



## BYLINES

### A Look Back, A Look Ahead

In November of last year, we held our annual Editorial Review Board (ERB) breakfast, a tradition that has been conducted for many years and precedes my tenure as Editor-in-Chief. The breakfast is one way we at the journal thank the board for their tireless efforts as advisors and reviewers over the previous year. It's also a time for us to review the current status of the journal and talk about what the future holds for *The Consultant Pharmacist*.

This year, as many of you know, was a year of great change at the journal. With the loss of our publisher Tim Webster and a change in both managing and associate editors positions, we have had a challenging year. The staff worked through these changes and continued to provide you with up-to-date information on geriatric pharmacotherapy, therapeutic reviews, and innovative research, much of which was conducted by members of ASCP.

Manuscript submissions continued to be brisk, and the editorial review board provided more than 50 reviews of unsolicited manuscripts to the journal this year. For all of you who reviewed a manuscript this year but didn't attend the breakfast, I want to thank you for your contributions. This is truly a labor of love and is the reason for the high quality of the manuscripts published in the journal each month.

Several manuscripts followed what I like to refer to as our "mentoring" path in which the reviewers and I provided substantial support to the authors, helping them to clarify their work. The journal has a philosophy of mentoring individuals who are new to medical publishing and can help authors through the process, from clarifying

their research hypotheses through structuring various manuscript components. All of these manuscripts resulted in ultimate acceptance and a "win-win" situation for the author and the journal.

An often fruitful arena for manuscripts—poster sessions at the ASCP annual meeting—proved productive again in 2003. The editorial staff of *The Consultant Pharmacist* makes an effort to speak to poster presenters, urging them to consider the journal as a venue for publication of their original research. Several times these chats resulted in discussion of a publication strategy. The November Annual Meeting in San Antonio had a number of posters that we hope will make their way into complete manuscripts, successfully complete the peer review process, and into print in 2004.

Another point of discussion at the ERB breakfast was the electronic processing of manuscripts. We have been providing reviewers with electronic manuscripts, on request, for the past few years. What was discussed was a global change in the management of manuscripts, including online (e.g., Internet) submission, online peer review processing, and online approval of the final manuscript (e.g., galley proofs) by the authors. This would be a huge undertaking, but something we will be looking into in the next few months. We will never be devoid of paper in this process, but selected steps—if converted to an electronic format—could save time and money and result in faster processing; this ultimately would result in a shorter submission to publication time.

Finally, we discussed the process of

reinstating the evidence-based medicine review column, "Journal Review." We took a departure from this semimonthly column early in 2003, mostly due to administrative changes at the journal. We hope to bring this exciting column back to you in the next few months.

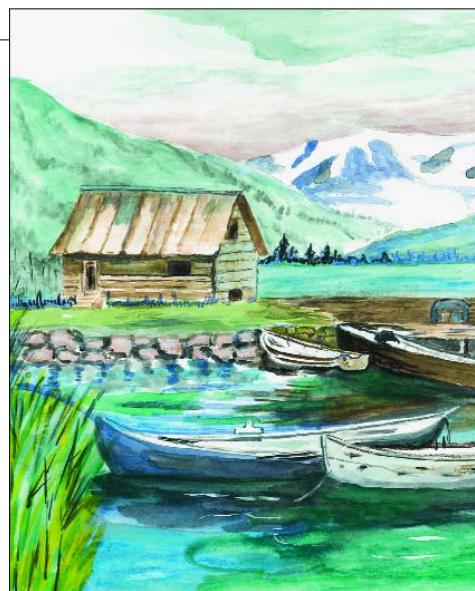
On another note, we continued our work with contributing writers and others who write about contemporary therapeutic issues in geriatric pharmacotherapy. We plan on continuing these relationships in 2004.

As a final recap to 2003, we had several manuscripts, features, and supplements this year that generated letters to the editor. As an editor, this is a very rewarding dialogue that challenges the readership and authors to critically evaluate the information at hand. We encourage you to comment on information published in the journal. I hope you don't agree with everything published in *The Consultant Pharmacist*; if you do, let us know that as well! We'd appreciate hearing from you.

H. Edward Davidson  
Editor-in-Chief

# THE Consultant Pharmacist

January 2004/Vol. 19, No. 1



*About the artist:* Ann Hall, 85, has had a life-long interest in painting. Most of her pictures, like *Maine Lobster Boat*, are of the ocean, surf, and rocks in Maine, where she and her husband had a summer cottage. She is now a great grandmother and lives in The Fairfax retirement community in Fairfax, Virginia.

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### A Primer

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1321 Duke Street  
Alexandria, VA 22314-3563  
703-739-1300 (ASCP-Production Office)  
703-739-1500 (ASCP-Production Office FAX)  
info@ascp.com

## EDITORIAL OFFICE

INSIGHT THERAPEUTICS, LLC  
129 W. Virginia Beach Blvd., Suite 105  
Norfolk, VA 23510  
757-625-6040; Fax 757-625-4538  
edavidson@inther.com

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## HEALTH TRENDS

### USE OF THIAZIDE DIURETICS REDUCES RISK OF HIP FRACTURE

Long-term use of thiazides was associated with a lower risk for hip fractures, according to an article in the *Annals of Internal Medicine* (Ann Intern Med 2003;139:476-82). Although this association was visible after short-term use, the risk reduction reached statistical significance only after one year of continuous use, according to researchers. This protective effect occurred independently of thiazide dose. After discontinuation of thiazide treatment, the protective effect disappeared after four months.

Since most hip fractures are related to osteoporosis, treating accelerated bone loss can be an important strategy to prevent hip fractures.

This study included 7,891 individuals 55 years of age and older. Hip fractures were reported by the general practitioners and verified by trained research assistants. Exposure to thiazides was divided into seven mutually exclusive categories: never use, current use for 1 to 42 days, current use for 43 to 365 days, current use for more than 365 days, discontinuation of use since 1 to 60 days, discontinuation of use since 61 to 120 days, and discontinuation of use since more than 120 days.

Researchers found that 281 hip fractures occurred. Relative to nonuse, current use of thiazides for more than 365 days was statistically significant and associated with a lower risk for hip fracture (hazard ratio, 0.46 [95% CI, 0.21 to 0.96]). There was no clear dose dependency. The study concluded that thiazide diuretics protect against hip fracture, but this

protective effect disappears within four months after use is discontinued.

### FIRST STUDY OF ALZHEIMER'S CAREGIVERS CITES BOTH REMARKABLE RESILIENCE, NEED FOR SUPPORT

The first detailed study of Alzheimer's caregivers showed a rapid recuperation from depression within three months of the death of their affected relatives, according to findings reported in the *New England Journal of Medicine* (N Engl J Med 2003;349: 1936-42). The study is based on data from REACH (Resources for Enhancing Alzheimer's Caregiver Health), a five-year, multisite initiative investigating interventions to support family caregivers.

"Depression often results when a family caregiver, who endures high levels of stress, is unable to alleviate the suffering of a loved one," said Richard Schulz, PhD, the University of Pittsburgh primary investigator. Knowing that the patient's death marks the end of his or her suffering may help cushion the blow of losing the loved one, according to the study.

"The home caregiver may begin to grieve while the patient is still alive. The caregiver may psychologically distance him or herself and rehearse what life will be like once he or she is gone," Schulz said. More than two-thirds of the home caregivers said they felt prepared for their loved one's death, and 72 percent of the caregivers said they were somewhat or strongly relieved by the relative's death.

The 18-month study, funded by the National Institute on Aging (NIA) and the National Institute for Nursing

Research (NINR), parts of the National Institutes of Health (NIH), followed 217 home caregiver/care recipient pairs and 180 caregiver/institutionalized care recipient pairs. The caregivers had a mean age of 65, were mostly women (84%), and had cared for their relatives an average of three years. The caregivers were divided evenly between spouses and offspring. Most of the patients were men who suffered moderate to severe dementia, with a mean age of 81. Information gathered from caregivers included the amount and type of care they provided, their subjective distress and depressive symptoms at baseline, 6, 12, and 18 months postbaseline, and their use of antidepressants.

Caregivers also were asked questions about their use and need for bereavement services. "The study fills important gaps in knowledge about how caregivers experience the end-of-life and the period immediately following the death of relatives with Alzheimer's disease (AD)," said Sidney Stahl, PhD, Chief of the Individual Behavioral Processes Branch of NIA's Behavioral and Social Research Program. "There is little research in this area due to the difficulty of predicting when a person with dementia is nearing the end of his or her life. With AD, there are long periods of progressive decline rather than abrupt shifts in health status."

The research suggests that services currently available only to patients who are hospice eligible (such as bereavement and counseling services before death for the family and pain control for the patient) would benefit caregivers and patients with dementia, he said. More than six million people provide long-term unpaid care to disabled

elders in the United States, according to the Administration on Aging.

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### **GENETICS OF PARKINSON'S DISEASE ZEROES IN ON ACTIVITY OF ALPHA SYNUCLEIN**

**S**cientists investigating a rare familial form of early-onset Parkinson's disease have discovered that too much of a normal form of the alpha-synuclein gene may cause Parkinson's disease. The finding, reported in the October 31, 2003, issue of *Science* (Science 2003;302:841), shows that abnormal multiplication of the alpha-synuclein gene can cause the disease.

The study provides major new clues into the process by which Parkinson's disease develops. Further, it suggests another way of looking at the consequences of abnormal protein deposition in a variety of neurological diseases, such as Alzheimer's disease, researchers say.

The findings are the product of collaboration among scientists at several institutions, including researchers at the National Institutes of Health, part of the Department of Health and Human Services. They were reported by Andrew Singleton, PhD, and colleagues at the National Institute on Aging's (NIA) Laboratory of Neurogenetics; Matthew Farrer, PhD, of the Mayo Clinic; and Katrina Gwinn-Hardy, MD, of the National Institute of Neurological Disorders and Stroke (NINDS). The team also included scientists from the National Human Genome Research Institute (NHGRI) and Georgetown University Medical Center, Washington, D.C.

Until very recently, researchers

focused on possible environmental factors as the culprit in Parkinson's disease.

In 1996, mutations in the alpha-synuclein gene were identified in a few large families in whom the disease was unusually common. Since then, mutations in several other genes have also been linked to familial forms of Parkinson's disease. In this new study, investigators analyzed blood samples from another affected family, the "Iowa kindred," in which many relatives developed Parkinson's disease or related neurological diseases.

In individuals in this family affected by Parkinson's disease, instead of the usual two copies of the alpha-synuclein gene in the chromosome 4 pair, the researchers found four copies of the alpha-synuclein gene. This multiplication of the alpha-synuclein gene (an abnormal triplication of three genes on one chromosome 4 and the normal one copy on the other chromosome 4) results in the individual's having too much synuclein. This protein buildup is believed to cause the Parkinson's disease symptoms.

"This study is an exciting step forward in our understanding of this disease," notes the NIA's Singleton. "It contributes to the growing body of evidence suggesting that genetic variations in alpha-synuclein contribute to Parkinson's disease. It suggests that in Parkinson's disease both mutated and normal alpha-synuclein behave in a way that is quantitatively different from the way the protein functions in people without Parkinson's disease."

The researchers said that the findings in their study are relevant to both familial and sporadic, or typical, Parkinson's disease. The pathology of

typical Parkinson's disease is similar to the pathology in this family, they note, and previous work from the group and others has suggested that the amount of synuclein produced might contribute to a person's risk of getting the disease.

Parkinson's disease is the second most common neurodegenerative disease, after Alzheimer's disease. It is estimated that the disease currently affects at least 500,000 Americans.

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### **MORE THAN ONE-THIRD OF HOSPITAL MEDICATION ERRORS INVOLVE SENIORS**

**M**ore than one-third of hospital medication errors that reach the patient involve seniors, according to the fourth annual report on hospital errors reported to the United States Pharmacopeia (USP). The study provides a comprehensive analysis of 192,477 medication errors voluntarily reported by 482 hospitals and health care facilities nationwide in 2002, including community, government, and teaching institutions. MEDMARX is USP's anonymous reporting database that hospitals and health care systems use to track and trend medication errors. USP created MEDMARX to help health care facilities understand the causes of medication errors and the factors that contribute to them to improve patient care and safety.

"The report data revealed that more than one-third of the medication errors reaching the patient involved a patient aged 65 or older," said Diane Cousins, RPh, vice president of the Center for the Advancement of Patient Safety at USP. "As the senior population continues to increase, USP is calling

for hospitals to focus on reducing medication errors among seniors. Seniors and their families need to become more involved in their care.”

A MEDMARX data report revealed a number of significant findings, including:

- A majority (55 percent) of fatal hospital medication errors reported involved seniors.

- When medication errors caused harm to seniors, 9.6 percent were prescribing errors.

- When harm occurred, wrong route (7 percent), such as a tube feeding given intravenously, and wrong administration technique (6.5 percent), such as not diluting concentrated medications, were the second and third most common errors among those aged 65 and older.

Omission errors (43 percent), improper dose/quantity errors (18 percent), and unauthorized drug errors (11 percent) were the most common types of medication errors among seniors.

Of the 192,477 medication errors documented by MEDMARX, the vast majority were corrected before causing harm to the patient. However, 3,213 errors, or 1.7 percent of the total, resulted in patient injury. Of this number, 514 errors required initial or prolonged hospitalization, 47 required interventions to sustain life, and 20 resulted in a patient's death. Compared with 2001 data, a smaller percentage of reported errors resulted in harm to the patient (1.7 percent in 2002 versus 2.4 percent in 2001).

Health care facilities attributed medication errors to many reasons and often cited workplace distractions (43 percent), staffing issues such as shift

changes and floating staff (36 percent), and workload increases (22 percent), as contributing factors. Although workplace distraction remains the leading factor contributing to medication errors, the data revealed a drop from 47 percent in 2001.

For more information on the report, *Summary of Information Submitted to MEDMARX in the Year 2002: The Quest for Quality*, see [www.usp.org](http://www.usp.org).

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### **CHANGES IN FORMULARIES AFFECT UTILIZATION AND SPENDING**

**C**hanges in formulary administration may have dramatically different effects on utilization and spending and may, in some instances, lead enrollees to discontinue therapy, according to an article in *The New England Journal of Medicine* (N Engl J Med 2003;349: 2224-32). The changes in copayments can substantially alter out-of-pocket spending, the continuation of the use of medication, and possibly the quality of care.

Many employers and health plans have adopted incentive-based formularies in an attempt to control prescription drug costs. Haiden A. Huskamp, PhD, and other researchers used claims data to compare the utilization and spending of drugs in two employer-sponsored health plans that implemented changes in formulary administration with those in comparison groups of enrollees covered by the same insurers. One plan simultaneously switched from a one-tier to a three-tier formulary and increased all enrollee copayments for medications. The second switched from a two-tier

to a three-tier formulary, changing only the copayments for tier-3 drugs. Researchers from Harvard Medical School, Brigham and Women's Hospital, and Medco Health Solutions examined the utilization of angiotensin-converting-enzyme (ACE) inhibitors, proton-pump inhibitors, and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins).

The study found that enrollees covered by the employer who implemented more dramatic changes experienced slower growth than the comparison group in the use of a drug and a major shift in spending from the plan to the enrollee. Among the enrollees who were initially taking tier-3 statins, more enrollees in the intervention group than in the comparison group switched to tier-1 or tier-2 medications (49 percent versus 17 percent,  $P<0.001$ ) or stopped taking statins entirely (21 percent versus 11 percent,  $P=0.04$ ). Patterns were similar for ACE inhibitors and proton-pump inhibitors.

“As is the case with other cost-containment strategies in health care, incentive-based formularies cannot solve a much larger problem—in this case, the high cost of drugs in the United States,” the study said. “But for now, a shifting of the costs and responsibility for health care decisions to consumers is a growing trend, and incentive-based formularies have a major role in this strategy. Important questions remain regarding the effect of these formularies on patients' health outcomes.”

Marlene Z. Bloom  
Managing Editor

# A Primer

## Understanding Aging in the 21st Century

### INTRODUCTION

Aging—everyone is doing it. And, as the 78 million aging baby boomers in the United States—those born between the years 1946 and 1964—join the ranks of the elderly, what has been termed “the demographic imperative” will arrive. In just a few short years, literally all of society’s institutions will be affected, in one way or another, by this massive demographic shift. The number of older adults in our country will more than double: from 35 million now to nearly 80 million older adults by the middle of the 21st century. The health care system and the professionals that work within this system will have a special role to play in this aging world.

This article has been prepared to provide a background in social gerontology to health care professionals and to raise some issues that are likely to influence the nature of the professional work of health care providers. The issues discussed not only will have relevance for the world of work, but also for our own family life as well. The article:

- Outlines and refutes some of the prevailing myths associated with aging

**Donna L. Wagner**  
**Kelly J. Niles**

- Provides an overview of the scope and magnitude of the demographic changes
- Discusses the changing social roles of elders and family relationships
- Lays out health care issues and discusses trends of the future and their implications for health care providers

### REFUTING MYTHS ABOUT OLD AGE

The story of Marjorie Smith, page 16, illustrates a new lifestyle for many of today’s elders. While Marjorie’s case may seem as if it might not fit the reality of an elderly woman living alone, Marjorie’s situation embodies a new model of aging for the 21st century. She is hooked

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**DONNA L. WAGNER, PhD**, is Director, Gerontology Program, Towson University, Towson, Maryland.

**KELLY J. NILES, MPA**, is a doctoral student, University of Maryland, Baltimore.

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THE AGING OF OUR POPULATION CARRIES WITH IT PROFOUND IMPLICATIONS FOR SOCIETY AND THE INDIVIDUAL.



## **MARJORIE SMITH: A THOROUGHLY MODERN ELDER**

At age 79, Marjorie Smith never imagined herself divorced and living by herself. Nonetheless she is living alone and loving her active and rewarding life. Initially, Marjorie's daughter suggested that her mother make arrangements after the divorce to move from her home of 30 years to live with her. Determined to remain independent, Marjorie found an apartment in a nearby urban area with access to many of the services and entertainment she would need, including public transportation, grocery stores, pharmacies, coffee shops, and book stores. Marjorie enjoys her new neighborhood and maintains links with old friends as well as new friends. Marjorie's closest friends live in the area—an important selling point when Marjorie was deciding where to live.

While Marjorie enjoys good health, her friends vary in their health conditions—another reason for Marjorie to be close. She spends some time each week with one old friend who now needs home health services and helps her to manage her daily activities, usually picking up things for her at the grocery store and pharmacy.

Marjorie has experienced some disappointment in her life and has had to make some sacrifices, but she feels that she has, over the years, been able to maintain her strength because of her commitment to herself as a woman and as a spiritual person. Marjorie checks her horoscope daily and is reinvigorated each day after completing her 30 minutes of meditation.

Years ago her grandson taught her how to use a computer, and now Marjorie keeps in contact with her extended family through e-mail and online photos. Marjorie's daughter e-mails her every morning, and although Marjorie appreciates her daughter's concern and advice, she is grateful for the delete button. Additionally, Marjorie explores this new chapter of her life as an older, single woman by connecting with others through an online dating service. While Marjorie reports that although her life took a turn she never expected—at an age she never expected—she is up to the challenge and looks forward to each and every day.

