Why the Elderly Need Individualized Pharmaceutical Care



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Table of Contents

Summary vi	ii
Introduction	1
Multiple Diseases	2
Optimal Therapy for Elderly Patients with Coexisting Conditions	6
Physiological Changes	6
■ Changes in the Way the Body Processes Drugs	7
Absorption	8
Distribution	8
Metabolism	8
Elimination	9
■ Aging Organ Systems	9
Variation in Drug Action	9
Enhanced Effects	9
Diminished Effects	0
■ Side Effects	1
Central Nervous System1	1
Anticholinergic	1
Cardiovascular	1
Obstacles to Individualized Drug Therapy for the Elderly	2
Switches	2
Limits 14	4
Conclusions: The Need for Coordinated Pharmaceutical Care	5
Appendix: Diseases of the Elderly	6
References	8

Summary

Advances in healthcare and pharmaceuticals have made it possible to treat many common diseases of the elderly. However, at a time when more innovative drug options are available, access to these agents is often limited or denied by restrictive aspects of drug benefit plans. For the elderly especially, such limitations are counterproductive. More than any other group, older people need access to a wide range of prescription drug options to safely meet their specific healthcare needs. A "one drug fits all" approach does not

work for elderly patients because they are exposed to unique health variables that are rare in younger patients. When these factors interact in an older patient, individualized drug therapy is

A "one drug fits all" approach does not work for elderly patients.

required, and restricted drug access could lead to ineffective or negative health outcomes.

Selection of pharmaceutical therapy for elderly patients can pose a significant challenge and is determined by three primary factors unique to this group. First, the prevalence of multiple chronic diseases, or comorbidity, is much higher in older individuals. For example, nearly 40% of the elderly suffer from arthritis plus another serious health condition, such as cardiovascular disease or diabetes. Second, an older body reacts to pharmaceuticals quite differently than a youthful one due to the physiological changes that accompany aging; metabolism rates change, organ function declines, and sensitivity to some drugs can be altered. Finally, compared with younger patients, there is generally a wider variation in pharmacological action of a drug across individuals. Taken together, these three factors create the need for flexibility in prescribing for the elderly.

Although there are many high-quality pharmaceutical agents to treat diseases of the elderly, optimal selection of medications can only be achieved if a wide range of drug options is available. If restrictive drug policies or inadequate insurance plans limit the availability of pharmaceuticals, pre-

scribers may be unable to choose the best drug therapy for their patients. Such restrictions may compromise the health of the elderly unnecessarily and result in increased utilization of other med-

ical services, thereby increasing overall costs. Such outcomes are deleterious to everyone involved: patient, provider, plan, and payer.

Furthermore, several additional factors increase the risk of sub-optimal pharmaceutical care for older Americans. These patients often have a number of physicians (specialists and sub-specialists included) providing for their care without any collaboration. Also, older patients, particularly the frail elderly, migrate among separate treatment sites, a practice that provides little continuity of care. What is greatly needed is the coordination of all drug treatments for an individual patient across sites, providers, and over time. Such a seamless continuum may represent the next stage in the evolution of geriatric pharmaceutical care.

Introduction

Pharmaceutical therapy is the most common medical intervention used to treat the elderly, a group which currently comprises 13% of total U.S. population and which accounts for approximately one-third of all annual healthcare costs, or \$300 billion.¹ Recent attention to prescription drug expenditures has stimulated discussions about how to design drug benefit plans, public and commercial, that adequately address

both medical and economic concerns of the elderly. An understanding of the complexity of pharmaceutical therapy in the elderly is essential to achieving this goal.

The elderly require individually tailored pharmaceutical care.

Medications, especially recently developed agents, can often improve the health and quality of life of older individuals suffering from many conditions, including the most prevalent diseases of the elderly listed in Chart 1. However, the elderly, a diverse population with specialized healthcare needs, require pharmaceutical care that is individually tailored to each patient based on his or her specific health status. Due to considerable variation from patient to patient, there may be no one "best practice" for treating every patient. The sources of variation include the presence of multiple chronic diseases, the physiological changes that accompany aging, and the wide variation in the properties of drugs used to treat diseases of the elderly. These separate factors, which are further discussed in this paper, interact to form a complex picture.

