



HEALTH NOTES



Drug Therapy Considerations in Older Adults

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HEALTH NOTES

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Drug Therapy Considerations in Older Adults

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William Powers
Chairperson, Communication and Public Education Committee
California State Board of Pharmacy

On behalf of the California State Board of Pharmacy, I am pleased to offer and recommend this publication on drug therapy for seniors to California's pharmacists, patients and other health care providers. The board encourages pharmacists to use the process offered in this monograph to earn continuing education credits for studying the information.

Health Notes is published by the California State Board of Pharmacy's Communication and Public Education Committee to assist California pharmacists and other healthcare providers to be better informed on topics of importance to their patients. Patients, too, should find this information highly useful.

According to the 2000 census, there were approximately 3.6 million seniors in California who were over age 64. This group comprises a large segment of those who take prescription drugs, yet these drugs are most effective when they are prescribed and taken appropriately.

This *Health Notes* addresses drug therapy issues affecting seniors with the intent to improve the quality of pharmacists' care provided to these patients. The articles are on a variety of diseases or issues related to drug therapy and management for seniors, and offer information from experts on such matters as therapeutic goals, metabolic issues affecting drug therapy, and patient counseling tips. The articles also confront and dispel a number of myths involving seniors and prescription medication therapy. These myths include:

- Geriatric patients do not learn new information.
- Older patients are less able to tolerate medication than younger adults.
- A person over the age of 65 will always experience more side effects from medication than someone younger than 65
- Seniors who take opioids for chronic non-cancer pain will become addicted in days to weeks.
- All vitamins are safe, even at large doses.
- Because over-the-counter medicines don't require a prescription, they're not as strong.
- Patients with health insurance do not qualify for patient assistance programs through the pharmaceutical industry.

As Dr. Bradley Williams concludes in his article:

“Older adults greatly appreciate the care and attention that comes with pharmaceutical care. They rely heavily on medications for disease management and successful treatment that enhances their quality of life. For pharmacists, interventions can be rewarding and ensure that their older patients retain their functions and activity despite the presence of chronic disease.”

We believe this issue of *Health Notes* will be of great benefit in advancing the health of our state's seniors.

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A Note From the Editors

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By now, most of us are well aware, either from census reports, newspapers, or by just looking in the mirror each day, of the increasing number of older adults in American society. In 2011, the 76 million baby boomers will begin turning 65 years old and this “age wave” is expected to have great political and social impact.

The statistics from the U.S. 2000 census are frequently in the media and raised in political debates:

- Elders (65 years and older) represent 12.4 percent of our population and number 35 million – or one in every eight Americans.
- Over 2 million people celebrated their 65th birthday in 2000. Their life expectancy is an additional 17.9 years.
- The elderly population is projected to double to 70 million in the next quarter century. By 2030, one in every four Americans will be “geriatric.”
- Americans 85 years of age or older are the fastest growing segment in our country. They numbered 4.2 million in 2000 and are projected to increase to 8.9 million by 2030.

Adults over 65 years of age are more likely to suffer from a chronic condition requiring drug therapy: 44 percent have arthritis, 39 percent have hypertension, 28 percent have some form of heart disease, and 20 percent have diabetes mellitus. On average, older adults visit a physician six times annually and receive twelve prescriptions per year (two prescriptions per visit), resulting in 365 million prescriptions written each year in the U.S.

Drug therapy for older adults is frequently less than optimal, which is of significant concern to health professionals and consumers alike. Medications have the potential to improve a person’s quality of life, but inappropriate drug therapy may cause adverse reactions and harm, increase health care costs, require emergency room visits or hospitalizations, and could be fatal. By taking an active role in optimizing drug therapy for older adults, pharmacists can improve therapeutic outcomes and reduce adverse consequences.

In this issue of *Health Notes*, we’ve chosen a case-based format to illustrate key points and to emphasize practical

applications of the information presented. The patient cases do not represent any specific individuals, but are rather a composite of typical older adults, common medical problems, and medications. The authors will discuss Mr. and Mrs. Brown, Mrs. Smith, and Mrs. Young throughout the issue, providing their own perspectives on the issues present. Our hope is that you will find this information informative, helpful, and applicable to your practice.

EDUCATIONAL OBJECTIVES

After reading this issue of *Health Notes*, the pharmacist should be able to:

1. Identify four factors that contribute to medication complications in older adults.
2. Give five examples of how aging can affect drug action in older patients.
3. Describe four principles that can be implemented to enhance positive medication outcomes in the elderly.
4. Discuss the role of drug therapy in Alzheimer’s disease.
5. Discuss the treatment philosophy for depression in the elderly and how it differs from treatment paradigms in younger adults.
6. Identify treatment options and use of medications in the treatment of osteoarthritis pain.
7. Discuss the treatment options for type 2 diabetes, including specific considerations for the elderly.
8. Discuss precautions for the elderly who self-medicate with over-the-counter medications and dietary supplements.
9. Describe prescription benefit options and cost saving strategies for adults over the age of 65 years.
10. List five strategies for maximizing counseling sessions with older patients.

Case Histories



Case I: Mr. And Mrs. Brown

Mr. and Mrs. Brown live in a small apartment in the inner city. Ted Brown is a 79-year-old retired accountant. His wife of 51 years, Judy Brown, continues to work part time as a substitute teacher. The Browns are active older adults and both enjoy ballroom dancing and taking walks in the park. Mrs. Brown takes no prescription medications, but does take a variety of herbal and nonprescription medications that she purchases by mail. Mr. Brown takes the following medications on a regular basis:

- aspirin 81mg once daily
- hydrochlorothiazide 25 mg once daily
- clonidine patch (Catapres-TTS-1®) weekly for hypertension
- ranitidine (Zantac®) 150 mg twice daily for gastric reflux
- naproxen (Naprosyn®) 375 mg twice daily as needed for arthritis pain
- lovastatin (Mevacor®) 40 mg daily at bedtime

- metformin (Glucophage®) 500 mg three times daily for diabetes
- nitroglycerin 0.4 mg sublingual as needed for chest pain
- diazepam 5mg as needed for occasional anxiety and insomnia

Mr. Brown had a heart attack three years ago, but has not experienced chest pain in over a year. He takes his medications as prescribed, but does occasionally forget to take his cholesterol medication and admits, “My cholesterol could be better.”



Case II: Mrs. Smith

Mrs. Smith is a 69-year-old recently retired sales clerk. She has just returned to her suburban home, where she lives alone, after being discharged from the hospital following a blood clot in her leg. During her five-day stay in the hospital, she was started on warfarin (Coumadin®) 5 mg daily. Her dose was increased from 3 mg to 5 mg per day on the day that she was discharged. She is now picking up her new prescription for Coumadin® 5 mg tablets from a community pharmacy. The prescription bottle is labeled, “Take as directed.” Mrs. Smith has her prescriptions filled at several pharmacies, because she finds the prices may vary from one pharmacy to the next. Her health insurance does not cover medications that are not administered in a hospital.

Mrs. Smith’s medications are:

- warfarin (Coumadin®) 5 mg per day
- digoxin (Lanoxin®) 0.125 mg daily for irregular heart beat
- fluoxetine (Prozac®) 20 mg per day for depression
- rofecoxib (Vioxx®) 25 mg daily for joint pain
- loratadine (Claritin®) one tablet daily for hay fever (OTC)
- omeprazole (Prilosec®) 20 mg per day for stomach distress

As she picks up her new prescription for Coumadin®, she brings Tagamet HB®, Pepto-Bismol®, ginkgo biloba capsules, vitamin C 500 mg tablets, vitamin E 1,000 unit capsules, and a bottle of Advil® to the checkout counter. She also mentions to the pharmacist that she feels her vision has worsened lately, she feels thirsty a lot, and has been getting up more often in the middle of the night to urinate.



Case III: Mrs. Young

Thelma Young is a 71-year-old retired teacher who was recently diagnosed with “probable mild-to-moderate Alzheimer’s disease.” Her husband accompanies her to the pharmacy today to purchase vitamin E and Advil®. Mrs. Young tells the pharmacist that she has been experiencing difficulty sleeping and states, “I am having very disturbing dreams that wake me up during the night. Then I can’t get back to sleep. The nonprescription sleeping pills that I’m taking help, but I feel groggy in the morning.” She demonstrates some difficulty in finding the correct words to say, but can otherwise communicate effectively. Her husband says that his wife frequently forgets where she puts household items and that she has burned several pans on the stove recently. He asks, “How fast will the new memory drug, Aricept®, work?” Mr. Young goes on to say that his wife has had difficulty sleeping off and on for years, but that the disturbing dreams are a change. He asks if it could be a result of her taking the new medicine. He also wants to know if Advil® and vitamin E will help her memory.



PRESCRIBING CHALLENGES IN THE ELDERLY PATIENT

Pharmaceutical Care in the Elderly



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Chronic medical conditions require treatment, and the treatment of choice often remains drug therapy. With increasing use of medications, the rate of noncompliance and the risks of adverse drug reactions, drug interactions, and drug-induced hospitalizations rise. Studies over the past 10-15 years have found that approximately one-quarter of all hospital admissions for people aged 65 years and older are associated with medication-related problems, typically adverse drug reactions or noncompliance. Factors that may contribute to this problem include polymedicineⁱ, prescribing of medications that are not appropriate for older adults, unsupervised use of non-prescription remedies, and inadequate counseling and education of patients about their medications.

Polymedicine

Polymedicine has been defined in many ways. Most definitions include some specific threshold, such as the use of five or more medications. A more appropriate definition, however, is simply the use of unnecessary medications. For example, Mr. Brown (Case I) requires several medications to manage multiple chronic diseases, but this is not polymedicine (although the choices of some of the medications are not ideal). Mrs. Brown, in contrast, purchases several remedies by mail and many of them may not be necessary. Consequently, she is the person more likely to be exhibiting polymedicine. Mrs. Smith (Case II) appears to be taking an antihistamine routinely, although hay fever is commonly a seasonal condition. Her ibuprofen purchase duplicates her rofecoxib (Vioxx®) prescription. Her Tagamet HB® and Pepto-Bismol® are probably being used to treat the same gastrointestinal problem for which she is taking omeprazole (Prilosec®). This illustrates the important point that polymedicine is not necessarily confined to the overprescribing of medications.

Several factors contribute to polymedicine, as shown in Table 1. In addition, the attitudes of health professionals toward older adults can contribute. Those who view older adults as complainers may respond by quickly writing prescriptions to bring the visit to an end, or they may not provide adequate

ⁱThe term *polymedicine* is sometimes used interchangeably with *polypharmacy*.

MYTHS & FACTS

- MYTH:** *Older adults are more noncompliant with medication regimens than younger patients.*
- FACT:** Noncompliance is more closely related to the numbers of medications and the complexity of the regimen. Because the elderly often take more medications, they have more opportunity for noncompliance.
- MYTH:** *Geriatric patients do not learn new information.*
- FACT:** Vision and hearing impairments and slower nerve transmission as we age make it more difficult for some elderly patients to register new information. When delivered in a manner that takes this into account, older adults learn very well.

Table 1. Factors That Contribute to Polymedicine

• Multiple disease states
• Time constraints on health professionals
• Multiple health care providers
• Use of nonprescription medications
• Patient-driven prescribing

counseling or education about the appropriate use of medications. As a general rule, the more complex the patient and the more fragmented the care, the greater the risk of polymedicine.

Pharmacists and other health professionals must be alert to the signs of polymedicine, which may not always be obvious. Identifying polymedicine (Table 2) requires effective communication between prescribers, pharmacists, other health care providers, and most importantly, patients. A prescribed medication may not have an apparent indication or the problem may no longer be active. For example, Mr. Brown is receiving diazepam for occasional anxiety and insomnia. These problems often do not require treatment if the frequency is occasional. In addition, non-drug treatment may be as or more effective than using a benzodiazepine. Mrs. Smith exhibits polymedicine by her use of several duplicate medications, as described previously. She also is at risk for the use of

Table 2. Evidence of Polymedicine

• Medications with no apparent current indication
• Use of duplicate medications
• Use of interacting medications
• Medications that are contraindicated in concurrent diseases or conditions
• Inappropriately high or low medicine dosages
• Pharmacotherapy of adverse drug reactions

several interacting medications, including cimetidine, fluoxetine, and warfarin. Omeprazole can also affect digoxin absorption and ginkgo biloba may increase the risk for bleeding when used with warfarin.

Mrs. Smith wishes to take ibuprofen, which may be contraindicated with her warfarin therapy because of the increased risk of bleeding. It also may worsen her stomach distress for which she is taking omeprazole and wishes to purchase Tagamet HB®. Other signs of polymedicine include the use of inappropriately high or low doses of medications, and the treatment of adverse drug reactions with other medications.

Nonadherence

The use of large numbers of medications increases the risk for noncompliance or nonadherence to therapy. Mr. Brown takes eight prescription medications, six of them routinely. The dosage frequencies range from once weekly to twice daily. Although he appears to take his medications conscientiously, he admits to occasionally forgetting to take his lovastatin. Several factors that can affect adherence to therapy, some of which apply to Mr. Brown, are listed in Table 3. A special problem is present with his Catapres-TTS®. It is a topically applied medication that includes two components, the patch containing the clonidine and an adhesive patch. Patients have been known to apply the adhesive cover patch only and discard the active patch containing the drug, not realizing that both must be applied.

Table 3. Factors That Contribute to Nonadherence

• Taking several medications with different schedules (e.g., combination of daily, twice daily, three times daily plus medications to be taken with or without meals)
• High-cost medications
• Delays in ordering medication refills
• Inability to travel to the pharmacy to pick up refills
• Confusing or difficult directions (e.g., bisphosphonates) or changes in directions
• Perceived or actual adverse effects
• Lack of understanding about a medication's intended effect or unclear expectations about outcomes

Adverse Drug Reactions

Elderly patients are often given prescriptions for medications that may be more likely to cause adverse drug reactions due to age-associated physiological changes. For example, Mr. Brown is taking Catapres-TTS® for his hypertension. This medication often causes orthostatic hypotension, dry mouth, and constipation in older adults and may also have an adverse effect on his mood. Given his history of myocardial infarction, an angiotensin converting enzyme inhibitor or a beta-blocker would be a more appropriate choice. He is also taking naproxen for arthritis pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) may antagonize the effect of his antihypertensive medication and worsen his gastric reflux. Acetaminophen is generally considered a more appropriate medication for arthritis pain and will not adversely affect his other conditions. Diazepam and other long-acting benzodiazepines are considered inappropriate for older adults because these drugs accumulate in the body and increase the risks of falls and cognitive impairment.

Patient Consultation

Mrs. Smith (Case II) illustrates the frequent and unsupervised use of nonprescription medications. She wishes to purchase Tagamet HB® and Pepto-Bismol®, which duplicate her omeprazole therapy. The Tagamet®, ginkgo biloba, and vitamin E may all have additive effects with Coumadin®, causing an increased risk of bleeding. The ibuprofen duplicates her Vioxx® and may cause intestinal bleeding that may be exacerbated by the anticoagulant.

These issues illustrate the importance of counseling and educating older adults about their medications. The pharmacist and prescriber play crucial roles in ensuring patient safety. An excellent initial strategy is for older adults to use a primary care physician who will coordinate services among other physicians and clinicians, such as dentists, podiatrists, and any others who may prescribe medications.

Elderly patients should purchase all of their prescription and nonprescription medications at a single pharmacy so that a comprehensive medication history is available. When seniors obtain nonprescription remedies from other sources, they should inform their pharmacist so that the information can be included in their patient profiles.

Pharmaceutical Care Principles

The use of pharmaceutical care principles provides a systematic approach to ensuring good patient education. These include assessment, development of a care plan, establishment of therapeutic goals, and follow-up. The assessment process includes an understanding of the patient, disease state, and drug therapy. Age-associated physiologic changes must be

considered. The older patient's lifestyle and activity level also may affect the response to medications. The use of alcohol, tobacco, and caffeine must be considered, as well as the effect of a disease state on mobility and function. Mr. Brown's arthritis pain may reduce his ability to exercise and less activity may compromise his cardiovascular conditioning. Mrs. Young has significant functional deficits due to her Alzheimer's disease. This will affect her ability to adhere to a medication regimen and impair her ability to reliably report adverse drug effects. The appropriateness of medication choices must be evaluated with regard to pharmacokinetics, pharmacodynamics, potential for drug interactions, and the ability to adhere to a therapeutic regimen.

High rates of medication use, complex drug regimens, the potential for adverse drug reactions and interactions, self-medication, and the likelihood of noncompliance with a therapeutic plan make developing a pharmaceutical care plan challenging. Suggestions for improving adherence to a medication regimen are listed in Table 4. The pharmacist must work closely with prescribers, the patient, and other care providers to ensure that the therapy maximizes benefit while minimizing risk. Mrs. Smith purchases her prescriptions from several pharmacies, making it difficult to implement a care plan. She compounds the problem by purchasing several nonprescription remedies concurrently. Her pharmacist should educate her about the risks of unsupervised medication use and should work with her to develop a mechanism that will encourage her to use only one pharmacy for all of her medication needs.

Therapeutic Goals and Follow Up

Therapeutic goals should be developed along with the care plan. It is important to recognize that older adults may have goals (e.g., quality of life) that may be very different from those of health professionals. Compliance with a medication regimen will be much better when the patient's lifestyle is considered and incorporated into the therapeutic plan.

Table 4. Strategies For Patients to Improve Compliance

<ul style="list-style-type: none"> • Use medication calendars, pillboxes, or similar reminder systems.
<ul style="list-style-type: none"> • Store medications in a location that will serve as a reminder system (e.g., keep mealtime medications at the dining table, or bedtime-only medications at the bedside).
<ul style="list-style-type: none"> • When traveling, keep medications with a cosmetic or toiletry kit, or some other item that is used on a daily basis.
<ul style="list-style-type: none"> • If visually impaired, set up a large-type calendar system and place an easily distinguishable marking on each different medication.
<ul style="list-style-type: none"> • Ask the pharmacist or prescriber if there are dosage forms available that can be taken only once or twice a day to reduce the likelihood of a confusing drug regimen.

Ensuring ongoing effective pharmacotherapy requires follow-up. Older patients will respond well when they understand the importance of treatment and know that the treatment is effective. Elderly patients should be instructed how to self-monitor for chronic diseases such as hypertension and diabetes. This provides them with immediate feedback and helps them reach their goals. Pharmacists should incorporate functional assessment into drug therapy monitoring (e.g., asking how far a patient with arthritis can walk without pain). Follow-up also includes maintaining an ongoing dialogue with prescribers, providing advice regarding self-medication, and offering positive reinforcement to patients regarding their drug therapy success.

Older adults greatly appreciate the care and attention that comes with pharmaceutical care. They rely heavily on medications for disease management and successful treatment enhances their quality of life. For pharmacists, interventions can be rewarding and ensure that their older patients retain their function and activity despite the presence of chronic diseases.

COUNSELING TIPS

- Actively offer counseling to elderly patients. Many are reluctant to interrupt the pharmacist to ask questions.
- Make sure the counseling area is quiet and free of distractions. Hearing aids amplify all sound, including background noise.
- Speak slowly and distinctly while looking at the patient. Older adults with hearing impairments rely to some degree on lip reading.
- Do not shout or raise your voice above normal. Shouting raises the pitch of the voice, and high tone hearing is reduced in older adults.
- Supplement written educational materials with verbal instructions to reinforce learning.
- Make sure written materials are in a type font large enough to be read by a person with impaired vision. High contrast (black type on white surface) is most easily read.
- Allow time for information to "sink in," then ask for feedback to ensure that the information was understood.
- Reinforce information at subsequent visits.
- For metered dose products, transdermal patches, and other unique delivery devices, show, don't just tell, the patient how to use. Have the patient demonstrate proper use and how to use the product.
- For topical ointments and creams, keep a jar of Eucerin or similar product handy and demonstrate how to apply the topical prescription "sparingly." For example, an amount of ointment the size of a green pea will cover the back of the hand. Show and Tell!
- Encourage the use of reminders such as medication calendars or pillboxes. Be sure that the patient can use the reminder system. If not, enlist the assistance of a caregiver or other person who can help set up and monitor the system.
- If a patient is getting refills beyond the expected refill date, ask about the reason for the delay. It may uncover problems with understanding or memory, or indicate prescriber-initiated changes that require the prescription to be updated for accuracy.