## **Understanding Aging in the 21st Century**

into technology, she is independent, relatively healthy, and enjoys a mature, sexually active lifestyle. Marjorie's case is useful as a way to bring to light and explore a few of the myths of aging.<sup>1</sup>

### **MYTH: The majority of elderly are alone and isolated from their families.**

As we see in the case study, Marjorie does in fact live alone. While living alone can be an indicator of unmet need in some instances, for Marjorie it was a conscious decision as well as a symbol of her desire to remain independent and autonomous. We also know from the case study that even though she is living alone, Marjorie is not at all isolated from her family. She enjoys a healthy relationship with the members of her family. Older adults can and do sometimes make decisions that may separate them from family members, but that's not always an indicator of unmet need or an unhealthy lifestyle.

### **MYTH: The majority of elderly are in poor health.**

Recent research on trends in disability and functional health reveal that disability rates among the elderly are in fact declining. Disability and morbidity are more likely to occur among the oldest-old—those over the age of 85. While many older people have chronic illnesses that require management, most report relatively high levels of satisfaction about their own health.

### **MYTH: Older people tend to become more religious as they age.**

The majority of research on religion and the elderly suggests that religiosity and spirituality remain stable throughout the life span. For example, in Marjorie's case reference was made to her as a spiritual person. While the meditation may be a new addition to her spiritual expression, chances are she has expressed herself as a spiritual person throughout her life.

### **MYTH: The elderly have no interest in, or capacity for, sexual relations.**

While Marjorie and her contemporaries may not express themselves as they did in their youth, or even as they did in their early adult years, sexual function and expression do not decline or diminish strictly as a result of age. The aging process does alter some functioning, but older adults who enjoy relatively good health as they age should be able to experience sexual intimacy throughout their aging lives. And many, like Marjorie, are discovering that the Internet is a good tool for meeting potential partners.

### **MYTH: The majority of elderly live in nursing homes or other long-term care facilities.**

In 1990 the United States Census reported that 5.1 percent of older adults resided in institutional settings. That figure dropped to 4.5 % in

## RECENT RESEARCH ON TRENDS IN DISABILITY AND FUNCTIONAL HEALTH REVEAL THAT DISABILITY RATES AMONG THE ELDERLY ARE DECLINING

2000.<sup>2</sup> The majority of older adults live in the community and, if needed, use home and community-based services that may be available to them, have friends or family members to assist them, or manage their own care.

The older population is the most heterogeneous group in our society. The 35 million Americans over the age of 65 have led 35 million different lives—with different experiences—all of which have shaped individual attitudes and perspective on life. It is important to understand that not every person over the age of 65 will desire or have the ability to live the lifestyle that Marjorie chooses to live. Different cohorts of elders, including the up-and-coming baby boomers, will have a shared social, political, and economic history. For example, the oldest-old “came of age”<sup>3</sup> during the Great Depression and may have certain beliefs and attitudes that differ from younger elders. It is critical, though, to keep in mind that while individuals may share time and space within a certain historical context, the way in which they experience these historical events may vary greatly based on race, gender, economics, and other factors.<sup>3</sup>

### KEEP IN MIND

It is important to keep in mind that the majority of elderly are not alone and are not isolated from their families, nor are they in poor health. Older people tend to remain stable with regard to religiosity as they age, and have an interest in, and capacity

for, sexual relations. In addition, the majority of elderly people live in the community, not in nursing homes. The elderly are a heterogeneous group, and the cohort effect does play a role in many aspects of the lives of elders.

### NORMAL AGING

Aging is a normal process. Human life span, or the maximum number of years we can live, is thought to be about 120 years. As we learn more about the biological foundations of aging, it may be possible to extend human life span. Life expectancy, or the number of years on average we can expect to live, has been increasing. It is projected that, by 2005, life expectancy at birth will be 74.9 years for men and 80.7 years for women. This contrasts sharply with the life expectancy of someone born in 1900—only 50 years. Experts disagree about whether we will be successful in increasing life expectancy in the future. However, there is evidence that gains in life expectancy may be possible as we examine other countries. Japan, for example, has the highest life expectancy—76.4 years for men and 82.9 years for women in 1995. The United States lags behind many countries in life expectancy, and some observers suggest that there is more we can do to extend life expectancy advantages to our population. In 1995, the highest life expectancies were found in European countries and Canada (as well as Japan).<sup>4</sup>

### AGING INDIVIDUALLY

Aging is an individual experience that is experienced by each of us in different ways depending upon overall general physical, mental, and social health.

Each of our body systems matures at a different rate and on a different schedule. Scientists studying longevity and human aging suggest that a number of factors including genetics, environment, and behavior play a role in the way aging is manifested on an individual basis. Nonetheless, there are a number of aging-related changes that are likely to occur in most people as they age. These include:

- Reductions in physical energy
- Changes in sleep patterns
- Reductions in flexibility, height, and coordination
- Increased skin wrinkling, graying hair, or hair loss
- Sensory changes related to vision, taste, smell, and hearing
- Hormonal changes<sup>5</sup>

### TIPS FOR THE HEALTH PROFESSIONAL DEALING WITH AGE-RELATED CHANGES

#### VISION

Normal age-related changes in vision include a condition known as presbyopia. Presbyopia occurs when the elasticity in the eye is diminished and people have difficulty reading small print and making accommodations when redirecting their focus from objects at a distance to objects near. In addition, it is common to experi-

ence a decline in the function of the lens and the iris, particularly for older persons who are on multiple medication regimes, and distinguishing color also becomes a problem. For example, an older adult may have difficulty distinguishing between violet, blue, and green.<sup>5</sup> Other vision problems that may accompany aging include glaucoma, cataracts, and macular degeneration.

To help address vision problems health professionals should make sure that:

- There is adequate illumination in office and other areas
- Information and instructions are printed in large letters, enabling someone with aging eyes to read it comfortably
- Medication instructions are not provided using the color of the pills as markers. It may be difficult, if not impossible, for an older patient to distinguish between a blue and green pill.

## HEARING

Hearing changes are common in older adults and include difficulty in hearing and understanding speech, difficulty in locating the source of sound, and less tolerance for background noise. "Presbycusis" is the term used to describe age-related hearing changes that include difficulty hearing high-frequency tones and, in some cases, difficulty hearing low intensity tones. Communication is often a problem with older adults who have low-level hearing loss since hearing speech and understanding all of the words that

are spoken can be difficult for many.

To help overcome hearing-related miscommunication:

- Try to communicate with the older person in a room that does not have background noise. Large open spaces like stores and restaurants can be extremely poor environments for good communication.
- Make sure that your message is being heard and understood by asking questions as you go along.
- When possible, have a printed sheet to aid you that the older person can take with him or her when providing health-related instructions.

## DEXTERITY

Dexterity also changes with age. It is more difficult to complete common tasks such as opening a package, jar, or pill bottle that is sealed. Arthritis, also common among the older population, can exacerbate the normal problems of dexterity, making everyday life much more complicated for many elders.

To make sure that health-related regimens can be easily followed:

- Provide the older person with containers that are easy-to-open and not child-proof.
- Suggest that a special container be used for everyday medication or health products as a strategy for addressing dexterity as well as memory and organizational issues.
- Make sure that the older person knows how products can be opened. Some new packaging requires special effort to understand and open.

## OTHER SENSORY CHANGES

Our sense of taste, smell, and touch are also diminished as we age. For example, in the over-80 age group, 75% experience significant loss of ability to smell.<sup>5</sup> Smelling, tasting, touch and feeling, hearing, and vision are all basic to our ability to perceive the world around us. Some believe that for the very old, diminishing sensory capacity is part of the reason older people sometimes appear to be slow in comprehending new situations or information or have difficulty making a decision about something. While we know that intelligence does not decline with age, the speed at which we are able to perceive things around us and process new information does. For this reason, it is important to take the time necessary to explain health care-related information an older person needs and to provide each person with enough time to make decisions and process the information.

Other common health-related issues in late life include problems with balance and an increased risk of falling. Falls are the leading cause of accidental death and the seventh leading cause of death for those over the age of 65.<sup>6</sup> While environmental factors can be important factors in fall risk, there are a range of other factors that increase the risk as well. These include alcohol use and medication side effects as well as physical disorders such as dementia, vision loss, and musculoskeletal conditions.

For many elders, the social consequences and personal fears about

aging are more debilitating than the actual age-related changes. Communication problems, changes in one's appearance, and functional limitations can all result in changes in our social interactions and, in some elders, a change in our own self-concept as well. Perceptual changes that accompany advanced aging—reduced speed in responding to stimuli and coming to closure in making decisions—can be troubling to an older adult and make it seem to others as if the individual is less capable of managing day-to-day matters.

It is important that health care providers recognize the age-related changes and anticipate the implications of these changes as they interact with their older patients.

### KEY POINTS

- Aging is not a disease, nor are all old people sick.

- Certain physiological changes occur in most individuals as a natural consequence of aging including sensory changes; reduction in energy levels; sleep, hormonal, and skeletal-muscular changes.

- While dementia is more common in older people than other age groups, it is not inevitable and is often a symptom of an acute condition that requires intervention.

- Health care providers should consider normal perceptual changes that occur with age when explaining new medications, their possible side effects, and when and if the older adult should contact his or her physician.

### IMPLICATIONS FOR HEALTH CARE PROVIDERS

America is experiencing population aging—decreasing birthrates and decreasing mortality rates. This shift from high fertility and high mortality rates carries with it a profound set of demographic imperatives, with implications for all sectors in our society. An increasing number of elders—both in absolute numbers and in their proportion of the total population—means that health care providers are more likely to have a graying patient practice. And although disability rates among the elderly are declining, old age remains a platform for disease and particularly for chronic disease.<sup>7</sup> The oldest-old are those most at risk for illness and disability, and their numbers are the fastest growing of all age groups.<sup>8</sup> In this section we will review the demographic shifts occurring within the nation and discuss selected implications of these shifts.

### THE OLD AMERICANS

The 2000 U.S. Census counted 35 million Americans over the age of 65. This represents an increase of 12% over the 1990 Census figure. The aging population has grown steadily in numbers since the Census began in 1790. Those over the age of 85 grew faster than their younger counterparts—38% increase between 1990 and 2000. In comparison, the population between 74 and 85 increased 23% and that between 65 and 74 years increased by less than 2%. This relatively low percentage of young-

old reflects the smaller birth cohort of the 1920s and 1930s and will dramatically change when the first baby boomers enter late life (starting in 2011).

The oldest-old are the group most likely to have chronic illnesses that lead to reduced function, morbidity, and disability. For example, although few elders over the age of 65 are in nursing homes (4.5%), almost one in five elders of the oldest-old are in a nursing home.<sup>8</sup> The oldest of this group, the centenarians, are growing rapidly, as well. The Census estimates that between 69,000 and 81,000 people are over the age 100. This number is likely to grow as high as 4.2 million in 2050.<sup>9</sup> And, if the trends continue in health status of the elders, the growth of this group—those over 85, 95, and 100—holds significant implications for our health care system.

Elderly Americans today are a very diverse population—in their lifestyles, habits, preferences, and attitudes about the world around them. In general, however, they are more educated as a group than their predecessors, healthier and, thanks to Social Security and pension reform, more financially independent than those who came before them. Women continue to have longevity advantages over men. There were 20.6 million women over the age of 65 in 2000 compared with 14.4 million men. And, as we look at the breakdown within the elderly population, we see that for those between the ages of 65 to 74 there were 82 men for every

## AN INCREASING NUMBER OF ELDERS MEANS THAT HEALTH CARE PROVIDERS ARE MORE LIKELY TO HAVE A GRAYING PATIENT PRACTICE

100 women; between ages 75 to 84 years, 65 men for every 100 women; and for these older than 85, only 41 men for every 100 women.

Florida continues to be the state most populated by elders, with an aging population of 17.6%. Pennsylvania, with 15.6%, and West Virginia, with 15.3%, are close behind. Nationally, 12%, or one out of eight Americans, is over the age of 65. In whatever geographic area

the elders may live, the vast majority are living in their community and living independently. Even among the oldest-old, more than 80% live in the community.

### **TOMORROW'S OLDER AMERICANS**

Each day, more than 6,000 Americans will celebrate their 65<sup>th</sup> birthdays. In 10 years, more than 10,000 Americans will turn 65 daily.<sup>10</sup> The aging of the baby boom generation

will have a profound effect on our demographic outlook. In seven short years, the first baby boomers will turn 65. The size of this generation guarantees an increase in the median age of Americans and an absolute, as well as proportional, increase in the elderly population. Just how much of an effect the aging of this very large cohort will have on America depends, in part, on the birth rates. Some projections suggest that in 2030,

when we will have 70 million older Americans, one out of four people living in the United States will be elderly. The growth of the elderly population will peak in 2050, at a projected 78.9 million persons.

Given the relatively good health of older Americans and our expectations that health improvements will continue as the baby boomers age, the true effects on society and on our health care system may not be felt until 2020 or later. In size, the oldest-old segment is likely to continue to experience rapid growth, from about 4 million today to almost 19 million by 2050.<sup>10</sup>

Of course, the overall effect of the baby boom generation also may be deferred if the majority of boomers remain healthy, in the workforce, or continue to work productively after the age of 65. Table 1 shows the involvement of persons over the age of 65 in the workforce between the years 1980 and 2000, demonstrating the increased involvement of every subgroup of the elderly population, including those over the age of 80. It is likely that we will continue to see relatively high labor force participation rates among older adults if two conditions persist—there are opportunities for them in the labor force and the health status of older adults remains at its current levels or improves. Table 2 demonstrates the projected labor-force participation rates into the future.

If, as some researchers suggest, we are making improvements in the com-

**TABLE 1. PERCENTAGE OF ELDERLY PARTICIPATION IN THE LABOR FORCE, BY AGE AND YEAR (1980-2000)**

Age	1980	1985	1990	1995	2000
65–69	21.0	18.4	21.0	21.8	24.4
70–74	11.9	10.7	11.3	12.5	13.5
75+	4.8	3.9	NA	NA	NA
75–79	NA	NA	6.1	6.9	7.5
80+	NA	NA	2.5	2.7	3.2

Abbreviation: NA = not available.  
Source: U.S. Department of Labor Statistics, 2000.

**TABLE 2. CURRENT AND PROJECTED PERCENTAGE OF ELDERLY PARTICIPATION IN THE LABOR FORCE PARTICIPATION RATES BY AGE AND YEAR**

Age	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
65–69	24.7	24.9	25.2	25.5	25.7	26.0	26.3	26.6	26.8	27.1
70–74	13.7	13.9	14.1	14.3	14.4	14.6	14.8	15.0	15.2	15.3
75–79	7.6	7.7	7.8	7.9	8.0	8.1	8.2	8.3	8.4	8.5
80+	3.3	3.3	3.4	3.4	3.4	3.4	3.4	3.5	3.5	3.5

Source: U.S. Department of Labor Statistics, 2000.

pression of morbidity into the very last years of life, we could also see a more dramatic increase in the next 10 years in the labor force participation of those over the age of 80. Working is not only a partial solution to the challenges of public support for an expanding older population, but also is symbolic of continued societal engagement of older adults. As the percentage of our population increas-

es, meaningful social roles for this group will be vital to our ability to manage the aging population on a societal level—and critical for the well-being of those aging individuals.

**HEALTH CARE IMPLICATIONS**

Those over the age of 65 are the most likely to use health care resources. Today, older adults, only about 12% of the population, consume the

### THE PICTURE OF AGING

- The aging population will increase from 35 million to nearly 80 million by the middle of the 21st century.
- In 2050, the percentage of elderly may increase from the current 12% to 25% of the U.S. population.
- The oldest-old—those over age 85—are the fastest growing sector of the older population.
- The majority of older Americans live independently in the community.
- Disability rates among the older population are falling, but chronic conditions continue to pose challenges to the oldest-old.
- Although elders are more likely than other age groups to use health care services, there are inadequate numbers of trained health care professionals to see to their needs. This problem will be exacerbated as the baby boom generation enters late life.
- Tomorrow's elderly may have higher labor force participation rates and expanded social roles than seen historically. The effect on society of population aging in the middle of the 21st century will depend upon our ability to provide a range of social opportunities to our expanding elderly population.

following percentage of health care services:

- 36% of hospital stays
- 49% of all days of hospital care
- 50% of physicians' time<sup>10</sup>

The average 75-year-old has three chronic conditions and uses more than 4.5 times the number of prescription medications than younger persons. And, although most elders report relatively good health, the oldest-old commonly have one or more disabling conditions that limit their mobility or the ability to manage their activities of daily living without some assistance or assistive device.

Common chronic illnesses among the elderly include arthritis, heart disease, respiratory conditions, and sensory deficits. And the incidence of certain cancers, such as prostate cancer, increases with age. Osteoporosis in late life also leads to falls, a serious risk for older adults that often results in hip fractures and other injuries that may reduce the individual's mobility. Depression also is underdiagnosed and believed to be common among elders.

Dementia also is a problem for some elderly. About four million people have Alzheimer's disease, a progressive, fatal condition. Unless a prevention or cure is developed for this disease, we are likely to see this number double in the next 20 years. This condition and related dementias present challenges for the health care system and extreme problems for the family of the patient. It is costly, financially as well as emotionally, to

provide care for people with dementia; expensive institutional care is almost always required, sometimes for many years. Some older adults may develop dementia symptoms—confusion and forgetfulness—as a result of drug interactions, vitamin deficiencies, or illness.

Not surprisingly, the elders with the lowest income and lowest educational attainment are at the most at risk as result of health problems.<sup>11</sup> For the older population, disability and poverty often go hand-in-hand.

Even if, as some predict, our health care technology and health care prevention strategies related to lifestyle result in a decrease in chronic illnesses in late life, we still are facing a very dramatic increase in older patients who need health care services as the baby boom generation enters late life. And one of the biggest challenges is the scarcity of trained geriatric professionals. An estimated 20,000 geriatricians are needed *today* to provide high quality care to our older patients, and there are only 9,000 qualified in geriatrics. By 2030, it is anticipated that our country will need as many as 36,000 geriatricians. In addition to geriatricians, professionals trained in geriatrics are needed in all aspects of health care. Less than one percent of the nurses are certified in geriatrics, less than one-third of one percent of physical therapists are trained in geriatrics, and there are only 720 pharmacists nationwide with geriatric certification.<sup>10</sup>

## MINORITIES AND THE ELDERLY

- By 2030, 25 percent of the elderly population will be composed of minority elders.
- A comprehensive understanding of the issues affecting specific populations is crucial.
- In addition to race and ethnicity, gender is an important consideration. For example, older African-American women experience poverty and reductions in health status at higher rates than African-American males.
- A sensitivity to the influence of cultural norms and values in seeking and using health care services will enhance the effectiveness of the health care professional.

## WHO TAKES CARE OF THE ELDERLY?

- Families will continue to provide the majority of care to their older family members.
- Home and community-based services will continue to evolve in response to shifting demands and needs of current and incoming cohorts of older adults (programs that enable participants to make their own care decisions).
- Many older people are providing care to an even older family member or spouse.
- Caregiving will continue to evolve into an issue inclusive of male caregivers.
- Long-distance caregiving will continue to be a common family caregiving pattern.
- Even though older persons are receiving care from a family member, they are still making their own decisions about care if they are cognitively able to do so.

## FAR-REACHING CONSEQUENCES

The demographic imperative of an increasing elderly population is far reaching. While we can't predict the future, there are some trends that will likely change the face of aging, as we now know it. These trends include an increase in ethnic diversity among the elderly, increasing educational attainment among older Americans, and changes in family structure.