> The paper also presents "vignettes" illustrating how these factors can combine with uncoordinated pharmaceutical treatment to result in compromised care. Created by physicians and pharmacists, each

vignette is a hypothetical account that underscores the need for coordinated pharmaceutical care within the larger context of the entire healthcare system.

The variations in response to medications among the elderly result in part from wide differences in numbers and patterns of coexisting conditions, organ function, frailty, cognitive ability, and capacity to perform activities of daily living. Since these



CHART 1: Disease Prevalence in the Elderly

Source: Centers for Disease Control and Prevention/National Center for Health Statistics. Current Estimates from the National Health Interview Survey, 1995. Report 199, 1995.

factors differ by age, drug therapy requirements and problems may differ across "younger-old" (ages 65-75), "older-old" (76-85), and "oldest-old" (86+) age cohorts.² While the oldest-old group (especially those over 100 years of age) is growing fastest, their general physiological characteristics, their pharmacological needs, and their ability to handle medications are poorly known.

In addition, the actions of medications for many conditions, such as hypertension and depression, may differ for elderly individuals of various racial and ethnic backgrounds. Over the past 20 years, research has revealed clinically significant differences in metabolism among some minorities. These individuals may be at greater risk of an undesirable outcome if prescribed the "standard" pharmaceutical remedy for many diseases. For instance, some studies have indicated that African-Americans are less responsive to some antihypertensive agents, specifically beta-blockers and ACE-

The actions of medications may differ in elderly individuals of various racial and ethnic backgrounds.

inhibitors. In many cases, treatment with a calcium channel blocker or a diuretic may be more effective for this population. Chinese-Americans may be more sensitive to the effects of certain antihypertensives, requiring a dosage adjustment or selection of an alternate agent for optimal therapy.³ For these reasons, the availability of many therapeutic options is necessary to adequately meet the needs of various ethnic and racial groups. Although information on the differences in therapeutic response among minorities has been growing, much more research is required, particularly now as the elderly population increases in its diversity. By 2030, the rate of population growth in older minority groups is projected to be almost three times that of the total elderly population.⁴

Multiple Diseases

Comorbidity, or the simultaneous presence of two or more chronic diseases, is common in the elderly and is an important reason why treatment must be tailored to the needs of individual patients. The rate of comorbidity in the elderly population has increased steadily since the early 20th century. This increase may be attributed to a rise in the number of diagnoses and to increased longevity.⁵ As people age, the incidence and impact of comorbidity increase, resulting in a decline in well being and functional abilities.⁶

Verbrugge and colleagues determined that a person over age 55 has an average of 2.68 chronic conditions,⁷ and Hobson cited an average of 5 coexisting conditions in patients 65 years and older.⁸ The common thread through almost all comorbidity studies is that the number of diseases per person increases with age.⁵ Chart 2 depicts the prevalence of chronic conditions and comorbidity in the elderly population. By the seventh decade of life, three out of four people suffer from at least one chronic disease and more than half have two or more diseases.⁵

Just as certain individual diseases are more common in the elderly, there are also frequently occurring disease pairs. The simultaneous presence of arthritis and high blood pressure is one such pair common in older people; more than 24% of people older than 60 suffer the effects of both diseases (see Chart 3). Such comorbidity requires careful selection of drug therapy to ensure safe and effective drug combinations. In Chart 3 the incidence of several common disease pairs is shown and potential drug interactions are highlighted.

Patients with multiple diseases require multiple medications. The NHANES III study found that approximately 30% of patients age 75 or older with two or more chronic conditions take at least 5 prescription drugs regularly.⁹ Another study reports that the average elderly person commonly takes 4.5 prescription medications;⁸ among nursing home residents this number may be as high as 7 or more drugs.¹⁰





Source: Guralnik, JM et al. "Aging in the Eighties: The prevalence of comorbidity and its association wih disability." Advance Data Report 170. 1989.

Certain disease pairs may have much

greater effects on the patient.

Prescribing multiple medications poses a challenge to healthcare providers. Often, older patients visit multiple physicians for treatment of various conditions. Coordinating medications among multiple physicians in most current healthcare systems is difficult, but without coordination,

elderly patients are at increased risk for adverse drug reactions (ADRs). As the number of medications increases, so does the risk of an ADR. An ADR can result in mild to serious injury to the patient.¹⁰ Patients tak-

ing 5 or fewer drugs have a 4% chance of an ADR. With 6 to 10 medications, the risk increases to 10%, and at 11 to 15 medications, the risk of an ADR skyrockets to 28%.¹¹ These numbers indicate a need to take extra caution when determining the best drug therapy for older patients.