Altered Drug Action with Aging

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As a person ages, a number of natural physiological changes occur that alter the way the body handles drugs. In older persons, alterations in drug disposition are related to changes in body composition and organ function. Such age-related changes are generally gradual and follow the normal physiology of aging. Furthermore, the elderly are prone to some pathological conditions that can significantly alter drug disposition (e.g., congestive heart failure). Geriatric patients may also be more sensitive to certain medications; as a result they are more susceptible to the effects of a drug than a younger patient. This places the elder patient at greater risk for experiencing adverse effects from doses of medications typically used in younger persons.

Conceptually, there are two ways to envision drug therapy in individual patients: what the drug does to the body, and what the body does to the drug. Pharmacodynamics is what the drug does to the body. It describes the action of the specific drug and the response of the patient. Conversely, pharmacokinetics is what the body does to the drug and includes such parameters as absorption of the drug, distribution of the drug to the various organs and tissues in the body, metabolism of the drug into other compounds, and renal excretion of the drug and metabolites with subsequent elimination from the body. These two concepts are interrelated in that pharmacokinetic parameters determine the amount of drug that reaches the blood circulation and the site of action, whereas the intensity of the pharmacodynamic effect is generally associated with the amount or concentration of drug at the site of action. Thus, in most cases, there is a concentration-response relationship such that the higher the drug concentration at the site of action, the greater the effect.

Absorption

When a medication is taken orally, the drug needs to be absorbed from the gastrointestinal (GI) tract to get into the blood stream. A number of changes in the GI tract occur with aging that can potentially affect drug absorption after oral

MYTHS & FACTS

MYTH: *Older patients are less able to tolerate medications than younger adults.*

FACT: Age-related changes in pharmacokinetics and pharmacodynamics are complex. For some medications, elderly patients are more sensitive and for some they are less sensitive. Many differences in dose-response observations can be predicted based on the changes in pharmacokinetic parameters.

administration. The rate and extent of absorption of a drug is influenced by a variety of factors, including changes in GI physiology and function. Alterations in absorption will affect how much and how rapidly a dose will be absorbed.

Physiological changes in the elderly that may potentially impact drug absorption include a slower rate of gastric emptying, a decrease in intestinal motility, a reduction in intestinal blood perfusion, and a diminished intestinal mucosal surface area. In addition, the extent of absorption may be increased in the elderly for drugs that undergo extensive first-pass metabolism in the liver. This may be expected when there is a decrease in the metabolic biotransformation of the drug, resulting in a greater fraction of a dose entering the systemic blood circulation.

The net effect of the above factors has proven difficult to predict and most frequently does not result in clinically relevant changes in drug absorption after oral administration. Reasons for this include the complex nature of the drug absorption process and bioavailability factors. However, it is prudent to anticipate that the rate of drug absorption and the onset of action may be prolonged in the elderly and that the extent of absorption of drugs that undergo extensive first-pass metabolism may be greater than in younger persons.

Geriatric patients may be prone to other factors that can alter drug absorption. These include: swallowing difficulties, poor nutritional status, erratic meal patterns, and interactions with other prescription and nonprescription medications. A

variety of gastrointestinal conditions not exclusive to older patients, such as Crohn's disease, ulcerative colitis, celiac disease, or surgical procedures (eg., gastrectomy or small bowel resection), may further alter GI absorption of medications.

Distribution

After a drug is absorbed and enters the blood circulation, it distributes to various organs and tissues throughout the body. The distribution of drugs in the body can significantly differ in geriatric patients as compared to younger adults. This difference reflects the various changes in body composition that normally occur as a person ages.

In general, the total body weight of a person declines in old age, particularly in the very old. Specifically, there is a general decline in lean body mass, and an increase in the proportion of body fat. This results in less drug distribution to muscle tissue for drugs such as digoxin, while fat-soluble drugs such as diazepam have a relative increase in drug distribution. Additional changes in body composition in the elderly include a decrease in total body water, a general reduction in the serum albumin concentration, and an increase in α_1 -acid glycoprotein. Changes in total body water affect the distribution of water-soluble drugs, such as lithium. A decrease in serum albumin concentration is significant for acidic drugs that are highly bound to this protein, while basic drugs bind to α_1 -acid glycoprotein. As the serum albumin concentration declines, the fraction of free or unbound drug increases. Thus, lower total (bound + unbound) drug concentrations are associated with greater pharmacological activity when the free fraction is increased, because the unbound drug is the active entity. This also complicates measuring serum drug concentrations for therapeutic drug monitoring purposes, because total concentrations of the drug are most often measured. This necessitates making some adjustment in the value for proper interpretation. Using phenytoin as an example, the proportion of free drug is normally 10 percent when the serum albumin concentration is 4.4 mg/dL, but it increases to 20 percent when the serum albumin concentration declines to 2.0 mg/dL. Thus, for any given total serum phenytoin concentration, the pharmacological activity would essentially be twice as great when the serum albumin concentration is 2.0 mg/dL versus the normal value of 4.4 mg/dL.

When there is less drug distribution, smaller loading doses of the medications are needed and the half-life of the drug (the time it takes for the blood concentration to decline by 50 percent) will be shortened. Failure to adjust the loading dose in response to a decrease in drug distribution will result in higher blood concentrations of the drug and places the patient at greater risk for toxicity and adverse effects. Conversely, when drug distribution is expanded, relatively

higher loading doses are required to achieve desired blood concentrations and the half-life of the drug is extended. Changes in the half-life of a particular drug influence the frequency of dosing when designing dosage regimens. Generally, the longer the half-life, the less frequently a medication needs to be administered, because the effect of the drug is prolonged. The shorter the half-life, the shorter the duration of drug action will be and the medication will need to be administered more frequently.

Metabolism

One of the body's primary mechanisms to detoxify compounds is to transform or metabolize them, which most often inactivates them and allows them to be excreted from the body more readily. For most drugs, metabolism occurs predominantly in the liver. A reduction in the rate of drug metabolism extends the half-life and prolongs the action of the drug. When this occurs, it is appropriate to lower the dose or give the doses less frequently.

Many variables determine metabolic capacity, including nutritional status, diet, genetics, gender, alcohol intake, smoking, environmental factors, and the concomitant use of other medications. In the elderly, several physiological changes are associated with altered drug metabolism, including: a decrease in liver mass, a decrease in blood flow to the liver, and a reduction in the intrinsic activity of drug-metabolizing enzymes. The decrease in liver blood flow essentially decreases the rate at which a drug reaches the liver to be metabolized, while a decrease in the number and activity of metabolic enzymes diminishes the metabolic capacity of the liver.

Drug metabolism is a complex process and there is considerable variability. However, several generalizations can be made in the geriatric patient. The rate of metabolism is often diminished for drugs that are dependent upon hepatic blood flow, such as lidocaine, propranolol, and meperidine. In addition, geriatric patients have been shown to have a reduced rate of Phase I metabolism of some drugs, which involves the oxidation, reduction, dealkylation, or hydroxylation of compounds. Furthermore, this difference may be gender related, with elderly women metabolizing some drugs (e.g., midazolam, doxylamine) as efficiently as younger adults. However, no significant change has been observed in the rate of Phase II metabolism in the elderly, which consists of glucuronidation, acetylation, and sulfation of compounds.

These age-related differences in drug metabolism should be considered when selecting a drug and dosage regimen. For example, chlordiazepoxide, diazepam, and flurazepam undergo Phase I metabolism, and thus, the rate of elimination will be slower than in younger adults. This may result in drug accumulation over time, potentially causing over-sedation,

impaired psychomotor skills, or confusion. Alternatively, lorazepam, oxazepam, and temazepam are metabolized primarily by Phase II reactions, which are not affected by the aging process. However, while their shorter half-life makes these drugs less likely to accumulate, they can also cause the same adverse effects as the previously listed benzodiazepines.

Because older patients are often on multiple medications, there is a greater potential for some medications to alter the metabolism of other medications the patient is taking. Moreover, there are some common conditions in the elderly (e.g., congestive heart failure) that also have a detrimental effect on metabolism of certain drugs. These factors must be taken into consideration when assessing drug therapy in this patient population.

Excretion

Renal excretion of drugs and their metabolites is the major route of elimination from the body. As with metabolism, a reduction in the clearance of a drug via renal excretion will extend the half-life and the duration of action, which often necessitates a reduction in dosage. (See Table 1.)

It is well known that kidney function declines with advancing age. The level of decline varies significantly between individuals, with some healthy older adults experiencing much less of a loss than patients with high blood pressure or diabetes. Physiological changes associated with this age-related decline in renal function include diminished blood flow to the kidneys, a decrease in kidney mass, and a reduction in the size and number of functioning nephrons. Consequently, there is a reduction in the filtration, active secretion, and tubular reabsorption of drugs.

Commonly, clinicians use creatinine clearance to estimate glomerular filtration rate, a standard measurement of renal function. Between the ages of 40 and 80 years, the creatinine clearance decreases at a rate of approximately 1 mL/minute each year. It is important to understand that although the cre-

atinine clearance gradually decreases, the measured serum creatinine concentration may not change significantly. This is because the decrease in creatinine clearance is often accompanied by decreased creatinine production in the aged, which is due to a decline in lean body mass. The net effect is little or no change in the serum creatinine concentration. Thus, age and body mass must be factored into assessments of renal function. One such method that incorporates these factors is the equation developed by Cockcroft and Gault:

$$Cl_{cr} = \frac{(140 - \text{Age})(\text{Wt})}{(72)(S_{cr})} \times S$$

where Cl_{cr} is the creatinine clearance in mL/min

Age is in years

Wt is the lean or ideal body weight in kg

S_{cr} is the serum creatinine concentration in mg/dL

S = 1.0 for males and 0.85 for females

Pharmacodynamics

Pharmacodynamics refers to the actions of a drug and the response that patients experience. With some medications, elderly patients often experience a different degree of response than in younger adults. It is difficult to determine if such differences are due to pure intrinsic pharmacodynamic changes (concentration-response relationships) or age-related alterations in the pharmacokinetics (amount of drug that reaches the site of action).

The normal aging process itself may predispose patients to be more or less sensitive to particular medications, especially drugs that affect the cardiovascular and central nervous systems. It is postulated that this is a result of changes at the receptor site (the site of drug action). Such differences may include changes in the binding affinity for the drug, changes in the number or density of active receptors at the target

Table 1. Medications Requiring Dosage Adjustment for Diminished Renal Function

Anti-infectives	H ₂ Blockers	Cardiac	Oral Diabetes Medications	Other
Aminoglycosides	Cimetidine	Atenolol	Chlorpropamide	Allopurinol
Cefixime	Famotidine	Benazepril	Glyburide	Furosemide
Cefodoxime	Ranitidine	Captopril	Metformin	Lithium
Cephalexin	Nizatidine	Digoxin		Methotrexate
Fluconazole		Enalapril		Metoclopramide
Penicillins (various)		Nadolol		
Ciprofloxacin		Procainamide		

organ, biochemical processes, homeostatic regulation, structural features, and physiological processes. Additionally, changes in the anatomy and physiology in the older patient may render them more susceptible to the effects and side effects of medications. For example, elderly patients with impaired balance are at greater risk for drug-induced falls, particularly when the medications cause sedation or dizziness.

Age-related changes at the receptor site may be responsible for an increase in sensitivity to warfarin, benzodiazepines, anticholinergics, and narcotic analgesics. Thus, lower doses are generally required to achieve the same degree of effect as in younger patients. In contrast, the elderly have been shown to be less sensitive than younger adults to beta-adrenergic agonists (e.g., isoproterenol), beta-adrenergic antagonists (e.g., propranolol), allopurinol, and insulin. The antihypertensive effect of calcium channel blockers (e.g., verapamil) has also been observed to be greater in the elderly, whereas the effect on cardiac conduction was less than in younger subjects studied.

Age-related changes occurring in the central nervous system may explain why dizziness, sedation, and confusion are common adverse drug effects experienced by older patients. Similarly, elderly patients are more prone to orthostatic hypotension from medications that affect the cardiovascular system, because they often have a diminished capacity to quickly compensate for postural changes in blood pressure.

Changes in pharmacodynamics in the elderly may be obscured by the age-related changes in pharmacokinetics. For example, elderly patients may be less sensitive to propranolol, but more propranolol may reach the systemic circulation for a given dose due to a decrease in the rate of metabolism. Although clinicians can anticipate these effects, the net effect may be difficult to predict.

Case Discussions

A number of these concepts can be applied to Mr. Brown (Case I) and Mrs. Smith (Case II). Mr. Brown takes diazepam for occasional anxiety and insomnia. The distribution of diazepam is generally increased in the elderly and its rate of metabolism is often reduced. Both of these changes contribute to an increased half-life of diazepam, which results in a prolonged duration of action. As a sleeping aid, drugs with a long duration of action should be avoided because daytime sedation is undesirable and can be problematic. Additionally, older patients are generally more sensitive to the sedative effects of benzodiazepines. This increases the risk of falls and the potential for broken bones. In Mr. Brown's case, such effects are a concern because he enjoys dancing and walks in the park. Sedation and impaired reflexes can also be dangerous in those who continue to drive.

Assuming Mr. Brown's lean body weight is about 60 kg and that his serum creatinine concentration is 0.8 mg/dL (normal: 0.6-1.2 mg/dL), his estimated creatinine clearance is approximately 64 mL/min. The recommended dose of ranitidine is 150 mg orally once daily in patients when $Cl_{cr} < 50$ mL/min. Since Mr. Brown is borderline with respect to a dosage adjustment, his dosage should eventually be reduced to account for the gradual decline in kidney function that occurs with normal aging. In addition, metformin should be avoided in patients with a creatinine clearance of less than 60 mL/min, because it is eliminated primarily by the kidneys and this may increase the risk of lactic acidosis.

Mrs. Smith's dose of Coumadin® was increased on the day of discharge from the hospital. Thus, the full therapeutic effect of Coumadin® will not be observed for several days because the half-life may be prolonged in older patients and because of the time it takes for a decrease in the synthesis of clotting factors in the liver. Furthermore, because of an increased sensitivity to the effects of warfarin, elderly patients generally require lower doses to achieve the desired degree of inhibition in blood clotting. Mrs. Smith also wishes to purchase Tagamet HB®, which can reduce the metabolism of warfarin. Thus, Mrs. Smith is at greater risk for bleeding complications. Her warfarin therapy should be monitored very closely and her dosage titrated accordingly, until her therapeutic response is stabilized.

Mrs. Smith is also taking digoxin (Lanoxin®), which is eliminated via both metabolic and renal pathways. Further, a decrease in muscle mass in the elderly reduces the distribution volume for digoxin, which binds extensively to skeletal muscle. She is also taking omeprazole (Prilosec®), which has the potential to increase the oral absorption of digoxin. For these reasons, Mrs. Smith should be monitored periodically to prevent concentration-related adverse effects of digoxin, which has a very narrow therapeutic range. Loading and maintenance doses of digoxin must be adjusted in elderly patients to account for reductions in the volume of distribution and elimination.

Conclusion

Age-related alterations in drug action reflect the changes in body composition and organ function associated with the natural aging process. For many medications, age-related changes in pharmacokinetics and pharmacodynamics can be anticipated. Additional factors, such as nutritional status, drug-drug interactions, and co-morbidity with other medical conditions may also contribute to the complexity of drug action in the older patient. Understanding these concepts enables pharmacists and other clinicians to rationally adjust drug doses for older adults and anticipate the effects of drug therapy.

Evaluating The Risks and Benefits of Drug Therapy



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Standards that ensure the safe and effective use of medications in older patients are essential. Adhering to four basic principles will enhance therapeutic outcomes:

- Avoid unsafe medications.
- Recognize when medications worsen activities associated with daily functioning.
- Use evidence-based medicine to determine first-line agents.
- Tailor drug therapy to the individual, considering concomitant disease states and medications.

The nursing home reform amendments contained in the 1987 Omnibus Budget Reconciliation Act (OBRA 87) provide a working template to improve optimal medication use in the frail elderly. This template is useful for the assessment of drug therapy in older individuals because it addresses many of the issues that enhance therapeutic outcomes. It advocates prescribing only when there is a definite indication, monitoring for efficacy and side effects of medications, and considering the effects of the medications on a patient's well being. OBRA 87 was the first major revision of federal nursing home requirements in almost two decades. At that time, excessive sedation of nursing home residents through the use of psychoactive medications was a significant concern. These chemical restraints were being used excessively to avoid troublesome behavior by the nursing home residents, despite the fact that they were known to cause significant side effects and lacked good scientific evidence to support their use.

OBRA 87 regulations require nursing facilities to meet the highest realistic physical, medical, and psychological standards for the well-being of each resident. A pharmacist reviews each resident's medication regimen every month and provides recommendations that improve drug therapy or the monitoring of

MYTHS & FACTS

MYTH: Older individuals do not derive real benefits from medication besides treating some symptoms of disease.

FACT: Appropriate medications, such as blood pressure medication, can reduce the incidence of stroke, heart failure, kidney damage and heart attack, regardless of age.

MYTH: A person over the age of 65 will always experience more side effects from medication than someone younger than 65.

FACT: Older individuals can be susceptible to side effects; however, careful selection of medicines proven to be safe in the elderly, along with careful dose titration, can significantly improve the tolerability of most medication.

therapy. The pharmacist ensures that the resident is not prescribed unnecessary drugs. Unnecessary drugs are defined as duplicate therapy, or a drug in an excessive dose, for an excessive duration, without adequate monitoring, without adequate indications for use, or in the presence of adverse effects that should result in a dose reduction or drug discontinuation. As a result of OBRA 87, drug regimens are screened specifically for psychoactive drugs to make sure that a specific condition documented in the clinical records is being treated, and that gradual dosage reductions are attempted in an effort to discontinue these drugs.

Unfortunately, the same government regulations for medication safeguards, including mandates for monthly drug regimen review, do not exist for older individuals outside of the extended care setting. Studies examining the impact of pharmacists working with older persons outside of the extended care setting have consistently shown that pharmacists identify and resolve medication-related problems, reduce unnecessary medications, decrease adverse medication effects, and help avoid unnecessary expenses. Overall, pharmacists promote safer prescribing and enhance medication compliance.

Avoid Unsafe Medications

Medications are necessary for many older adults to treat illness, improve quality of life, and sometimes extend life. For example, isolated systolic hypertension is a condition where the systolic pressure is too high, but the diastolic pressure is not. It occurs primarily in older individuals. At one time, older persons were assumed to require an elevated systolic blood pressure in order to properly supply the brain and other vital organs with blood. Thus treating isolated systolic hypertension was thought to actually worsen clinical outcomes. On the contrary, when the effects of antihypertensive medications were evaluated in older individuals with isolated systolic hypertension, the evidence showed that elderly individuals derived significant health benefits from medication. Numerous studies have now demonstrated that treating hypertension, and in particular, elevations in systolic pressure, with medications such as thiazide or thiazide-like diuretics (e.g., hydrochlorothiazide or chlorthalidone), beta blockers (e.g., metoprolol, atenolol), and dihydropyridine calcium channel blockers (e.g., nitrendipine), significantly reduces the incidence of total mortality, stroke, heart failure, and myocardial infarction, as compared to placebo.



In general, these medications are well tolerated. However, some place older individuals at greater risk for side effects. In 1997, Beers published criteria that helped to define medications that should be avoided in the elderly. (See Table 1.) Many were included because of their significant anticholinergic side effects (e.g., sedation, confusion, constipation, dry

Table 1. Drugs to be Avoided in the Elderly*

Therapeutic Category	Examples	Reason(s) to Avoid
Tricyclic Antidepressants	Amitriptyline (Elavil®), Doxepin (Sinequan®)	Significant anticholinergic effects
Gastrointestinal antispasmodic drugs	Dicyclomine (Bentyl®), Hyoscyamine (Levsin®), Propantheline (Pro-Banthine®), Belladonna alkaloids (Donnatal®), Clidinium-chlordiazepoxide (Librax®)	Significant anticholinergic effects
Antidiabetic drugs	Chlorpropamide (Diabinese®)	Prolonged and serious low blood sugar and a syndrome of inappropriate antidiuretic hormone
Antihypertensive Drugs	Methyldopa (Aldomet®)	May lower the heart rate and exacerbate depression
Antiarrhythmic Drugs	Disopyramide (Norpace®)	May induce heart failure and produce anticholinergic side effects
Benzodiazepines	Flurazepam (Dalmene®), Chlordiazepoxide (Librium®), Diazepam (Valium®)	Prolonged sedation and increased risk of falls and fractures
Narcotic analgesics	Pentazocine (Talwin®)	Causes more confusion and hallucinations than other narcotic agents and does not have pure pain blocking effects
	Meperidine (Demerol®)	Must be given frequently to attain pain control; can cause central nervous system stimulation and seizures in individuals with reduced kidney function
Barbiturates	All, except phenobarbital	Highly addictive and cause more side effects than other sedative or hypnotic drugs
Antiplatelet drugs	Ticlopidine (Ticlid®),	More toxic than other alternatives such as aspirin
Cardiac Drugs	Digoxin for heart failure (doses greater than 0.125mg daily)	Kidney clearance of the drug may be decreased, increasing potential for toxicity

* Rated most problematic ("high severity") by Beers, 1997

mouth, blurred vision, urinary retention, and increased heart rate). Others were listed because they have greater potential for toxicity in this population. In addition to the drugs listed in Table 1, other drugs associated with less severe complications in the elderly were identified. These included indomethacin, propoxyphene, phenylbutazone, trimethobenzamide, reserpine, diphenhydramine, and muscle relaxants. Medication profiles of older individuals should be screened for these drugs and whenever possible, they should be replaced with safer alternatives.