## ETHNICITY AND DIVERSITY

Increasing ethnic and racial diversity among our elders has important implications for health care and human service professionals working with elders, as have family changes.

The older population is increasing in ethnic diversity and, by 2030, it is expected that minority elders will make up 25 percent of the elderly population.<sup>11</sup> For example, by 2030 the percentage of older Hispanics is expected to grow by 238%; African-Americans, 134%; Asian-Americans, 354%; and Native Americans and Alaskan Natives, 159% compared with a growth rate of only 79% for Caucasian, non-Hispanic elderly.<sup>12</sup> With these projections in mind, it is quite clear that a comprehensive understanding of the issues affecting these populations is crucial when providing care and services. The key issues affecting specific elderly minority populations follow.

### Hispanic Elders<sup>1</sup>

- The Hispanic population is heterogeneous. It includes Mexicans,

Puerto Ricans, Cubans, and groups from South and Central America.

- Hispanics tend to have low incomes and low levels of education.
- Language barriers may exist for elderly Hispanics in particular—some of who may be reluctant to depend on younger family members for support with regard to health-related issues.

### African-American Elders<sup>1</sup>

- Older African-Americans generally experience poorer health than whites.
- This population has a reduced life expectancy, compared with other groups.
- Older African-Americans have higher rates of poverty, compared with other groups.
- Religion and family play an important role in the life of African-American elders.

### Asian-American Elders<sup>12</sup>

- Cultural barriers often exclude them from receiving public benefits.
- Asian-American elderly commit suicide at a rate three times the national average.
- Asian-American elderly may be the most neglected by programs developed to serve all elderly populations.

### Native American and Alaskan Native Elders<sup>12</sup>

- Average life expectancy at birth for these groups is eight years less than that of whites.

■ This population is 10 times more likely to develop diabetes than whites.

■ Many factors affect this population's ability and reluctance to receive medical assistance including, geographic isolation, lack of transportation, limited financial resources, and folk and ritual healing traditions that may preclude traditional services.

Cultural beliefs and norms influence the extent to which individuals welcome and value health care services as well as the extent to which they will adhere to health care protocols. A sensitivity to cultural differences and a willingness to work with diversity will enhance a health care professional's effectiveness with an aging population.

#### **FAMILY AND SOCIAL SUPPORTS OF OLDER ADULTS**

Family dynamics and the norms that operate within and around them have undergone transformations in the last few decades. For example, families today have many more opportunities for intergenerational exchanges than was typical just a few decades ago. Four- and five-generation families are not uncommon and provide resources to family members not available in times past.<sup>13</sup> Families have undergone some basic structural changes such as reduced fertility rates, which have dropped from a rate of 3 children per family to the current rate of 1.5. There also have been changes in timing of events such as births and marriages. In general, we can look forward to spending as many as eight

decades with our siblings, five decades or more with our parents, and three or more decades with our grandchildren. Some researchers have defined the new look of our aging families as the "bean-pole" family since there are fewer people but more generations.

Our family norms are being modified to accommodate the increasing longevity of our relationships. For example, adults are redefining relationships with their parents and their adult children based upon adult relationships, not merely those based on childrearing.

Many of our family norms and relationship patterns have withstood the test of time. In particular, the norm of filial obligation has remained strong. Today there are an estimated 22 million American households who report they are providing assistance to an older family member.<sup>14</sup>

Research suggests that more than 90% of care to community-dwelling older adults is provided informally by family, friends, and neighbors.<sup>14</sup> Additionally, according to the National Long-Term Care Survey, only nine percent of this population relies on formal support mechanisms.<sup>15</sup>

While the structure of today's family has changed and norms have shifted, it is clear that one thing remains the same—the overwhelming portion of care to older adults continues to be provided informally. This becomes increasingly important as shortages in

the long-term care workforce become more apparent. Families not only act to fill the gap in the work force but provide billions in unpaid assistance and out-of-pocket expenses.<sup>16</sup>

Although family caregiving is normative today, it is important to remember that older adults do not rely solely upon family members for decision-making or advice. Most older adults look to their physician and health care provider to advise them on health care matters and continue to remain their own health care decision-maker. Only in the case of older adults with cognitive impairment will we reliably see family members as decisionmakers. And because of concern about the well-being of the elder, some family members may question an older adult's ability to make good decisions. Health care providers can be caught between two opposing forces when advising an older adult and need to be aware any existing personal bias about decision-making and advanced age. Despite concerns on the part of well-intentioned family members, older individuals continue to be directing their own care unless they are physically unable or have been determined by a court to require a guardian or legal health care proxy. And finally, it is very important to remember that many of the caregivers to an older person are older persons themselves. Today it is not uncommon to find a 75-year-old caregiver to a 95-year-old mother or an 80- or 90-year-old who is caring for his or her spouse of the same age.

## CONCLUSION

The aging of our population carries with it profound implications for society and the individual. Financial and health security for an aging population is and will continue to be a key focus of public policy. The current health care system, designed to meet the needs of acutely ill patients, is challenged by the needs of a rapidly expanding population, primarily affected by chronic illness.

Many gerontologists are wondering if the private sector is up to the task of modifying businesses, products, and systems to accommodate the changing needs of an aging population. At the same time, we as individuals are aging and discovering on a personal level the full effect of aging on our families and our loved ones. Baby boomers are caring for aging parents and grandparents while trying to explore their own aging and setting an example that their children may follow when they become very old.

Medical science is trying to keep pace with the changing needs of an aging population as well, and the new "anti-aging" medicine movement is seeking to defer aging effects for as long as possible and redefine biological aging. Health care professionals are in the middle of our changing social norms and population trends, advancing science and changing medical options and practice. These health care professionals are the gatekeepers and guides for people who are seeking to improve their quality of life and well-being, despite age-related

changes. Understanding the larger issues in aging and how these issues may affect individuals will be of critical importance in providing high quality care to an aging population. ☉

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Same Disorder,

**LATE-ONSET PSYCHOSIS REPRESENTS A SIZABLE PROPORTION OF NEW SCHIZOPHRENIA CASES, BUT DIAGNOSIS IS CHALLENGING.**

# LATE-ONSET

Different Presentation

Mrs. Green, age 62, insisted her neighbors were talking about her; she could hear their voices through the wall, even though they lived in detached houses. At first her adult children dismissed these complaints. When they found her wearing a gas mask while cooking Sunday dinner (to combat what she thought were the poison gases being forced through her floors and ceilings), they sought professional help. Mrs. Green was admitted to a private psychiatric hospital and, after several diagnoses were considered, was diagnosed with late-onset schizophrenia. Her symptoms went into complete remission after two months of treatment with risperidone 0.5 mg daily.

Clinicians tend to think of schizophrenia as an illness that starts in early adulthood. Late-onset psychosis, however, represents a sizable proportion of new schizophrenia cases, but diagnosis is challenging—its symptoms are easily confused with other age-related disorders, substance abuse, or adverse effects of medications. Although data are lacking on incidence rates in long-term care facilities, consultant pharmacists need to be aware of late-onset schizophrenia's unique disease progres-

sion, distinguishing characteristics, and prognosis.

Late-onset schizophrenia was only recently added as a formal diagnostic description with the 1994 publication of the *Diagnostic and Statistical Manual* (4th edition), simply referred to as DSM-IV.<sup>1</sup> Earlier diagnostic systems dating back to the turn of the century used the term paraphrenia to describe various psychotic symptoms with late-onset. Paraphrenia remained a frequently used category, although clinicians often used the diagnosis inconsistently, applying it both to late-onset schizophrenia and organic disorders with psychotic features.

Despite the adoption of DSM-IV, development of research and treatment guidelines have been hampered by a lack of clear and consistent terminology and age criteria. A group of international experts resolved this ambiguity by publishing a consensus statement in 2000 that defines late-onset schizophrenia (first onset after age 40) and very-late-onset (first onset after age 60).<sup>2</sup>

## **SCHIZOPHRENIA'S POSITIVE AND NEGATIVE SYMPTOMS**

Schizophrenia is among the most devastating forms of psychotic

# SCHIZOPHRENIA

mental illness, with emotional and cognitive symptoms that affect major areas of functioning. Symptoms of schizophrenia are classified as positive and negative.

*Positive symptoms* are exaggerated distortions of normal functioning and include delusions and other false beliefs, distorted sensory perceptions such as hallucinations, disorganized speech and thinking, and grossly disorganized or inappropriate behaviors such as social disinhibition and catatonic behaviors. Only the rare patient will experience every positive symptom, but distorted sensory perceptions are ordinary. Auditory hallucinations are the most frequent, affecting approximately 70% of patients.<sup>3</sup> Paranoid delusions of being followed, watched, or victimized are also common.

*Negative symptoms* reflect a diminution of normal cognitive and behavioral functioning such as flattened affect, poverty of speech, reduction or inability to initiate and persist in goal-directed behavior, impaired information processing, and memory recall.

Again, patients rarely present all symptoms; individual symptoms vary in intensity and may go into remission. Delusion intensity, for example, can range from the mild (e.g., someone is secretly listening to me) to the

## ISAAC NEWTON AND LATE-ONSET SCHIZOPHRENIA

One of the most interesting pre-modern descriptions is that of the scientist Isaac Newton, who, at age 51, developed late-onset schizophrenia with predominate symptoms of persecutory delusions. During his 18-month episode, he often made references to conversations with colleagues that never occurred and accused them of slandering his reputation. Although historical records support the diagnosis, not all historians agree; critics contend Newton's symptoms were consistent with metal poisoning resulting from his alchemy studies, which included the handling of mercury. While metal poisoning is associated with psychotic-like symptoms, this theory is weakened by a key finding: metal poisoning leads to the loosening of teeth. Newton died at age 84 with all but one of his secondary teeth, a remarkable accomplishment prior to the rise of preventive dentistry.

Sources: References 5,6

**GUIDO R. ZANNI, PhD**, former Commissioner for the District of Columbia's Commission on Mental Health Services, is a Health Systems Consultant based in Alexandria, Virginia.

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bizarre (e.g., God is communicating with me through the television). Likewise, cognitive deficits often fluctuate with illness duration.<sup>4</sup>

Schizophrenia is clinically and diagnostically divided into five subtypes: paranoid, catatonic, undifferentiated, disorganized, and residual. A schizophrenia diagnosis is based on a pattern of positive and negative symptoms—not a single symptom. The American Psychiatric Association lists diagnostic criteria in its DSM-IV.<sup>1</sup>

## EPIDEMIOLOGY AND COSTS

Schizophrenia's worldwide prevalence is approximately 1%, affecting 24 million people.<sup>7,8</sup> Two million people in the United States are affected: 1.3% of adults 18 to 54 years of age and 0.6% of those age 55 and older.<sup>4,9</sup> Schizophrenia typically presents around adolescence. Incidence increases rapidly during the second, third, and fourth decades. Both genders are affected equally, but average age for onset differs: males evidence onset three years earlier, 27.6 years, compared with females, age 30.6.<sup>10,11</sup> Onset graphs illustrate a bimodal distribution for females, with a second peak after age 44; new cases for males, however, continue to decline.<sup>12</sup>

Schizophrenia's costs are staggering. It consumes one-fourth of all mental health costs and one-third of psychiatric hospital beds.<sup>13</sup> In 1996, costs totaled \$65 billion yearly, with \$19 billion in direct medical costs and \$46 billion in indirect costs.<sup>13</sup> Direct costs for schizophrenia

account for 2.5% of all health care dollars, with inpatient treatment accounting for the single greatest share of total direct costs.<sup>14</sup>

## LATE-ONSET SCHIZOPHRENIA

Prevalence for late-onset schizophrenia is estimated at 0.6%. Because studies have employed different age criteria and diagnostic screening tools, experts interpret estimates for late-onset cases cautiously. Overall, schizophrenia onset after the age of 40 represents 23.5% of cases, approximately 517,000 people. Schizophrenia's prevalence for individuals between ages 24 and 64 is 0.6%, and for those older than 65, prevalence estimates range from 0.1% to 0.5%. Annual incidence for those over the age of 44 is estimated at 12.6 per 100,000.<sup>2</sup>

Up to 87% of late-onset cases are female. Reported female-to-male ratios range from 2.2:1 to 22.5:1.<sup>26</sup> Observed gender differences cannot be explained by gender-related mortality rates. Studies attempting to control for such variables still report higher ratios of females to males in late-onset schizophrenia compared with early-onset.<sup>26</sup>

Clinically, late-onset schizophrenia presents differently. Patients are *more likely* to:

- Experience visual, tactile, and olfactory hallucinations
- Have accusatory and abusive auditory hallucinations
- Struggle with persecutory delusions and partition delusions (beliefs

## COMORBID CONDITIONS

Schizophrenia has been described as a "life-shortening disease." Life expectancy for people diagnosed with schizophrenia is 20% shorter than that of the general population. Medical comorbidity accounts for 60% of premature deaths, excluding those related to suicide. Consider the following:

- Approximately 50% of schizophrenia sufferers meet diagnostic criteria for alcohol or drug abuse, and substance abuse is four times higher than that of the general population.
- One-fourth to one-third suffer from depression. Approximately 10% of patients commit suicide, and five times that many attempt suicide.
- Comorbid obsessive-compulsive disorders are found in up to 15% to 20% of patients.
- Schizophrenia sufferers smoke more, ingest more alcohol, and have poorer diets and exercise less compared with nonsufferers. These risk factors lead to numerous comorbid conditions including cardiac and pulmonary diseases, infectious diseases, hyperlipidemia, osteoporosis, and hyperglycemia.
- Schizophrenia sufferers are more likely to have impaired glucose tolerance, which can present as new-onset type 2 diabetes, hyperglycemia, or ketoacidosis. Type 2 diabetes may be two to three times more prevalent in patients with severe mental disorders.
- HIV infection affects 5% to 8% of the seriously mentally ill, and concurrent substance abuse can escalate incidence to 20%.

Source: References 15-25

**BECAUSE STUDIES HAVE EMPLOYED DIFFERENT AGE CRITERIA AND DIAGNOSTIC SCREENING TOOLS, EXPERTS INTERPRET ESTIMATES FOR LATE-ONSET CASES CAUTIOUSLY**

that persons and objects can pass through impermeable barriers)

■ Babble on with third person running commentary, i.e., auditory hallucinations where patients hear voices talking about them in the third person, e.g., “she hates the cat—she’s a witch.”

Late-onset patients are *less likely* to display formal thought disorders or flattened affect. Formal thought disorder and negative symptoms are rare when onset occurs after age 60.<sup>2</sup>

Research demonstrates that persecutory delusions are one of the most common late-onset symptoms, affecting up to 92% of patients.<sup>27</sup> Consequently late-onset schizophrenia has a higher frequency of paranoid subtype, some studies reporting up to 75%.<sup>28</sup> Late-onset and early-onset cases do not differ on the prevalence of hallucinations, although a greater range of hallucinatory categories of visual, tactile, and olfactory are observed in late-onset cases.

Level of functioning prior to onset also distinguishes early-onset from late-onset cases. Late-onset patients are more often premorbidly suspicious and paranoid, socially isolated, and argumentative. Psychosocial histories reveal higher premorbid functioning in adolescence and early adulthood.<sup>28</sup> Many late-onset patients were married, educated, and main-

tained steady employment, demographics which also differentiate them from early-onset patients.<sup>26</sup>

**ETIOLOGY AND RISK FACTORS**

Late-onset schizophrenia’s underlying etiology and precipitating factors are believed to be similar to those in early-onset: core symptoms are attributed to dysfunctions in the brain circuitry itself.<sup>4</sup> Neurobiology of schizophrenia is linked to specific activity of neurotransmitters, serotonin levels, and dopamine processes. Nevertheless, it remains unclear if dopamine and neurotransmitter activity cause schizophrenia or if they are a byproduct of more fundamental metabolic dysfunctions.

Disease pathology for late-onset schizophrenia is believed to be identical to that of early-onset, but risk factors appear to differ. Genetic, sensory deficits, premorbid disorders, neuropsychological abnormalities, and gender have received particular attention.

*Genetics.* The genetic basis for schizophrenia is unquestionable. While schizophrenia’s prevalence rate is 1%, families with members diagnosed with schizophrenia have disproportionately higher rates. Immediate biological relatives, excluding twins, have a 5% to 10% increased lifetime risk for schizophrenia that is directly

related to the degree of genetic closeness. First cousins, for example have a 2% risk, half-siblings have a 6% risk, full siblings have a 9% risk, and monozygotic (identical) twins have a 48% risk.<sup>29</sup>

This genetic profile appears to differ for late-onset cases. Relatives of very-late-onset patients have a lower risk for schizophrenia than relatives of early-onset sufferers, leading some to speculate that late-onset schizophrenia may be genetically distinct from early-onset cases.<sup>2</sup> An intriguing association between depression and relatives of late-onset patients exists: 16.3% of relatives suffer from depression compared with 4.4% on non-relatives, giving rise to speculation that late-onset schizophrenia and affective disorders may overlap in genetic and other etiological links.<sup>26</sup>

Since few studies have examined the prevalence of psychiatric disorders among relatives of late-onset cases, theories about varying genetic models await further support. This is particularly true when citing the prevalence rate in relatives, especially considering the methodological problems of following patients’ family members into their old age to ensure every case is detected.<sup>30</sup>

*Sensory Impairment.* Sensory deficits, particularly hearing and vision loss, are more prominent among late-onset

## RESEARCH DEMONSTRATES THAT PERSECUTORY DELUSIONS ARE ONE OF THE MOST COMMON LATE-ONSET SYMPTOMS, AFFECTING UP TO 92% OF PATIENTS

cases than those observed in matched controls. Increased incidence of cataracts and bilateral conductive hearing loss are found among late-onset schizophrenia, paranoid types.<sup>30</sup> One case-controlled study examining younger cohorts found the association was primarily related to uncorrected sensory deficits.<sup>31</sup>

*Brain Abnormalities.* Studies examining nonspecific structural brain changes find those observed in late-onset cases are similar to those observed in younger counterparts (e.g., late-onset cases manifest higher ventricle-to-brain ratio and third-ventricle volume and volume reductions in the left temporal lobe). These nonspecific brain changes are distinct from abnormalities observed in patients suffering from the dementias.<sup>2</sup>

*Premorbid Traits and Gender.* Because late-onset symptoms differ from those observed in early-onset, researchers have searched for distinguishing clues in late-onset patients' prediagnosis behavior. Retrospective review of pre-onset psychosocial characteristics reveals a distinct profile: many patients were socially isolated, suspicious, and frequently had paranoid tendencies prior to onset.<sup>28</sup> Although these are confirmed differences, it is difficult to know if they represent valid risk factors or if

they were early symptoms of a slow, insidious onset process.

Gender is a definite risk factor for late-onset schizophrenia, but its role continues to be baffling. Some explanations focus on gender-specific stressors. Females tend to live longer, increasing exposure to psychosocial stressors such as financial difficulties, bereavement, death of peers, and physical disabilities. While these stressors are significant for aging females, few studies have systematically examined their effects. Overall, studies examining the role of stress in schizophrenia's etiology fail to identify clearly defined stressors.<sup>4</sup>

*Etiological Heterogeneity.* No single etiological risk factor emerges as more important than another. Prevailing theories maintain schizophrenia's causes are multifactorial, with genetics creating vulnerability and psychosocial and other stressors galvanizing its onset. These theories postulate a model of etiological heterogeneity, suggesting additive effects of genetic vulnerability and environmental stressors until patients reach a yet unknown threshold and succumb to schizophrenia.<sup>32</sup> People with late-onset schizophrenia reach this threshold in their geriatric years. Possible explanation for delayed onset is that sufferers either lacked earlier exposure

to contributing factors or had some protection from their effects for several decades.