For patients with comorbid conditions for which they receive multiple medications, two types of ADRs, drug-drug and drug-disease interactions, are of particular concern. Drug-drug interaction can occur when the medications prescribed for two conditions do not mix well. For example, an older

> patient who has hypertension and depression may be taking guanethidine to reduce blood pressure and a tricyclic antidepressant concurrently. However, certain antidepressants interact with guanethidine, reducing its antihyper-

tensive effect.¹² This could be potentially dangerous for a patient with severe hypertension. To avoid this drug-drug interaction, an alternate antidepressant which does not reduce the effectiveness of guanethidine would be preferable.

Managing Multiple Medications: Finding Combinations that Work

Mr. K is an 80-year-old widower who lives alone, but near his daughter who looks in on him. He has a history of heart disease and high blood pressure, conditions for which his cardiologist prescribes digoxin and an antihypertensive drug, respectively. One year after his wife's death, Mr. K still does not seem to be his "old self." He has lost touch with friends, appears lethargic during the day but cannot sleep at night, and seems increasingly sad. His daughter becomes concerned and brings him to the family physician. A benzodiazepine for insomnia and a tricyclic antidepressant are prescribed. The drugs initially improve Mr. K's mood, but he soon becomes confused and for-getful. Also, he complains of dizziness and even falls once. This close call results in another trip to the physician, where his blood pressure is found to be extremely low.

Upon review of Mr. K's medications, the family physician realizes the problem. In attempting to control Mr. K's rising blood pressure, his cardiologist had increased the dosage of the antihypertensive agent. The antidepressant, the insomnia medication, and the hypertension medication together had produced the disorientation and dizziness. Further worsening the situation was the non-prescription antihistamine that Mr. K takes frequently for his hay fever and other allergies.

The doctor contacts the cardiologist to discuss the dosage of the antihypertensive and to suggest a different blood pressure medication, possibly a diuretic. He also revises the antidepressant and insomnia therapy by discontinuing the benzodiazepine and replacing the antidepressant with one also having sedative effects, with instructions to take before bedtime. For the hay fever, the doctor advises replacing the non-prescription antihistamine with a new intranasal steroid spray for his allergies that would not add to his lethargy. The new drug regimen allows Mr. K to take fewer pills while getting better results.

Drug-disease interaction occurs in patients with comorbidity when a drug prescribed for one condition worsens another condition. An example is when beta-blockers are used to treat heart disease in a patient who also has respiratory problems. Although the use of beta-blockers after a heart attack has been associated with significantly

An additional concern for the older patient with multiple conditions is the possibility of synergism.

reduced mortality rates, these medications can exacerbate breathing problems in patients who also have asthma or other respiratory dysfunction.¹³ Potential drug-disease interactions should always be considered when prescribing for elderly patients with comorbidity.

... comorbidity diminishes the practical value of single-disease standards for treatment and management

Certain disease pairs may have much greater effects on the patient than the singular effects of the two component diseases.⁷ Such pairs may substantially reduce functional ability. Diabetes plus depression or diabetes plus heart disease are two synergistic pairs yielding exacerbated effects. For patients with multiple diseases, simply combining

> the standard treatments for each disease may not be effective. As explained in a 1993 article in *The Journal of Epidemiology,* "As the natural course and therapeutic interventions of one disease will influence the co-existing second (or even third) dis-

ease, comorbidity diminishes the practical value of single-disease standards for treatment and management."¹⁴ Many drugs on the market are tested in single-disease trials and may include few elderly