Recognize When Medications Worsen Activities Associated with Daily Functioning

A significant number of people in their seventies and beyond continue to enjoy excellent health, vitality, and cognition. Significant changes in physical or cognitive health warrant an evaluation by health care professionals. Braun and colleagues described geriatric failure to thrive as a gradual decline in physical or cognitive function usually associated with body weight loss, decreased appetite, and social withdrawal that occurs without immediate explanation. It is important to note that medications can often worsen functional ability, such as performing activities of daily living. (See Table 2).

Medications can affect mood and cognition, ambulation, bodily functions such as urinary or fecal continence, nutritional intake through a variety of mechanisms, and can cause fatigue and weakness. Mr. Brown (Case I) is taking diazepam for occasional anxiety and insomnia. Diazepam and other

benzodiazepines can predispose older individuals to falls, depression, fatigue, weakness, confusion, memory impairment, and daytime sedation. Ideally, non-pharmacological strategies (e.g., avoiding daytime naps, eliminating stimulants such as caffeine from mid-afternoon onward, maintaining an active lifestyle that includes physical and mental exercise) should be implemented to manage occasional anxiety and insomnia. Mrs. Young (Case III) has Alzheimer’s disease and has been self-treating her insomnia with nonprescription sleeping agents. Alzheimer’s disease is associated with decreased effects of the neurotransmitter acetylcholine. Unfortunately, nonprescription sleep aids containing diphenhydramine or doxylamine have significant anticholinergic side effects. It is possible that part of the cognitive impairment associated with her Alzheimer’s disease is due to her sleeping pills. Aricept®, an acetylcholinesterase inhibitor, blocks the breakdown of acetylcholine in the brain, thereby increasing central nervous system concentrations. Use of medications with anticholinergic side effects should generally be avoided in patients with Alzheimer’s disease, because they may worsen symptoms or diminish the effects of prescription medications.

Use Evidenced-based Medicine to Determine First-Line Agents

Evidence-based medicine is the process of using the results from well-designed clinical trials to develop treatment strategies. These trials involve a very large number of patients, include a comparison of two or more medications or one medication with a placebo, are continued for a reasonable length of time, and have safeguards to ensure that the interpretation of the results is not biased. Fortunately, nationally published treatment guidelines, created by panels of experts in their field using evidence-based medicine are available for most common disease states. (See Table 3.) The experts decide, based on the published evidence, which agents have superior efficacy and safety. It is prudent in most situations to use these recommended first-line agents.

An application of published guidelines for the treatment of hypertension could result in modifying the drug therapy for Mr. Brown (Case I). According to the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-VI), the clonidine patch (Catapres-TTS-1®) is considered a second-line agent for hypertension. Clonidine has a central mechanism of action and therefore may lead to a greater

Undesirable Effect	Medications Implicated
Constipation	Anticholinergics (e.g., diphenhydramine), diuretics, narcotic analgesics (e.g., codeine, morphine), resins (e.g., cholestyramine), cations (e.g., iron, aluminum), verapamil, vincristine
Urinary Incontinence	Sedatives, diuretics, anticholinergics, alpha receptor blockers (e.g., terazosin in women) and adrenergic agonists (e.g., pseudoephedrine in men)
Falls	Benzodiazepines (e.g., diazepam), anti-hypertensive agents (e.g., prazosin), antidepressants (e.g., amitriptyline), antipsychotics (e.g., chlorpromazine), cancer chemotherapy agents
Cognitive Impairment (delirium, depression, dementia)	Anticholinergics, sedatives, dopamine agonists (e.g., levodopa), antihypertensive agents (e.g., methyldopa), opiates (e.g., morphine), steroids (e.g., prednisone), digoxin, muscle relaxants

Table 3. Selected Websites for Treatment Guidelines

- | |
|---|
| • High Blood Pressure – http://www.nhlbi.nih.gov |
| • Diabetes – http://www.diabetes.org |
| • High Cholesterol - http://www.nhlbi.nih.gov |
| • Asthma - http://www.nhlbi.nih.gov |
| • Obesity - http://www.nhlbi.nih.gov |
| • Chronic Heart Failure – http://www.acc.org |
| • Coronary Heart Disease - http://www.acc.org |

degree of central nervous system side effects such as sedation or depression. Mr. Brown is receiving hydrochlorothiazide, a recommended first-line agent, in an acceptable dose. If blood pressure is not controlled with one first-line agent alone, the addition of another first-line agent should be considered in place of the clonidine patch.

Tailor Drug Therapy to the Individual

Treatment guidelines are important to enhancing therapeutic outcomes for the general population. However, guidelines are never so specific as to consider each and every individual encountered in daily practice. Tailoring therapy to an individual requires considering the patient's concomitant diseases, concomitant drugs, and wishes when developing a treatment plan. Mr. Brown is receiving two medications to lower blood pressure. However, he also has coronary heart disease as is evidenced by his prior myocardial infarction (heart attack). As a result, therapy with an angiotensin converting enzyme (ACE) inhibitor (e.g., enalapril or ramipril) and a beta-blocker (e.g., atenolol or metoprolol) is warranted. ACE inhibitors and beta-blockers are first-line therapy for hypertension and are recommended for patients with coronary heart disease, particularly those who have had a previous heart attack. Tailoring therapy in this patient could result in replacing clonidine with an ACE inhibitor or beta-blocker. The pharmacist should also encourage compliance with his cholesterol-lowering agent since Mr. Brown is at risk for another cardiovascular event, such as heart attack or stroke.

Tailoring therapy also takes into account the need to use some medications with caution. Mr. Brown was prescribed Naprosyn® for his arthritis pain. Naprosyn®, a nonsteroidal anti-inflammatory drug (NSAID), may worsen his gastric reflux and can increase blood pressure by increasing sodium

and water retention by the kidneys. In addition, advancing age is a risk factor for gastrointestinal bleeding with NSAID therapy. If Mr. Brown's arthritis pain is due to osteoarthritis, a trial of acetaminophen (Tylenol®) is warranted. Mrs. Smith (Case II) has gastric distress and has been prescribed warfarin. It would be prudent to determine if the distress has been associated with any bleeding or erosions before treatment with warfarin. Tailoring therapy for Mrs. Smith would involve a great deal of discussion regarding drug-drug interactions. Bleeding effects of warfarin can be potentiated by Tagamet HB®, Advil®, Pepto-Bismol®, high doses of ascorbic acid and vitamin E, and a variety of natural medicines. These agents prevent the metabolism of warfarin or inhibit the ability of platelets to form a clot, thereby placing the patient on warfarin at greater risk for bleeding.

Conclusion

Older individuals can derive significant benefits from appropriate pharmacotherapy. In order to optimize the benefits of drug therapy and minimize the risk of adverse medication outcomes, careful assessment of risk and benefits of drug therapy must be performed. Agents with superior safety and efficacy proven in well-designed clinical trials should be utilized. Once appropriate medication therapy is implemented, pharmacists should monitor individuals to ensure that patients receive therapeutic benefits and do not endure drug-induced illness that might be inappropriately attributed to the aging process.

COUNSELING TIPS

- Encourage adherence to medications. Never assume that the patient is convinced that they need the medication. Explain the benefits of treatment.
- Supply adherence devices and regularly monitor adherence.
- Suggest strategies that reduce potential side effects. If a significant adverse drug reaction occurs, have the patient contact the prescriber.



MANAGEMENT OF COMMON GERIATRIC DISORDERS

Alzheimer's Disease

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In recent years, more successful treatments for Alzheimer's disease have been developed. Currently, four drugs have been approved to treat it, with many more in clinical trials. Alzheimer's disease, although not yet curable, is now more readily diagnosed and treatable.

Drug therapy for Alzheimer's disease is of great interest to patients, families, loved ones, and clinicians. Not surprisingly, individuals diagnosed with probable Alzheimer's disease and their caregivers are very interested in both approved and unapproved treatments. Many individuals like Thelma Young (Case III) take prescription, nonprescription, and herbal/alternative remedies concurrently. Alzheimer's disease offers the pharmacist an opportunity to act as a consultant to patients, caregivers, and other healthcare practitioners.

What is Alzheimer's Disease?

Alzheimer's disease is a progressive neurological disease that results in extensive brain damage and impaired memory. It has a gradual onset and patients generally become aware that they are having difficulty remembering recent events, finding words, or performing tasks that were once routine. A condition called minimal cognitive impairment, characterized by mild memory impairment that has not yet reached a level of clinical significance, but is noticeable to the individual, is being studied to determine if people diagnosed with it eventually develop Alzheimer's disease. Several clinical drug trials, some using combinations of donepezil and vitamin E, are examining a possible role for drug therapy in minimal cognitive impairment.

As Alzheimer's disease progresses, patients experience changes in personality, increasing confusion, impaired judgment, and difficulty following simple directions. These changes take place at various rates in different patients, but are exemplified by a slow, steady decline. A rapid change in cognitive function strongly suggests a problem other than Alzheimer's disease. Hallucinations, delusions, Parkinson-like gait disturbances and/or seizures may appear in the later stages.

MYTHS & FACTS

MYTH: *Vitamin E improves memory.*

FACT: High doses of Vitamin E may reduce the time to nursing home placement in Alzheimer's disease, but do not appear to improve memory or cognition.

MYTH: *Alzheimer's disease can be diagnosed by imaging the brain.*

FACT: Various types of radiological imaging have improved the ability to diagnosis Alzheimer's disease by ruling out certain conditions, but today it is not possible to diagnosis it with reasonable certainty only by imaging.

MYTH: *Currently available drugs to treat Alzheimer's disease can cure the disease.*

FACT: Unfortunately there is no cure for Alzheimer's disease. Drugs may improve symptoms of the disease and appear to slow its progression.

Eventually the patient with severe Alzheimer's disease is unable to manage even basic physical functions. Death is due to secondary complications, usually an infection. Currently, the average life expectancy is about seven years from the time of diagnosis, with a range of two to twenty years.

Neurological damage caused by Alzheimer's disease is responsible for approximately 50 percent of reported dementias. A combination of Alzheimer's disease and vascular dementia (previously called multi-infarct dementia) and primary vascular dementia comprise another 25 percent. Dementia of the Lewy body type and frontotemporal dementia comprise perhaps another 15 percent. The remaining 10 percent includes Picks' disease, Parkinson's disease, Huntington's chorea, Creutzfeld-Jakob disease, and a new variant of Creutzfeld-Jakob disease commonly called mad cow disease. Thus, the term dementia does not necessarily mean the patient has Alzheimer's disease. Rather, it signifies a cluster of symptoms.

Increasingly sensitive diagnostic skills and advances in imaging and medical technology are enabling medical practitioners to identify specific dementia disorders that will improve and expand the options for treatment and research. A reversible

dementia is detected in 10–20 percent of suspected Alzheimer’s disease cases. These are most often caused by electrolyte imbalances, thyroid disorders, trauma to the head (e.g., subdural hematoma), vitamin B₁₂ deficiencies, psychiatric conditions (e.g., depression), medications, or substance abuse (e.g., alcoholism). Medications are the most common reversible cause.

What Happens to the Brain?

In Alzheimer’s disease, plaques develop first in the areas of the brain used for memory and other cognitive functions. These plaques are primarily composed of beta-amyloid, which is a fragment of a protein derived from a larger protein called amyloid precursor protein. Beta-amyloid is intermingled with portions of neurons and with other cells, such as microglia (cells that surround and digest damaged cells or foreign substances, which cause inflammation) and astrocytes (cells that serve to support neurons.) It is still not clear whether amyloid plaques themselves cause Alzheimer’s disease or whether they are a by-product of the disease process. Many researchers believe that the formation of amyloid plaques is the primary culprit.

Brains afflicted with Alzheimer’s disease show numerous clusters of degenerated nerve endings and tangles of fibers in excess of those found in the normal aging brain. These findings, which assure the diagnosis, can only be confirmed after an autopsy. In recent years, we have learned that patients with Alzheimer’s disease also suffer from a depletion of certain essential chemicals in the brain called neurotransmitters. Neurotransmitters, such as acetylcholine, serotonin, norepinephrine, and dopamine, are vital to facilitating communication between nerve cells. Acetylcholine is significantly reduced in the Alzheimer’s disease patient’s brain, leading to attempts to increase its concentration by either adding more acetylcholine or preventing its normal enzymatic destruction. Other neurotransmitters may play a role in modulating the activity of acetylcholine.

Who Is At Risk?

Over four million people in the United States have been diagnosed as having Alzheimer’s disease. Approximately 1.6 million of these patients have severe deficits, requiring daily supervision or nursing home care. The prevalence (the number of individuals diagnosed as having Alzheimer’s disease at any one time) in the 65 and older age group doubles every five years. In general, women over 75 years of age are at greatest risk for developing Alzheimer’s disease. Genetics play a role in both younger and older adults, with most cases of Alzheimer’s

disease occurring before the age of 60 displaying a significant genetic link. While Alzheimer’s disease is not just a disease of the old, the vast majority of cases are identified in people over 65 years of age. Except in specific genetically-related disorders (e.g., Down’s syndrome), Alzheimer’s disease, if it does occur, generally emerges late in life, usually after 75 years of age.

Habits of lifelong learning, male gender, estrogen supplementation, and regular NSAID use may offer some degree of protection from developing Alzheimer’s disease. Estrogen therapy does not appear to be an effective treatment for Alzheimer’s disease. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been suggested to reduce the risk of developing it, but this also remains to be proven. The pharmacist can tell Thelma Young and her husband (Case III), that as of yet, there is no evidence that ibuprofen improves memory. In fact, several clinical studies found NSAIDs are not effective to treat Alzheimer’s disease, refuting an older study of indomethacin that suggested NSAIDs might be helpful. At present, the risks of NSAID-related side effects do not warrant recommending these drugs.

Caregivers

Families or other caregivers provide most of the care for patients with Alzheimer’s disease and are usually responsible for medication management. Most recent estimates place the cost to the family at \$18,000 per year for patients diagnosed with mild Alzheimer’s disease and approximately \$37,000 per year for those suffering from severe Alzheimer’s disease. The toll on families and caregivers can be devastating, not only in financial cost, but personal costs as well. Caregivers display up to a 50 percent increased risk for depression and stress-related conditions.

An important role for pharmacists is counseling Alzheimer’s disease patients and their caregivers regarding the safe and effective use of medications. When counseling, use short sentences, avoid complicated words, be clear, be brief, and break down tasks into simple, one-step instructions. Remember that Alzheimer’s disease patients, especially early in the disease, may suffer from anxiety, depression, and irritability as well as confusion. The pharmacist should direct attention to the client (patient) as well as to the caregiver.

Drug Therapy

Over the years, numerous drugs and other agents have been used to treat senile dementia (i.e., improve memory and reduce confusion), including ergoloid mesylates

(Hydergine®), cyclandelate (Cyclospasmol®), papaverine (Pavabid®), niacin, choline hydrochloride, and lecithin. Although published research suggested many of these drugs should be effective in treating dementia, this was not generally observed in practice. Many of the early research trials used small numbers of patients, and frequently the study design was flawed. At this time, there appears to be little reason to prescribe any of these drugs for Alzheimer's disease.

Cholinesterase Inhibitors

Tacrine (Cognex®), donepezil (Aricept®), rivastigmine (Exelon®) and galantamine (Reminyl®) have been approved for the treatment of Alzheimer's disease. Their most prominent pharmacological action is to inhibit the degradation of acetylcholine in the brain. This is accomplished by inhibiting the action of acetylcholinesterase or butyrylcholinesterase, which are the primary naturally occurring enzymes that break down acetylcholine. By preventing the destruction of acetylcholine, overall brain concentrations are increased.

To date there have been no head-to-head studies comparing the efficacy of these drugs. It is important to remember that a positive response to the cholinesterase inhibitors may not be reflected in a noticeable improvement, but rather in a temporary stabilization or reduction of specific symptoms. Clinical experience suggests one-third of patients will demonstrate an observable improvement, one-third will remain stable or decline more slowly, and in one-third there will be no observable improvement and they will continue to steadily decline.

It is important to counsel patients and caregivers about the appropriate use of these agents. If any of these agents, particularly rivastigmine, is discontinued for more than three days, the dosage titration should be restarted from the beginning. Patients taking cholinesterase inhibitors should be monitored closely when they have medical conditions that might be worsened by a cholinergic drug (e.g., asthma, gastrointestinal disorders, seizures, incontinence, muscle cramps). Drugs with anticholinergic activity should be avoided whenever possible.

Tacrine (tetrahydroaminoacridine, THA, Cognex®)

Tacrine's use in medicine dates from the 1940s. It was used for a variety of medical purposes including reversal of the delirium caused by anticholinergic drugs. Cognitive function improves in about 30 percent of patients taking tacrine in doses of at least 120 mg to 160 mg per day. Unfortunately, few people tolerate these doses. Given the frequent side effects, drug interactions, need for multiple daily doses, and required testing

to avoid liver toxicity, tacrine has been replaced by newer, less problematic drugs. Tacrine served a useful purpose, however, by raising awareness that Alzheimer's disease could be treated.

Donepezil (Aricept®)

Donepezil, though modestly efficacious, represents a significant advance in the treatment of Alzheimer's disease. It is more active in the central nervous system and less so in peripheral tissues. There is good evidence that donepezil has a beneficial effect on cognition, although it has little impact on activities of daily living. It may delay the time to nursing home placement in Alzheimer's disease patients. As with other drugs in this group, gastrointestinal side effects (nausea, diarrhea, anorexia) are by far the most common adverse effects associated with donepezil. These can be minimized or avoided by increasing the dose slowly. Insomnia, usually described by patients as nightmares that awaken them, can occur. Switching the dose to the morning hours usually corrects this problem.

Given its relatively benign side effect profile and the similar costs of the 5-mg and 10-mg tablets, donepezil should be titrated to the maximum suggested dose of 10 mg per day when possible. The usual regimen is to start patients on 5 mg per day in the evening, allowing the patient/caregiver to change to a morning dose if insomnia occurs. The dosage should be increased to 10 mg per day after 4–6 weeks. A few patients will not tolerate the 5 mg per day dose and can be started at 2.5 mg per day. If so, the dose should be titrated up more slowly to the maximum dose tolerated. Dividing the dose into two daily dosages may enable patients who are encountering gastrointestinal side effects to reach a therapeutic dose.

Rivastigmine (Exelon®)

Rivastigmine, a carbamate derivative, is a long-acting, reversible, noncompetitive acetylcholinesterase inhibitor that acts on both cholinesterase and butyrylcholinesterase. In comparison, tacrine acts preferentially on butyrylcholinesterase, while donepezil inhibits acetylcholinesterase sites. The clinical importance of the different sites of action is not known. Even though it has a short half-life, rivastigmine has a rather long duration of action, which allows twice daily dosing.

A dose-related response has been identified with rivastigmine and a minimum dose of 6 mg/day is necessary for therapeutic effect. Some patients treated with doses of 6–12 mg/day experience substantial cognitive improvement. Side effects associated with rivastigmine are also dose related, with more rapid titration being associated with more adverse effects. Gastrointestinal side effects occur most commonly and include

nausea, vomiting, anorexia, and dyspepsia. Side effects are generally transient and mild to moderate in severity, unless the dose is increased too rapidly. Weight loss has been reported with rivastigmine therapy. In one clinical trial, 26 percent of women and 18 percent of men in the high-dose group experienced weight loss of 7 percent or more of their baseline body weight.