### ESTROGEN AND SCHIZOPHRENIA

The second surge of new cases observed in females older than 44 fuels hypotheses on the relationship between estrogen and schizophrenia. The estrogen hypothesis maintains estrogen exerts a protective effect against schizophrenia.<sup>12</sup> Support for this theory comes from observed gender differences in age of onset, premorbid adjustment, treatment response, and disease progression. Consider the following:

- Earlier menarche age is correlated with later onset of schizophrenic symptoms.
- Forty-seven percent of psychiatric admissions occur during paramenstrual phases, when estrogen levels are at their lowest.
- A correlation exists between estradiol levels and psychosis scores.
- Cognitive performance scores are positively associated with estrogen levels.
- Pregnant schizophrenia sufferers require less medication during pregnancy.<sup>12</sup>

These data suggest estrogen modulates symptoms. Clinical findings are further supported by animal studies that demonstrate estrogen reduces

## ESTROGEN AS A TREATMENT FOR SCHIZOPHRENIA

Given the intriguing association between estrogen and schizophrenia, several researchers have investigated estrogen as a treatment intervention. In one double-blind, placebo-controlled study, groups of females with schizophrenia were treated with antipsychotic medication plus 50 mcg transdermal estradiol, 100 mcg transdermal estradiol, or placebo. At the end of 28 days, women on 100 mcg showed greater improvement than those on 50 mcg, who in turn showed more improvement than the placebo group. Improvement for symptoms of hallucinations, thought disorders, and delusions was particularly striking in the 100-mcg group. Despite the small sample size and brief follow-up period, these results reinforce the need for additional studies examining estrogen's role on symptomatology and outcome.

Source: Reference 33.



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the dopamine concentration in the striatum, affects the number of dopamine receptors, and has a modulating effect on serotonin systems. These systems are implicated in schizophrenia's pathogenesis, and estrogen appears to mimic the effects of antipsychotic medications such as haloperidol.<sup>12,33</sup>

The relationship between estrogen and schizophrenia suggests practice guidelines should address the potential need for dose increments in menopausal women.<sup>33</sup> Augmenting current treatments for schizophrenia with estrogen is under serious investigation. Although well-controlled human trials are limited, many schizophrenia researchers believe available evidence favors acceptance of estrogen's role in schizophrenia's etiology and treatment.<sup>12,33</sup> The current controversy on the risks of hormone replacement therapy, however, necessitates treatment recommendations on an individual care basis.

## ASSESSMENT ISSUES

All patients with new-onset schizophrenia require comprehensive evaluation; late-onset cases create additional challenges because schizophrenia's symptoms overlap with many other syndromes and neurological conditions. Assessment minimally should include:

- Comprehensive medical and psychosocial histories, including medications
- Physical and neurological examinations

- Laboratory diagnostics and CT neuroimaging

- Psychiatric and cognitive evaluation<sup>26</sup>

Comprehensive laboratory and physical examinations will determine if the patient's symptoms are linked to organic disorders or current medications. Symptom history, however, must be viewed with caution because onset may have occurred earlier than reported. Families frequently fail to report cognitive and emotional symptoms, confusing them with normal aging. Also, as a result of the reclusive lifestyle of many late-onset schizophrenia sufferers, symptoms may have gone unnoticed for some time.

Despite limited research investigating the relationship between cognitive deficits, aging, and schizophrenia, psychological and cognitive assessment assist with differentiating schizophrenia from neurodegenerative disorders such as Alzheimer's disease and other dementias. Schizophrenia sufferers, for example, retain their ability to learn new material and recall it at a later time, unlike Alzheimer's patients in which both learning and recall of new material are seriously impaired. As noted earlier, late-onset patients have nonspecific structural brain changes similar to early-onset sufferers (e.g., higher ventricle-to-brain ratio and third-ventricle volume), which—once identified via neuroimaging techniques—helps to differentiate schizophrenia from the dementias.<sup>2</sup>

Approximately 50% of geriatric

inpatients manifest paranoid symptoms; late-onset schizophrenia must be differentiated from both mood disorders with psychotic features and other types of delusional disorders—two disorders that are also more likely to have onset during middle and old age.<sup>30</sup> Generally, clinicians consider a diagnosis of late-onset schizophrenia when mood symptoms have been brief in duration relative to primary psychotic symptoms; this is unlike true mood disorders, which are marked primarily by affective symptoms over a longer duration and coupled with distinct symptom cycles.

Delusional disorders can easily be confused with late-onset schizophrenia. An important distinction is late-onset schizophrenia presents with more bizarre delusional content, frequently accompanied by pronounced visual, auditory, tactile, or olfactory hallucinations.

Hallucinations are often absent in other types of delusional disorders, and the delusions tend to be less bizarre.<sup>30</sup>

## TREATMENT ISSUES

Patients with late-onset schizophrenia respond to much smaller doses of medication than early-onset patients. Very-late-onset patients respond to half the dose required for younger counterparts.<sup>26</sup> Others report substantial symptom reduction with a fourth of typical doses for antipsychotic medications including clozapine (Clozaril), haloperidol

## PATIENTS WITH LATE-ONSET SCHIZOPHRENIA RESPOND TO MUCH SMALLER DOSES OF MEDICATION THAN EARLY-ONSET PATIENTS

(Haldol), thioridazine (Mellaril), and fluphenazine (Prolixin).<sup>34</sup>

Overall, older patients on conventional neuroleptics face an increased risk of extrapyramidal symptoms,<sup>26</sup> and tardive dyskinesia (TD) continues to be a concern with neuroleptic use. The severity of TD is a function of gender and age at diagnosis. Prevalence rates for TD are similar for males and females under age 50.

Over age 50, more women than men develop TD, once again suggesting estrogen's modulating effects. Studies controlling for onset age, neuroleptic dose, and illness duration find that women with late-onset and men with early-onset have more severe dyskinesia than women with early-onset and men with late-onset.<sup>35</sup>

While atypical antipsychotics are the preferred line of treatment for younger patients, prescribers must exercise caution when treating older adults. Side-effect profile may suggest different strategies for older adults. While most older patients appear to tolerate atypical antipsychotics, their association with weight gain, elevated serum triglycerides, and glucose dysregulation must be evaluated against their benefits.

Similarly, the association of traditional neuroleptics with TD may worsen other comorbid conditions. Tremor and rigidity in patients with

preexisting Parkinsonian symptoms may worsen with high-potency neuroleptics such as haloperidol. Because low-potency neuroleptics (e.g., thioridazine) have significant anticholinergic activity, they should be avoided in patients with prostatic hypertrophy.<sup>30</sup>

Considering the likelihood for medication effects on comorbid conditions, drug interactions, and age-related dosing, treatment protocols for late-onset schizophrenia generally adhere to the "start low, go slow" guideline.

### OUTCOME

Schizophrenia's disease progression and outcomes vary extensively, with most patients experiencing periods of symptom exacerbation and remission. Outcome studies, however, suggest late-onset patients fair better than their early-onset counterparts.

Consider the following general statistics on schizophrenia's progression:

- Approximately 10% of patients remain severely ill.
- Approximately 50% to 67% improve significantly or recover.
- Some studies suggest up to 31% patients experience complete remission.
- Most patients relapse at least once.
- Gradual onset and delayed treatment prolong acute episodes.<sup>3,4</sup>

Relapse is common among people with schizophrenia. One study, for example, found that 82% of patients have at least one additional episode within five years of onset. Treatment nonadherence increases relapse further; studies report patients who stop taking maintenance medication double their risk of worsening or relapse.<sup>3</sup>

Outcomes are significantly brighter for late-onset cases. Patients respond favorably to treatment, and studies report partial remission or full remission, ranging from 48% to 76%.<sup>26,27</sup> The duration of illness also is shorter.<sup>36</sup> Particularly striking is that late-onset patients require much smaller doses to achieve favorable outcomes, even though positive symptoms such as hallucinations present with the same frequency.

Long-term follow-up studies tracking late-onset cases are few; valid relapse data are lacking. Many speculate that late-onset schizophrenia may actually be a precursor for neurodegenerative disorders. One small five-year follow-up study matched 27 late-onset cases with controls. Five years later, nine of the late-onset cases were found to have dementia (five Alzheimer's disease-type, one vascular, and three dementia of unknown type) compared with zero cases of dementia in the controls.<sup>35</sup> While the

possibility exists that the late-onset patients may have had undetected dementia at the study's start, one also would have expected similar occurrences in the controls.

Because this study employed a small sample and several participants either died or refused follow-up examinations, findings are viewed cautiously. The relationship between aging, schizophrenia, estrogen, cognitive decline and late-onset of dementia deserves additional scrutiny. Until then, prevailing theories maintain that late-onset schizophrenia is distinct from neurodegenerative disorders.

## ENDNOTES

Schizophrenia's etiology remains elusive. Much of what is known about etiology, treatment effectiveness, and outcome is derived from studies involving younger cohorts. While etiology and pathogenesis of late-onset is not viewed as distinct from early-onset, unique characteristics of older populations complicate both diagnosis and treatment regimens. Overall, treatment of the first episode with antipsychotic medication has emerged as a significant predictor of long-term positive outcome.<sup>4</sup> Large scale treatment studies on the use of antipsychotics in the elderly are needed along with data on the number of late-onset patients in long-term care facilities. With late-onset cases expected to increase as America ages and longevity increases, prudent consultant pharmacists will keep abreast of cutting edge research. ☉

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## PREVALENCE OF LOW BONE-MINERAL DENSITY AMONG MENTALLY RETARDED AND DEVELOPMENTALLY DISABLED RESIDENTS IN INTERMEDIATE CARE

Elmer V. Schmidt  
James R. Byars  
David H. Flamuth  
Jeff J. Schott  
Craig M. Sever

**Objective:** To explore the prevalence of low bone-mineral density (BMD) and related fractures among mentally retarded and developmentally disabled residents in intermediate care settings.

**Design:** Cross-sectional study.

**Setting:** Intermediate care facilities for mentally retarded and developmentally disabled (>16 beds) and group homes ( $\leq$ 16 beds) in the mid-western United States.

**Participants:** A total of 360 residents were selected for the initial study group; 119 were excluded, 241 remained to study completion.

**Intervention:** Antiresorptive therapy with alendronate 10 mg daily and calcium 500 mg with vitamin D 200 IU, three times daily, for participants in the osteoporosis range; calcium 500 mg with vitamin D 200 IU three times daily for participants in the osteopenia range.

**Main Outcome Measures:** Low BMD and related fractures. Secondary measures included medications associated with bone loss, mobility level, medical diagnoses associated with bone loss, diagnosis of bone disorders, level of mental retardation, pharmacotherapy and calcium supplementation, and demographic characteristics.

**Results:** The prevalence of low BMD in this study group was 78.8% (n=189), with 157 (65.1%) participants in the osteoporosis range and 32 (13.3%) in the osteopenia range. The average age was 45.8 years, with residents ranging from 20 to 91 years; 67.6% (n=163) were male. Nearly three-fourths of participants were in either the severe or profound range of mental retardation. Forty residents received multiple medications, contributing to bone loss. The incidence of documented nontraumatic fractures was 3.5%.

**Conclusions:** Low BMD is prevalent in mentally retarded and developmentally disabled residents in intermediate care settings with low mobility and other risk factors. Consultant pharmacists have the opportunity to suggest appropriate pharmacotherapy for the treatment of low BMD in this setting.

**Key Words:** Alendronate, Calcium supplementation, Developmental disabilities, Mental retardation, Osteopenia, Osteoporosis.

**Abbreviations:** BMD = bone-mineral density; DEXA = dual-energy x-ray absorptiometry; ICF/MRDD = intermediate care facilities for the mentally retarded and developmentally disabled; PIXI = peripheral-DEXA-bone densitometer; .

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### INTRODUCTION

In the United States, intermediate care facilities for the mentally retarded and developmentally disabled (ICF/MRDD) serve residents with a primary diagnosis of mental retardation or related conditions such as cerebral palsy, epilepsy, Down syndrome, or any other condition found to be closely related to mental retardation.<sup>1</sup> Mental disease and disorders such as schizophrenia, bipolar disorder, dementia, psychosis, autism, and others may coexist with the primary diagnosis of mental retardation.<sup>2</sup>

Low bone-mineral density (BMD) and related fractures in the ICF/MRDD population are suspected to be more severe and prevalent at earlier ages than in the general population as a result of multiple risk factors unique to this population. In the United States today, 10 million individuals are estimated to have severe bone loss or osteoporosis and another 34 million individuals are estimated to have low BMD or osteopenia, which increases risk for osteoporosis and related fractures.<sup>3</sup> Among the 10 million Americans with osteoporosis, eight million are female; 55% of Americans 50 years of age and older have low bone mass.<sup>3</sup> Menopausal estrogen loss and the aging process are primary contributors to osteoporosis. Secondary forms of osteoporosis include those seen with systemic illness, intestinal malabsorption, or medication exposure. Therefore, osteoporosis is not limited to the elderly female population.<sup>4</sup> The complexity of neuromuscular disorders, cognitive function disorders, and behavioral and psychological disorders associated with the medical and mental diagnoses common in the ICF/MRDD population contribute to diminished mobility, medication use, and nutritional deficiencies, all of which increase risk for low BMD and fractures. Several of these risk factors have been studied in

**ELMER V. SCHMIDT, PHARM.D, FASCP, CGP**, is Consultant Pharmacist, Home Pharmacy Services, LLC, Belleville, Illinois. **JAMES R. BYARS, PHARM.D, FASCP, CGP**, is Director of Clinical Services, Home Pharmacy Services, LLC, Belleville, Illinois. **DAVID H. FLAMUTH, PHARM.D, FASCP**, is Vice President and Director of Public Relations, Home Pharmacy Services, LLC, Belleville, Illinois. **JEFF J. SCHOTT, PHARM.D**, is Consultant Pharmacist, Home Pharmacy Services, LLC, Belleville, Illinois. **CRAIG M. SEVER, PHARM.D**, is Consultant Pharmacist, Home Pharmacy Services, LLC, Belleville, Illinois.

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**ADDRESS FOR CORRESPONDENCE:** Elmer V. Schmidt, PharmD, FASCP, CGP, Home Pharmacy Services, LLC, 1520 Mascoutah Avenue, Belleville, IL 62220

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similar populations and settings and are reported in the literature.

Henderson et al.<sup>5</sup> reported that fractures are common in children and adolescents with moderate-to-severe cerebral palsy, and many of those who sustain a fracture will sustain repeated fractures. Cummings and Melton<sup>6</sup> also found that primary osteoporotic fractures (i.e., vertebrae, proximal femur, and distal forearm) occur more frequently in patients with low BMD, and adults who sustain a fracture are 50% to 100% more likely to sustain another fracture in a different location. Among those with cerebral palsy, low bone density, stiff joints, poor balance, and violent seizures are contributing factors for fractures.

A study by Jeffrey et al.<sup>7</sup> on bone metabolism disorders in severely handicapped children and young adults attributed osteopenia to immobility; nutritional deficiencies, particularly calcium and vitamin D; and interference with normal bone mineral metabolism by drugs such as anticonvulsants.

Relationships between medication use and osteoporosis, and dietary patterns and osteoporosis also have been reported by Prestwood<sup>8</sup> and Tucker et al.,<sup>9</sup> respectively, though their studies were in older adults.

King et al.<sup>10</sup> reported an increased prevalence of reduced bone mass in children and adults with spastic quadriplegia. The investigators stated that few, if any, of these patients had primary diseases of the bone; however, immobilization predisposes one to bone resorption, reducing BMD and increasing the risk of fractures. Tyler et al.<sup>11</sup> screened for osteoporosis in community-dwelling adults with mental retardation and reported an increased incidence of risk factors for osteoporosis. Another study by Center et al.<sup>12</sup> of a community-dwelling population of 94 young adults with mental retardation showed a higher prevalence of osteoporosis and

osteopenia among the study group than among an age- and gender-matched group. For the study group, 67.5% were in the osteoporosis range and 13.3% were in the osteopenia range.

While prevalence and risk factors for low BMD and related fractures have been studied and reported for the United States population overall, and for older Americans specifically, few studies were found in the literature on the prevalence of low BMD among mentally retarded and developmentally disabled individuals. Of those studies that were found, all were among community-dwelling populations. Therefore, the primary purpose of this study was to explore the prevalence of low BMD and related fractures in an ICF/MRDD population.

## METHODS

To meet the stated objective, a population study was designed and conducted. The population for the study included all residents of selected ICF/MRDD (>16 beds) and group homes ( $\leq$ 16 beds) in the mid-western United States (N=568). The inclusion criteria for the study included individuals with the following conditions: decreased mobility, poor dietary intake (i.e., inability to follow dietary regimens due to level of mental retardation or psychiatric disorder), Down syndrome, cerebral palsy, thyroid disorder, quadriplegia, history of hysterectomy, or seizure disorder. Individuals receiving any one of the following medications known to be associated with bone loss were also included: carbamazepine, corticosteroids, gabapentin, phenobarbital/primidone, phenytoin, thyroid medications.

Residents were identified for study inclusion by the consultant pharmacist and nursing staff. Dietary intake information was provided by direct care staff.

Three hundred sixty residents were identified for BMD testing. The facility medical

director and administrator gave written authorization to conduct the study as a quality improvement initiative. Consent for participation also was obtained from the legal guardian for each subject. Each subject's primary care physician ordered the test.

Baseline data were collected on medications associated with bone loss, mobility level, medical diagnoses associated with bone loss, diagnosis of bone disorder, level of mental retardation, dietary regimens, calcium supplementation, and demographic characteristics.

The data collection tool for BMD was the peripheral-DEXA-bone densitometer (PIXI). The PIXI scan technology was selected for ease of testing in the study sites. Other advantages of the PIXI scan include low x-ray dose (limited to heel or forearm), no clothing restrictions, and immediate results (within five seconds).<sup>13</sup> The PIXI scan technology does have limitations compared with the dual-energy x-ray absorptiometry (DEXA) scan. The DEXA scan is the most accurate and advanced test available for measuring bone mass at the spine and hip, with excellent resolution; however, it requires patients to lay motionless in a horizontal position on a large table for approximately 10 minutes.<sup>14</sup> Individuals in this study group would not be able to undergo this procedure without a sedative/hypnotic agent. Limitations of the PIXI scan include the underestimation of bone loss since the heel has a slower bone-loss rate than other sites in the body.<sup>13</sup> While not advocated as a measurement of monitoring effectiveness of treatment for bone loss, the PIXI scan is advocated as an effective instrument for screening.<sup>13</sup>

Therefore, the PIXI scan technology was determined to be more practical than the DEXA scan for this study since it is portable, fast, and effective. The diagnostic criteria for the categories of bone loss based upon PIXI

scan results are as follows: osteoporosis, a T-score of  $<-1.6$  standard deviations; osteopenia, T-scores within a range of  $-0.6$  and  $-1.6$  standard deviations; and normal, a T-score of  $>0.6$  standard deviations. For comparison, the World Health Organization and International Osteoporosis Foundation have established the diagnostic criteria for assessments done with a central DEXA as follows: normal hip BMD T-score, osteopenia range—hip BMD T-score  $<-1$  and  $>-2.5$ , and osteoporosis—hip BMD T-score  $>-2.5$ .<sup>14</sup>

Baseline data on medications associated with bone loss, mobility level, and medical conditions and diagnoses associated with bone loss, diagnosis of bone disorder, level of mental retardation, calcium supplementation, and demographic characteristics were collected through computer-generated surveys and manual reviews of the study participants' pharmacy and facility records. Data on dietary regimens were collected through the dietary management corporation.