CHART 3:	Comorbid	lity and	Drug	Interact	tions*

Comorbid Disease Pair	Percentage Population Over Age 60	Potential Drug Interactions	Adverse Effects
Arthritis and High Blood Pressure	24.1%	NSAIDs + Digoxin	Some NSAIDs may increase digoxin levels resulting in potential toxicity.
		NSAIDs + ACE Inhibitors	Some NSAIDs may blunt the antihypertensive effects of some ACE inhibitors.
Depression and Other Comorbid Disease	15.0%	Tricyclic Antidepressants + Clonidine (for hypertension)	The concomitant use of these agents may significantly increase blood pressure and cause potential hypertensive crisis.
Arthritis and Heart Disease	8.0%	NSAIDs + Coumadin	With NSAID use, the anti-coagulant (blood- thinning) effect of coumadin may be enhanced. Also, there is increased risk of bleeding in the GI tract.
		NSAIDs + Beta-blockers	This combination could result in a reduced anti- hypertensive effect and increased blood pressure, negatively impacting heart disease.
High Blood Pressure and Heart Disease	8.0%	Digoxin + Calcium channel blockers	Digoxin and some calcium channel blockers show additive effects increasing the potential for digoxin toxicity.
		Diuretics + Digoxin	Arrhythmia can result from the concomitant use of digoxin with loop diuretics.
High Blood Pressure and Diabetes	5.7%	Thiazides + Insulin	Thiazides reduce the effectiveness of insulin.
Arthritis and Diabetes	5.5%	Cortisone + Insulin	Harmful increase in blood glucose levels in diabetics.

* This chart illustrates only a few examples of drug interactions and is not intended to represent the scope of all potential interactions.

Drug-Disease Interaction in a Patient with Arthritis and Heartburn

Mrs. R is a 63-year-old woman with a history of moderate heartburn for which she self-medicates with an over-the-counter medication. She has recently noticed painful aching in her hands. Her doctor diagnoses her with mild arthritis and orders a prescription for ibuprofen, an anti-inflammatory pain reducer. However, Mrs. R does not mention her use of a non-prescription drug for heartburn.

After several weeks of regular ibuprofen use, Mrs. R experiences severe chest pain. She is rushed to the emergency room, but after a series of tests, the ER doctor rules out heart attack as the cause of the pain. Instead, he believes that Mrs. R has had a drug-disease interaction; the ibuprofen aggravated her heartburn severely, causing the intense chest pain. To alleviate the condition, the ER doctor contacts Mrs. R's primary care physician to propose an alternate arthritis drug, which does not result in gastrointestinal side effects such as heartburn. In addition, he suggests an evaluation to determine the root causes of Mrs. R's persistent heartburn.

participants with comorbidities. This underscores the need for individually tailored and routinely monitored drug therapy regimens.

Optimal Therapy for Elderly Patients with Coexisting Conditions

The range of pharmacological actions now available for the treatment of many diseases allows physicians to choose optimal medications for patients with one or more comorbidity. Chart 4 explains how antidepressant therapy can be optimized for patients with depression and a coexisting illness or condition. The chart lists the major classes of drugs used to treat depression, and outlines conditions that exist commonly with depression. Because of the high prevalence of comorbidity and the plethora of possible disease combinations, there is no one preferred treatment of depression in older individuals. Rather, as the chart indicates, the selection must be based on the pharmaceutical characteristics of the drug and the conditions of the patient; a medication that is a good choice for one patient may not be the best choice for another. This also holds true for the pharmaceutical treatment of diseases other than depression. The wide availability of drug options for the treatment of specific diseases helps to ensure that optimal care can be obtained for older

patients with varying health status.

In addition, some illnesses may actually represent a cluster of related diseases, with many common symptoms but differing in many aspects. Depression may be an example of such a cluster, since depressive symptoms vary among patients. For example, depression is associated with agitation in some patients, but not in others. These variations in symptomatology may reflect differences in the patterns of neurotransmitter imbalance underlying the disease. Although a decrease in serotonin appears to play a central role, norepinephrine and dopamine are implicated as well. The available antidepressant medications differ in their relative effects on these neurotransmitters, and differences exist even among agents of the same pharmacological class. Prescribers can take advantage of these differences in optimizing therapy for individual patients.

