage-directed therapy (the approach to initial drug selection); 2) titration of medications to minimize side effects and drug discontinuation; 3) identifying indications for switching, adding, or using combination therapy; 4) importance of a gradual and persistent approach to drug dosing, up- and down-titration, and route of administration; and 5) differentiating indications for cholinesterase inhibitors and NMDA inhibitors based on disease staging.

During later stages of AD, AL care providers can be helpful in identifying behavioral disturbances that trigger introduction of antipsychotics, mood stabilizers, anticonvulsants, and/or benzodiazepines. However, as emphasized in earlier sections, nonpharmacologic measures should be attempted first, prior to starting antipsychotic agents to address behaviors.

Care providers in the AL setting challenged with caring for residents with AD should recognize that monitoring resident response to drug therapy can be difficult, especially when other, intervening medical conditions can precipitate exacerbations of cognitive dysfunction, delirium, or disturbed behaviors. Failures in drug response frequently must be differentiated from intercurrent events causing clinical deterioration.

The hallmark role of the ABCs (Activities of Daily Living [ADLs], Behavior, Cognition, and Cost) criteria in determining management strategies is important, as is the need to focus on both cognition and behavioral domains as trigger points for drug therapy. Moreover, critical to the PROCLAIM approach of Monitoring resident response is the understanding that the spectrum of improvement with drug-based therapy frequently crosses domains; that is, cognitive, behavioral, and functional preservation may occur in one domain but not another.

**Monotherapy vs. Combination Therapy.** Although the majority of published studies evaluating the role of pharmacologic therapy in AD patients have compared cholinesterase inhibitor or NMDA receptor antagonist monotherapy to placebo, there is increasing evidence suggesting that AD patients with moderate-to-severe disease may derive additional benefit from treatment combining two drug classes (i.e., addition of an NMDA inhibitor such as memantine to a cholinesterase inhibitor such as donepezil). Although methods for identifying AD patients who are most likely to benefit from combination therapy are not yet developed, the AD-AL Panel, in general, took the position that combination therapy should be considered, especially in persons with moderate-to-severe disease.

**Monitoring.** The AD-AL Panel emphasizes the PROCLAIM strategy of Monitoring residents to guide drug therapy and the need to identify and pre-specify end points that should trigger drug discontinuation or change in therapy.

**DRUG THERAPY: THE FOUNDATIONAL ROLE OF NMDA RECEPTOR ANTAGONISTS AND CHOLINESTERASE INHIBITORS (CHEIS)**

**Memantine: NMDA Receptor Antagonist.** Memantine (Namenda®) is a low- to moderate-affinity, uncompetitive Nmethyl-D-aspartate receptor antagonist. Controlled trials have demonstrated the safety and efficacy of memantine monotherapy for patients with moderate-to-severe AD, and the agent is approved as monotherapy in these patient subgroups. Additional studies have also demonstrated the usefulness of memantine for mild stage AD, although the drug does not have a formal indication for this stage.

Glutamate is the main excitatory neurotransmitter in the CNS and has a role in neurotransmission and plasticity. Glutamate receptors are divided into NMDA, AMPA, and kainate subtypes. The NMDA receptor has a complex structure with several binding sites for NMDA and glutamate and a central ion channel capable of binding phencyclidine. NMDA-receptor activation generates a long lasting influx of Ca2+ into neurons, which is thought to be involved in long-term potentiation—a cellular process that underlies learning and memory.22,23

In pathogenesis, such as the neurodegeneration of AD, an increase of extracellular glutamate is thought to lead to excessive activation of NMDA receptors with consequent intracellular accumulation of Ca2+. This intracellular accumulation of calcium then initiates a cascade of events that results in further neuronal death.24,25 It is postulated that memantine, which has a moderate-affinity for phencyclidine site NMDA antagonist, might protect neurons from glutamate-mediated excitotoxicity without preventing physiological activation of the NMDA receptor.

Under pathologic conditions, excessive activation of receptors by glutamate kills cells; hence the term “excitotoxicity.”26 There is considerable evidence that the pathologic cascade of AD includes an excitotoxic component.27-29 Chronic, excessive glutamatergic stimulation of NMDA receptors can result in degeneration and death of cortical and subcortical neurons.