Rivastigmine is dosed twice daily, with food to reduce gastrointestinal side effects. Food reduces the peak blood level, but does not reduce the extent of absorption. Few drug interactions would be expected since rivastigmine exhibits minimal protein binding and is metabolized to only a small degree by cytochrome P450. Doses should be reduced in patients with hepatic or renal impairment, which is also true for tacrine, donepezil, and galantamine.

Galantamine (Reminyl®)

Galantamine was first isolated from the bulbs of the common snowdrop and several amaryllidaceae plants such as daffodils. It is a selective, competitive acetylcholinesterase inhibitor as well as a modulator of nicotinic receptors. This dual action may enhance the impact of acetylcholine; however, this remains to be proven. Recent clinical trials confirm galantamine's efficacy at doses of 16–24 mg/day, administered in divided doses. There are apparent benefits in cognitive, functional, and behavioral symptoms. It appears that galantamine, if titrated slowly, has tolerable side effects.

Gingko biloba

Gingko biloba is used in patients with Alzheimer's disease, both as a prescribed therapy and as a non-prescribed dietary supplement. Egb 761, an extract of gingko biloba, is the predominant form currently being investigated. While some studies have shown statistically significant benefits, these were not always apparent to clinicians. Previous studies generally used 120 mg daily in divided doses. Currently, doses of 240 mg/day of gingko biloba are being studied in a multi-site trial.

Gingko biloba has demonstrated a potent antioxidant effect and is known to possess antiplatelet activity. A possible interaction exists with other antiplatelet agents such as aspirin, clopidogrel, ticlopidine, or dipyridamole. It is prudent to advise patients that they may be at an increased risk for bleeding or bruising. Opinion differs regarding whether patients taking anticoagulants (e.g., warfarin) should also take gingko biloba. Several case reports have associated the combination with cerebral and intraocular hemorrhages. In one controlled trial, gingko biloba did not increase the

anticoagulant effect in patients stabilized on warfarin. Patients taking both gingko biloba and warfarin should be monitored closely.

Behavior Problems Associated with Alzheimer's Disease

A significant number of patients diagnosed with Alzheimer's disease will experience behavioral problems. These include hallucinations (usually visual), delusions, paranoia, depression, aggressive behavior (both verbal and physical), inappropriate sexual behavior, restlessness/wandering, and screaming. It is not uncommon for the term "agitation" to be used to describe an aberrant behavior. However, it is important for the health care provider to note exactly what the behavior is, when it occurs, what may have provoked it, and the environment in which it occurred. Some problems like wandering, restlessness, poor grooming, aggressive behavior, and mild-to-moderate agitation are best managed by careful assessment and non-drug interventions. Non-drug interventions should generally be attempted prior to initiating drug treatment. Physical, psychological, pharmacological, and environmental factors should be assessed prior to selecting drug therapy to treat the behavior. Drugs are usually not the first choice for treatment. They rarely make the behavior disappear and when effective, may only reduce the behavior by 50 percent. A variety of drugs are being prescribed, with variable success, for psychiatric behavioral problems associated with Alzheimer's disease and other dementias. (See Table 1.) Hallucinations, paranoia, delusions, severe agitation with aggressive/combatative features, and depression are more apt to respond to psychotherapeutic agents.

Case Discussion

Mrs. Young's (Case III) disturbing dreams may be the result of administering donepezil at bedtime, which is often done to spare the patient mild gastrointestinal problems that may occur when the drug is first started. Some individuals find dreams may be more vivid and not disturbing, some report no changes in their dreams, and some, as with Mrs. Young, may find the dreams disturbing. If so, donepezil should be given in the morning, which usually resolves the problem. Most OTC sleeping products contain antihistamines such as diphenhydramine or doxylamine, which have anticholinergic properties and should be avoided. If Mrs. Young's sleeping problem persists, she should be referred to her physician.

Mr. Young asks, "How fast will Aricept® work?" As noted

Table 1. Medications for Behavioral Symptoms Associated With Alzheimer’s Disease

Drug Class	Examples	Comments
Antidepressants	Fluoxetine Sertraline Citalopram Escitalopram	SSRIs are considered first-line therapy. Citalopram and sertraline may be effective in behavioral disturbances, even when depression is not present. Tricyclic antidepressants should be avoided.
Cholinesterase inhibitors	Donepezil Rivastigmine Galantamine	Case reports, uncontrolled and retrospective studies suggest possible role in management of behavior. May be drugs of choice for hallucinations in Lewy Body Type dementia.
Antipsychotics	Typical: Haloperidol Fluphenazine Atypical Antipsychotics: Clozapine Risperidone Olanzapine Quetiapine Ziprasidone	Side effects (tardive dyskinesia, extrapyramidal side effects, orthostatic hypotension) limit use. Clozapine rarely used, due to side effects. Risperidone 1mg usually effective; more side effects with 2 mg. Olanzapine 5 mg/day appears effective; 15 mg same as placebo. Risk of diabetes and some anticholinergic activity problematic. Quetiapine appears useful in Lewy Body, Parkinson’s with minimal EPS. Ziprasidone efficacy unknown, possible arrhythmias.
Antiseizure medications	Valproic acid Divalproex Carbamazepine	Mostly uncontrolled studies; appear more effective for aggression, impulse control, rare liver toxicity (adults) and thrombocytopenia. Possibly effective, but numerous drug interactions; side effects limit use.
Antianxiety drugs	Benzodiazepines Buspirone	Limit to short-term therapy for acute episodes. Choose intermediate-acting agents (lorazepam, oxazepam). Avoid long-acting agents (diazepam), except clonazepam may be useful. Side effects include increased risk of falls, impaired coordination, possible memory impairment. Lorazepam is not safer than other drugs in this class. Must be dosed consistently for 2 weeks to see benefit (not prn). Varying reports as to efficacy. Minimal side effects.

earlier, some individuals do not exhibit improvement on drugs like Aricept®. However, they do not decline as rapidly, which is considered a positive response. Mr. Young should be told to look for improved alertness, reduced apathy, and possible improvement in activities of daily living (ADLs), such as bathing, toileting, or dressing. Memory may or may not improve. Some prescribers will discontinue the cholinesterase inhibitor if improvement or stabilization cannot be identified after six months.

Neither NSAIDs (e.g., ibuprofen) nor vitamin E have demonstrated an ability to improve memory or cognition in Alzheimer’s disease. NSAIDs may reduce the risk of developing Alzheimer’s disease, but this remains to be proven. At the present time, NSAIDs should not be recommended for prevention or treatment of Alzheimer’s disease, because the risk of adverse drug reactions (e.g., gastric ulcers, bleeding) outweighs potential benefits.

Conclusion

Approximately 10 percent of people over 65 years of age suffer from Alzheimer’s disease, which increases to 47 percent in nursing home residents over 85 years of age. It is a pro-

gressive neurological disease that can burden both patients and family with emotional, financial, and social costs. Patients and families/caretakers have numerous questions regarding medications. Recent advances in drug therapy and conflicting information in both the professional and consumer media make it difficult for patients and their caregivers to make informed decisions. The pharmacist is an ideal person to answer their questions and provide advice.

COUNSELING TIPS

- Speak slowly and ask only one question at a time. If there is a need to repeat the question, repeat it exactly as first stated.
- When the patient is having difficulty expressing a thought or statement, help supply the words. Take a guess at the words, then ask if that is correct. Be patient.
- Do not openly disagree with the person. This may lead to agitation. Don’t provide too much information at one time. Don’t interrupt as Alzheimer’s disease patients can lose concentration quickly. Remember, the patient’s behavior is a result of the disease. These patients can’t improve their behavior by trying harder. In fact, the frustration may make their behavior worse.
- Remain calm. Speak in a calm voice, low and well modulated. As with any verbal interaction, the feelings you express in your voice are as meaningful as the words.

Depression

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Depression is a potentially serious medical disorder that often causes significant impairment to daily functioning and quality of life. Despite the risk of increased mortality and morbidity, depression is often underdiagnosed in the elderly. When it is diagnosed, it is often undertreated. Depression represents a major economic burden to the U.S. health care system. Annual costs related to depression are reported to be over \$50 billion, of which only 28 percent, in one analysis, were for medical treatment. The remaining 72 percent were attributable to morbidity and mortality associated with depression. Morbidity associated with a major depressive episode includes inability to manage daily living activities, decreased productivity and increased absence from work, longer stays for acute hospitalizations, prolonged rehabilitation, and worse health outcomes than for non-depressed persons. An increase in mortality is also associated with depression. The lifetime risk of death by suicide is 15 percent for patients with a history of major depression, as compared to less than 1 percent for the general population. The rate of suicide among older depressed patients, especially males, is almost twice that of the general population.

Major depression is defined as a loss of interest and/or pleasure or a depressed mood that lasts at least two weeks. Additionally, five or more of the following symptoms must be present: weight loss or gain, insomnia or hypersomnia, motor agitation or retardation, decreased energy, feelings of guilt, inability to concentrate, and thoughts of suicide. The lifetime prevalence of depression in the general U.S. population is reported to be 17 percent. The Epidemiological Catchment

MYTHS & FACTS

MYTH: *Depression is a natural part of aging.*

FACT: Depression is a medical disorder of unknown cause that may be precipitated by environmental, physiological, and/or biochemical factors. These factors, while often present in older persons, are not necessarily associated with aging or the aging process.

MYTH: *Depression that results from loss (death of a loved one, loss of job) is a normal reaction to life adversity and should not be treated.*

FACT: For some, bereavement and loss may precipitate major depression. Marked functional impairment, feelings of worthlessness, suicidal ideation, and psychomotor retardation may indicate major depression. Treatment is appropriate, especially if these symptoms persist two months after the loss.

MYTH: *If response to an antidepressant is not evident 4-6 weeks after initiation of therapy in an older patient, another antidepressant drug should be substituted.*

FACT: Response to antidepressant drug therapy in older patients occurs later than in younger patients and treatment should be continued for at least 6 to 12 weeks.

Area Study reported symptoms of depression occurred in 15 percent of community dwelling residents over the age of 65, a lower prevalence than in younger people. Higher prevalence rates (up to 42 percent) have been reported for elderly nursing home residents. Depression in elderly patients is associated with significant risk of mortality. A four-fold increase in mortality risk for depressed older adults compared to non-depressed controls has been reported. Furthermore, the presence of depression in a resident of a long-term care facil-

ity increases risk of death in the first year following admission by almost 60 percent.

Depression is often inadequately diagnosed and treated in elderly persons. This occurs even though newer, presumably safer, antidepressant drugs have become available. Barriers to diagnosing depression in older adults include the perception by clinicians, patients, and caregivers that depression is a natural part of aging. Coexistence of depression with one or more chronic diseases and disabilities, including dementia and anxiety, may mask or make the diagnosis of depression in elderly persons difficult. Medication prescribed to treat concomitant medical or neurological conditions (e.g., hypertension, pain, Parkinson’s disease, arthritis) may complicate diagnosis by causing or contributing to depression. (See Table 1.) There is also a tendency for older patients to under report psychiatric symptoms and focus instead on somatic symptoms when communicating with their medical care providers. Finally, older persons are more likely to experience losses (e.g., loss of a loved one, loss of home) and other stressors (e.g., financial difficulties) that may contribute to depression or cause depressive symptoms to be dismissed as a normal response to life adversity. However, depression in response to stressors such as bereavement and losing one’s home are not necessarily consequences of adversity and should be treated. This is especially true if depressive symptoms persist two months following the loss.

In addition to underdiagnosis of depression in elderly patients, barriers to treatment include cost of therapy for many who subsist on fixed-incomes without prescription drug insurance. Another barrier to optimal therapy is lack of studies

Table 1. Medications That May Cause or Contribute to Depression
• Carbidopa/levodopa
• Beta-blockers
• Clonidine
• Benzodiazepine
• Barbiturates
• Anticonvulsants
• H ₂ antagonists
• Alcohol
• Corticosteroids
• Interferon
• Narcotics

and data in depressed older adults, especially those in the “old-old” age group (over 85 years old). This necessitates extrapolation of treatment recommendations from experiences with younger patients. Heterogeneity in response to therapy further complicates treatment of depression in the elderly, and patients with late-onset depression (i.e., depression that first appears in old age rather than earlier ages and continuing into old age) may be more resistant to treatment. When medications are used to treat late-life depression, significant response generally takes longer to become evident, often requiring at least six to twelve weeks of therapy.

Appropriate and effective treatment of depression in the elderly, just as in younger adults, can improve signs and symptoms of depression, enhance quality of life, reduce relapse and recurrence, decrease mortality especially with respect to suicide, and lower the cost of health care. Both biological therapy (defined as drug therapy and electroconvulsive therapy), and psychosocial therapy have been shown to be effective in the treatment of late-life depression. The following discussion will focus on drugs that have been used and shown to be effective in the treatment of depression in the elderly.

Drug Therapy

Antidepressants currently available in the United States are generally considered equally effective. Antidepressants are primarily chosen based on the prescribing preference of the health care provider, their formulary status, and their side effect profiles. The most commonly prescribed are discussed below.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) were the mainstay of therapy prior to the introduction of the selective serotonin reuptake inhibitors (SSRIs) and other newer agents. Examples of TCAs are amitriptyline (Elavil®), nortriptyline (Pamelor® and Aventyl®), desipramine (Norpramin®), doxepin (Sinequan®), and imipramine (Tofranil®). The mechanism of action of TCAs includes activity with multiple neurotransmitters. They inhibit the reuptake of norepinephrine and serotonin and they also antagonize histamine, dopamine, and cholinergic receptors. The TCAs are effective for the treatment of depression, but burdened with side effects of special relevance to the elderly. Orthostatic hypotension is a serious complication of TCAs that may lead to falls. They may also delay cardiac conduction and exacerbate the risk of sudden death due to arrhythmia in persons with ischemic heart disease. Additionally, TCAs have anticholinergic side effects,



including constipation, dry mouth, urinary retention, and blurred vision. The latter two are of particular concern in men with benign prostatic hyperplasia and persons with certain types of glaucoma, respectively. Due to these bothersome and significant side effects, TCAs have fallen to second- or third-line therapy for the treatment of depression. When TCAs are considered for treatment of late-life depression, nortriptyline and desipramine are the preferred agents, because they have less anticholinergic activity.

Trazodone

Trazodone (Desyrel®) is a weak inhibitor of serotonin uptake and a norepinephrine antagonist, which causes orthostatic hypotension. Dizziness related to orthostatic hypotension and sedation caused by the drug may limit full therapeutic dosing in the elderly. Additionally, trazodone is associated with priapism (prolonged, persistent abnormal erections) that may, in rare cases, require medical intervention. Thus, trazodone is used primarily for its sedative effects at relatively low doses.

Selective Serotonin Reuptake Inhibitors (SSRIs)

The SSRIs are second-generation antidepressants that impact the serotonergic system in the central nervous system

via the selective inhibition of the reuptake of serotonin. They provide a major improvement in antidepressant tolerability, because they are safer than TCAs in an overdose and are essentially free of cardiac and anticholinergic effects (although paroxetine does have some anticholinergic activity). However, these drugs also have significant side effects, including nausea, vomiting, headache, insomnia, weight loss, and a high rate of sexual dysfunction. Products currently available in the U.S. include fluoxetine (Prozac®), sertraline (Zoloft®), paroxetine (Paxil®), citalopram (Celexa®), and escitalopram (Lexapro®).

The SSRIs are all given as a single daily dose, in the morning or at bedtime. Fluoxetine has a long half-life and, therefore, may take up to six weeks to be completely eliminated from the body. They affect the cytochrome P450 hepatic enzyme system, which leads to potential drug-drug interactions. Fluoxetine and paroxetine have the greatest potential to inhibit the metabolism of other medications through their effect on this enzyme system. Sertraline, citalopram, and escitalopram are also metabolized by this enzyme system, but have much less impact on the metabolism of other drugs. Fluoxetine has been associated with elevated INRsⁱ in persons previously stabilized on warfarin therapy. Additionally, all of the SSRIs have been associated with changes in platelet function and abnormal bleeding in individuals not taking anticoagulants.

Venlafaxine (Effexor®)

In addition to inhibiting serotonin reuptake, venlafaxine also inhibits norepinephrine reuptake at doses above 150 mg/day. At high doses, it also inhibits the reuptake of dopamine. Venlafaxine is effective; however, it requires multiple daily dosing. A sustained-release product, Effexor XR®, allows once daily dosing. At higher doses, venlafaxine causes a predictable elevation in blood pressure in nine percent of patients.

ⁱINR refers to International Normalized Ratio, the common laboratory test for blood clotting.

Mirtazapine (Remeron®)

Mirtazapine is an alpha-2 antagonist that leads to increased concentrations of central norepinephrine. Mirtazapine also has activity at the cholinergic and histamine-1 receptors, which explains its side effect profile. It is sedating, causes weight gain, and has several anticholinergic side effects similar to the TCAs. However, mirtazapine does not significantly affect cardiac conduction. The combined use of clonidine, an antihypertensive central alpha-2 agonist, and mirtazapine may lead to hypertensive urgency, which can result in stroke and/or death. Similar drug interactions have been reported with TCAs and clonidine.

Bupropion (Wellbutrin®)

Bupropion is thought to produce an antidepressant effect via the relatively weak inhibition of norepinephrine, serotonin, and dopamine reuptake. It is effective and well tolerated in the elderly. Bupropion has been studied in elders with significant cardiac disease and has been shown to be safe and effective. Its use is limited by a significant seizure risk; thus it is contraindicated in persons diagnosed with a seizure disorder. Doses must be limited to not more than 150 mg per dose and 450 mg per day (400 mg per day for the sustained-release product) to minimize seizure risk. Bupropion is also associated with agitation and insomnia; therefore, the last dose of the day should be given in the late afternoon. It has little or no impact on sexual function. Ritonavir, an antiviral medication used in the treatment of HIV/AIDS, inhibits the metabolism of bupropion, resulting in large increases in serum bupropion levels. Because of the increased risk of seizures, this combination should be used cautiously, if at all.

Nefazodone (Serzone®)

Nefazodone is structurally related to the first generation antidepressant trazodone. Its mechanism of action is weak inhibition of serotonin reuptake and weak antagonism of norepinephrine. There are limited data regarding the use of nefazodone in the elderly. Nefazodone, like trazodone, also causes sedation and dizziness, which may limit full therapeutic dosing in the elderly. It has been associated with significant liver toxicity leading to liver transplant or death. Although rare, the severity of this reaction warrants increased caution. Nefazodone should not be initiated in persons with underlying liver disease and patients taking the medication should be counseled to watch for the symptoms of liver dysfunction (jaundice, anorexia, gastrointestinal complaints, malaise, dark-

ening of the urine) and to notify their healthcare provider immediately if any of these occur. Due to the risk of hepatotoxicity, nefazodone is considered -third or fourth-line therapy. Additionally, nefazodone inhibits the cytochrome P450 3A4 enzyme, resulting in its inhibition of the metabolism of several drugs (e.g., benzodiazepines, cyclosporine, statins).

St. John's Wort

No discussion of the treatment of depression today is complete without mention of St. John's Wort (*Hypericum perforatum*). This popular herbal product inhibits the reuptake of serotonin, norepinephrine, and dopamine. St. John's Wort has been beneficial in the short-term treatment of mild-to-moderate depression. However, it is not effective in the treatment of severe depression. St John's wort induces cytochrome P450 isoenzymes 3A4 and 2C9 and can significantly reduce plasma levels and activity of cyclosporine, warfarin, protease inhibitors, digoxin, and other drugs.

Pharmacotherapeutic Considerations

Product Selection

All of the antidepressant drugs currently marketed in this country are equally effective in the treatment of geriatric depression. However, not all patients will respond uniformly to all agents. Among the drug therapy options, the second-generation agents (SSRIs, venlafaxine, bupropion) have fewer undesirable effects in older patients (e.g., dry mouth, urinary retention, sedation) than first-generation agents (e.g., TCAs, trazodone). Some adverse effects, such as orthostatic hypotension, may be associated with both first- and second-generation agents. The potential for drug-drug interactions also exists for the first-generation tricyclic agents and some of the second-generation antidepressant drugs.

Dose and Duration of Therapy

The potential to undertreat the elderly with depression should not be overlooked. Pharmacokinetic studies for several antidepressants (e.g., nefazodone, citalopram, paroxetine, bupropion) demonstrate age-related decline in the elimination rates of these agents. This highlights the importance of starting with a low dose and titrating up slowly. Clinical trials indicate that standard doses of antidepressants are well tolerated in the elderly and all efficacy studies in the elderly have utilized standard target doses. Drug therapy should be reassessed on a routine basis for both efficacy and side effects. If

side effects emerge, dose reduction, slowing the rate of dose escalation, or changing to a different medication may be appropriate. Persons who fail to respond to one antidepressant may benefit from a trial of an alternative antidepressant within the same class or in a different class.