Physiological Changes

Many studies have demonstrated that age-related physiological changes affect the outcomes of drug therapy.¹⁵ As a group, the elderly span the continuum from near perfect health to extreme physiological decline. Dr. Robert M. Oskvig of the University of Rochester Medical Center concurs:

CHART 4: Optimal Therapy for Depression in Elderly Patients with Coexisting Conditions

	Antidepressants by Class						
Coexisting Conditions	Tricyclic Antidepressants (TCA)	Tetracyclic Antidepressants	Triazolopyridines	Aminoketones	Monoanine Oxidase Inhibitors (MAOI)	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin/ Norepinephrine Reuptake Inhibitors
Arrhythmia	Ø	Ø	Ø	0	\bigcirc		\bigcirc
Constipation	Ø	Ø		\bigcirc	Ø	•	\bigcirc
Hypertension	Ø	0	0	\bigcirc	Ø	$\bigcirc 1$	Ø
Insomnia	2	\bigcirc		Ø	\bigcirc	Ø	Ø
Hypotension	\bigotimes^3	Ø	Ø	٠	Ø		
Mobility Problems	Ø	Ø	Ø	•	Ø	•	•
Vision Problems	Ø	Ø		0	Ø	٠	\bigcirc
Good choice	ate choice	e in most	circum	istances	Ø Us	e with ca	ution

Sources: Drug Facts and Comparisons, 2000; Wells BG, Mandos LA. Depressive Disorders. In: Pharmacotherapy, Dipiro J editor. 3rd ed. 1997:1395-1415.

Note: This chart illustrates the range of antidepressant medications available for patients with varying conditions and characteristics, and is based on information from the sources cited and the opinions of several physicians. It is NOT, however, intended to be used as a tool to assist with prescribing.

¹ Possible interaction between specific SSRIs and specific antihypertensives.

² Due to greater sedative effects, one sub-class of tricyclic antidepressants may be preferable to another sub-class for patients with insomnia.

³ One tricyclic antidepressant, nortryptiline, is not associated with exacerbated hypotension (Wells and Mandos, 1997).

"There is consensus that physical and medical heterogeneity increases as the population gets older; that is, this population is unique for its non-homogeneity."¹⁶ Trends indicate that of the entire elderly population, the younger-old are the most homogeneous in their health status; conversely, the physiological integrity of the oldest-old varies considerably from individual to individual.¹⁶ With so much variation, many drug options are necessary to meet the health needs of specific elderly individuals and groups safely and effectively.

Changes in the Way the Body Processes Drugs

Changes in the rate at which drugs are absorbed, distributed, metabolized, or eliminated by the body can affect the level of drug in the blood stream. Higher blood levels mean greater drug action and potentially greater toxicity, and vice versa. Each of these four "pharmacokinetic" processes may be greatly altered in elderly individuals, so all drug therapy regimens must reflect a consideration of these changes.¹⁷

Absorption

As people age, drug absorption rates fluctuate due to changes in certain organs.¹⁸ For example, the changes in an older gastrointestinal tract can affect the absorption of drugs taken by mouth.¹⁹ Likewise, the absorption of drugs administered transdermally (across the skin) may be slowed by the decreased vascularity in older patients.¹⁹ Of the four pharmacokinetic processes, absorption has the least significant impact on the choice of pharmaceuticals for the elderly patient.

Distribution

Depending on their chemical structure, drugs will distribute to different places in the body. Some drugs distribute to lean body tissue, while others

... this population is unique for its non-homogeneity.

distribute to fatty tissue. As the body ages, it maintains less lean body tissue and acquires greater stores of fatty tissue. These changes will affect the dosage amount needed to produce the desired therapeutic outcome. If dosage is not appropriately adjusted for the elderly, toxicity can occur.²⁰ Toxicity refers to levels or conditions under which a drug causes an unanticipated, deleterious reaction. This is an important consideration with a drug such as digoxin, which is used to treat heart disease. Digoxin has a narrow therapeutic range, or "window" between the level at which the drug is effective and the level that results in toxicity.⁸ Also, digoxin distributes to the lean body mass, of which there is less in most elderly. Combined, these two conditions require great care in prescribing this agent for older patients. For some patients, an alternative treatment choice may be required due to these age-related changes. Other examples of drugs that may be affected by agerelated changes in distribution are gentamicin, a potentially toxic antibiotic; lithium carbonate, indicated for severe agitation;²¹ and some benzodiazepines, used to treat anxiety and sleep disorders.²²

For some patients, an alternative treatment choice may be required due to these age-related changes.

In addition to changes in body composition, diet can affect the body's distribution of drugs. According to nutrition screening programs in a wide variety of institutional and community settings, the risk rates for malnutrition in the elderly population range from 25% to 85%.²³ Malnutrition alters the therapeutic effect of some drugs that utilize protein for distribution. Although improving the diet is the best solution, sometimes this is not possible, especially for community-dwelling elders who live alone. When malnutrition is suspected, the use of a non-protein-binding drug may be the best choice.