Neurochemical and neuropathological studies of the AD
brain show degeneration of glutamatergic pathways occurring early in the disease in a pattern corresponding with the distribution of plaques and tangles, and there are regional decreases in cortical and hippocampal NMDA and AMPA receptor mRNA and protein in AD.

**Clinical Evidence.** As clinical experience with memantine grows, the precise role of this medication in treating persons with AD has been better defined. Because memantine currently is only one of two agents (along with donepezil) approved for persons with severe AD, and because combination therapy with an agent from the NMDA receptor antagonist (memantine) and a cholinesterase inhibitor (donepezil) is becoming more common, this agent plays an important role for progressing residents in the AL setting.

A published trial in a nursing home population with mixed dementias (AD and vascular dementia [VaD]) showed functional improvement and a reduction in care dependence with memantine. In another trial in moderately to severely impaired outpatients with probable AD, memantine treatment significantly slowed the rate of cognitive and functional decline. An open-label extension of this trial was conducted, with preliminary reports suggesting encouraging results among patients switched from placebo to memantine.

More recently, a large placebo-controlled, double-blind, clinical trial of memantine in combination with the cholinesterase inhibitor donepezil showed that memantine (10 mg bid) administered to patients with moderate-to-severe AD maintained on stable doses of this cholinesterase inhibitor improved treatment response relative to the outcomes observed solely with cholinesterase inhibitor maintenance therapy.

Based on this evidence, memantine can be considered an important therapeutic approach for AD based on criteria applied to other therapies that have been approved. Because memantine has a lower incidence of GI side effects than some cholinesterase inhibitors, some experts recommend using it as the initial agent in patients with moderate or severe stage AD.

**Cholinesterase Inhibitors.** The cholinergic hypothesis of AD is now generally well accepted. Based on this framework, a therapeutic approach has been developed that consists of the potentiation of cholinergic transmission in affected cerebral areas. Cholinesterase inhibitors achieve this by delaying the degradation of acetylcholine (ACh).

The central nervous system contains two kinds of cholinesterase: acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE). Initial cholinergic research focused on inhibition of AChE, but it has recently been demonstrated that BuChE also plays an important role in the degradation of ACh in normal and AD brains. Therefore, both cholinesterases constitute a rational target for the treatment of AD. Over the course of AD, AChE activity appears to be diminished to 33-45%, whereas the total activity of BuChE in the brain increases by up to 40-90%.

**Overview of Available Agents.** The cholinesterase inhibitors donepezil (Aricept®), rivastigmine (Exelon®), and galantamine (Razadyne®) have been proved effective in clinical trials. The rationale for the efficacy of these agents is based on the cholinergic hypothesis of AD, in which the decline in learning and memory is attributed to a cholinergic deficit mediated by impairments of attentional processing and perhaps excitatory amino acid excessive activity.

All three drugs have a low incidence of serious reactions, but they may produce such mild-to-moderate cholinergic side effects as nausea, anorexia, vomiting, and diarrhea. Fortunately, tolerance to these side effects often develops, especially when a systematic, gradual titration schedule is employed, and if individuals on agents such as rivastigmine and galantamine are advised to consume their medication after a full meal. Recently, rivastigmine has been approved as a once-daily skin patch, with initial studies showing a reduction in adverse GI side effects and improved caregiver and patient acceptance to this new formulation and route of administration.

However, if therapy with a cholinesterase inhibitor is interrupted for more than several days, the drug should be restarted at the lowest dosage and retitrated because of renewed susceptibility to side effects. Instruments that measure cognition, behavior, and functional ability have shown that cholinesterase inhibitors are beneficial in persons with AD.

While discussion of these instruments and their quantitative implications is beyond the scope of this report, it is safe to conclude that individuals who tolerate and respond to acetylcholinesterase inhibitors will experience modest cognitive improvements. In fact, deterioration of cognition will be delayed by one year in about 20% of treated patients (as measured by a 7-point improvement on the Alzheimer's Disease Assessment Scale, Cognitive Section).

An evidence-based review by the Quality Standard Subcommittee of the American Academy of Neurology investigated important issues in the management of dementia. These reviewers concluded that cholinesterase inhibitors should be a first-line treatment in patients with mild-to-moderate AD.