Consultant pharmacists, as part of their routine drug regimen review function, recommended treatment based upon the subject's bone scan results and risk factors. Risk factors were assessed through review of medical records and consultation with nursing staff. For study participants whose BMD was in the osteoporosis range, the consultant pharmacist recommended that the physician prescribe antiresorptive therapy with the bisphosphonate alendronate, 10 mg daily, and calcium 500 mg with vitamin D 200 IU, three times daily. In the United States, bisphosphonates are the most widely prescribed, and alendronate was the only bisphosphonate available at the time.<sup>15</sup> Alendronate was recommended over miacalcin based upon evidence supporting efficacy in a broad range of patients; miacalcin is recommended for treating osteoporosis in postmenopausal females. Efficacy data for miacalcin did not

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support its choice as a first line agent in this population.<sup>16</sup> Furthermore, estrogen replacement therapy was not recommended as a result of scientific evidence indicating that overall health risks exceed benefits.<sup>17</sup> Alendronate was not recommended, however, if the study participant had contraindications, including gastrointestinal symptoms (e.g., gastrointestinal esophageal reflux disease, bleeding, etc.), could not sit in a upright position for 30 minutes following therapy, or could not swallow the medication. For study participants for whom alendronate therapy was contraindicated, recommended treatment was calcitonin-salmon nasal spray and calcium 500 mg with vitamin D 200 IU three times daily. Finally, for study participants whose BMD was in the osteopenia range, the recommended treatment was calcium 500 mg with vitamin D 200 IU three times daily. Eighteen months postbaseline, data were collected on implementation of the recommended pharmacologic treatment and fractures among the study group.

Descriptive statistical analyses on discrete variables were performed utilizing chi-square tests of independence. Continuous variables were analyzed via linear regression with dichotomous variables (comorbid diagnoses and concomitant medications) as independent variables and the dependent variable being the T-score stratified as osteoporosis, "yes" or "no." Residents with a T-score indicating osteopenia were considered as "no" for this analysis. Post-hoc Pearsons Correlation testing was performed as part of the regression model. In addition to the regression analysis, univariate and multivariate associations of concomitant disease states and medications on BMDs were performed. The odds ratio (OR) value is the probability of the outcome among the exposed (concomitant disease/medications) divided by the probability of the outcome in the unexposed. Level of

significance was set at 0.05, and statistical significance was determined if the probability was less than 0.05. Chi-square tests of independence were performed with Minitab for Windows software, version 12.21. All other statistical testing was performed with SPSS for Windows version 11.0.

## RESULTS

A total of 360 MRDD individuals from selected ICFs were selected for the study; 119 were excluded in accordance with exclusion criteria and 241 participants remained to completion. Exclusion criteria included 1) grossly retracted heel muscles, 2) too combative to perform bone scan, 3) not present at site on the day of the scan, 4) less than 20 years of age, 5) current medication therapy to prevent bone loss, and 6) calcium or vitamin D supplementation.

For the initial study group screened (n=241), the majority were male (n=163; 75.6%) and white (n=205; 85.1%). Thirty-one (12.9%) were African American. The mean age was 45.8 years, ranging from 20 to 91 years. By level of mental retardation, 55.6% had profound mental retardation, and 17.0% severe mental retardation. Demographic data are presented in Table 1.

Results for the main outcome measure, BMD, indicate that a majority of participants had either osteoporosis (n=157; 65.1%, mean T-score=3.124, SD=1.205) or osteopenia (n=32; 13.3%, mean T-score = -1.124, SD = 0.340). By gender, more males (n=114; 69.9%) than females (n=43; 55.1%) had osteoporosis. By race, 8.7% of blacks (n=21) had osteoporosis, compared with 55.2% of whites (n=133).

Univariate analyses of medications associated with bone loss are presented in Table 2. Among those participants whose screening results indicated a bone density in the osteoporosis range, 13.7% (n=33) were

prescribed phenytoin and 12.5% (n=30) carbamazepine. Results indicated that 40 participants were on multiple medications associated with bone loss.

In the logistic regression shown in Table 3, several conditions were shown to have a statistically significant association with having osteoporosis; seizure disorder, cerebral palsy, quadriplegia, thyroid disorder, immobility, phenytoin, thyroid medication, and carbamazepine.

Analysis of BMD by level of mobility (normal = no restriction on mobility, restricted = some type of mobility restriction or use of adaptive device for mobility, none = no mobility), indicated the highest frequencies of osteoporosis among those with normal mobility (n=73; 30.3%) and no mobility (n=59; 25.5%). The highest percentage of osteopenia was also observed in the normal mobility group (n=23; 9.5%). However, low BMD was present in all mobility groups, with findings of osteoporosis in 10.4% (n=25) of residents in the restricted mobility group.

Results indicated that 142 participants (58.9%) had two or more risk factors for osteoporosis. From the study group, the frequency of osteoporosis (n=61; 25.5%) was highest among those with two risk factors (n=81; 33.6%).

Results of the prescribing physician response to the pharmacologic treatments suggested by the consultant pharmacist following the PIXI scans indicated that 29 (12.0%) of study participants received antiresorptive therapy, 4 (1.7%) received calcitonin-salmon nasal spray, and 124 (51.5%) received calcium 500 mg with vitamin D 200 IU or calcium 500 mg only, three times daily. Finally, 5 (2.1%) received conjugated estrogen and 1 (0.4%) received raloxifene. Over 18 months of observation following PIXI scans, 3.5% of the initial

**TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION (N=241)**

Characteristics	Results
Mean age, years (range)	45.8 (20–91)
Male gender	163 (67.6%)
Race	
White	205 (85.1%)
Black	31 (12.9)
Other	5 (3%)
Bone-mineral density scans	
Osteoporosis	157 (65.1%)
Osteopenia	32 (13.3%)
Normal	52 (21.6%)
Medical conditions	
Cerebral palsy	52 (21.6%)
Down syndrome	22 (9.1%)
History of hysterectomy	6 (2.5%)
Quadriplegic	28 (11.6%)
Seizure disorder	91 (37.8%)
Thyroid disorder	39 (16.2%)
Concomitant medications	
Carbamazepine	33 (13.7%)
Corticosteroids	11 (4.6%)
Gabapentin	11 (4.6%)
Phenobarbital/Primidone	31 (12.9%)
Phenytoin	44 (18.3%)
Thyroid supplements	41 (17%)
Mobility status	
Normal	142 (58.9%)
Restricted	29 (12%)
Immobile	70 (29%)

**TABLE 2. UNIVARIATE ASSOCIATIONS OF COMORBID DISEASE STATES/MEDICATIONS WITH T-SCORE (OSTEOPENIA/NORMAL VERSUS OSTEOPOROSIS)**

	Normal or Osteopenia n (%)	Osteoporosis n (%)	P Value
Seizure Disorder	16 (17.6)	75 (82.4)	0.0031
Cerebral Palsy	6 (11.5)	46 (88.5)	0.0012
Quadriplegia	5 (17.9)	23 (82.1)	0.0098
Thyroid Disorder	15 (38.5)	24 (61.5)	0.041
Down Syndrome	9 (40.9)	13 (59.1)	0.16
Hysterectomy	4 (66.7)	2 (33.3)	0.194
Immobility	11 (15.7)	59 (84.3)	0.0039
Phenytoin	11 (25)	33 (75)	0.0064
PB/Primidone	6 (19.4)	25 (80.6)	0.18
Gabapentin	3 (27.3)	8 (72.7)	0.31
Thyroid Medication	16 (39)	25 (61)	0.041
Carbamazepine	3 (10)	30 (90)	0.035
Corticosteroid	2 (18.2)	9 (81.8)	0.38

**TABLE 3. MULTIVARIATE ASSOCIATIONS OF COMORBID DISEASE STATES/MEDICATIONS WITH T-SCORE (OSTEOPENIA/NORMAL VERSUS OSTEOPOROSIS)**

	RR	95% CI
Seizure Disorder	2.89	1.84–3.65
Cerebral Palsy	3.04	2.39–4.01
Quadriplegia	2.41	1.72–2.90
Thyroid Disorder	1.89	1.36–2.39
Down Syndrome	1.00	0.51–1.32
Hysterectomy	1.08	0.64–1.50
Immobility	3.88	2.98–4.95
Phenytoin	1.80	1.34–2.65
PB/Primidone	1.15	0.87–1.27
Gabapentin	1.08	0.83–1.21
Thyroid Medication	1.56	1.27–1.92
Carbamazepine	1.68	1.35–1.99
Corticosteroid	1.12	0.76–1.43

Abbreviations: CI= confidence interval, RR=relative risk.

study sample suffered a fracture, excluding 24 residents who were discharged or died, had a fracture of the hip, clavicle, or ankle.

## DISCUSSION

This study explored the prevalence of low BMD and related factors among mentally retarded and developmentally disabled residents in intermediate care settings in the mid-western United States. Findings indicated that 78.4% (n=189) of the study group (n=241) had low BMD, of whom 65.1% (n=157) had osteoporosis and 13.3% (n=32) had osteopenia. These findings support results of two similar studies reported in the literature on BMD among the MRDD. Center et al.<sup>12</sup> found that among a community-dwelling population of 94 young adults with mental retardation, 80.8% (n=76) had low BMD, with 67.5% (n=63) in the osteoporosis range. Tyler et al.<sup>11</sup> also studied 107 community-dwelling adults with mental retardation and found 55.1% (n=59) had low BMD. Demographic data across the three study groups are similar in terms of age and gender; however, in this study a higher percentage of participants had severe and profound mental retardation.

Results of this study also support previous studies related to risk factors for low BMD unique to the MRDD population, including medications associated with bone loss, mobility level, medical diagnoses associated with bone loss, diagnosis of bone disorders, and level of mental retardation.<sup>7-11</sup> This study also is consistent with previous studies looking at the relationship between anticonvulsant use in individuals with mental retardation and low BMD. In this study, statistically significant relationships were found for phenytoin and carbamazepine; 86.3% (n=38) of those on phenytoin and 97.0% (n=32) of those on carbamazepine had either osteoporosis or osteopenia. Regarding the

factors of medical diagnoses and mobility level, 100% (n=52) of those with cerebral palsy had low BMD, with 88.5% (n=46) in the osteoporosis range.

Henderson et al.,<sup>5</sup> however, found an increased incidence of fractures in children and adolescents with cerebral palsy. We did not attempt to correlate fractures with osteoporosis in this study. One limitation of this study was that fracture data were collected through medical records of documented nontraumatic fractures. Fractures could have occurred that were unrecognized and unreported due to the high percentage of the study group in the severe-to-profound level of mental retardation. These residents have a nonverbal functioning level and communicate by gestures, sounds, or changes in behavior or dietary patterns. Therefore, it is possible that a resident could have had a vertebral or other BMD-related fracture that went undetected and undiagnosed.

At the point in the study where the consultant pharmacist suggested treatment for residents with low BMD and other risk factors (e.g., medication, mobility level, low dietary intake of calcium and vitamin D, etc.) to the prescribing physician, alendronate was the only bisphosphonate available. Current treatment options for low BMD include bisphosphonates, calcitonins, and selective estrogen receptor modulators. However, bisphosphonates are the most widely prescribed agents.<sup>15</sup> Comparison of the results of the bone-density scans at baseline with the results of the prescribing physician response to the suggested pharmacologic treatments 18 months later indicate that even though more than 60% of the sample had screenings in the osteoporosis range, only 12% (n=29) received antiresorp-

tive therapy. However, 51.5% (n=124) of participants did receive calcium 500 mg with vitamin D 200 IU or calcium 500 mg only, three times daily. One limitation of the study in regard to the treatment recommendations is that residents with poor dietary intake of calcium or vitamin D may not have been identified for supplementation. While the dietary regimens for residents consisted of an average daily intake of 1130 mg elemental calcium and vitamin D 200 IU daily, dietary intake may be limited because of the inability to consume foods as a result of physical, cognitive, and other disabilities.

Other limitations of this study include a population sample that may have been biased because of the inclusion criteria. The population for this study included MRDD residents in intermediate care settings in one geographical region. In one facility, all residents were wheelchair bound. Further, direct care staff may have identified residents for the study sample who did not meet any of the inclusion criteria or excluded residents who met inclusion criteria. Therefore, based on the aforementioned limitations, these results may not be able to be generalized to other ICF/MRDD populations.

## CONCLUSION

This study supports previous data recognizing the high prevalence of low BMD among mentally retarded and developmentally disabled residents in intermediate care settings. The opportunity exists for consultant pharmacists to identify residents at risk for osteoporosis and to recommend appropriate pharmacotherapy. Screening for osteoporosis using a BMD scan may identify individuals who may benefit from therapy.

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## A SYNOPSIS OF THE PRACTICE PARAMETERS ON DEMENTIA FROM THE AMERICAN ACADEMY OF NEUROLOGY ON THE DIAGNOSIS OF DEMENTIA

Janet K. Pitner  
David L. Bachman

**Objective:** The objective of this paper is to review the current practice guidelines as developed by the American Academy of Neurology (AAN) for the diagnosis of dementia.

**Data Sources:** The data sources were the Report of the Quality Standards Subcommittee of the American Academy of Neurology paper, which was published in the May 2001 issue of the journal *Neurology*.

**Study Selection:** The studies used in this paper are those reviewed by the AAN Practice Parameter Committee, which reviewed the literature for evidence-based human studies pertaining to the diagnosis of dementia. Studies on Alzheimer's disease (AD) included had to have more than 25 subjects. Each article was classified based on the quality of evidence. After review of the evidence, the committee drafted recommendations and placed the evidence into Practice Standards, Guidelines, or Options.

**Data Synthesis:** The main results of this review were the guidelines for diagnosing dementia of various forms. To diagnose dementia, the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) should be used. For AD, the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association) criteria should be used. The Modified Hachinski Ischemic Score criteria can be used in the diagnosis of vascular dementia. The Consortium for DLB (Dementia with Lewy Bodies) criteria may be of use in clinical practice. Neuroimaging with a noncontrast CT or MRI scan in the routine initial evaluation of persons with dementia is appropriate; other methods of neuroimaging are not recommended at this time. Genetic testing and use of apolipoprotein E (ApoE) genotyping is not recommended at this time. Depression, B<sub>12</sub> deficiency, and hypothyroidism should be screened for and treated in patients with dementia. Unless the patient lives in an area in the United States with a high rate of syphilis, screening for tertiary syphilis is not warranted.

**Conclusion:** The guidelines and their clinical applications are pertinent and important knowledge for consultant pharmacists. This practice parameter will need to be updated every few years to include new studies and information that becomes available.

**Key Words:** Alzheimer's disease, Dementia, Geriatrics, Practice guidelines, Vascular dementia.

**Abbreviations:** AAN = American Academy of Neurology; AD = Alzheimer's disease; HIS = Hachinski Ischemic Score; VaD = Vascular dementia.

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With the aging of the baby boomer generation, Alzheimer's disease (AD) and other types of dementia will generate major public health issues over the next 50 years. There are many controversial areas in the diagnosis of dementia. In an effort to address these issues and provide an educational service, the American Academy of Neurology (AAN) has formulated evidence-based practice parameters for the diagnosis of dementia.<sup>1</sup> This is the second of these practice parameters to be reviewed in this series. These are useful articles for consultant pharmacists because they are evidence-based reviews with practice guidelines and recommendations. The reader is encouraged to obtain the articles and read the full text to obtain complete understanding of the process and findings of the committees. The full text of the articles, the evidence tables, and summaries for physicians and caregivers can be downloaded from the AAN Web site at [www.aan.com](http://www.aan.com) or the articles can be found in the journal *Neurology* in May 2001. The following is a synopsis of the practice parameters on the diagnosis of dementia.

### CLINICAL QUESTION STATEMENT

This diagnostic practice parameter addresses four major issues in the diagnosis of dementia and recommends practice standards, guidelines, and options based on the available evidence. In this article, four questions were addressed:

- Are the current criteria for the diagnosis of dementia reliable?
- Are current diagnostic criteria sufficiently accurate to establish a diagnosis for the prevalent dementias in the elderly?
- Do laboratory tests improve the accuracy of the clinical diagnosis of dementing illness?

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JANET K. PITNER, PHARM.D., CGP, BCPS, is Senior Scientific Liaison, Neuroscience, Ortho-McNeil Pharmaceutical, Charleston, South Carolina. DAVID L. BACHMAN, MD, is Associate Chief of Staff, Geriatrics and Extended Care, Ralph H. Johnson Veteran's Affairs Medical Center, Charleston, South Carolina.

**ADDRESS FOR CORRESPONDENCE:** David L. Bachman, MD, Associate Chief of Staff, Geriatrics and Extended Care, Ralph H. Johnson Veteran's Affairs Medical Center, 109 Bee Street, Charleston, SC 29401.

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■ What comorbidities should be evaluated in elderly patients undergoing an initial assessment for dementia?

### PARAMETER DEVELOPMENT PROCESS

Within the AAN organization, a Quality Standards Subcommittee (QSS) was formed and charged with the mission of developing scientifically sound, clinically relevant practice parameters in areas of neurology using a standard process. A panel of experienced clinicians from a variety of disciplines was appointed. Literature was identified by searching the following databases: MEDLINE, Excerpta Medica, and BIOSIS. Only human studies published in English were sought. Dementia was the principal search term, but other terms searched were neuroimaging, diagnostic techniques, diagnostic imaging, biologic markers, cerebrospinal fluid (CSF), diagnostic errors, differential diagnosis, and neuropsychological tests. The search yielded 1,175 articles, but these were narrowed down to approximately 300 relevant articles. An additional 300 articles were identified by committee members or obtained from bibliographies of articles identified in the search.

Each article was classified based on the quality of evidence (Class I through IV) as shown in Table 1. After review of the articles, recommendations were drafted, reviewed by all committee members, and categorized as a Standard, Guideline, Practice Option, or Practice Advisory as shown in Table 2. The parameter was reviewed by the QSS, the AAN Practice Committee, interested AAN members, the AAN Geriatric and Behavioral Neurology Sections, representatives of the American Geriatrics Society, and the Alzheimer's Association. The QSS and the AAN Practice Committee gave final approval for the practice parameter.

**TABLE 1. CLASSIFICATION OF EVIDENCE**

Class	Description
I	Evidence provided by a well-designed, blinded, prospective study of a broad spectrum of patients with the suspected condition, using a "gold standard" for case definition that used the appropriate tests for diagnostic accuracy.
II	Evidence provided by a well-designed, blinded, prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed, blinded, retrospective study of a broad spectrum of persons compared with a broad spectrum of controls with the appropriate tests of diagnostic accuracy.
III	Evidence provided by a blinded, retrospective study in which either persons with the established condition or controls are of a narrow spectrum.
IV	Any design in which the test was not blinded or evidence is provided by expert opinion alone or descriptive case series (without controls).