In general, older depressed patients take longer to demonstrate a response to drug therapy than younger patients. Twelve weeks of drug therapy may be necessary to see a response in some elderly patients. Older patients should be treated for a minimum of six to twelve weeks (instead of the usual four to six weeks) before a determination of therapeutic failure or decision to change to another treatment agent or modality is made.

Maintenance therapy in the pharmacological treatment of depression should extend for at least six months beyond the resolution of symptoms, because earlier discontinuation leads to high recurrence rates. Persons who have experienced more than one previous episode of depression may be candidates for life long therapy. The decision to continue or discontinue maintenance therapy must be weighed by the patient and healthcare provider, taking into account the impact on quality of life.

Serotonin Syndrome

Serotonin syndrome is a severe adverse reaction characterized by irritability, increased muscle tone, shivering, myoclonus (involuntary muscle twitching or spasms), and altered consciousness. Many of the antidepressants discussed above modify serotonin concentrations in the central nervous system as part of their proposed mechanism of action. These agents can induce rapid accumulation of serotonin in the central nervous system when used in combination (e.g., monoamine oxidase inhibitors with other antidepressants) or when co-administered with other serotonergic agents (e.g., selegiline [Eldepryl®], St. John's Wort, sumatriptan [Imitrex®], zolmitriptan [Zomig®]). The antidepressants most frequently linked with serotonin syndrome are monoamine oxidase inhibitors, SSRIs, and venlafaxine. If the reaction occurs, discontinue the offending agent and provide supportive medical care.

Case Discussions

Mrs. Smith (Case II) illustrates several points related to depression. First, her antidepressant is an SSRI, which is the drug class of choice for first-line therapy because of its minimal cardiac and anticholinergic side effects. However, fluoxetine (Prozac®) has been reported to increase the effect of

warfarin (Coumadin®), increasing the risk of bleeding. Fluoxetine inhibits the enzyme (CYP 3A4) responsible for the metabolism of warfarin and also impairs platelet function. Both effects may lead to bleeding. Since she has already been stabilized on the antidepressant, her anticoagulation provider will likely adjust for this drug interaction. Choosing an alternative SSRI (e.g., sertraline or citalopram) is another option, but impractical. It takes five to six weeks for Prozac® to be eliminated from the body and a similar amount of time for the new agent to become effective. Finally, Mrs. Smith has selected an over-the-counter product, Cimetidine (Tagamet HB®), which may contribute to her symptoms of depression. A pharmacist, working in conjunction with her primary care provider, can optimize Mrs. Smith's pharmacotherapy.

Conclusion

Despite the serious consequences of decreased quality of life and increased risk of suicide, depression is underdiagnosed in the elderly. A number of barriers to the diagnosis of geriatric depression exist, the most insidious being the general perception that depression occurs as a natural part of aging. When diagnosed and appropriately managed, depression in the elderly is highly treatable. Although electroconvulsive and psychosocial therapy are effective, pharmacotherapy remains the cornerstone for treating depression in the elderly.

COUNSELING TIPS

- Advise elderly patients how and when to take their prescribed antidepressant.
- Be sure to rise slowly from a supine position when taking nortriptyline, doxepine, trazodone, or mirtazapine, to minimize orthostatic hypotension and dizziness.
- Sedating antidepressants, such as trazodone or nefazodone, are best taken at bedtime.
- Activating antidepressants, such as sertraline or bupropion, are best taken when the patient is normally awake.
- Discuss how long to take the drug. Response to therapy may not be seen for up to twelve weeks in older patients. Patients should continue the drug for at least that length of time, even if they feel they are not receiving benefit from it. Depending on the onset of symptoms and number of previous major depressive episodes, duration of therapy may vary.
- Caution patients against abrupt withdrawal of prescribed antidepressant therapy. This could produce symptoms similar to those of serotonin syndrome (e.g., agitation, insomnia, sweating, restlessness, seizures).

Osteoarthritis Pain

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Pain is the most common reason that patients visit their healthcare providers. Acute pain usually has a cause and usually resolves. Chronic pain, also referred to as persistent pain, is an individual's unpleasant sensory or emotional experience that continues for a prolonged period of time and may or may not be associated with a recognizable disease. Osteoarthritis, also called degenerative joint disease, probably accounts for more than two-thirds of pain complaints among older adults and, thus, is the focus of this article. Pain is a highly subjective, personal experience for which there are no objective tests. Persistent pain can impair a person's ability to perform daily activities and decreases quality of life. Elderly patients expect pain as they age; thus, they may be reluctant to complain or report it fearing an unfavorable medical evaluation and treatment side effects. Significant persistent pain may result in anxiety, depression, insomnia, difficulty concentrating, decreased ability to exercise, and inability to enjoy usual activities.

Older people are more likely to suffer from diseases that cause pain. An estimated 21 million Americans (women more commonly than men), most of whom are older than age 45, are affected with osteoarthritis. It is the most common form of arthritis in this country and is also one of the most expensive and debilitating diseases. It results in more than 7 million physician visits per year and the cost to the U.S. economy is nearly \$65 billion per year in expenses, lost wages, and productivity. Osteoarthritis of the knee can be as debilitating as any cardiovascular disease, with the exception of stroke.

There are many risk factors for developing osteoarthritis. Age and obesity may lead to osteoarthritis of the knees and lower joints. People with joint injuries due to sports, accidents, or work activity may be at increased risk of developing osteoarthritis. Discomfort usually results from breakdown of cartilage, which is the part of the joint that provides a cushion between the ends of bones. As the cartilage erodes, the bones rub against each other causing pain and loss of movement. Osteoarthritis pain typically worsens with weight bearing activity and improves with rest. The most commonly involved joints include the knees, hips, feet, ankles, and the joints near

MYTHS & FACTS

MYTH: *Nonsteroidal anti-inflammatory medications are the safest and preferred medications to treat mild-to-moderate osteoarthritis pain in older adults.*

FACT: There is often little inflammation with osteoarthritis. Acetaminophen is the recommended first-line agent for mild-to-moderate arthritis pain.

MYTH: *Opioids should not be used for moderate-to-severe non-cancer pain in the elderly.*

FACT: Opioids are recommended for moderate-to-severe pain when other medications and non-pharmacologic interventions provide inadequate pain relief and the patient's quality of life is affected by the pain.

MYTH: *Elderly patients who take opioids for chronic non-cancer pain will become addicted in days to weeks.*

FACT: Patients taking opioids regularly for pain may become physically dependent, but addiction is rare. The pharmacist should be able to distinguish between physical dependence and addiction.

the fingertips. Patients often experience morning stiffness, tenderness, bony enlargements, and/or limited joint motion of the affected area(s). Unlike rheumatoid arthritis, inflammation is usually mild and localized to the affected joint(s).

Treatment Strategies

There is no known cure for osteoarthritis. Treatment focuses on decreasing pain, improving joint mobility, and improving quality of life. Recommended treatment strategies include:

- Exercise to keep joints flexible and to improve muscle strength and mobility
- Analgesic or pain medications
- Heat or cold therapy for temporary pain relief
- Joint protection to prevent strain or stress
- Weight control to minimize extra stress on joints

Other non-pharmacologic treatment strategies include physical and occupational therapy (strengthening exercises and rest), assistive devices such as braces and footwear, traction to immobilize joints, and transcutaneous electrical nerve

stimulation to alleviate pain. Surgical treatment is considered when drug therapy is ineffective or function is severely impaired, before severe deformity develops.

Drug Therapy

Pharmacologic therapy should be combined with non-pharmacologic strategies to optimize pain management. Pharmacologic management usually involves the use of analgesic medications. Generally, acetaminophen is the first-step drug. Patients should expect pain relief, but it may not be realistic for them to expect to be completely pain free. Analgesic medications are generally as safe and effective in older adults as in younger patients. However, two patients rarely respond in the same way to medications, so therapy should be tailored to the individual. There may be health, dosing, and side effect variables to consider in older adults.

A fundamental principle of treating persistent pain, which applies to osteoarthritis, is to use pain medications on a regular schedule to provide continuous pain relief. Long-acting medications that only need to be taken once or twice daily may improve adherence to the regimen. The use of as-needed medications should be reserved for intermittent pain or exacerbations of pain. The goals of treatment should be to decrease the patient's pain and improve function, mood, and sleep. Older adults are more likely to experience the side effects of pain medications and they also appear to be more sensitive to their pain relieving effects, thus, a low starting dose is generally recommended. The exception is acetaminophen, which can be started at regular doses for moderate pain.

Acetaminophen

Acetaminophen (up to 4,000 mg daily in divided doses) is the drug of choice for mild-to-moderate arthritis pain. Patients who drink more than two alcoholic beverages a day or have liver disease should reduce the dose to a maximum of 2,500 mg per day. Tylenol Long Acting® (650 mg per tablet) dosed every eight hours may offer some individuals an easier regimen.

Non-acetylated Salicylates

Non-acetylated salicylates offer a viable alternative to acetaminophen or nonsteroidal anti-inflammatory medications. Salsalate (Disalcid®) 500 mg three or four times daily may be increased to 1,000 mg three or four times daily if necessary. Another product, choline/magnesium trisalicylate (Trilisate®), is available as a tablet or liquid, and should be taken in doses of 500 mg to 1,500 mg every 8 to 12 hours, up to a maximum dose of 5,500 mg per 24 hours. Nonacetylated salicylates have fewer gastrointestinal side effects and are less likely to impair kidney function, as compared to NSAIDs. Unlike aspirin and

the NSAIDs, they do not affect platelet function. The non-acetylated salicylates are relatively safe and are less expensive alternatives to COX-2 NSAIDs.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and naproxen are commonly used for moderate-to-severe arthritis pain. Older adults seeking relief from osteoarthritis pain take an estimated 50 percent of all NSAIDs produced. All NSAIDs should be used cautiously in persons with hypertension or edema. Some patients may benefit from taking non-specific NSAIDs together with a medication to prevent GI bleeding (e.g., misoprostol or a proton pump inhibitor). NSAIDs should be used with caution in the elderly. High-dose, long-term NSAIDs use should be avoided and when used chronically, NSAIDs should be dosed on an as-needed rather than an around-the-clock basis. They should also be avoided in patients with a history of peptic ulcer disease or impaired renal function. Avoid the use of more than one NSAID at a time.

COX-2 Inhibitors

The selective cyclo-oxygenase (COX-2) inhibitors (celecoxib, rofecoxib) should be considered when NSAIDs are indicated in the elderly, because they have less potential for gastrointestinal side effects. The COX-2 NSAIDs have minimal effects on platelet aggregation, so if a patient is taking low dose aspirin for heart or stroke prevention, it should be continued. When COX-2 NSAIDs and aspirin are used together, there is probably a similar risk for GI bleeding as with non-selective NSAIDs. The American Geriatrics Society recommends non-acetylated salicylates as relatively safe and less expensive alternatives to COX-2 NSAIDs.

Tramadol

Tramadol (Ultram®), a centrally-acting analgesic, may be used alone or in combination with acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs). Tramadol should be started at low doses (50 mg every 4-6 hours) and increased slowly to minimize side effects such as drowsiness and nausea in the elderly. The maximum dose recommended in the elderly is 300 mg daily in divided doses, which should be decreased in the presence of kidney or liver disease.

Opioids¹

Opioid medications such as oxycodone, morphine, hydrocodone, or other mu-receptor agonists, are recommended for moderate-to-severe arthritis pain for which other treatments do not provide substantial relief. Extensive experience

¹Opioid refers to a pain medication class that is similar to or derived from morphine. This class is often referred to as "narcotic," but this is a legal term for controlled substances that are not specific to pain medications.



and evidence supports the use of long-acting opioids to improve patient adherence, minimize medication blood level peaks and valleys, and to minimize side effects when managing cancer pain. These advantages also appear to apply in the management of arthritis pain. Although the literature supports the use of opioid analgesics to treat moderate-to-severe chronic non-cancer pain, these drugs continue to be underused. Reluctance to prescribe or administer opioids (as well as patient and family reluctance to use them) may be unduly influenced by fear of addiction and side effects as well as social pressure to control illicit drug use. Although the true rate of addiction among chronic pain patients is not established, addictive behavior among elderly patients taking opioid drugs for medical reasons is reportedly low. The use of codeine and propoxyphene should be avoided because of their side effects and limited efficacy.

Glucosamine

Glucosamine sulfate is a synthetic version of a bodily substance that helps to make cartilage. The American Pain Society recommends that adults with osteoarthritis be encouraged to take 1,500 mg of oral glucosamine sulfate daily. A recent study compared 1,500 mg of oral glucosamine versus a placebo for three years in osteoarthritis patients. Glucosamine decreased pain and improved physical function by about 20-25 percent, as compared to the placebo. By X-ray examination, the cartilage remained stable in those patients taking glucosamine and shrank in the group taking a placebo, suggesting worsening of arthritis in the placebo group.

Chondroitin

Chondroitin sulfate, another dietary supplement, may stimulate production of cartilage and has been shown in a small number of trials to improve pain and function with daily use. The effects usually take weeks to months to occur. There are preparations containing both glucosamine and chondroitin, but no long-term studies have shown the combination to be superior to either agent alone.

Case Discussions

When counseling Mr. Brown (Case I), the pharmacist should ask about his arthritis pain and how often he takes his Naprosyn®. If Mr. Brown is taking his Naprosyn® one or two times a day with good relief, he may be a candidate for acetaminophen. Since he is also taking Zantac®, he may have GI distress. Acetaminophen is preferred, because of the potential for GI bleed with NSAIDs. The COX-2 inhibitors may not have the advantage of a lower risk for GI bleed in Mr. Brown, because he takes low-dose aspirin for its anti-platelet effects. Low dose aspirin offsets any GI protective effect of the COX-2 inhibitors. If Mr. Brown is experiencing moderate-to-severe pain despite the use of a nonsteroidal analgesic or if he is experiencing GI distress from his NSAID, he could be a candidate for opioid therapy in combination with acetaminophen. Opioid therapy should be initiated with the lowest dose of a short-acting drug given on a scheduled basis. Often an initial dose at bedtime may be helpful with sleep and may allow the patient to sleep through any side effects. Mr. Brown should not be taking a long-acting benzodiazepine (e.g., diazepam) with the opioid.

If an opioid is initiated, Mr. Brown should also be asked about any history of constipation. He should be reminded to drink plenty of water and exercise as permitted by his physician. He may consider taking a stimulant laxative (e.g., senna, bisacodyl) and a stool softener to avoid or minimize opioid-induced constipation. If his fluid intake is adequate, bulk forming laxatives may be considered. Stool softeners alone are rarely, if ever, effective in managing opioid-induced constipation.



tion. Mr. Brown is also on the diuretic hydrochlorothiazide and a Catapres® patch, which can both also cause constipation.

Mrs. Smith (Case II), who is already taking a COX-2 inhibitor (Vioxx®), is purchasing Advil®. Because Advil® has effects on platelet aggregation and can affect bleeding time, it should not be taken with her Coumadin®. She, too, should be questioned about her pain relief from the Vioxx® and why she needs the Advil®. Acetaminophen is the preferred agent for treating mild-to-moderate pain. If her arthritis pain is not relieved by her Vioxx®, Mrs. Smith may also be a candidate for an opioid. She seems to be having some GI distress, because she plans to supplement her Prilosec® with OTC Tagamet® and Pepto-Bismol®. Use of a chronic opioid would decrease her risk for GI bleed and drug interactions. She should be monitored carefully, as an opioid could exacerbate depression.

Conclusion

The elderly may suffer from significant pain of different origins. Pain is not normal and should not be expected to occur with aging. Patients should be encouraged to discuss their pain with their primary care providers and the underlying causes should be treated if possible. There are a variety of

medical interventions available to minimize the pain and disability caused by osteoarthritis, resulting in improved physical function and quality of life.

COUNSELING TIPS

- Encourage scheduled use of pain medications for osteoarthritis. One exception is nonsteroidal anti-inflammatory agents, which when taken, should be dosed on an as-needed basis.
- When an elderly patient is taking an NSAID, ask about a history of peptic ulcer, GI bleed, and stomach distress. Evaluate aspirin and other NSAID intake from nonprescription drugs.
- When a COX-2 NSAID is started for a patient's pain, ask the patient if he or she is to continue taking low dose aspirin to prevent cardiac events. Generally, the low dose aspirin should be continued since COX-2 inhibitors do not affect platelet aggregation.
- When a patient is started on an opioid, discuss the possibility of constipation. Patients do not usually become tolerant to this side effect. Recommend adequate fluid intake, appropriate exercise, and possibly a prophylactic stimulant laxative.

Diabetes

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Diabetes is a condition that affects the body's ability to produce or respond to insulin, a hormone that allows blood sugar (glucose) to enter the cells of the body and be used for energy. This results in a high blood glucose level. Over time, diabetes can be associated with serious complications, such as heart, eye, kidney, and nerve disease. Nearly 17 million Americans have diabetes, representing approximately six percent of the population. The majority of people with diabetes have type 2 diabetes (formerly called non-insulin dependent diabetes or adult-onset diabetes), whereas approximately 1 million people have type 1 diabetes (formerly called insulin-dependent diabetes or juvenile-onset diabetes). Approximately, one-third of people with type 2 diabetes are undiagnosed. As people get older, the prevalence of type 2 diabetes increases; over 20 percent of people age 65 or older and 18 percent of nursing home residents have diabetes. Diabetes costs the U.S. over \$98 billion annually, with people age 65 or older accounting for two-thirds of these costs. The annual per capita expenditure for a person with diabetes is four-fold that of a person without diabetes. Table 1 lists risk factors for diabetes other than aging.

Recognizing Diabetes

Mrs. Smith (Case II) is experiencing symptoms consistent with diabetes. She complains of thirst, blurred vision, and increased urination during the night. Common symptoms of diabetes include frequent urination (polyuria), excessive thirst (polydipsia), extreme hunger (polyphagia), unusual weight loss, increased fatigue, blurry vision, and irritability.

While people with type 1 diabetes tend to develop these symptoms abruptly and severely prior to diagnosis, people with type 2 diabetes often develop them more gradually and less severely. As a result, people tend to attribute their symptoms to other causes. For example, the elderly may attribute vision problems, increased need to urinate, and fatigue with general signs of aging, and may not seek medical care. Also,

MYTHS & FACTS

MYTH: Only people on insulin need to monitor their blood glucose.

FACT: People with diabetes that monitor their blood glucose can better self-manage their diabetes. People taking an oral medication that can cause hypoglycemia (e.g., a sulfonylurea, repaglinide, and nateglinide) should self-monitor their blood glucose.

Table 1. Major Risk Factors for Developing Type 2 Diabetes

Table 2. American Diabetes Association Glycemic Goals

Index	Normal	Goal	Additional Action Suggested
Premeal glucose (mg/dL)			
Blood	<100	80-120	<80 or >140
Plasma	<110	90-130	<90 or >150
Bedtime glucose (mg/dL)			
Blood	<110	100-140	<100 or >160
Plasma	<120	110-150	<110 or >180
A1C (%)	<6	<7	>8

Note: A1C is referenced to a non-diabetic range of 4-6 percent.

hyperglycemia may be less symptomatic in the elderly since the renal threshold for glycosuria (spilling of glucose into the urine) increases with age. Typically the renal threshold is an ambient blood glucose of 180 mg/dL. This can increase to over 270 mg/dL in the elderly, meaning one would not experience the symptom of increased urination until the blood glucose level reached levels greater than 270 mg/dL.

Treatment Goals for Diabetes

The overall treatment goals set forth by the American Diabetes Association (ADA) are categorized in Table 2. The ADA's Standards of Care appear in Table 3. Recently, the American Association of Clinical Endocrinologists released tighter goals than the ADA, recommending the A1Cⁱ to be <6.5 percent, fasting plasma glucose <110 mg/dL, and a 2-hour post-meal glucose of <140 mg/dL. Plasma glucose concentrations are 10-15 percent higher than blood glucose concentrations. Thus, it is important to know whether the glucose monitor being used by the patient reads out plasma or blood values in order to interpret the readings properly.