It should be noted that comparing the clinical efficacy of different cholinesterase inhibitors in AD directly across trials is problematic since each trial used slightly different entry criteria and different populations; in addition, these trials were performed at different centers and may have used different outcome assessments. Consequently, a direct comparison of the efficacy of the different cholinesterase inhibitors requires head-to-head clinical trials, which currently are lacking.

The cholinesterase inhibitors generally appear to produce symptomatic effects in patients with AD following different lengths of treatment. The clinical efficacy in drug trials has revealed an improvement in the Alzheimer's Disease Assessment Scale-Cognitive Subscale score (ADAS-Cog) varying between 1.8 and 4.9 points compared with placebo.
In some cases, these drugs appear to have salutary effects not only on cognition, but also on behavioral abnormalities, including apathy, anxiety, and delusions.40

**Treatment Response.** A meta-analysis study45 confirms that AD patients treated with cholinesterase inhibitors demonstrate statistically significant global improvement compared with those treated with placebo, supporting current guidelines advocating treatment.41,46-48 The therapeutic benefit reported in this meta-analysis is consistent with the modest benefits described in previous qualitative reviews.41,49-51

The number needed to treat (NNT) of 12 for one additional patient to demonstrate a global response is similar to NNTs previously calculated for AD.52 By comparison, reported NNTs are three for antipsychotics in schizophrenia,53,54 four for antidepressants for depression in medical illness,55 and 29 to 86 (5-year NNT) for antihypertensives to prevent major event (myocardial infarction, stroke, or death).56

Although minimal improvement or better was the definition in the main analysis, many authors use stabilization as the definition in studies lasting six months or more.57-59 The definition of treatment response had an important impact. These results confirm that cholinesterase inhibitor treatment is associated with significantly better global improvement than placebo treatment for all three definitions of response (stabilization or better, minimal improvement or better, marked improvement).

Finally, tolerability of cholinesterase inhibitors is an important consideration when evaluating their place in therapy. The proportion of patients in whom adverse events emerged during treatment was only 8% higher in those receiving cholinesterase inhibitors than in those receiving placebo, confirming that these medications are well tolerated. The adverse events were mostly gastrointestinal, and no related deaths were reported. The rates of dropout and dropout due to adverse events were higher with cholinesterase inhibitors than with placebo (8% and 7%, respectively). The rates seen in clinical practice may be lower when dosage and administration techniques for specific agents are tailored to the individual.

**Switching Agents.** A significant percentage of individuals will experience lack or loss of therapeutic benefit with the initial agent, or alternatively, discontinue the drug due to safety and/or tolerability issues. In many instances, physicians may be reluctant to offer such patients an alternative treatment option (i.e., another agent within the class or a medication from a different drug class) once the initial medication has been discontinued.

This approach may compromise patient management, since for many patients, total duration of treatment is relatively short in comparison with the chronic nature of AD, and switching to another agent may produce benefits even though the initial agent has produced less-than-satisfactory results.

Guidelines for switching agents used in AD are in evolution. It must be emphasized that, in general, individuals with AD should not have their medications switched if they are responding to current treatment, with no safety/tolerability issues.Switching should only be considered in persons who: 1) show initial lack of efficacy; 2) initially respond to treatment but subsequently lose clinical benefit (loss of efficacy); and/or 3) experience safety/tolerability issues.

Before the decision to switch is made, dose adjustment always should be considered (i.e., dose increase for lack/loss of efficacy, dose reduction for safety/tolerability problems), providing the new dose falls within the recommended therapeutic range. If this strategy proves unsuccessful, then a treatment switch should be considered.60

A minimum treatment period of six months, beginning when the individual has reached an optimal dose of initial cholinesterase inhibitor therapy, should be allowed before any firm decision regarding the efficacy of treatment is made. This time frame permits the dose of cholinesterase inhibitor to be escalated to an optimal level and allows the clinician to form an accurate picture of clinical progression, which will assist in judging the efficacy of treatment.