Source: Reference 1.

**TABLE 2. DEFINITIONS FOR PRACTICE RECOMMENDATIONS BASED ON CLASSIFICATION OF EVIDENCE**

Recommendation	Description
Standard	Principle for patient management that reflects a high degree of clinical certainty (usually Class I evidence or overwhelming Class II evidence).
Guideline	Recommendation for patient management that reflects moderate clinical certainty (Class II or strong Class III evidence).
Practice Option	Strategy for patient management for which the clinical utility is uncertain (evidence is inconclusive or conflicting or it is expert opinion).
Practice Advisory	Practice recommendation for emerging or newly approved therapies or technologies based on evidence from at least one Class I study. A limited statistical or clinical response, cost-benefit issues, or disagreement among practitioners and/or payers may exist.

Source: Reference 1.

**TABLE 3. DSM III-R DIAGNOSTIC CRITERIA FOR DEMENTIA AND DEMENTIA OF THE ALZHEIMER'S TYPE (DAT)****Diagnostic Criteria for Dementia**

- A. Demonstrable evidence of impairments in short- and long-term memory
- 1) Impairment in short-term memory may be indicated by inability to remember three objects after five minutes.
  - 2) Impairment in long-term memory may be indicated by inability to remember past personal information or facts of common knowledge.
- B. At least one of the following:
- 1) Impairment in abstract thinking, such as:
    - Inability to find similarities and differences between related words
  - 2) Impaired judgment:
    - Inability to make reasonable plans to deal with interpersonal or family problems and issues
  - 3) Other disturbance in higher cortical function, such as:
    - Aphasia (disorder of language)
    - Apraxia (inability to carry out motor activities despite intact comprehension and motor function)
    - Agnosia (failure to recognize or identify objects despite intact sensory function)
    - Constructional difficulty (inability to copy three-dimensional figures, assemble blocks, or arrange sticks in specific patterns)
  - 4) Personality changes, such as:
    - Alteration or accentuation of premorbid traits
- C. The disturbance in A and B significantly interferes with work or usual social activities or relationships with others.
- D. Not occurring exclusively during the course of delirium
- E. Either 1) or 2):
- 1) Evidence from history, physical examination, or laboratory tests of a specific organic factor(s) judged to be etiologically related to the disturbance.
  - 2) In the absence of such evidence, the disturbance cannot be accounted for by any nonorganic disorder.

**Diagnostic Criteria for Dementia of the Alzheimer's Type**

- A. Dementia per criteria above
- B. Insidious onset with a generally progressive deteriorating course
- C. Exclusion of all other specific causes of dementia by history, physical examination, and laboratory tests

Source: Adapted from Reference 3.

**ANALYSIS OF EVIDENCE***Question 1: How reliable are the diagnostic criteria for dementia?*

The first two questions deal with the reliability of available diagnostic criteria for dementia and the ability to establish a diagnosis and differentiate the prevalent types of dementia. The criteria that are the most widely used in North America to diagnose dementia are those established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's and Related Disorders Association (NINCDS-ADRDA);<sup>2</sup> the Diagnostic and Statistical Manual of Mental Disorders, Third Edition; Revised (DSM-III-R);<sup>3</sup> and the DSM-IV.<sup>4</sup> The NINCDS-ADRDA criteria are a result of a Work Group on the Diagnosis of Alzheimer's Disease, which was established by NINCPS-ADRDA. These criteria were published in 1984 and are used most often by neurologists. This work group developed criteria for the diagnosis of the dementia syndrome, as well as possible, probable, and definite Alzheimer's disease.

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is a manual used by psychiatrists that provides diagnostic criteria for all types of mental disorders. Since mental disorders are illnesses of symptoms without signs, this manual was developed to give diagnostic clarity to mental disorders for clinical practice as well as research. As new information and understanding of disease processes and symptomatology for mental disorders comes to light, the DSM task force and working groups update the manual, hence the ascending versions, i.e., DSM III-R published in 1987 (R for revised from DSM III), DSM IV, published in 1994, and the newest DSM-IV-TR, which was published in 2000 (TR for Text Revision). This manual contains criteria for diagnosing dementia (per se), as well as dementia of the Alzheimer's

**TABLE 4. NINCDS-ADRDA DIAGNOSTIC CRITERIA FOR ALZHEIMER'S DISEASE**

Criteria for the Clinical Diagnosis of <b>Probable AD</b>	<ul style="list-style-type: none"> <li>a. Dementia established by clinical examination and documented by a rating scale (e.g., MMSE, Blessed Dementia Scale, etc.) and confirmed by neuropsychological tests</li> <li>b. Deficits in two or more areas of cognition</li> <li>c. No disturbance of consciousness</li> <li>d. Onset between ages 40 and 90, usually after age 65</li> <li>e. Absence of systemic disorders or other brain diseases that in and of themselves could account for the progressive deficits in memory and cognition</li> </ul>
Supports the Diagnosis of <b>Probable AD</b>	<ul style="list-style-type: none"> <li>a. Progressive deterioration of specific cognitive functions such as language, motor skills, and perception</li> <li>b. Impaired activities of daily living</li> <li>c. Altered patterns of behavior</li> <li>d. Family history of similar disorders</li> <li>e. Laboratory results of               <ul style="list-style-type: none"> <li>1. Normal lumbar puncture</li> <li>2. Normal or nonspecific EEG</li> <li>3. Evidence of cerebral atrophy on CT scan with progression documented by serial scans</li> </ul> </li> </ul>
Other Clinical Features Consistent With the Diagnosis of <b>Probable AD</b>	<ul style="list-style-type: none"> <li>a. Plateaus in the course of progression of the illness</li> <li>b. Associated symptoms of depression: insomnia; incontinence; delusions; illusions; hallucinations; catastrophic verbal, emotional, or physical outbursts; sexual disorders; weight loss</li> <li>c. Abnormal neurologic motor signs, especially with advanced illness, such as increased muscle tone, myoclonus, or gait disorder</li> </ul>
Features That Make the Diagnosis of <b>Probable AD Unlikely</b>	<ul style="list-style-type: none"> <li>a. Sudden, apoplectic onset</li> <li>b. Focal neurological findings, such as hemiparesis, sensory loss, visual field deficits, and incoordination</li> <li>c. Seizures or gait disturbances at onset or early in disease</li> </ul>
<b>Possible AD Criteria</b>	<ul style="list-style-type: none"> <li>a. Made of the basis of the dementia syndrome, in the absence of other neurological, psychiatric, or systemic disorders that cause dementia</li> <li>b. May be made in the presence of a second disorder sufficient to cause dementia that is not considered to be the cause of the dementia</li> </ul>
<b>DEFINITE AD Criteria</b>	<ul style="list-style-type: none"> <li>a. The clinical criteria for probable AD are met <b>and</b></li> <li>b. Histopathologic evidence obtained from biopsy or autopsy</li> </ul>

Abbreviations: AD = Alzheimer's disease, MMSE = Mini-Mental State Examination, NINCDS-ADRDA = National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association.

Source: Reference 2.

type (DAT); vascular dementia; and dementia due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease (CJD), general medical conditions, substance-induced, and multiple etiologies. The diagnostic criteria for dementia in the DSM-III-R revision were not changed in the DSM-IV revision. These diagnostic criteria are shown in Table 3.

The committee searched for and evaluated published studies that evaluated the sensitivity, specificity, and reliability of these criteria for diagnosing dementia. Most of the studies evaluated looked at the DSM-III-R<sup>3</sup> criteria specifically; few looked at the criteria as named DSM-IV. They found the DSM-III-R<sup>3</sup> criteria to have "good" to "very good" reliability (kappa ranges from 0.5 to 0.9). The NINCDS-ADRDA and the DSM-IV criteria, although very similar to the DSM-III-R, had not been assessed for reliability at the time of this panel review. The practice recommendation is that the DSM-III-R<sup>3</sup> diagnostic criteria are reliable and should be used to diagnose dementia (guideline). Even though identical, the DSM-III-R criteria were studied, and this is what must be recommended, but the authors infer that the DSM-IV criteria are identical to the DSM-III-R and can be used as well, even though not as many studies have evaluated them by name.

**Question 2: How reliable are the diagnostic criteria for the most common subtypes of dementia?**

### ALZHEIMER'S DISEASE

The committee evaluated the accuracy of the NINCDS-ADRDA<sup>2</sup> criteria for "Probable AD" and the DSM-III-R<sup>3</sup> criteria for DAT in diagnostic studies that used neuropathologic confirmation as the gold standard. In the majority of studies, both criteria had either good sensitivity (average = 81%, range

**TABLE 5. NINDS-AIREN CRITERIA FOR VASCULAR DEMENTIA**

The criteria for the clinical diagnosis of probable VaD shall include all of the following and should be severe enough to interfere with activities of daily living:

1. Presence of dementia (cognitive decline from a previously higher level of functioning) manifested by:
  - Impairment of memory AND
  - Two or more of the following:
    - Orientation, attention, language, visuospatial functions, executive functions, motor control, praxis
2. Cerebrovascular disease:
  - Presence of focal signs on neurologic exam, e.g., hemiparesis, lower facial weakness, Babinski sign, sensory deficit, hemianopia, dysarthria consistent with stroke
  - Evidence of relevant CVD by brain imaging
3. Relation between the above two disorders:
  - Dementia within three months after a stroke
  - Abrupt deterioration in cognitive function
  - Fluctuating, stepwise progression of cognitive deficits

**Clinical features consistent with VaD diagnosis:**

- Early presence of gait disturbance
- History of unsteadiness and frequent falls
- Early urinary incontinence
- Pseudobulbar palsy
- Personality and mood changes

**Features that make the diagnosis of VaD unlikely:**

- Early onset of memory or cognitive decline in the absence of corresponding focal lesions on brain imaging
- Absence of focal neurological signs
- Absence of CV lesions on brain imaging

Abbreviations: CVD = cardiovascular disease, NINDS-AIREN = National Institute of Neurologic Disorders and Stroke, the Association of Internationale pour la Recherche et l'Enseignement en Neurosciences, VaD = vascular dementia.

Source: Adapted from reference 6.

49%–100%) or low specificity (70%, 47%–100%), or vice versa. The panel concluded that either of these can and should be used to accurately diagnose Alzheimer's disease (guideline). The NINCDS-ADRDA criteria for "Possible AD" was found to have high sensitivity (93%, range 85%–96%) although lower specificity (48%, range 32%–61%). The panel participants felt that this was because of the many overlapping features that non-AD dementias share with AD. Table 3 gives the DSM-III-R Diagnostic Criteria for DAT, and Table 4 shows the NINCDS-ADRDA Criteria for Probable, Possible, and Definite AD.

**VASCULAR DEMENTIA**

Four criteria for vascular dementia (VaD) exist and were evaluated for validity. These were the State of California AD Diagnostic and Treatment Centers Criteria (the California criteria),<sup>5</sup> the National Institute of Neurologic Disorders and Stroke, the Association of Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria,<sup>6</sup> the Hachinski Ischemic Score as modified by Rosen (MHIS),<sup>7</sup> and the DMS-IV.<sup>4</sup> The California criteria, the DSM, and the NINDS-AIREN criteria were found to have low sensitivity with higher specificity in studies that compared clinical diagnoses with neuropathologic findings. Balancing sensitivity against specificity is a problem for all diagnostic criteria for vascular dementia. Some vascular pathology is present in 29% to 41% of community cases of autopsied dementia. The California criteria, NINDS-AIREN, and MHIS share similar degrees of specificity for identifying "pure" VaD. Although lacking in neuroimaging analysis, the committee felt that the MHIS was more suitable for identification of those with at least some cerebrovascular pathology. For this reason, the panel

suggests that the MHIS may be of use in the diagnosis of cerebrovascular disease in dementia (option). Table 5 shows the NINDS-AIREN diagnostic criteria for VaD, and Table 6 shows the MHIS, which is a scored scale. Scores of  $\geq 4$  on the MHIS are consistent with vascular dementia.

### DEMENTIA WITH LEWY BODIES

The only criteria for the diagnosis of Dementia with Lewy Bodies (DLB) are the Consortium for DLB Diagnostic Criteria.<sup>8</sup> These criteria were found to have low inter-rater reliability, low sensitivity (22%–75%), although higher specificity (71%–91%). The panel concluded that these criteria may be used in clinical practice (option). The consensus criteria for diagnosing DLB are shown in Table 7. These criteria do not exclude the presence of concomitant Alzheimer pathology, and some patients may meet criteria for both. The presence of two or more core features for a diagnosis of probable DLB confers higher diagnostic specificity and is suitable for research. For clinical practice, a requirement of only one core feature may be appropriate. Neither neuropsychological testing nor neuroimaging differentiates DLB from AD or VaD.

### FRONTEROTEMPORAL DEMENTIA

The committee looked at criteria for frontotemporal dementia (FTD). The Lund-Manchester criteria<sup>9</sup> were the first criteria for this disorder and from these, Consensus Diagnostic Criteria<sup>10</sup> were developed by an international workshop. The Lund-Manchester criteria were found to differentiate FTD from AD in one Class II study, but were unable to differentiate the two types of dementia in other studies. The committee recommended that the Consensus Diagnostic FTD criteria might be used in clinical practice (option).

**TABLE 6. MODIFIED HACHINSKI ISCHEMIC SCALE**

Feature	Point Value
Abrupt onset	2
Stepwise deterioration	1
Somatic complaints	1
Emotional incontinence	1
History or presence of hypertension	1
History of strokes	2
Focal neurological symptoms	2
Focal neurological signs	2

Source: Reference 7.

**TABLE 7. CONSENSUS CRITERIA FOR THE CLINICAL DIAGNOSIS OF DEMENTIA WITH LEWY BODIES (DLB)**

#### Clinical Diagnostic Criteria for Dementia with Lewy Bodies

- Progressive cognitive decline which interferes with normal functioning
- Core features
  - Fluctuating cognition with variations in attention and alertness
  - Recurrent visual hallucinations that are well-formed and detailed
  - Spontaneous motor features of Parkinsonism
- Supportive features
  - Repeated falls
  - Syncope
  - Transient loss of consciousness
  - Neuroleptic sensitivity
  - Systematized delusions
  - Hallucinations other than visual
- Features which do not support DLB diagnosis
  - Stroke
  - Other brain disorders
- Two features must be present for diagnosis of probable DLB; 1 for possible DLB.

Source: Reference 8.

**TABLE 8. CONSENSUS DIAGNOSTIC CRITERIA FOR FRONTOTEMPORAL DEMENTIA****Clinical Profile:**

- Character change and disordered social conduct are the dominant features
- Perception, spatial skills, praxis, and memory are relatively well preserved

**Core Diagnostic Features:**

- Insidious onset and gradual progression
- Early decline in social interpersonal conduct
- Early impairment in regulation of personal conduct
- Early emotional blunting
- Early loss of insight

**Supportive Diagnostic Features:**

## A. Behavioral disorder:

- Decline in personal hygiene and grooming
- Mental rigidity and inflexibility
- Distractibility and impersistence
- Hyperorality and dietary changes
- Perseverative and stereotyped behavior
- Utilization behavior

## B. Speech and language difficulties:

- Altered speech output – spontaneity and economy of speech
- Stereotypy of speech
- Echolalia
- Perseveration
- Mutism

## C. Physical signs:

- Primitive reflexes
- Incontinence
- Akinesia, rigidity, and tremor
- Low and labile blood pressure

## D. Testing:

- Neuropsych: significant impairment on frontal lobe tests
- EEG: normal
- Brain imaging: predominant frontal and/or anterior temporal abnormality

Sources: References 9 and 10.

The clinical diagnostic features of FTD are shown in Table 8. The clinical profile listed in the table summarizes the neurobehavioral profile necessary to fulfill the criteria for the diagnosis of FTD. All of the core features must be present in an individual patient for a diagnosis of FTD. The supporting clinical features may not be present in all patients, although they are considered characteristic of FTD and their presence adds substantial weight to the diagnosis. The diagnosis becomes more likely when more supportive features are present. Physical symptoms support the diagnosis of FTD, but their absence does not rule FTD out. To assist in diagnosis of FTD, neuropsychological testing is often helpful since it typically reveals problems with verbal fluency (e.g., FAS test), abstraction, and executive function.

**PRION DISEASES**

Creutzfeldt-Jakob Disease (CJD), the most well known type of prion disease, is a fatal, nontreatable dementia. Correctly diagnosing this illness is important for two reasons:

- 1) to ensure that rare, rapidly progressive, treatable dementias, such as Hashimoto's encephalitis, are not misdiagnosed, and
- 2) to provide pertinent information to families and caregivers on which to base life decisions. The study by Poser et al. comparing clinical criteria<sup>11</sup> to autopsy-confirmed cases found good sensitivity and specificity, and the practice recommendations are to use these clinical criteria in rapidly progressive dementia syndromes for CJD diagnosis. These criteria are based on clinical symptoms; characteristic electroencephalographic (EEG) patterns and are listed in Table 9.

**Question 3: Which are the optimal laboratory or imaging tests to assist in the diagnosis of dementia?**

## NEUROIMAGING

The data support the use of structural imaging, such as a noncontrast computed tomography (CT) or magnetic resonance imaging (MRI) scan, at the time of initial dementia diagnostic workup to identify pathology such as a brain neoplasm or a subdural hematoma. The sensitivity of functional neuroimaging with single photon-emission-computed tomography (SPECT) was found to be lower than that of clinical diagnosis, especially in mild disease. For that reason, it is not recommended in the routine evaluation of the patient with dementia. In one study evaluating positron emission tomography (PET) scans in the diagnosis of dementia, PET scans had a sensitivity of 93% but a specificity of only 63%. PET scans were felt to have promise as an adjunct to clinical diagnosis, but further studies are needed to establish its value over and above a competent clinical diagnosis. However, SPECT and PET may be helpful in differentiating FTD from AD (guideline).

## BIOMARKERS

Much has been made of the predictive value of the apolipoprotein E4 (APOE E4) genotype. However, the presence of two copies of the "bad" APOE E4 allele does not guarantee a diagnosis of AD, but does increase the risk. Testing for APOE E4 does increase the positive predictive value of AD diagnosis, but since the genotype itself is not diagnostic for AD, routine genetic testing for APOE status is not recommended.

No genetic markers for other types of dementia have been found to be useful thus far. There has been intense interest in other types of biomarkers, especially those found in the CSF of affected patients. Levels of  $\beta$ -amyloid<sub>1-42</sub>, tau protein, AD7C-NTP, CSF 14-3-3 protein, and neuron-specific enolase in the CSF have been evaluated as markers

**TABLE 9. CLINICAL DIAGNOSIS OF CREUTZFELDT-JAKOB DISEASE (CJD)**

### Probable CJD may be diagnosed by:

- Rapidly progressive dementia
- Periodic sharp waves in the EEG

At least two of the following:

- myoclonus
- visual disturbance
- pyramidal and/or extrapyramidal signs
- akinetic mutism
- gait ataxia

### Laboratory test results considered typical of CJD:

- EEG with periodic sharp wave complexes
- MRI bilateral areas of increased signal intensity predominantly affecting the caudate nuclei and putamen
- Presence of 14-3-3 protein in cerebrospinal fluid
- CT scan with atrophy in the temporobasal and hippocampus region

### Definite diagnosis of CJD—confirmation by autopsy

Source: Reference 11.