Metabolic goals must be individualized. For patients with advanced diabetes complications, life-limiting co-morbid illness, or cognitive or functional impairment, the ADA states it is reasonable to set higher target goals. Glycemic goals are

the targets for the glucose levels and the A1C. The A1C reflects the average blood glucose over the past 2-3 months. An A1C of 6 percent reflects an average blood glucose of approximately 120mg/dL; 7 percent and 8 percent are 150mg/dL and 180mg/dL, respectively. Thus for each 1 percent increase in the A1C, the average blood glucose rises by approximately 30 mg/dL. If the A1C is greater than 8 percent, additional action is recommended by the ADA (i.e., modifying the treatment plan to improve the glycemic control).

Support for these glycemic goals came from the United Kingdom Prospective Diabetes Study (UKPDS), which assessed whether intensive treatment reduced the development of complications over a ten-year period. The people in the intensive group (sulfonylurea, metformin, or insulin) had an A1C 0.9 percent lower than the standard group (lifestyle interventions), which resulted in a 25 percent reduction in the microvascular complications of diabetes (i.e., eye and kidney disease). For every 1 percent reduction in the A1C there was a 35 percent reduction in developing microvascular complications. Although a reduction in the cardiovascular complications was observed (specifically a 16 percent reduction in the risk of heart attack and sudden death), it did not reach statistical significance.

While the UKPDS provided good evidence of the need for improved glycemic control, intensive treatment had disadvan-

Table 3. American Diabetes Association Standards of Care

Procedure	Frequency	Goal
A1C	2-4 times/year (twice a year if treatment goals are met; otherwise quarterly)	<7%
Lipids	yearly	LDL-C ≤100 mg/dl TG <150 mg/dl HDL-C ≥45 mg/dl in men HDL-C ≥55 mg/dl in women
Urine albumin	yearly	Negative (normal is < 30 mg albumin/gm creatinine)
Blood Pressure	each medical visit	<130/80 mm Hg
Dilated eye exam	yearly	no retinopathy
Influenza vaccine	yearly	no infection
Pneumococcal vaccine	at least once ¹	no infection
Foot examination	yearly (comprehensive); each medical visit (visual)	no ulcerations; those at risk should self-inspect feet daily
Dental exam	twice yearly	no periodontal disease
Self-Monitoring of Blood Glucose (SMBG) ²	individualized	detect hypoglycemia; include in self-management program

¹ A one-time revaccination is recommended for people >64 years of age if previously vaccinated at age <65 years and administered more than 5 years ago.

² Medicare covers testing supplies (strips, lancets, meters) whether or not one uses insulin. A physician needs to prescribe the blood glucose testing supplies and document how often to test the BG on the prescription.

ⁱOlder names for A1C were glycosolated hemoglobin or hemoglobin A1C.

tages: more weight gain (~6 pounds) and hypoglycemic episodes (1.4 percent versus 0.7 percent). Also, the mean age of participants in the UKPDS was 54 years and none was over the age of 65. Thus, clinical trial data is still lacking for the elderly. In light of this, the ADA glycemic goals need to be tailored to the individual.

Treatment Options for Diabetes

The six classes of oral medications for type 2 diabetes are listed in Table 4. The first three, which stimulate insulin release from the pancreas, are referred to as insulin secretagogues.

While the available medications provide various treatment options, they have led to confusion among health care providers and patients about which one to start first and which combinations are rational. Many practitioners use a stepped-care approach to managing type 2 diabetes, as is done with hypertension.

Step 1. Lifestyle Changes: Diet, Exercise, and Management of Cardiovascular Risk Factors

Diet and exercise are essential components to managing diabetes. Even if a person requires medication, this step remains. A complete discussion of medical nutrition therapy is beyond the scope of this article. However, a few basic principles can be followed. It is important that a meal plan be tailored to the individual and is realistic for that person, taking into account cultural and socioeconomic factors. Initial referral to a dietitian, if possible, is extremely useful. Spacing of meals, particularly balancing and spreading carbohydrate intake throughout the day, is one simple strategy.

Carbohydrates are converted to glucose in the body. Therefore, it is not only the obvious sources of glucose (candy,

cola, sweets) that increase the blood glucose, but the carbohydrates that one eats. A few examples of high carbohydrate foods are: potatoes, rice, tortillas, bread, pita bread, pasta, cereal, starchy vegetables (corn and green peas), fruit, and milk. Many people with type 2 diabetes are overweight. Even a moderate weight loss (e.g., 10-20 pounds) can reduce blood glucose levels significantly and improve blood pressure and cholesterol. While many weight-loss methods exist, one that reduces saturated fat intake and includes some type of regular physical activity (such as walking) is most often effective.

If a person smokes, she/he should be strongly advised to quit and be referred for tobacco cessation counseling. The ADA recommends people with diabetes who have heart disease, or those at risk for it, also take an enteric-coated aspirin daily (81-325 mg a day). People with diabetes at high risk for heart disease are those with a family history; smoke cigarettes; have hypertension, kidney disease, or a cholesterol disorder; are obese; and are over 30 years of age. Mr. Brown (Case 1) has already had a heart attack, so he appropriately takes an aspirin daily to prevent another one from occurring.

Step 2. Single Oral Medication (Added to Diet and Exercise)

When diet and exercise are no longer sufficient to maintain glycemic goals, a single oral medication may be added. All oral type 2 medications are options. Metformin (Glucophage®) is often used in overweight patients, since it does not cause weight gain. Sulfonylureas, repaglinide (Prandin®), and nateglinide (Starlix®) can all cause weight gain. Since the thiazolidinediones require liver monitoring every other month for the first year, they are often reserved for combination therapy.

Table 4. Oral Agents for Type 2 Diabetes

Class	Drug(s)	Primary Mechanism of Action
Sulfonylureas	glyburide (Micronase®, DiaBeta®) gliipizide (Glucotrol®) glimpiride (Amaryl®) tolazamide (Tolinase®) tolbutamide (Orinase®)	stimulation of insulin release from the pancreas
Meglitinides	repaglinide (Prandin®)	stimulation of insulin release from the pancreas
Amino-acid derivatives	nateglinide (Starlix®)	stimulation of insulin release from the pancreas
Biguanides	metformin (Glucophage®)	reduction of glucose output from the liver
Alpha-glucosidase inhibitors	acarbose (Precose®) miglitol (Glyset®)	delayed digestion and absorption of carbohydrates from the meal
Thiazolidinediones	pioglitazone (Actos®), rosiglitazone (Avandia®)	reduction of insulin resistance in the body



Special Considerations in the Elderly

Kidney and Liver Function

When selecting a type 2 diabetes medication for an elderly person, the kidney and liver function need to be assessed. Certain sulfonylureas are preferred in the elderly because they are metabolized to compounds with negligible activity (e.g., glipizide, tolbutamide), have a shorter duration of action (e.g., tolbutamide) or have been studied in patients with kidney problems (e.g., glimepiride). Longer acting sulfonylureas or those with active metabolites (e.g., glyburide, chlorpropamide) should be avoided because of an increased risk of hypoglycemia. Because repaglinide (Prandin[®]) and nateglinide (Starlix[®]) have a very short duration of action and have been studied in patients with reduced kidney function, these may also be preferable.

Pioglitazone (Actos[®]) and rosiglitazone (Avandia[®]) may be used in patients with reduced kidney function, but not in those with liver problems. Acarbose (Precose[®]) and miglitol (Glyset[®]) should be avoided in patients with severe kidney impairment (serum creatinine >2.0 mg/dL). Severe kidney impairment can cause injected insulin to last longer, so people on insulin therapy may require a reduction in their insulin doses.

Metformin (Glucophage[®]) should not be used in patients with kidney or liver problems. It should also not be used if a person has congestive heart failure requiring medications or has an acidotic condition. Metformin (Glucophage[®]) is predominantly eliminated from the body by the kidneys, so reduced kidney function will result in its accumulation and increase the risk for lactic acidosis. Lactic acidosis, a very rare side effect (approximate incidence is 1/33,000), can be life threatening. Metformin (Glucophage[®]) should not be used in men or women with serum creatinine concentrations of ≥ 1.5 mg/dL or ≥ 1.4 mg/dL, respectively. In elderly patients, an estimate of creatinine clearance (using the Cockcroft and Gault equation described in the previous article, Altered Drug Action With Aging) may be a better and earlier indicator of reduced kidney function. Metformin (Glucophage[®]) should be avoided in patients with a creatinine clearance <60 ml/min. It should also not be used in patients who are >80 years unless their creatinine clearance suggests that kidney function is not significantly impaired. Other predisposing factors for lactic acidosis include shock, acute heart attack, liver failure, surgery, severe infection, an illness that causes severe dehydration, and excessive alcohol ingestion.

Step 3. Combination Oral Medications

When single oral therapy is no longer sufficient to achieve glycemic goals, a second medication can be added for additional blood glucose lowering. The key is to combine medications that work at different sites. Triple therapy may also be useful if two oral agents are inadequate.

Step 4. Oral Medication Therapy Plus Insulin

Over time, as type 2 diabetes naturally progresses, the pancreas produces less and less insulin. The UKPDS demonstrated that additional drug therapy was needed every four to six years, on average. Insulin can be added to oral therapy.

Step 5. Insulin Alone

Many people with type 2 diabetes are on insulin alone to control their diabetes. Some people who are on insulin alone were never tried on the newer oral agents such as metformin (Glucophage[®]) or a thiazolidinedione. In these cases the addition of oral medication may enhance glycemic control and reduce the daily insulin requirement.

Eating Habits

People who have irregular eating habits or skip meals are at increased risk for hypoglycemia if taking a sulfonylurea. A short-acting agent, such as tolbutamide, repaglinide (Prandin®) or nateglinide (Starlix®), is preferable in such patients who require an insulin secretagogue.

Hypoglycemia

The ability to self-monitor blood glucose (SMBG) is an important consideration in the selection of the pharmacologic regimen for an elderly person. If a regimen may cause hypoglycemia, a person should SMBG. Of the sulfonylureas, tolbutamide, glipizide, and glimepiride have been associated with lower incidences of hypoglycemia. Although metformin (Glucophage®) should not cause hypoglycemia when used alone, hypoglycemia can occur when it is combined with other medications.

Intensive therapy may increase the incidence of hypoglycemia, as demonstrated in the UKPDS. In the elderly, hypoglycemia (blood glucose <70 mg/dL) is of special concern, because, over time, some people may not recognize the symptoms of hypoglycemia. This can delay treatment of low sugar reaction (hypoglycemic episode). Thus, if a patient has hypoglycemia unawareness, their metabolic treatment goals may need to be liberalized taking this into account.

Adherence

People with diabetes often take many other medications, as in Mr. Brown's case. Therefore, treatment regimens that are easy to follow and suited to a person's lifestyle are important considerations. For example, metformin (Glucophage®) can be taken either two or three times daily with food. Mr. Brown could take metformin twice a day (e.g., 500 mg in the morning and 1000 mg at dinner), if he is able to tolerate a 1000 mg dose. Also, he admits that he occasionally forgets to take lovastatin at bedtime. To improve adherence, he could try taking it with his other medications, and then monitor the cholesterol to see if it is adversely affected.

Insulin Therapy Considerations

Patients with vision or dexterity problems can have difficulty handling the insulin vial/syringe and injecting insulin. Insulin syringes are available in 1/3 ml (holds 30 units), 1/2 ml (holds 50 units), and 1 ml (holds 100 units) sizes. For patients whose insulin doses are less than 30 units, use of the 1/3 ml syringe is preferable, because its markings and lines are much easier to read. For

patients with dexterity problems, an insulin delivery device, such as a pen device, may allow for easier handling and administration of insulin. Syringe magnifiers may also be of value.

Conclusion

People with diabetes often do not just have diabetes. They may also have hypertension, a cholesterol disorder, kidney disease, and/or heart disease, and thus may take many medications. It is important to periodically assess the safety and effectiveness of all medications, especially in older persons.

COUNSELING TIPS

- Teach patients how to recognize symptoms of low blood sugar (hypoglycemia) These include rapid heartbeat, hunger, sweating, irritability, shakiness, dizziness, headache, confusion, and anxiety.
- If any of these symptoms occur, the patient should check his or her blood glucose. If it is below 70 mg/dL, take a fast-acting source of 15 grams of glucose*.
- Recheck the blood glucose in 15 minutes; if it is still below 70 mg/dL, take another 15 grams of glucose.
- Sources of glucose that contain fat (e.g., candy bar) do not act fast enough to treat low blood glucose, because the fat delays absorption.
- If the blood glucose remains below 70 mg/dL call the emergency medical system.
- All people who use insulin should have a glucagon emergency kit at home. A family member or caregiver should be trained on how to administer it in case the person becomes unconscious.
- Patients taking insulin or other medications that can cause hypoglycemia should be told to wear some form of medical identification indicating that they have diabetes. These products, such as a bracelet or pendant, provide vital medical information during an emergency.
- Patients taking metformin should be familiar with the symptoms of lactic acidosis, even though it rarely occurs. These include feeling very weak, tired or uncomfortable; unusual or unexpected stomach discomfort; trouble breathing; feeling dizzy, light-headed or cold; or suddenly developing a slow or irregular heartbeat. If any of these symptoms occur, they should stop taking metformin and call their physician.
- It is important to temporarily stop metformin when undergoing an x-ray procedure that necessitates an injection of a dye (contrast agent). Metformin should be stopped at the time of or before the procedure and not restarted until 48 hours after the procedure and after kidney function has been re-evaluated and found to be normal.

*Examples of 15 grams of fast-acting glucose include:

- 1 cup (8 oz) of skim milk
- 1/2 cup (4 oz) apple, orange, or grapefruit juice
- 1/3 cup grape or cranberry juice
- 1/2 cup regular (not diet) soda (e.g., colas)
- 1 tablespoon honey
- 3-4 glucose tablets
- 1 tube glucose gel



RESOURCES AND INFORMATION
FOR THE PATIENT AND
THE PHARMACIST

Geriatric Self Care



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People over the age of 65 consume one-third of all prescription and nonprescription medications. The average older adult takes five to six prescription medicines and three to four nonprescription products on a daily basis. The over-the-counter (OTC) market is continuously growing as prescription medications are converted to over-the-counter (nonprescription) status. The dietary supplement market (herbs, nutritional supplements) is growing as well. The practice of self-medicating has become confusing for many older adults. Reliance on the advice of a neighbor, friend, or family member is not uncommon. The pharmacist's knowledge of a person's prescription and nonprescription medication use can assist greatly in improving self-care.

Pharmacists can educate and counsel older adults on product selection. Before recommending an OTC product, ask the person about specific symptoms that are bothersome and when they began to occur. The pharmacist should also ask what makes these symptoms better or worse and what has the person already tried for relief. A thorough health and medication history is necessary in order to select an appropriate medication without creating drug-disease or drug-drug interactions. Patients must be told how quickly their symptoms will improve, what side effects to expect, and when to seek medical care if symptoms do not resolve. In some instances, direct referral to a physician may be indicated.

For most people, information on health management is best acquired through effective communication with physicians, nurses, and pharmacists. The patient should therefore be encouraged to bring all medicines, or at least a complete list of them, to their physician at each visit. They should write out any questions they have in advance to assure that nothing is overlooked. The community pharmacist is an ideal resource for information on side effects, interactions, and contraindications, for both prescription and nonprescription products.

Common Conditions For Which The Elderly Seek Self Care

Dry skin

Dry skin is common in the elderly. Skin thinning, reduced water retention in the stratum corneum, and decreased sebum

MYTHS & FACTS

MYTH: *Because over-the-counter medicines don't require a prescription, they're not as strong.*

FACT: The ingredients in OTC medicines can be just as strong as prescription medications. Always tell your doctor about all prescription and nonprescription medications you're taking so that potentially dangerous side effects and interactions can be avoided. Some nonprescription medicines are not recommended in the elderly. Do not use them without medical advice.

MYTH: *Because herbs are natural, they are safe.*

FACT: Just like traditional medicines, some herbs are safe and some are toxic. Many herbs have serious side effects and need to be monitored. They can also interact with traditional medicines.

MYTH: *I must buy expensive "natural vitamins" to get the best ones.*

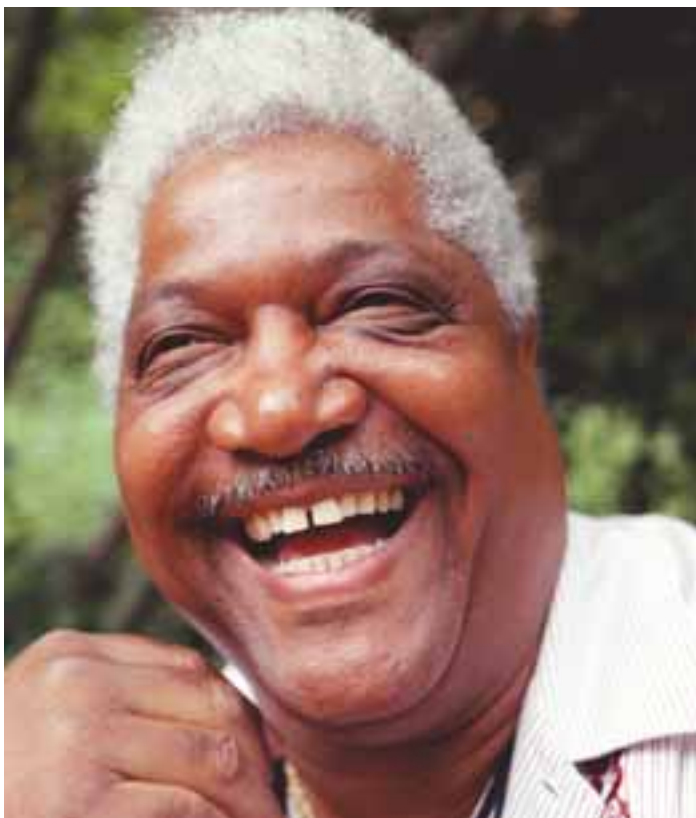
FACT: Synthetic, cheaper vitamins and minerals are just as effective as the more expensive natural ones.

MYTH: *All vitamins are safe even at large doses.*

FACT: Fat soluble vitamins are not easily eliminated from the body. Large doses may lead to toxic reactions and can interact with certain prescription medicines.

production produce tight, rough skin. Common skin problems in the elderly include scaling, fissures, inflammation, and pruritus, which often accompany dryness. One treatment goal is to maintain skin hydration, which can be done by simply maintaining adequate water intake (eight 8-oz. glasses per day). Hot baths and detergent soaps, which remove natural oils and lead to additional skin drying, should be avoided. Warm baths every other day, mild soap, gently patting skin rather than vigorously drying, and applying an emollient or moisturizing lotion immediately following a bath or shower may also help.

Common brand names of moisturizing products include Vaseline®, Curel®, Eucerin®, and Keri®. They contain combinations of emollients (e.g., petrolatum, lanolin, cocoa butter), which promote water retention through occlusion, and humectants (e.g., glycerin, propylene glycol), which promote water retention through hydration. Other products such as U-lactin®, Lachydrin®, and Lacticare® contain keratin-softening agents such as urea, lactic acid, or allantoin.



Constipation

Among community-dwelling elders over the age of 65, approximately one-quarter of men and one-third of women suffer from chronic constipation. Many diseases commonly seen in the elderly, as well as some medications used to treat them, exacerbate the problem. Medications that cause constipation should be eliminated, if possible. Pharmacists can help identify such medicines and recommend less bothersome alternatives.

Management of constipation should begin with non-pharmacologic strategies. These include increasing dietary intake of fruits, vegetables, and grains high in fiber; drinking at least 8 glasses of liquid daily; and regular exercise. If unsuccessful, medications may be tried. Bulk-forming or fiber laxatives add enough bulk to the diet to regulate bowels and are safe and effective with chronic use. They usually take several days to produce a bowel movement and need to be continued on a daily basis to stay regular. Fiber laxatives must be taken with sufficient fluids, such as 1–2 eight-ounce glasses of water several times daily. Failure to do so may result in the exacerbation of constipation or even fecal impaction.

A stool softener, such as docusate, is another safe alternative for long-term use. It works by causing the stool to absorb more water, making it easier to evacuate. Like fiber laxatives, docusate takes about 72 hours to work and must be taken regularly. A combination of a fiber laxative and stool softener is

safe, effective, and may be used chronically.