The decision to switch from one agent to another must be based upon realistic treatment expectations, particularly in a disorder such as AD, which causes all patients to undergo symptomatic deterioration over time.60 Switching guidelines for rivastigmine and galantamine stipulate that a switch with no washout period generally can be safely performed if no safety/tolerability issues are evident with the initial agent. This approach is favorable as it provides treatment continuity for the patient and uninterrupted cholinergic stimulation. If, however, the patient has experienced safety/tolerability issues with their initially prescribed agent, a washout period (for up to 7-14 days or until side-effects resolve) should be implemented.60

**BEHAVIOR AND MOOD DISORDERS**

A detailed discussion focusing on management of disturbed behaviors and mood disorders in AD is beyond the scope of this report. Nevertheless, a few important principles are worthy of emphasis as they relate to the AL environment.

Cholinesterase inhibitors and NMDA receptor antagonists should already be on board in residents with AD who manifest behavioral derangements. For acute exacerbations of behavioral symptoms, short-term use with other agents may be indicated and also useful in chronic treatment of these symptoms once optimization of NMDA receptor antagonist or cholinesterase inhibitor therapy is no longer effective.

Depression can—and, in general, should—be treated with antidepressants, which may improve quality of life. Psychotic symptoms, typically visual hallucinations or paranoid delusions, should be treated with atypical antipsychotic medications, but only if the resident functions poorly because of disturbing psychotic features, and if nonpharmacologic methods have been attempted.
Apathy can be extremely difficult for residents and families. Anticholinesterase inhibitors often help. Behavioral symptoms such as agitation or an abnormal sleep/wake cycle may be improved with medications, but all have side effects. Benzodiazepine use is discouraged in dementia because of risks of sedation, falls, inhibition of learning and memory, and paradoxical excitation. Anticonvulsive agents, such as divalproic acid, carbamazepine, and trileptal have been used to treat paroxysmal and aggressive behavior without concomitant psychosis, but supporting data are limited in this population; side effects include drug-drug interactions and excessive sedation.

Atypical antipsychotics, particularly risperidone, quetiapine, and olanzapine, have been used for agitation as well as psychosis in elderly patients with dementia. Improvement is modest; they are not FDA-approved for this indication, and long-term effects are unknown. The manufacturers of risperidone and olanzapine recently added a warning to the label of a possible increased risk of ischemic cerebrovascular disease, and other complications also have been reported. As emphasized, their use should be selective, and in general, should be limited to situations in which other methods have proven ineffective.

**OTHER THERAPIES FOR AD: SEPARATING FACT FROM FICTION**

The possible benefits in AD of other agents—among them, folic acid, vitamin E, selegiline, estrogen, statins, and anti-inflammatory agents—still is widely debated. While acknowledging that agents other than cholinesterase and NMDA inhibitors may produce benefits in selected patients, conclusive evidence supporting the use of the agents discussed below is lacking, and none of these agents carry an indication for AD.

**Folic Acid.** It is imperative that adequate folic acid is provided in the diet, in the form of vitamin supplements, or adequate nutrition.

**Vitamin E.** Support for use of vitamin E primarily is derived from the Alzheimer’s Disease Cooperative Study, which evaluated the effects of 10 mg of selegiline once daily and/or 1000 IU of vitamin E twice daily as treatments for AD. The study’s authors concluded that these agents delayed disability and nursing home placement but not deterioration of cognitive function.

Despite these results, it should be noted that the study population appeared to be highly selected. Most notable is the fact that subjects were younger, but had more severe dementia, than control patients and were not taking psychoactive medications. Consequently, there have been questions about whether the results of the study are applicable to a clinical setting. A recent Cochrane review concluded that after adjusting for differences between patient groups in the Alzheimer’s Disease Cooperative Study, there was insufficient evidence to recommend vitamin E. The Cochrane review also found weak evidence of side effects associated with the use of vitamin E.

**Selegiline.** A number of studies have examined evidence for the use of selegiline, a selective monoamine oxidase inhibitor, in the treatment of AD. Most of these studies have shown some improvement in cognition, behavior, and mood, but little evidence of a global benefit in cognition, functional ability, and behavior. In 2000, the authors of a meta-analysis of 15 clinical trials concluded that there was not enough evidence to recommend selegiline as a treatment for AD. Because of the risk of stupor, rigidity, severe agitation, and elevated temperature, selegiline therapy is contraindicated in patients who are taking meperidine, and this precaution often is extended to other opioids. Concurrent use of selegiline with tricyclic antidepressants and selective serotonin reuptake inhibitors also should be avoided. These restrictions discourage the use of selegiline in persons with AD.