**TABLE 10. GERIATRIC DEPRESSION SCALE-SHORT FORM**

### Questions Asked:

- Are you basically satisfied with your life?
- Have you dropped many of your activities and interests?
- Do you feel that your life is empty?
- Do you often get bored?
- Are you in good spirits most of the time?
- Are you afraid that something bad is going to happen to you?
- Do you feel happy most of the time?
- Do you often feel helpless?
- Do you prefer to stay at home, rather than going out and doing new things?
- Do you feel you have more problems with memory than most?
- Do you think it is wonderful to be alive?
- Do you feel pretty worthless the way you are now?
- Do you feel full of energy?
- Do you think your situation is hopeless?
- Do you think that most people are better off than you are?

Source: Reference 12.

**TABLE 11. HAMILTON DEPRESSION SCALE**

Parameter	Description
Depressed Mood	Feelings of sadness, hopelessness, helplessness, worthlessness
Feelings of Guilt	Self-reproach, rumination over past errors
Suicide Ideation	Feelings that life is not worth living, suicidal gestures
Insomnia, Early	Difficulty falling asleep
Insomnia, Middle	Middle of night awakenings
Insomnia, Late	Early morning awakenings
Work and Activities	Any decrease in usual
Retardation	Slowness of thought and speech, impaired ability to concentrate, decreased motor activity
Agitation	Fidgetiness, can't be still
Anxiety/Psychic	Tension, irritability
Anxiety/Somatic	Physiological manifestations of anxiety, such as: <ul style="list-style-type: none"> <li>■ Gastrointestinal symptoms (dry mouth, indigestion, diarrhea, etc.)</li> <li>■ Cardiovascular (palpitations, headaches), respiratory (hyperventilation)</li> <li>■ Urinary frequency</li> <li>■ Sweating</li> </ul>
Somatic Symptoms/GI	Loss of appetite, difficulty eating
Somatic Symptoms/	Loss of energy, fatigue, aches, heaviness in limbs
<b>General</b>	
Genital Symptoms	Loss of libido, menstrual disturbances
Hypochondriasis	Ranges from preoccupation with frequent complaints to delusions
Loss of Weight	Documented loss of weight
Insight	Denial of being ill or lack of insight into situation

Sources: Adapted from references 14 and 15.

for AD and other dementias. For the most part, they do not appear to improve diagnostic accuracy and are not recommended for routine use in the diagnosis of dementia. The CSF 14-3-3 protein assay may, however, be useful for confirming the diagnosis of CJD when recent stroke or viral encephalitis can be excluded (guideline).

*Question 4: Which comorbidities should be screened for in elderly patients undergoing an initial assessment for dementia?*

Many laboratory tests may be done in the routine assessment for dementia, both to find other causes of cognitive impairment and to look for correctable types of dementia (including complete blood count, serum electrolytes, glucose, blood urea nitrogen (BUN), serum creatinine, folate, B<sub>12</sub>, thyroid function, syphilis serology, heavy metal screening, and serum toxicology). This practice parameter evaluated studies that have been done to address the diagnostic value of depression, vitamin B<sub>12</sub> levels, thyroid function analysis, and syphilis screening.

**DEPRESSION**

Depression is a common illness in the elderly and in those with dementia. Prospective studies show that persons who present with cognitive impairment as a manifestation of depression are likely to have dementia on longitudinal follow-up. In addition to this condition, dementia and depression may coexist in as many as 12% of patients throughout the span of dementia. Although treatment of depression may not completely reverse cognitive dysfunction, the practice parameter committee recommended that depression be screened for and treated if found (guideline). Many validated instruments are available to assess depression, such as the Geriatric Depression Scale (GDS) (short form)<sup>12,13</sup> and the Hamilton Depression Scale (HAM-D).<sup>14</sup> The Short Form of the GDS is a 15-item scale that may be used in patients who are cognitively intact or have mild AD, and is shown in Table 10. It was developed primarily for greater brevity than the original 30-item GDS and takes approximately five to seven minutes to administer. A score of 5 or more corresponds to a clinical diagnosis of depression. The HAM-D scale

assesses 17 areas (shown in Table 11), and scores are based on the presence and severity of the parameters assessed.

### **VITAMIN B<sub>12</sub> DEFICIENCY**

Vitamin B<sub>12</sub> deficiency has been suggested to be a reversible, treatable cause of dementia in the elderly. However, studies have found only a very small number of patients with dementia caused by B<sub>12</sub> deficiency. Reports of improvement in cognition with treatment of B<sub>12</sub> deficiency have been equivocal. The committee felt that B<sub>12</sub> deficiency should be screened for and treated if found (guideline).

### **THYROID FUNCTION**

Hypothyroidism is a common disorder in the elderly population. Some studies have found that persons with hypothyroidism may have lower mental status test scores, word fluency, visuospatial abilities, and learning compared with euthyroid patients. An elevated TSH level was found to carry an increased risk for dementia in one population-based study, but was unrelated to the presence of dementia in two additional studies. Although numbers are small, treatment of hypothyroidism may partially or completely reverse the symptoms of dementia. The practice parameters recommend screening for and treating elderly persons for hypothyroidism, when appropriate (guideline).

### **SYPHILIS TESTING**

Apparently there are only a few areas now in the United States with high numbers of current syphilis cases. Within the last 20 years, there have been no reported cases of tertiary

syphilis in any epidemiological studies conducted in North America. The current tests for syphilis (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin, and fluorescent treponemal antibody) are nonspecific. Unless the patient has some specific risk factor, evidence of prior syphilitic infection, or resides in one of the few areas in the United States with high rates of syphilis, screening for this disorder in patients with dementia is not well supported and not recommended by the practice parameter (guideline).

### **SUMMARY AND CONCLUSION**

New studies are being published constantly, and in a few years these guidelines may be out of date as new data, information, and technology emerge. For example, the newest version of the DSM is the DSM-IV-TR, which was not mentioned in the original practice guideline because it had not been published at that time. Current practice guidelines have been reviewed in this paper and are summarized below. The intent of the Practice Parameter committees was to provide an evidence-based approach to the diagnosis of dementia, based on available scientific and clinical information. It is not intended to include all possible methods of care or all criteria for choosing to use specific procedures. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and his or her physician based on the individual patient circumstances. The guidelines are summarized in Table 12, page 62.

**TABLE 12. AMERICAN ACADEMY OF NEUROLOGY SUMMARY GUIDELINES AND PRACTICE PARAMETERS****REFERENCES**

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**DIAGNOSTIC CRITERIA**

- To diagnose dementia, the DSM-III-R (DSM-IV) should be used routinely. (Guideline)
- To diagnose Alzheimer's disease, the NINCDS-ADRDA for probable AD or DSM-III-R criteria for Dementia of the Alzheimer's Type should be used routinely. (Guideline)
- The Hachinski Ischemic Index criteria as modified by Rosen may be of use in the diagnosis of cerebrovascular disease in dementia. (Option)
- The Consortium for Dementia with Lewy Bodies (DLB) diagnostic criteria may be of use in clinical practice. (Option)
- The Consensus Diagnostic Criteria for Frontotemporal dementia may be of use in clinical practice. (Option)
- Clinical criteria for Creutzfeldt-Jakob Disease (CJD) should be used in rapidly progressive dementia syndromes. (Guideline)

**NEUROIMAGING**

- Structural neuroimaging with either a noncontrast CT or MRI scan in the routine initial evaluation of patients with dementia is appropriate. (Guideline)
- Linear or volumetric MRI or CT measurement for the diagnosis of Alzheimer's disease (AD) are not recommended for routine use at this time. (Guideline)
- For patients with suspected dementia, SPECT (single photo-emission-computed tomography) cannot be recommended for routine use in either initial or differential diagnosis as it has not demonstrated superiority to clinical criteria. (Guideline)
- PET imaging is not recommended for routine use in the diagnostic evaluation of dementia at this time. (Guideline)

**LABORATORY TESTS**

- Genetic testing of patients with suspected DLB and CJD is not recommended. (Guideline)
- Routine use of APOE genotyping in patients with suspected AD is not recommended at this time. (Guideline)
- There are no other genetic markers, CSF, or other biomarkers recommended for routine use in the diagnosis of AD. (Guideline)
- Testing for tau mutations or AD gene mutations is not recommended for routine evaluation in patients with FTD at this time. (Guideline)
- The cerebrospinal fluid 14-3-3 protein is recommended for confirming or rejecting the diagnosis of CJD in clinically appropriate circumstances. (Guideline)

**COMORBID ILLNESS**

- Depression should be screened for in patients with dementia. (Guideline)
- B<sub>12</sub> deficiency should be screened for in routine assessments in the elderly. (Guideline)
- Hypothyroidism should be screened for in elderly patients. (Guideline)
- Unless the patient has some specific risk factor or evidence of prior syphilitic infection, or resides in one of the few areas in the United States with high numbers of syphilis cases, screening for this disorder in patients with dementia is not justified. (Guideline)

Abbreviations: APOE = apolipoprotein E; DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; NINCDS-ADRDA = National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association.

**GLOSSARY OF TERMS**

**Agnosia:** Failure to recognize or identify objects despite intact sensory function.

**Aphasia:** Disorder of language.

**Apraxia:** Inability to carry out motor activities despite intact comprehension and motor function.

**Constructional Difficulty:** Inability to copy three-dimensional figures, assemble blocks, or arrange sticks in specific patterns.

**Delusion:** A fixed belief maintained in the face of irrefutable evidence to the contrary.

**Echolalia:** Purposeless, often involuntary repetition of words spoken by a person; seen in schizophrenia and dementia.

**Gold Standard:** Accepted reference standard or diagnostic test for a particular illness.

**Impairment in Long-term Memory:** The inability to remember information that was known in the past, either past personal information (where one lives, birthplace, occupation) or facts of common knowledge (past presidents, known dates).

**Impairment in Short-term Memory:** the inability to learn new information.

**Kapp Statistic:** A measure of interobserver variation. It quantifies the extent to which the observed agreement exceeds that which would be expected by chance.

**Interrater Reliability:** Variability among the different persons who observe or rate the changes being evaluated.

**Perseveration:** Involuntary, pathological repetition of words or activity.

**Positive Predictive Value:** The percentage of people with a positive test result who actually have the disease.

**Pseudobulbar Palsy:** A clinical syndrome usually due to disease of both cerebral hemispheres, involving the centers of paths of the tracts to cranial nerves in the brainstem. Symptoms include some or all of the following: paralysis of swallowing, articulation, chewing movements, and emotional lability.

**Pyramidal:** Pertaining to motor movements through the pyramidal tract, which are a system of fibers that connect the motor neurons in the frontal cortex adjacent to the rolandic fissure to spinal or bulbar motor neurons.

**Reliability:** The reproducibility of the results of a test.

**Sensitivity:** The ability of a test to accurately identify people with a specified disease.

**Specificity:** The ability of a test to accurately identify people who do not have the disease.

**Stereotypy:** Persistent repetition of an activity or mannerisms that may be seen in schizophrenia or other psychotic or neurological illness.

**Validity:** The performance of a diagnostic test or the ability of a test to distinguish between who has a disease and who does not. Sensitivity and specificity are the two major parameters that define this.

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## POLICY CURRENTS

### Medicare Reform, New Drug Benefit Signed into Law on December 8th

**P**resident Bush has signed into law legislation drastically revamping Medicare and giving its beneficiaries a new prescription drug benefit. The legislation was passed by Congress before Thanksgiving and signed into law on December 8, 2003.

The House approved the bill by a 220–215 vote just before dawn on November 22. Republican leaders used a three-hour voting window into the early morning hours—the longest roll call vote in history—to convince two lawmakers, Reps. C.L. Butch Otter (R-Idaho) and Trent Franks (R-Arizona) to change their votes. Otter and Franks were convinced to vote in favor of the bill after negotiating with leadership and receiving phone calls from President Bush.

Three days later, the Senate passed the Medicare bill by 54–44. The final vote came after the Republican majority, with Democratic help, broke a filibuster led by liberal democrats to block the measure in favor of action next year on an alternative. The Senate also defeated a budget challenge to the measure.

The support of the AARP, announced in mid-November, was a key development in the eventual passage of the legislation. Republicans used the endorsement to counter Democratic criticism of the proposal.

Democrats opposed the bill for a variety of reasons including the use of private health plans and the gap in prescription drug coverage known as “the doughnut hole” (see below). Some Democrats argued that the legislation was designed to conceal the actual costs older Americans would have to pay. Democrats also wanted to

have more low-income seniors completely covered by the benefit.

Some AARP members were angered by the group’s endorsement of the legislation. They complained on the AARP Internet message board and destroyed membership cards.

#### **NEW MEDICARE STRUCTURE**

The new law redefines Medicare’s structure—it no longer is a universal program charging the same fees for service despite income level. Instead, the size of benefits that beneficiaries receive will depend on their incomes. Starting in 2006, Medicaid will no longer be available for Medicare beneficiaries.

For Medicare Part B, wealthier seniors, with incomes of \$80,000 or more, will have to pay higher premiums for doctor’s visits and other outpatient services. The amount would increase on a sliding scale, topping out at 80% for people with incomes above \$200,000. The annual deductible for outpatient care will rise from its traditional fixed rate of \$100 to \$110 in 2005, and continue to increase annually.

#### **PRESCRIPTION DRUG CARD**

In 2004 and 2005, Medicare recipients will be able to purchase a drug discount card that is expected to save them 10% to 25% on their prescription costs. At least 20 different companies, charging different annual fees and prices for the same medicines, are expected to provide the competing cards. The drug card will be the main benefit until the full benefit program starts in 2006. By then, plan participants will be able to buy more prescriptions for the same money they

spend today. This is because private companies providing the coverage may be able to negotiate lower prices with drug manufacturers based on the large volume in demand by beneficiaries. This standard card will not be able to be used in nursing facilities.

Additionally, those with low incomes of \$12,123 (\$16,362 for couples) will get \$600 a year for prescription drugs in 2004 and 2005. This transitional discount drug card will be able to be used in nursing facilities.

#### **MEDICATION THERAPY MANAGEMENT**

Under the new Medicare law, prescription drug plans are required to provide medication therapy management services for targeted beneficiaries who take multiple drugs, have multiple chronic diseases, or incur significant drug spending. The medication therapy management services will be designed to optimize therapeutic outcomes, improve medication use, reduce the risk of adverse events and drug interactions, and increase patient adherence and compliance with prescribed regimen. The language specifies that these medication therapy management services may include special packaging for medications. (See ASCP Reports, page 76).

#### **ROLE OF PRIVATE HEALTH PLANS**

Once the plan takes effect in 2006, beneficiaries will have two choices for coverage:

- New or separate policies for prescriptions
- Private health plans that also

provide the rest of their care

For any region that does not have one stand-alone drug plan and one private health plan, the government will provide the drug coverage.

### **HOW PRESCRIPTION COSTS ARE COVERED**

Whether a beneficiary chooses a separate policy for prescriptions or a private health plan, all patients will pay an estimated \$35 per month premium for the first year and an annual deductible of \$250. The government will pay 75% of drug costs up to \$2,250. At that point the coverage stops (the "donut hole") until the beneficiary pays \$3,600 out of pocket in "catastrophic" prescription expenses. Then the coverage kicks in again, with the government paying 95% of the remaining costs for the year. Under these catastrophic provisions beneficiaries would pay \$2 for generic drugs and \$5 for brand-name drugs, or 5% of the total cost of the drug, whichever is more.

### **GENERIC DRUG PROVISIONS**

Prescription medications could get to the market faster under the new bill, which closes loopholes in the 1984 Hatch-Waxman Act. The new law limits the ability of pharmaceutical companies to block cheaper equivalents to their brand-name drugs.

### **REIMPORTATION**

The Medicare legislation says reimportation of medications from Canada may occur only if the Secretary of the Department of Health and Human Services certifies that the drugs are safe. A reimportation law already is on the

books, but it was never implemented because HHS would not provide such certification. This remains a controversial issue because some lawmakers still see reimportation as a good way to decrease prescription costs, despite warnings by the Food and Drug Administration that medications imported back into the United States from other countries could be counterfeit or tainted, and thus, unsafe.

### **IMPACT ON DUAL ELIGIBLES**

Beneficiaries who are eligible for both Medicare and Medicaid, otherwise known as "dual eligibles," will be moved into the Medicare program under the new bill. This means they could pay more out-of-pocket for their medications because some state Medicaid programs cover 100% of prescription costs. The new Medicare legislation requires copayments, which are optimal for states under Medicaid coverage.

### **HEALTH PLAN COMPETITION**

One controversial provision of the bill is an experiment to have Medicare's original fee-for-service plan compete against private health plans for patients based on price. Starting in 2010, this experiment will take place for six years in six metropolitan areas in which at least two private plans enroll at least 25% of Medicare beneficiaries. Some lawmakers believe it will foster greater market competition.

### **EMPLOYER INCENTIVES**

To prevent companies from dropping coverage of their retirees once the Medicare prescription drug benefit

begins, the bill includes \$86 billion in payments and tax advantages over 10 years to employers who provide prescription coverage for their retired workers.

### **HEALTH SAVINGS ACCOUNTS**

This provision will be available to all Americans, not just the elderly. People under the age of 65 who have medical policies with high annual deductibles of at least \$1,000 for singles or \$2,000 for families could establish "tax-free" health savings accounts. They or their employers could give them a pretax amount equal to the deductible. These accounts could be used to pay health care expenses; withdrawals would be tax free.

### **COST CONCERNS**

Some conservative lawmakers are concerned the Medicare bill will result in higher spending and a larger federal deficit. Due to the costs of antiterrorism measures, consequences of the war with Iraq, and recently passed tax cuts, the deficit is expected to reach \$500 billion in the fiscal year that started October 1, 2003. The new Medicare benefits are expected to cost \$400 billion dollars over the first 10 years and more than \$1 trillion in the next decade. A cost-containment measure in the bill requires congressional response if general revenue contributions exceed 45% of Medicare program spending.

### **BOOST TO PHARMACEUTICAL INDUSTRY**

Critics of the bill say the legislation is a boost to big pharmaceutical compa-

nies because they will not be required by the government to lower the prices of prescriptions.

Biotechnology companies, which are smaller and produce treatments that can cost about \$10,000 or more per year, are hoping the Medicare bill will increase their revenues. In 2002, Medicare changed its rules for reimbursement, lowering its payments for some drugs used for hospital outpatient treatments by an average of 35%. The Medicare bill includes language sought by the biotech industry that would help set a floor for reimbursement of biotech drugs used for hospital outpatients.

### **DEMOCRATS RAMP UP TO REPEAL BILL PROVISIONS**

Shortly after the Senate passed the Medicare bill, Minority Leader Tom Daschle (D-S. Dak.) took action to oppose some of its key provisions.

With the introduction of his own bill, the "Medicare Preservation and Drug Price Fairness Act," Daschle hopes to eliminate premium support—the experiment juxtaposing traditional fee-for-service Medicare against health plans in metropolitan areas for six years. He also wants to change the requirements for a fallback government-run drug plan, making fallback an option if there are not at least two stand-alone drug plans in a region. The fallback is triggered if there is not at least one stand-alone and one private plan available.

Daschle also wants to rescind \$12 million in funding to encourage preferred provider options to expand regional coverage and revoke \$6 million for health savings accounts,

instead using the \$18 million to further encourage employees not to drop their retiree drug plans.