Other laxatives (e.g., stimulants, saline laxatives, lubricating agents) should be used on an as-needed basis only. Chronic use of stimulant laxatives like bisacodyl, castor oil, and milk of magnesia may lead to cramping, dehydration, and electrolyte imbalance. Frequent use of mineral oil is associated with malabsorption of fat-soluble vitamins. Although suppository or enema laxatives work very quickly, they can cause significant cramping and anal irritation and should only be used when other laxatives fail. Bowel evacuant (e.g., magnesium citrate, Fleet's Phospho Soda®) are available for over-the-counter use. However, they should not be used without a physician's advice, because unmonitored use can lead to severe dehydration in the elderly.

Urinary Incontinence

Urinary incontinence, defined as involuntary loss of urine or a sensation of urinary frequency or urgency, is predominately a problem of old age. Studies show that 56 percent of community-dwelling elderly and 80 percent of nursing home residents suffer from this disorder. The first step in treating it is to eliminate reversible causes. (See Table 1.) Non-pharmacologic approaches to management include timed or prompted voiding (i.e., bladder training) and Kegel exercises (20 minutes three times a day) to strengthen voluntary pelvic floor muscles, which improves periurethral structure support and bladder storage. If incontinence persists, prescription drug therapy may be indicated, which is beyond the scope of this article. The patient should be referred to his or her physician for thorough evaluation, which includes determining the underlying pathology.

Insomnia

Among healthy seniors, 12–25 percent report chronic insomnia. The incidence of insomnia appears to increase as the number of medical problems increases. Lifestyle changes, poor sleep habits and hygiene, anxiety, depression, dementia, age-associated reduction in deep sleep cycle, certain medical conditions (e.g., diabetes, pain, cardiac or respiratory disease), urinary incontinence, and medications can all contribute to insomnia in the elderly. Prolonged insomnia can result in daytime fatigue, impaired functioning, and reduced quality of life.

The most effective, long-term management of insomnia is non-pharmacologic. Although medications provide immediate relief from insomnia, non-pharmacologic measures can lead to permanent resolution of symptoms. Sleep hygiene measures include decreasing afternoon caffeine intake, exercising regularly before 6 pm, avoiding naps, establishing regular sleep hours, treating nighttime pain, addressing nocturia, and managing the bedroom environment (e.g., temperature, noise level). When drug therapy becomes neces-

sary, shorter-acting prescription drugs are preferred (e.g., zolpidem, zaleplon). Antihistamines commonly used in OTC sleep products (e.g., diphenhydramine, doxylamine) are associated with impairment of daytime functioning, even at low doses. They also have undesirable anticholinergic effects (e.g., delirium, confusion, disorientation).

Melatonin is a dietary supplement frequently used for sleep. Produced by the pineal gland, endogenous levels increase in the evening and peak during the normal hours of sleep. Older adults who suffer from insomnia appear to have lower levels of melatonin. Several small studies have shown that melatonin may be effective for sleep-onset insomnia

(trouble falling asleep), but it has not been shown to be effective in sleep-maintenance insomnia (trouble staying asleep), which is common in the elderly. Side effects are generally mild and include headaches, daytime drowsiness, dizziness, fatigue, irritability, and stomach upset. Melatonin should not be taken concurrently with alcohol or other sleep aids, because the combination may cause dizziness and excessive sedation.

Weight Loss

Involuntary weight loss represents a serious health concern in the elderly. Malnutrition is reported to occur in 55 percent of nursing home residents and low body weight is a major risk

Dietary causes	Medical conditions	Medications
Excess fluid intake More than 6 oz of fluid after 6:00 PM Caffeinated drinks Alcohol High sugar foods	Delirium Depression Restricted mobility Urinary tract infection Atrophic vaginitis Fecal impaction Polyuria due to poorly controlled diabetes, congestive heart failure	Acetylcholinesterase inhibitors Alpha agonists/antagonists ACE Inhibitors Anticholinergics Antihistamines Anti-Parkinson's drugs Diuretics Lithium Tricyclic antidepressants Antipsychotics Sedatives/hypnotics

Drug name	Effect
SSRIs Bupropion	Reduced carbohydrate craving
Digoxin	GI side effects in 25 percent of patients; loss of appetite is often the first sign of toxicity
Metformin	GI side effects and increased insulin sensitivity
NSAIDs	Decreased appetite, possibly due to nausea and stomach upset
Theophylline, oral albuterol, pseudoephedrine	Stimulant effect, decreased appetite
Cholinergic drugs for Alzheimer's disease (e.g., donepezil, rivastigmine, galantamine)	GI side effects
Sedatives/hypnotics	Loss of appetite due to sedation
Cholestyramine	Nutrient malabsorption
Levodopa	Increased fat breakdown, altered taste
Cancer chemotherapy, gold therapy, phenytoin, potassium, doxycycline, alendronate, theophylline	Stomatitis, gingival hyperplasia, mucosal injury
Hydrochlorothiazide, captopril, enalapril, nifedipine, diltiazem, metformin, some inhaled or intranasal products	Changes in taste (bitter or metallic) or smell
Ma huang (ephedra), guarana	Stimulants, decreased appetite
Thyroid hormone	Decreased appetite, particularly if dose is excessive

factor for functional decline and mortality. Causes of involuntary weight loss include:

- Social—loss of dining companion, not wanting to cook for oneself
- Psychological—bereavement, depression, dementia
- Medical—malabsorption, gastrointestinal disease, infection, trouble swallowing, cancer
- Pharmacologic—drug induced weight loss
- Physiological—decreased food intake resulting from decline in physical activity and resting metabolic rate

Pharmacists should refer patients who report a rapid weight loss (e.g., 4 percent weight loss within a year) to their physicians, because this often signals an underlying medical cause. After ruling out medical and psychological causes, the medication regimen should be reviewed to ensure that these are not causing or contributing to weight loss. (See Table 2.)

Nonprescription Drugs

Nonprescription or over-the-counter (OTC) medicines have always been an important aspect of geriatric self-care. However, patients must be reminded that while only a limited number of

ingredients are approved for over-the-counter use, thousands of brand name products are available and many contain combinations of identical medications. While some OTC drugs can be effective in managing symptoms safely, others can cause bothersome side effects. (See Table 3.) In some cases they create more problems than they treat, resulting in significant declines in health and functional ability. Therefore, patients selecting an over-the-counter medicine should be taught to look for specific drug names on the label, select a product that contains only those medicines needed for their particular symptoms, and ask a pharmacist for advice if they have any questions.

Dietary Supplements

One in three Americans uses a dietary supplement. However, consumers often lack accurate and objective medical information about the safety and efficacy of products before self-medicating.

The Dietary Supplement Health and Education Act (DSHEA) of 1994, amends the Federal Food Drug and Cosmetic Act pertaining to dietary supplements (defined as vitamins, minerals, herbs or other botanicals, amino acids, or other dietary supplements). This prevents manufacturers from claiming that herbs may be used

Table 3. OTC Ingredients That Can Cause Problems in the Elderly

Drug name	Indications	Side effects	Precautions
Pseudoephedrine	Nasal congestion	Nervousness, insomnia, agitation, decreased appetite, weight loss, increased blood pressure	Use cautiously in hypertension, cardiac disease, diabetes, or anxiety disorders.
Diphenhydramine Chlorpheniramine Brompheniramine	Allergies, runny nose, itchy eyes, itching, allergic rashes	Excessive sedation, dry mouth, constipation, urinary retention, tachycardia, confusion, mental status changes, delirium	Avoid in patients with dementia or BPH. Chlorpheniramine and brompheniramine may have milder side effects, but still bothersome.
Ibuprofen Naproxen Ketoprofen Aspirin	Arthritis, pain, fever reduction, inflammation, blood thinning (ASA)	Stomach upset, pain, ulcers, GI bleeding, acute kidney problems, water retention, increased blood pressure	Do not use without physician supervision. Always take with food. Can cause serious bleeding or acute kidney disease without warning. Increased risk of bleeding if taken with warfarin.
Bisacodyl senna	Stimulant laxatives for constipation	Related to purgative action	Not recommended as initial therapy; try bulk-forming product and docusate first. Use only as needed, for no more than 1 week at a time (except in patients on chronic narcotics). Chronic use can degrade colon function.
Magnesium citrate Sodium phosphate Magnesium hydroxide	Saline laxatives for constipation, bowel evacuation	Dehydration, weakness, fecal incontinence	Use only if clearly indicated. Unsupervised use can lead to severe dehydration, resulting in mental status changes, cardiac toxicity, and electrolyte imbalance.
Mineral oil	Lubricant laxative for constipation	Decreased absorption of fat-soluble vitamins, lipid pneumonia	Use only as needed; most problems are associated with chronic use.

to treat diseases such as high cholesterol, dementia, high blood pressure, anxiety, and depression. But it also limits the FDA's oversight. The manufacturers bear the responsibility for safety and effectiveness. The FDA is only allowed to remove products from the market after they have been proven to be hazardous.

Likewise, the FDA cannot impose the same strict manufacturing requirements on dietary supplements as it does on traditional pharmaceuticals. This results in batch-to-batch and manufacturer-to-manufacturer variation in concentrations and purity of ingredients. Chemical analysis of popular supplements used by the elderly, such as echinacea, ginkgo

biloba, ginseng, St. John's wort, saw palmetto, melatonin, glucosamine, and chondroitin, have shown significant variations from labeled potency. Pharmacists can help inform consumers about safe use of these products. (See Tables 4 and 5.)

Vitamin and Minerals

Relatively little information is available on the vitamin and mineral requirements of older adults. The usual standards for assessing vitamin and mineral requirements are based on the recommended dietary allowance (RDA), which provides nutrient requirements for all age groups. Older adults fall into the

Table 4. Dietary Supplements Commonly Used by the Elderly

Herb or Supplement	Common Uses	Precautions
St. John's wort	Depression and anxiety	May cause GI distress, restlessness, sedation, headaches, confusion, and sun sensitivity. Drug interactions with many prescription medications.
Ginkgo biloba	Memory loss and to improve cognitive function; often used in Alzheimer's disease	Increases antiplatelet effects of NSAIDs and may increase risk of bleeding with warfarin. Should not be used 7–10 days pre- or postoperatively. Generally well tolerated, although rarely leads to mild GI upset, headache, anxiety, or insomnia.
Garlic	High cholesterol, although efficacy not established	May cause body odor, GI upset, decreased blood pressure. Potentiates antihypertensive medications and blood thinners. Should not be used 7–10 days pre- or postoperatively.
Ginseng	Performance enhancement and to increase energy, although efficacy not established	May cause insomnia, hypertension, and nervousness. Potentiates CNS stimulants and blood-thinning medications. Should not be used 7–10 days pre- or postoperatively.
Valerian root	Anxiety and insomnia	May cause daytime sedation, additive effects with other CNS drugs. Should not be used with other sedatives and hypnotics. Hepatotoxicity has been reported and one case of precipitating benzodiazepine withdrawal.
Melatonin	Insomnia and jet lag	May cause headaches, daytime drowsiness, dizziness, fatigue. Additive effects with other CNS drugs.
Glucosamine Chondroitin	Osteoarthritis	May cause mild GI effects. Avoid chondroitin from bovine sources.
Saw palmetto	Improved urinary flow in men with enlarged prostates	May cause headaches and GI upset.

Table 5. Potentially Ineffective or Dangerous Dietary Supplements

Herb or Supplement	Common Uses	Precautions
Zinc	Preventing or reducing the duration of a cold. Not proven effective	May cause nausea, vomiting, zinc toxicity (flu-like symptoms, CNS symptoms, fatigue, anemia). Doses used for colds far exceed RDA. Safety of large doses not established.
Kava	Anxiety, sedation	Taken alone or in combination with other sedatives or alcohol, may impair driving ability. Reports of serious liver toxicity requiring organ transplants.
Ma huang (Ephedra)	Weight loss. At low doses also used for bronchospasm, asthma, congestion	Causes rapid heartbeat, elevated blood pressure, CNS stimulation, anxiety, insomnia, agitation, and weight loss. Contraindicated in cardiac disease, diabetes, or hyperthyroidism.
Guarana	Weight loss, to enhance athletic performance, reduce fatigue	Contains caffeine, theophylline, theobromine, tannins, trace amounts of timbonine (fish poison). Tolerance, psychological dependence with chronic use. Withdrawal syndrome: headaches, irritability, fatigue. May cause painful urination, GI spasms, insomnia, nausea, vomiting, CNS excitation, diuresis, palpitations, arrhythmias, muscle spasms, tinnitus, headache, delirium, convulsions.
DHEA	Increased energy, sexual potency	Potentiates effects of estrogen, testosterone. May cause deep voice, facial hair, acne, breakthrough bleeding in women and breast or prostate enlargement in men. May increase risk of breast and prostate cancer.



“51 and over” group, which does not consider the variability in requirements for people in later years. The best source of vitamins and minerals is a well-balanced diet. However, since many seniors eat irregularly or have poor nutrition, a daily multiple vitamin that does not exceed the RDA may be beneficial.

Water-soluble Vitamins (Vitamins B and C)

Vitamin C is present in all citrus fruits, strawberries, kiwi, papaya, red peppers, broccoli, and fortified juices. The RDA is 75–90 mg/day. There is no evidence that vitamin C absorption or utilization is impaired in older adults. Complete absence of vitamin C from the diet (rarely seen in the United States) results in scurvy. More commonly, vitamin C deficiency is associated with poor wound healing, easy bruising, inflammation of the mucosa, and capillary fragility.

The optimal dose of vitamin C is uncertain. Researchers often advocate doses that exceed the RDA. It is thought that 140 mg per day is necessary to saturate tissues and may be desirable for its antioxidant properties. Other sources report

no increase in bioavailability with doses above 400 mg. Vitamin C toxicity is rare; excess vitamin C is usually excreted, with the only side effect being discolored urine. Doses over 2 gm per day may contribute to diarrhea, nausea, stomach cramping, and kidney stones. There is little evidence that such doses prevent colds or cancer, or aid in wound healing.

Vitamin B₆ and B₁₂ deficiencies are common in geriatrics and have been associated with anemia, impaired cognitive function, and cell-mediated immunity. Daily requirements do not substantially change with age. Vitamin B deficiency is sometimes due to poor gastric absorption. B vitamins are present in many foods, including rice, grains, meat, peas, beans, avocados, potatoes, milk, and fish. Many vitamin B-complex formulations are available on the market. Toxicity is rare.

Niacin (vitamin B₃) deficiency is rare in the elderly. The RDA for people over age 50 years is 13–15 mg/day. This amount is easily attainable through a balanced diet including grains, vegetables, and fish. Doses of 500–3,000 mg daily are used for lowering cholesterol. At these larger doses, niacin has been associated with flushing, itching, headache, fatigue, ulcers, elevations in uric acid and glucose concentrations, and liver toxicity. For this reason, patients should be discouraged from self-medicating with niacin to lower cholesterol.

Fat-soluble Vitamins (Vitamins A,D,E, and K)

Vitamin A is present in fish, butter, cream, eggs, milk, liver, carrots, and broccoli. The RDA is 800–1000 mcg daily. The risk of toxicity is greater than that of deficiency. Although vitamin A supplementation (as beta carotene) has been associated with a lower risk of some types of cancer, studies are controversial and long-term effects have not been explored. Large doses of vitamin A are associated with toxicity and include symptoms like nausea, vomiting, fatigue, malaise, and joint pain.

Vitamin D is necessary for adequate calcium absorption and maintaining strong bones. It is present in milk, eggs, and fish and may be obtained from sunlight, but daily intake is often inadequate. Deficiency is common in the geriatric population, particularly those who are homebound or institutionalized. The RDA is 200 IU daily, although larger doses (400–800 IU) are recommended for patients at risk for osteoporosis. Toxicity is associated with daily doses of 50,000–100,000 IU. Symptoms of toxicity include anorexia, nausea, weakness, aches and pains, joint stiffness, weight loss, constipation, hypertension, and renal failure.

Vitamin E is present in plant oil, margarine, green vegetables, and grains. The RDA is 12–15 IU daily. Deficiency is rare in older adults and is usually not a concern. Larger doses (400–800 IU) have been recommended for their antioxidant properties and for cancer prevention. Until recently, vitamin E was thought to reduce cardiovascular risk; however, two controlled trials (HOPE and GISSI) have cast doubt on that benefit.

Vitamin E 1000 IU twice a day is currently recommended for delaying progression of Alzheimer's disease, although no evidence exists to support its use in improving memory. Toxicity is rare, but large doses have an antiplatelet effect, reduce vitamin K levels, and increase the effect of warfarin.

Vitamin K aids in blood clotting. The only vitamin manufactured by bacteria in the gastrointestinal tract, it is also present in green leafy vegetables, dairy products, and fruits. The RDA is 65–80 mcg daily and the average diet contains 300–500 mcg/day. Vitamin K deficiency is usually associated with antibiotic or anticoagulant administration. Patients on warfarin should keep a diet constant in vitamin K to avoid fluctuations in their INRs.

Calcium

Calcium is necessary to maintain strong bones and prevent fractures. It is present in all milk products, broccoli, and fortified orange juice. The daily requirement for older adults is 1000–1500 mg/day of elemental calcium. Elderly patients often do not get enough calcium in the diet or through supplementation (e.g., an 8-oz. glass of milk contains only 300 mg of calcium). Most multivitamins, even those intended for older adults, do not contain sufficient amounts of calcium (e.g., 200–300 mg per dose). Additional calcium sources are usually needed and any calcium salt (e.g., calcium carbonate, citrate, or gluconate) may be used. Calcium carbonate and calcium citrate provide the most elemental calcium per dose. Calcium citrate may be better absorbed by older adults and those taking H₂ blockers or proton pump inhibitors. A typical elemental calcium regimen is 500 mg three times a day. Calcium supplementation is rarely associated with gas or bloating and there is no good evidence that it causes constipation.

Case Discussions

Mr. Brown (Case I) is taking diazepam for sleep, which is not recommended. His pharmacist should review good sleep hygiene with him to see whether any changes in his daily routine would help with his occasional insomnia. Following those adjustments, if medication is still necessary, he should ask his physician for something more appropriate. Mrs. Brown should make a list of all her over-the-counter medicines and herbs and bring it to her pharmacist, so that he or she can evaluate whether they are safe for her to take. Certain nonprescription medicines and herbs are not appropriate for older adults.

Because Mrs. Smith's (Case II) different medicines can potentially interact, she should choose one pharmacy, where a pharmacist can properly screen her drug regimen for drug interactions. Her warfarin interacts with many nonprescription medicines that she is planning to buy, including Tagamet

HB®, Vitamin E (at doses greater than 1000 IU), Advil®, ginkgo biloba, and Pepto-Bismol®. She should be counseled to avoid taking these potentially dangerous combinations.

Other issues to consider discussing with her include the lack of an indication for vitamin E 1000 IU (she does not have Alzheimer's Disease) and lack of evidence that ginkgo improves memory in non-Alzheimer's disease patients. It is also important to find out why she is buying Tagamet HB® and Pepto-Bismol®. Both Vioxx® and Prozac® can cause stomach discomfort. If she is having stomach problems, her physician needs to be notified.

Mrs. Young's (Case III) OTC sleep aid likely contains diphenhydramine, which is not recommended in the elderly. It can cause excessive sedation, confusion, and other mental status changes, particularly in patients with dementia. If improving sleep hygiene does not help, her doctor should consider a short-acting sedative hypnotic. Vitamin E 1000 IU twice daily has been shown to slow down the progression of dementia in Alzheimer's disease and may be worth a try. It is not likely to cause any dangerous side effects and she may benefit from a trial. Taking Advil® for Alzheimer's disease is more controversial. The risk of bleeding from Advil® outweighs any benefits it may have; thus, it should not be recommended at this time.

Conclusion

Elderly patients, even those who can manage their own regimens adequately, often have many questions about their medications. Pharmacists are an ideal source of information and can counsel patients about their medications, educate them about the benefits and the potential dangers of self-medication, and screen their drug regimens for dangerous adverse reactions or drug interactions.

ADVICE TO PATIENTS WHEN SELF-MEDICATING

- When buying a new OTC product, ask your pharmacist whether it is safe for you.
- Tell your physician or pharmacist about all the nonprescription products you take. It is always a good idea to remind your physician what medicines you take, particularly if you are seeing more than one doctor.
- Read the label. Know what side effects to expect from each OTC product you take.
- Know how quickly you should see a response from an OTC medicine.
- Learn which medicine(s) you need for your symptoms and look for products containing only those ingredients.
- Learn which OTC medicines older adults should not use.
- Generic OTC products are just as effective as the more expensive brand names.
- Seek medical care if symptoms get worse or don't resolve.