**Estrogen.** Several descriptive studies have shown that postmenopausal women who take estrogen have a lower incidence of AD. In addition, a recent review of estrogen and neuroimaging studies demonstrated improved cerebral metabolism in women taking estrogen. Although estrogen may have a neuroprotective effect, it does not appear to improve cognition or function in patients with AD, and the combination of estrogen and progestin may increase the risk for dementia and stroke.

**Nonsteroidal Anti-inflammatory Drugs.** Inflammation surrounding beta-amyloid plaques with resultant destruction of neurons is thought to be an important factor in the pathogenesis of AD. Observational studies have found that persons who regularly use nonsteroidal anti-inflammatory drugs (NSAIDs) have a decreased incidence of AD. While NSAIDs may have some neuroprotective effect, several studies of anti-inflammatory drugs do not show a clear benefit for treatment, and the other adverse effects of NSAIDs on cardiovascular and gastrointestinal end points do not justify their use in AD.

**SUMMARY**

The AD-AL Expert Consensus Panel has developed the PROCLAIM action tool and care strategy for caregivers working in the assisted living setting. The PROCLAIM mandate can be viewed as an awareness and caregiver action plan that encourages a commitment to providing compassionate, effective, and optimal care for AL residents with Alzheimer’s dementia.

This approach attempts to account for the complex psychological, medical, financial, and emotional needs of afflicted individuals and their families, and stresses a proactive, professional, multidisciplinary approach based on the complex care needs of residents with AD.
on communication, consultation, and life enrichment. The AD-AL Consensus Panel has created the PROCLAIM acronym to help identify the most important dimensions of caring for persons with AD, and that can serve as a guide for comprehensive, multidisciplinary care of individuals with dementia residing in the assisted living environment.

REFERENCES


CME Questions

1. Goals of pharmacologic therapy in Alzheimer’s disease may include:
   A. Symptomatic stabilization
   B. Preservation and/or slowing of inevitable decline in cognition
   C. Abating functional impairment
   D. Delaying onset of disturbed behaviors
   E. All of the above

2. Documented or claimed benefits for cholinesterase inhibitors include all of the following except:
   A. Delaying institutionalization
   B. Reducing requirements for antipsychotic use
   C. Improvement or delay in decline of cognition
   D. Reversal of the underlying disease process and cure
   E. Improvement in global impressions

3. The following factors should be considered when determining the optimal approach to drug therapy in AD:
   A. Stage-directed therapy (the approach to initial drug selection)
   B. Titration of medications to minimize side effects and drug discontinuation
   C. Identifying indications and factors for switching, adding, or using combination therapy
   D. Differentiating indications for cholinesterase inhibitors and NMDA inhibitors based on disease staging
   E. All of the above

4. DSM-IV diagnostic criteria for dementia includes which of the following?
   A. Memory impairment
   B. At least one of the following: aphasia (language difficulties), apraxia (diminished ability to perform motor activities in the presence of intact motor function), agnosia (inability to recognize or name objects despite intact sensory function), or disturbance in executive function (diminished ability to plan or organize);
   C. Impaired social or occupational functions
   D. All of the above
   E. None of the above

5. Caregivers in the assisted living environment should address the following concerns and/or should be involved in communicating information about the following actions on behalf of residents:
   A. Assessment and monitoring of residents
   B. Consultation and referral
   C. Activities of daily living
   D. Medication side effects
   E. All of the above

Answer key: 1. E; 2. D; 3. E; 4. D; 5; E

TABLE 1
The PROCLAIM Strategy for AL Residents with Dementia and Related Conditions

PRO — PROfessional, PROactive, PROtect, PROvide, PROlong
C — Commitment, Compassion, Consultation, Communication,
L — Life enhancement, Life activities
A — Attentiveness, Assessment, Action
I — Interventions, Improvement, Identification
M — Medical Management, Medications, Monitoring

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SUGGESTED READING


8. PRIMARY CARE CONSENSUS REPORTS JUNE 15, 2004