His bill would make prescription drugs more affordable by Medicare negotiating with the industry for lower prices and allowing reimportation of American medications from Canada without federal approval.

### **OTHER BENEFITS**

The Medicare legislation makes other changes that could benefit seniors, such as broadening coverage for preventive care. Starting in 2005, newly enrolled Medicare beneficiaries would be covered for an initial physical examination, and all beneficiaries would be covered for heart disease and diabetes screenings. Additionally, beneficiaries who choose a private plan would have no lifetime limit for inpatient hospital care and would be protected against high bills for hospitalization.

However the key issue in the legislation—coverage of prescription drugs—left some seniors skeptical that Medicare will end up reducing the costs of their prescriptions.

A more detailed summary of the new Medicare bill, as approved by Congress, is available on the ASCP website, [www.ascp.com/public/ga/](http://www.ascp.com/public/ga/).

### **SCULLY RESIGNS AS HEAD OF CMS**

Thomas Scully, the administrator of the Centers for Medicare and Medicaid Services, has resigned, effective December 16. Scully, one of President Bush's key advisors on Medicare, said that he stayed in the administration a year longer than

he intended because he wanted to work on the Medicare reform bill, recently passed by Congress and signed into law.

"It has been a great run, and has been great fun working with, and learning from [Health and Human Services Secretary Tommy] Thompson, who has been a great friend and mentor," said Scully. "Watching the President and the Secretary drive the Medicare bill across the finish line in the last few weeks was a very rewarding culmination to a very exciting and fulfilling three years

Scully became the ninth administrator of the agency formerly known as the Health Care Financing Administration on March 22, 2001. He led an intensive effort to improve the responsiveness of the agency, with a new name, adopted from suggestions made by agency employees.

Diana Duvall  
Associate Editor

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## New Hypertension Trials: What Do the Results Mean for the Elderly?

### INTRODUCTION

Hypertension affects approximately 50 million people in the United States, including one out of four adults. About half of people who have a first heart attack and two-thirds who have a first stroke have blood pressures higher than 160/95 mm Hg.<sup>1</sup> Hypertension precedes the development of heart failure (HF) in 91% of cases and is associated with two to three times higher risk for developing heart failure.<sup>2</sup> High blood pressure was listed as a primary or contributing cause of death in about 118,000 United States deaths in 2000.<sup>1</sup>

Hypertension in the elderly was generally thought to be a natural process that occurred over time. Systolic blood pressure that increases with age is no longer considered "normal." Recent research suggests that treated hypertension in the elderly population results in decreased cardiovascular morbidity and mortality. As with younger patients, it is recommended that the overall blood pressure goal for the elderly to be less than 140/90 mm Hg.<sup>3</sup>

Therefore, the results of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and the Second Australian National Blood Pressure Study (ANBP2) are of interest to our audience. But how do they relate to the care of seniors, including those in nursing homes?

### ALLHAT

#### OVERVIEW

ALLHAT was designed to determine whether occurrence of fatal coronary heart disease (CHD) or nonfatal myocardial infarction (MI) is lower for high-risk hypertensive patients treated with newer agents (calcium channel blocker [CCB], angiotensin-converting enzyme inhibitor [ACEI], or alpha-blocker) compared with an older agent (thiazide diuretic). When ALLHAT was initiated, the use of diuretics and beta-blockers for hypertension was declining. A diuretic was selected over a beta-blocker for the study's traditional arm for two reasons: diuretics have been studied more extensively and were considered clinically advantageous for the types of patients to be selected for ALLHAT—older patients and those at higher risk of cardiovascular disease (CVD) complications.

ALLHAT was a randomized, double-blind, active-controlled, multicenter clinical trial that enrolled men and women ages 55 and older. The patients had to have a blood pressure less than or equal to 160/100 mm Hg on treatment, or a blood pressure greater than or equal to 140/90 mm Hg but less than or equal to 180/110 mm Hg without treatment. At least one of the following risk factors were present: previous (>6 months) MI or stroke; left ventricular hypertrophy; history

of type 2 diabetes; current cigarette smoking; high-density lipoprotein cholesterol less than 35 mg/dL; or other atherosclerotic CVD. Major exclusion criteria included recent (within past six months) MI, stroke, HF, angina, or an ejection fraction less than 35%; known renal insufficiency (serum creatinine 2 mg/dL or greater); or requiring diuretics, CCBs, ACEIs, or alpha-blockers for reasons other than hypertension.<sup>4</sup>

#### KEY FINDINGS

There were 42,418 participants in ALLHAT, making it the largest outcome trial in the treatment of hypertension to date. The study population consisted of the following: mean age was 66.9 ± 7.1 years; baseline blood pressure was 145/83 mm Hg or 156/89 if the patient was untreated; 47% female; 35% black; 19% Hispanic; mean body mass index (BMI) was 30; and 22% smoked. Of this population, 15,255 were randomized to the thiazide diuretic chlorthalidone (12.5–25.0 mg/day), 9,048 to the dihydropyridine CCB amlodipine (2.5–10.0 mg/day), and 9,054 to the ACEI lisinopril (10–40 mg/day).<sup>5</sup> The alpha-blocker doxazosin arm was stopped early because of a 25% higher rate of cardiovascular events compared with the chlorthalidone arm.<sup>6,7</sup> The remaining patients stayed on the study drugs through the end of the study for an average of 4.9 years. Approximately 43% of patients required more than one drug in the ALLHAT trial, but details were not reported.<sup>5</sup> Step two and step three drugs were mostly limited to atenolol, clonidine, reserpine, and hydralazine, which do not belong

to the four first-line classes. Other drugs, including low doses of step one drug classes, were permitted, if clinically indicated.<sup>4</sup>

The systolic blood pressure was significantly higher in the amlodipine group (~1 mm Hg) and the lisinopril group (~2 mm Hg for all participants, ~4 mm Hg in blacks, and ~3 mm Hg in those 65 years or older) compared with chlorthalidone. The diastolic blood pressure was significantly lower in the amlodipine group (~1 mm Hg). The mean final blood pressure among all groups was 135/75 mm Hg.<sup>5</sup>

In terms of the primary end point (fatal CHD + nonfatal MI) or all-cause mortality, no agent proved to be superior. However, chlorthalidone was significantly superior to lisinopril in preventing aggregate CV events (relative risk [RR] – 1.10; 95% CI (confidence interval), 1.05–1.16], principally stroke, HF, angina, and coronary revascularization). The relative risks of lisinopril versus chlorthalidone were 1.15 (95% CI, 1.02–1.30) for stroke, 1.19 (95% CI, 1.07–1.31) for HF, 1.11 (95% CI, 1.03–1.20) for hospitalized or treated angina, and 1.10 (95% CI, 1.00–1.21) for coronary revascularizations. There was a significant differential effect of age for combined CHD (fatal CHD, nonfatal MI, coronary revascularization or hospitalized angina). Patients less than 65 years of age tended to favor lisinopril (RR – 0.94; 95% CI, 0.84–1.05), while patients 65 years or older tended to favor chlorthalidone (RR – 1.11; 95% CI, 1.03–1.20). It is also important to note that chlorthalidone was markedly more effective than lisinopril in blacks than in nonblacks. The RRs

for stroke [1.40 (95% CI, 1.17–1.68) versus 1.00 (95% CI, 0.85–1.17)] and combined CVD [1.19 (95% CI, 1.09–1.30) versus 1.06 (95% CI, 1.00–1.13)] were significantly higher with lisinopril in blacks than nonblacks, respectively.

Amlodipine had a significantly higher risk of HF (RR – 1.38; 95% CI, 1.25–1.52) than chlorthalidone. This suggests that diuretics are particularly beneficial in the prevention of HF. However, other factors should be considered. In ALLHAT, 90% of the patients were on antihypertensive drugs before randomization, which were continued until they received the randomized study drug. We do not know the details of the prior medication.<sup>8</sup> A number of patients could have been on diuretics previously and then were suddenly switched to a CCB. This may have caused fluid retention, thus, contributing to HF. Also, as fluid retention is a major symptom of HF, the diuretic may have masked development, delaying diagnosis.

Biochemical effects were more severe with the diuretic. The chlorthalidone group reported lower potassium levels, which could cause rhythm disturbances in those predisposed to arrhythmias (elderly), slightly higher mean serum cholesterol levels, and a significant increase in the incidence of diabetes development over four years of follow-up (due to thiazides' diabetogenic nature) compared with the lisinopril group. Fasting hyperglycemia in the nondiabetics increased to 11.6% at four years in those on the diuretic compared with 9.8% on the CCB and 8.1% on the ACEI. However, as noted, these biochemical changes did not

result in significantly increased rates of clinical events, such as sudden cardiac death, MI, or end-stage renal failure during the time course of this trial.

Overall, ALLHAT showed that diuretics are superior at preventing CVD events compared with CCBs, ACEIs, and alpha-blockers. Each of the newer drugs had significantly higher rates of one or more forms of CVD (lisinopril and doxazosin had higher rates of combined CVD, amlodipine had a higher rate of HF). However, none of the treatments differed significantly from chlorthalidone in rates of major CHD events and all-cause mortality.

## **ANBP2**

### **OVERVIEW**

Recently, a similar study was published with somewhat contrasting results. The ANBP2 compared ACEIs to diuretics for hypertension in the elderly. ANBP2 was a randomized, open-label trial conducted in 1,594 family practice clinics in Australia that enrolled 6,083 patients, ages 65 to 84 years. The following are ANBP2 patient characteristics: no cardiovascular events in the previous six months; mean age was 72 (30% were 75–85 years); baseline blood pressure was 168/91 mm Hg; 95% white; mean BMI was 27; and 7% smoked. In contrast to ALLHAT, these patients were predominantly white and overall healthy and active with few previous cardiovascular events. The ACEI enalapril and the thiazide diuretic hydrochlorothiazide were recommended as initial therapy; however, family practitioners could choose another agent of their choice.

## KEY FINDINGS

There was a significant 11% reduction in the total burden of cardiovascular events or death from any cause with the ACEI (RR = 0.89; 95% CI, 0.79–1.00). Among elderly male patients, the beneficial effects of the ACEI were more evident. This group experienced a significant 17% reduction in the rates of both all cardiovascular events and first cardiovascular events (RR for both end points = 0.83; 95% CI, 0.71–0.97). There was not a significant difference in these primary endpoints among female patients. The ACEI group showed a significant reduction in the rate of the first myocardial infarction (RR = 0.68; 95% CI, 0.47–0.98); however, there was also a significantly higher incidence in fatal strokes with the ACEI group (RR = 1.91; 95% CI, 1.04–3.50).<sup>9</sup>

The ANBP2 study does not provide enough evidence to recommend an ACEI as initial therapy for all elderly patients. The trial does suggest that there is benefit in prescribing ACEIs to healthy, active, white, elderly males. This trial reinforces the fact that therapy must be individualized. Treatment should depend on co-morbid illnesses, potential drug interactions, and adverse drug reactions. The baseline characteristics of the patients enrolled in the ANBP2 study cannot be extrapolated to most nursing home patients here in the United States.

## CLINICAL IMPLICATIONS FOR THE OLD, OLD

Approximately 40% of the 1.5 million nursing home patients are 85 years or older, and between 32% and 44% have hypertension.<sup>10</sup> Currently, no outcome

trials using antihypertensive drugs have been published specifically targeting the “old, old” patient, but a meta-analysis revealed a cardiovascular benefit in patients with hypertension who were at least 80 years of age.<sup>11</sup> The data were collected from 1,670 participants in seven different trials using first-line treatment (beta-blockers, thiazides, CCBs, and alpha-blockers). This meta-analysis suggested that treatment prevented 34% of strokes in this population (95% CI 0.48–0.92). Major cardiovascular events and HF significantly decreased by 22% and 39%, respectively. There does not seem to be an age threshold above which hypertension should not be treated.

There is a large variability in the underlying health of those older than 80. According to an analysis of data taken from 300,000 nursing home residents, it is unclear whether the benefits of antihypertensive agents may outweigh the risks among those severely impaired.<sup>12</sup> Also, incorrect blood pressure technique and white coat hypertension may result in misclassification of hypertension in many elderly patients.<sup>13,14</sup> Elderly patients are more susceptible to volume depletion and sympathetic inhibition. Several investigators have reported the elderly to have an increased risk of falls when using diuretics.<sup>15-17</sup> Furthermore, excessive lowering of diastolic blood pressure to reach systolic blood pressure goals could conceivably result in coronary ischemia.

Multiple comorbid conditions and medications are not uncommon in older persons. The risk for adverse effects and drug interactions is increased. Therefore, the treatment

of hypertension in the very elderly must be highly individualized. Attempts should be made to achieve control with as few medications as possible. CCBs are the most frequently used antihypertensive drugs used in nursing homes. However, diuretics are formally preferred for systolic hypertension in the elderly,<sup>3</sup> although dihydropyridine CCBs also have strong evidence of benefit.

According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) guidelines,<sup>3</sup> thiazide-type diuretics should be the drug of choice for first-step therapy of hypertension. ALLHAT used chlorthalidone, but it seems very likely that the benefits will be obtained with any diuretic with sustained action. For the patient who cannot take a diuretic (which should be an unusual circumstance), beta-blockers, CCBs, and ACEIs may be considered. Contraindications to thiazides may include patients that are susceptible to hypokalemia (digitalis administration, hepatic cirrhosis), hyperuricemia (gout), or hypercalcemia. Thiazides should not be used in patients with significant renal impairment (creatinine clearance <30 mL/min), as their antihypertensive efficacy is diminished.

Most hypertensive patients will require more than one drug to adequately control blood pressure. For hypertensive patients not controlled on another drug, a thiazide diuretic in a low to moderate dose should generally be added. For hypertensive patients controlled on other drugs, a thiazide diuretic may be substituted. However,

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if hypertensive patients have a compelling indication for another drug class, they should not automatically be switched to a diuretic. Nonetheless, young and elderly patients are likely to benefit from the enhanced effectiveness of the diuretic as well as the reduced cost of the drug.

Brianne Fairchild, PharmD, is a Pharmacy Practice Resident with the Veteran's Administration, Pittsburgh, Pennsylvania. Chris Terpening, PhD, PharmD, is Assistant Professor, Departments of Clinical Pharmacy and Family Medicine, West Virginia University, Charleston, West Virginia.

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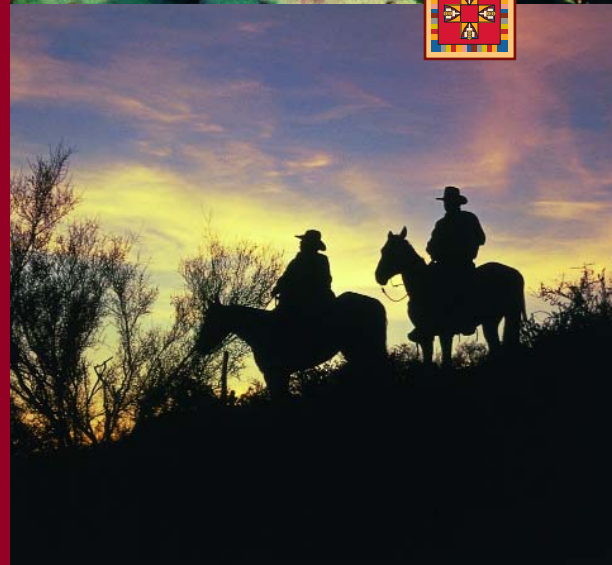
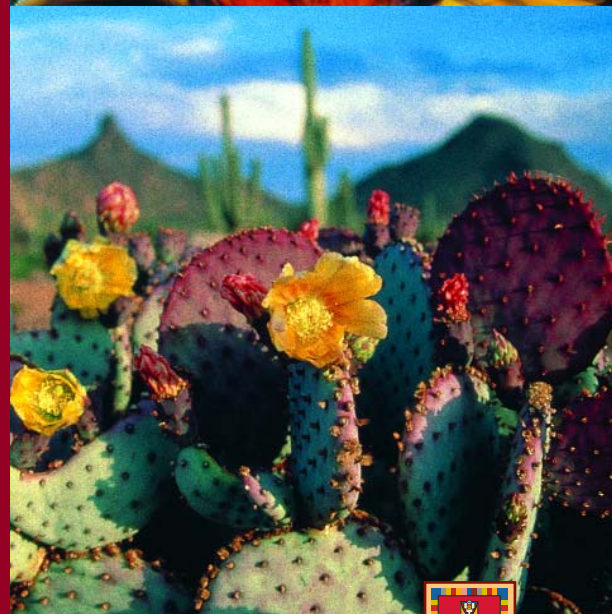
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Association,

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Washington, DC 20037;

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Care Pharmacy,

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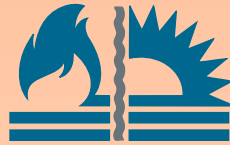
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# ASCP REPORTS

## ASCP Lobbying Results in New Medication Management under Medicare

**P**harmacists will be paid for medication therapy management services under the “Medicare Prescription Drug, Improvement and Modernization Act of 2003” recently passed by Congress and signed into law by President Bush on December 8, 2003. The bill requires that prescription drug plans take into account the resources and time associated with medication therapy management services.

This is a victory for ASCP, which, as a member of the Pharmacist Provider Coalition, urged lawmakers to include medication therapy management services in the final Medicare bill.

The Pharmacist Provider Coalition is composed of six national pharmacy associations that represent pharmacists working in all sectors of pharmacy practice. The coalition partners joined forces in 2001 to educate members of Congress and the public about the role pharmacists play in the safe and effective use of medications, and to provide patients access to medication therapy management services by pharmacists.

Under the new Medicare law, prescription drug plans are required to provide medication therapy management services for targeted beneficiaries who take multiple drugs, have multiple chronic diseases, or incur significant drug spending. The medication therapy management services will be designed to optimize therapeutic outcomes, improve medication use, reduce the risk of adverse events and drug interactions, and increase patient

adherence and compliance with prescribed regimens. The language specifies that these medication therapy management services may include special packaging for medications. Special packaging is one element of medication therapy management for which ASCP lobbied.

Efforts by ASCP also included promoting that the Certified Geriatric Pharmacist (CGP) credential is the most reliable way to determine if an individual has “expertise in the care of the elderly or disabled.” The Medicare bill says the medication therapy management will be developed in cooperation with licensed and practicing pharmacists and physicians.

Pharmacist Provider Coalition members expect seniors to embrace the medication therapy management services. A national survey conducted in 2002 found that 83 percent of Americans would be interested in having a pharmacist work closely with them and their physician to monitor how well their medications are working. Ninety-three percent of respondents also indicated support for such a new Medicare benefit.

Medication therapy management services will greatly help the elderly population, which was another goal of ASCP in its advocacy efforts for a Medicare outpatient drug benefit for seniors. Medication-related complications represent up to 11.5% of all hospitalizations. Recently published research indicates that medication-related problems cost the U.S. health

care system as much as \$177 billion a year. A substantial portion of this expense is preventable through medication management services provided by pharmacists collaborating with physicians.

In addition to ASCP, the Pharmacist Provider Coalition partners are: the Academy of Managed Care Pharmacy, American Association of Colleges of Pharmacy, American College of Clinical Pharmacy, American Pharmacists Association, American Society of Health-System Pharmacists, and the College of Psychiatric and Neurologic Pharmacists.

Diana Duvall  
Associate Editor

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