Reimbursement and Access to Care

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Access to affordable prescription drug coverage is arguably the most critical healthcare issue facing older adults today. It is well documented that individuals 65 years of age and over consume a disproportionate amount of the healthcare services and dollars. They pay a larger out-of-pocket share of the cost than do their younger counterparts, particularly for prescription drugs. Total spending on prescription drugs was estimated to have been \$90.6 billion in the United States in 1998. Older Americans comprise 13 percent of the population; yet they consume 34 percent of all prescription drugs and account for 42 percent of the drug expenditures. When accessing the healthcare system, including obtaining prescription drugs, reimbursement for services must be considered. This article will address the reimbursement options for prescription medications available to older adults and provide some practical strategies to aid pharmacists in minimizing out-of-pocket expenses for the elderly.

Prescription Drug Coverage for Seniors

With drug expenditures expected to increase at double-digit rates through 2007, older Americans, who have the greatest reliance on prescription drugs, do not have prescription drug coverage as part their basic Medicare benefit. Although Medicare has never provided an outpatient prescription drug benefit, it was estimated in 1996 that 69 percent of Medicare beneficiaries had some form of drug coverage from sources other than Medicare. The primary sources of drug coverage were a mix of employer-sponsored retiree benefits, Medicare+Choice managed care plans, Medigap plans, Medicaid, and veteran's benefits.

Employer-sponsored retiree benefits comprise the largest source of prescription drug coverage for the elderly. However, this benefit is on the decline as employers struggle to afford the rising premiums associated with providing care. Among firms of all sizes, the overall percentage of those offering retiree benefits dropped from 40 percent in 1994 to 28 percent in 1999.

The Medicare managed care plan, Medicare+Choice, pro-

MYTHS & FACTS

MYTH: *Generic drugs are inferior to their brand name counterparts*

FACT: Generic drugs are regulated and rated by the FDA. If a generic drug has an "AB" rating it is therapeutically equivalent to the brand name medication

MYTH: *Patients with health insurance do not qualify for patient assistance programs through pharmaceutical industry*

FACT: Each pharmaceutical manufacturer has different eligibility criteria. Typically, a patient can have health insurance but the person may not qualify if he/she has a pharmacy benefit associated with the health insurance plan.

MYTH: *Because Medicare does not cover outpatient prescription drugs, most older Americans have no prescription drug coverage.*

FACT: Over 60 percent of older Americans have some form of prescription drug coverage either through Medigap plans, Medicare +Choice, Medicaid, and Veteran's Administration benefits.

vided some prescription drug coverage to 13 percent of Medicare beneficiaries in 1999. Medicare+Choice plans, however, have become a less reliable source of prescription drug coverage of late. They are not offered in every state and some health plans have stopped offering Medicare+Choice, while others have dropped or limited drug coverage because reimbursement from Medicare has been unable to keep pace with the rising cost of prescription drugs. Enrollees in these plans have also experienced shrinking benefits for a higher price tag. Examples of this shrinking benefit include annual spending limits placed on prescriptions, large co-pay differences between generic medications (\$7-\$10) and brand name medications (\$30), drug benefits that only include generic drugs (i.e., brand name drugs are no longer covered) and the institution of a monthly premium.

Medigap insurance is another alternative for older adults. These insurance policies serve as supplemental coverage to the Medicare benefit. Of the ten Medigap policies available, only three offer prescription drug coverage. These three poli-

cies provide roughly 8 percent of Medicare recipients with prescription drug coverage and each requires that the patient pay for the first \$250 of their medication costs per year. After this \$250 has been paid, the member must then pay for half of the cost of each prescription (i.e., a 50 percent co-pay). Prescription coverage is limited to \$1,250 - \$3,000 annually, depending on the plan. The amount that a senior would pay in monthly premiums to get this prescription coverage ranges from \$1,900-\$3,250 annually, making these options very expensive for most seniors.

Medicare beneficiaries who are low income and have limited resources may qualify for state Medicaid (e.g., Medi-Cal) to help them pay for expenses not covered by Medicare. Those eligible for both Medicare and Medicaid are called dual eligible beneficiaries. The Medicaid benefits available to dual eligible patients vary depending upon income and resources. For dual eligible patients, Medicaid supplements Medicare and provides coverage for additional services such as outpatient prescription drugs (usually at no cost to the patient), eyeglasses and hearing aids, as well as nursing facility care beyond the 100 days covered by Medicare.

Medicare patients who have served in the armed forces may be eligible for veteran benefits either through the Department of Veterans Affairs (VA) or TRICARE insurance. If veterans are enrolled in the VA system and are eligible for medical benefits, they are also entitled to a pharmacy benefit that may or may not require a co-payment for prescription medications. TRICARE is a regionally managed health care program for active duty and retired members of the uniformed services, their families, and survivors. When combined with Medicare, TRICARE serves as a supplement to Medicare and provides a prescription drug benefit. This benefit provides medications either for no co-payment or a small co-payment, depending upon where the prescription is filled.

For over one-third of the Medicare-eligible seniors without a prescription drug benefit, the escalating cost of drugs is particularly problematic. These individuals may be low-income but may have non-liquid assets that prevent them from qualifying for state Medicaid programs. The amount that these individuals spend on prescription drugs can consume a large portion of their income, thus leaving them with difficult choices as to what essentials they are going to do without.

Pharmacist Interventions

Regardless of practice setting, pharmacists are in a position to assist this vulnerable population. Most pharmacies are equipped with software for drug utilization review to detect duplicate therapy, drug interactions and allergies. Pharmacists are also able to evaluate drug regimens to determine sub-optimal dosing and unnecessary drugs. Pharmacists have



immediate access to drug prices, formularies, third-party billing, therapeutic alternatives, and most importantly, the patients themselves. Along with therapeutic interventions, the opportunity for cost-saving interventions occurs each time the patient is counseled on appropriate medication use. Once the pharmacist has identified an opportunity for cost savings, it is important to engage the physician and the patient as team members to ensure the best outcome, both financially and therapeutically.

If the pharmacist determines that there are financial issues that may interfere with medication adherence, there are several strategies that can be employed to decrease the amount seniors are paying for prescription drugs (See Table 1).

Most pharmaceutical companies have a program that provides free or low cost brand name drugs to patients in need. These are sometimes referred to as indigent programs or patient assistance programs. Unfortunately, the programs can be confusing and difficult to use, as each company has different forms, eligibility criteria, renewal processes, and mechanisms for the patient to obtain medications. For these reasons many of the programs are underutilized. There are, however, several useful websites to assist patients and providers in obtaining this information (See Table 2).

Pharmaceutical manufacturers have recently introduced

new drug discount card programs that differ from their patient assistance programs. These discount card programs are intended for those patients whose income is above the levels necessary to qualify for patient assistance programs. Many of these applications do not require a physician's signature and medications are obtained through the patient's pharmacy. Each company's program differs in qualifications and discounts, but they too can provide savings to the patient on brand name medications. Before these programs and discount cards are considered, the pharmacist should review the patient's medication regimen, because expensive brand name medications can often be converted to generic equivalents or to other drug classes that have generics available.

California pharmacists have another cost-saving measure to offer Medicare patients. In 1999, SB 393 was passed in

California, which enables Medicare recipients to obtain their prescription drugs at a cost no higher than the Medi-Cal price for those drugs. Subsequent legislation enacted in 2002 has made these provisions permanent. Medicare patients must present their Medicare card to the pharmacy to be eligible for the discount.

Case Discussions

Although Mr. Brown (Case I) is a retired accountant and his wife is a part-time teacher, their only health insurance is Medicare parts A and B, which do not include an outpatient prescription drug benefit. Therefore, the Browns pay for their entire drug bill out of their own budget. Although Mr. Brown is the only one that takes prescription medications, his wife's nonprescription and herbal medications factor into their drug bills. Mr. Brown's drug regimen is predominantly generic; yet, his monthly bill still remains relatively high at about \$190/month. Several steps could be taken to decrease this amount. First, he has a brand-name antihypertensive medication that may be substituted with a generic, either by changing him to the tablet formulation of clonidine or by switching therapeutic classes to one that has generics, such as a beta-blocker. A beta-blocker may also be indicated for cardio-protection, because he had a heart attack several years ago. If the Catapres® is changed, the pharmacist must contact the physician for a new prescription.

The other strategy that may save Mr. Brown money is pill-splitting his cholesterol medication. Although Mevacor® recently became available generically, it may take months to years before the price falls significantly below the brand-name medication. If a medication comes in a higher strength that is twice the dose and if the price is less than double the lower

Table 1. Cost Saving Strategies	
• Ensure that the patient has maximized their reimbursement potential.	
• Maximize generic drug use.	
• Consider lower cost brand name medications.	
• Consider tablet spitting where appropriate.	
• Utilize all available assistance programs <ul style="list-style-type: none"> – Pharmaceutical industry-sponsored patient assistance programs – Pharmaceutical industry-sponsored discount cards – Offer Medicare patients the Medi-Cal contracted price of the drug. (SB 393) 	
• Determine whether mail-order provides cost-savings	
• Patients should periodically review all medications with the prescribing health care provider and ask, "Is this drug necessary to maintain my health?"	

Table.2 Useful Patient Assistance Websites and Resources	
http://www.benefitscheckup.org/	A free, easy-to-use service that identifies federal and state assistance programs for older Americans. BenefitsCheckUp was developed to address a concerning problem: millions of older adults are eligible for benefits, but not receiving them. Ranging from health coverage to supplemental income to help pay utility bills, there are millions of older adults who could benefit from a wide array of public programs if they knew about them and how to apply for them.
www.rxassist.org	This site is very useful. It contains information about the federal poverty level, detailed information on individual patient assistance programs (including eligibility, contact and processing information and forms that can be downloaded). This site also allows for easy searching for patient assistance programs by drug class, brand name, generic name and the company that manufactures the drug.
www.phrma.org	This site provides an annually updated patient assistance program directory and some useful links.
www.needymeds.com	This site is another catalog of available programs listed according to drug name and the manufacturer. It also has some useful references to several information resources that could be convenient to use. Overall it has a similar format to rxassist.org but it might be easier to navigate.
Rx Assist Plus	This is a useful patient-tracking device that interfaces with the Internet to quickly complete the appropriate patient assistance forms. It also has a tickler feature, which reminds the advocate to provide the patient with timely refills and re-enrollment into programs when the patient is due.

Table 3. Example of Pill-Splitting Cost Savings.

Drug	Strength	Directions and Quantity	Cost/month
Mevacor®	40mg	Take 1 tablet daily, #30	\$124
Lipitor®	20mg	Take 1 tablet daily, #30	\$101
Lipitor®	40mg	Take 1/2 tablet daily, #15	\$52

strength, one can use a higher strength tablet and split it to obtain cost savings. Unfortunately, the price of Mevacor® doubles as the strength doubles. However, it may be worthwhile to switch to a lower cost brand-name drug that can be split in half for cost savings. For example, he could be switched to Lipitor® 20mg. The cost savings by switching brands and pill-splitting is illustrated in Table 3.

When considering pill-splitting as a cost-saving technique, the pharmacist must first determine if the formulation of the tablet allows for it and whether the tablet size and shape allow for even pill splitting. Second, the pharmacist must evaluate whether the patient understands the concept of pill-splitting and if he or she has the dexterity to do it. Once these factors have been taken into consideration, the pharmacist should recommend a pill-splitter and demonstrate its use. If the pharmacist is going to recommend a change in the strength of the medication in order to split tablets, the physician must be contacted for a new prescription. The total savings to Mr. Brown if both of these medication changes are made is approximately \$100 per month.

Mrs. Smith (Case II) has no outpatient drug coverage and her income from Social Security and her pension total \$1,100/month, or \$13,200/year. Her monthly drug bill is \$400. She does not qualify for Medicaid, but her income does qualify her for patient assistance programs for Vioxx® and Prilosec®. Her Prozac® and her Coumadin® have generic equivalents. After these switches are made and the patient and doctor agree to complete the paperwork necessary for patient assistance programs on a quarterly basis, her new monthly drug bill is \$100.

Because her Coumadin® was changed to the generic equivalent it is important for the pharmacist to explain to the patient that she may require a blood test to check her INR after she has been on the generic warfarin for a week or 10 days. Inform the patient to contact her anticoagulation provider to let him or her know that she has switched to the generic version.

After discussion with her pharmacist, Mrs. Smith realizes that she is doubling up on some of her medications with non-prescription products that she purchases at the pharmacy. Some

of these over-the-counter medications can interfere with her prescription medications. She agrees to stop taking the non-prescription medications, which results in further cost savings.

As a retired schoolteacher Mrs. Young (Case III) may have a retiree benefit and therefore may have prescription drug coverage for her new drug, Aricept®. Because the drug is a brand name medication, she will most likely pay a co-pay ranging between \$10-\$30/month. Although there are no generic equivalents available for this class of medications, one possible cost-savings strategy is to purchase it through her insurance company's mail-order pharmacy. Many insurance companies offer a mail-order service for prescriptions allowing patients to obtain a 90-day supply of medication for the equivalent of one or two monthly co-payments, which saves one to two co-payment amounts every 90 days. If the patient has a high co-pay, these savings can be substantial. Mail-order may be considered for those medications that the patient takes chronically. Explain to the patient that if they choose to use a mail-order pharmacy to be sure that the company provides a telephone number that allows them to talk to a pharmacist. It is also important to let the mail-order pharmacy know about all of the medications they take, even if they are not filled by the mail-order pharmacy so that the pharmacy can perform drug utilization review.

Conclusion

Unfortunately, until there is a Medicare outpatient prescription drug benefit, older adults are at risk for non-adherence due to the cost of prescription medications. The pharmacist can identify these non-adherence issues and help solve these problems as a member of the healthcare team and as an advocate for the patient.

COUNSELING TIPS

- Explain health care coverage and prescription drug benefits available to older adults.
- Ask patients if their prescription costs are an issue or if their benefit has changed.
- Look for signs of non-adherence (refill dates that are extended, patients not refilling medications and no substitutes are on file, patients only getting partial fills of medications, inquiries about OTC alternatives to prescription drugs, repeated inquiries for generic alternatives to brand name medications).
- Ask the patient what they are realistically able to budget for prescription medications and what their income level is to determine eligibility for assistance programs.

NATIONAL TELEPHONE NUMBERS AND WEB SITES FOR COMMUNITY-BASED SERVICES

Senior Centers and Aging Network Services

Administration on Aging	(202) 619-7501
National Association of State Units of Aging	(202) 898-2578

Continuum of Services

Eldercare Locator	(800) 677-1116	www.ageinfo.org/elderloc/elderlo.html
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Specific Senior Services and Specific Diseases

ABA Commission of Legal Problems of the Elderly	(202) 662-8690	www.abanet.org
Assisted Living Federation of America	(703) 691-8100	www.alfa.org
National Academy of Elder Law Attorneys	(520) 881-4005	www.naela.org
National Alliance for the Mentally Ill	(800) 950-6264	www.nami.org
National Association of Home Care	(202) 547-7424	www.nahc.org
National Hospice Foundation	(800) 658-8898	www.nho.org
American Pain Society		www.ampainsoc.org
Alzheimer's Association	(800) 272-3900	www.alz.org
American Cancer Society	(800) 227-2345	www.cancer.org
American Diabetes Association	(800) 324-2383	www.diabetes.org
American Heart Association	(800) 242-8721	www.americanheart.org
American Parkinson's Disease Association	(800) 223-2732	www.the-health-pages.com/resources/apda
Arthritis Foundation	(800) 283-7800	www.arthritis.org

Drug Therapy Considerations in Older Adults

A Continuing Education Program for California Pharmacists



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TEST QUESTIONS

- Which of the following is an indicator of polymedicine?
 - the use of two medications to treat hypertension
 - an elderly patient who is taking seven medications
 - the use of four or more medications on an as-needed basis
 - the use of a prescription medication with no accompanying diagnosis
- Which of the following factors is the most common cause of drug-induced hospitalization in the elderly?
 - adverse drug reactions
 - use of nonprescription medications
 - dispensing of incorrect medications by pharmacists
 - multiple prescribers, each prescribing independently
- Older adults are more likely to be nonadherent with medication regimens than younger adults, because the elderly person:
 - has impaired vision and hearing
 - is unable to remember instructions
 - takes more medications than younger patients
 - refuses to follow proper instructions for taking prescriptions
- Which of the following can change, altering the distribution of drugs in the elderly?
 - total body water
 - serum protein concentrations
 - total body fat
 - all of the above
- Renal function decreases significantly with aging, which necessitates a dosage decrease for those agents that are renally eliminated.
 - True
 - False
- Which of the following statements is false with respect to physiological changes in the elderly patient:
 - total body weight generally declines
 - α_1 -acid glycoprotein concentrations increase
 - serum albumin concentrations increase
 - renal function progressively declines
- Which of the following statements is true regarding drug action in the aged:
 - patients may become more sensitive to certain medications
 - patients may become less sensitive to certain medications
 - dizziness, sedation and confusion are common side effects
 - they are more prone to experience orthostatic hypotension
 - all of the above
- Medications with significant anticholinergic effects can worsen
 - mental confusion
 - urinary retention
 - constipation
 - all of the above
- Nationally published treatment guidelines tailor therapy for each individual.
 - True
 - False
- A patient with a history of a recent fall and complaints of difficulty with balance should be evaluated to see if which of the following agent(s) is (are) prescribed:
 - diazepam
 - ascorbic acid
 - aspirin
 - all of the above
- The most frequently diagnosed dementia in the U.S. is:
 - Lewy Body dementia
 - Alzheimer's Disease
 - frontotemporal dementia
 - pseudodementia
- Alzheimer's disease may be treated with:
 - anticholinergic drugs
 - cholinergic drugs
 - antispasmodic drugs
 - antidepressant drugs
- Because elderly patients are more sensitive to drugs, response to antidepressant therapy occurs earlier (e.g., sooner than 4-6 weeks of drug therapy) than in younger patients.
 - True
 - False
- The following are all reasonable choices for the treatment of depression in an elderly patient, except:
 - paroxetine
 - amitriptyline
 - sertraline
 - bupropion
 - venlafaxine
- Orthostatic hypotension is a significant side effect commonly associated with which of the following antidepressants:
 - imipramine
 - trazadone
 - sertraline
 - doxepin
 - a, b, and c above
 - a, b, and d above
- Which of the following medication regimens should be recommended first line for moderate osteoarthritis pain?
 - nonsteroidal given routinely
 - nonsteroidal given on an as-needed basis
 - acetaminophen given on as-needed basis
 - acetaminophen given routinely
 - a low dose opioid given routinely
- Which of the following is not a diagnostic characteristic of osteoarthritis?
 - bony enlargements
 - severe inflammation
 - decreased cartilage on x-ray
 - morning stiffness
- Opioids should be avoided in the treatment of moderate to severe osteoarthritis, because of their potential for addiction at therapeutic doses.
 - True
 - False
- Of the following diabetes medications, which one is more likely to cause hypoglycemia?
 - glyburide
 - glipizide
 - metformin
 - rosiglitazone
 - acarbose
- If a person is on a diabetes regimen that can cause hypoglycemia, it is important for that person to self-monitor their blood glucose.
 - True
 - False
- Diphenhydramine should be avoided in the elderly, because it can cause:
 - excessive sedation and cognitive impairment
 - dry mouth
 - constipation
 - all of the above
- Which of the following vitamins can be toxic at high doses?
 - vitamin B complex
 - vitamin E
 - vitamin A
 - vitamin C
- Medicare+Choice plans are offered in select states and counties and may offer prescription drug coverage as well as other benefits not covered by Medicare.
 - True
 - False
- Pharmaceutical industry-sponsored patient assistance programs provide free brand name medications to all Medicare-eligible patients.
 - True
 - False
- When counseling elderly patients about medications, the pharmacist should:
 - discuss very detailed and extensive information about any possible adverse effect or drug interaction
 - explain the information quickly to ensure that all medications are covered
 - talk very loudly to be heard above the background noise in the pharmacy
 - provide written information as a supplement to verbal instructions

HEALTH NOTES

Drug Therapy Consideration in Older Adults

This issue of HEALTH NOTES is a collaborative effort of the California State Board of Pharmacy
and the School of Pharmacy, University of California, San Francisco

**The UCSF School of Pharmacy
Center for Consumer Self Care
"Helping People Help Themselves"**

The Center for Consumer Self Care is an emerging collaborative center whose mission is to ensure optimal and responsible use of medication and dietary supplements by individuals and the public at large. The Center will accomplish its mission through the following program cores: Consumer Education, Research, Professional Education and Public Policy.

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