Metabolism

Drugs are broken down (metabolized) primarily in the liver, and there is great variation in the rate of decline in liver function among elderly individuals. As people age, two important metabolic changes occur. First, blood flow through the liver is reduced.²⁴ Therefore, drugs that depend on blood flow to metabolize in the liver, such as isosorbide and lidocaine, should be started at lower doses and increased as necessary to achieve the desired therapeutic effect.⁸ Secondly, certain metabolic pathways that metabolize drugs change as people age. Some pathways are affected by aging, but some are not.²⁵ If there is a decline in function of a certain metabolic pathway, drugs that use this pathway are less preferable than ones that use other pathways. For example, metabolic reactions such as oxidation, reduction, and hydrolysis occur in the liver and are affected by aging. Therefore, drugs that use these processes could have altered effects in the elderly. Such drugs include the anti-anxiety agent diazepam, the cardiovascular agent quinidine, and the antidepressant nortriptyline.²⁶

Elimination

Many drugs are eliminated from the body through the kidneys. Unlike metabolism in the liver, the rate of decline in elimination by the kidneys is fairly predictable. In elderly patients, kidney function may be reduced by as much as 50% by age 75.²⁷ Of particular concern are renally eliminated drugs with a narrow therapeutic range. If kidney function is reduced, toxicity may occur before the body can rid itself of these drugs. Some examples of drugs of this type include digoxin,⁸ aminoglycoside antibiotics, lithium, cimetidine²⁸ and coumadin.²⁵

Aging Organ Systems

Although almost every organ system in the body is vulnerable to the effects of aging, there is great variation in organ function among elderly individuals, especially the younger-old.²⁷ Factors that effect organ aging are heredity, disease, and lifestyle. With declining organ function, the body responds differently to pharmaceuticals. Chart 5 details the effects of aging on various organ systems and the related implications for prescribing.¹⁶

Variation in Drug Action

As pharmaceutical innovation continues, the number of drugs that exist to treat diseases of the With declining organ function, the body responds differently to pharmaceuticals.

elderly will increase, offering the potential for increased longevity and improved quality of life. As of October 1999, 600 new drugs were in development by American pharmaceutical companies to treat diseases of the elderly.²⁹ But, like existing agents, new medications for a given disease are likely to vary greatly in effect. This is not to assert that one drug is better than another necessarily; rather, that different drugs prescribed for an illness can produce different responses, particularly in elderly individuals. This section examines these variations and their impact on drug selection for older patients.

Enhanced Effects

With age, organ systems can become more sensitive to the effects of certain drugs. When compared to younger patients, the elderly are more likely to experience atypical, enhanced drug effects at the target site — the organ or organ system where the drug acts. For example, the elderly are generally more sensitive to certain drugs that act in the central nervous system²⁸ The phenothiazines, chlor-

Older Bodies Need Different Drugs

Mr. P, a 67-year-old ex-sports columnist and tennis enthusiast, fell during a match and broke his arm. In the emergency room, an intern prescribes the narcotic meperidine to relieve the pain. After several days Mr. P has an unexplained seizure. Apparently, although Mr. P appears to be in top physical condition for a man of his age, his kidney function is declining. His doctor explains that aging of the kidneys can result in poorer renal function, causing a build up of some drugs and drug by-products that are renally eliminated. The drug Mr. P was given for pain produced a by-product that built up in his system and caused the seizure. Although meperidine can work well for younger patients, his doctor says, older patients who may have compromised renal function have better luck with other painkillers. Because of Mr. P's fit and youthful appearance, the intern had not considered this possibility of age-related renal impairment. Mr. P is switched to morphine, which does not have the seizure-inducing by-product. Soon after, the dosage of morphine is reduced and then completely discontinued.

CHART 5: Aging Organ Systems and Prescribing Implications

Organ System	Effects of Aging	Prescribing Implications		
Respiratory system	Increased sensitivity to certain pharmaceuticals	Problems with sleep apnea and periodic breathing with narcotics		
	Increased rigidity of chest wall	Exacerbation with opioids		
	Reduced lung muscle strength and endurance	Decreased strength and endurance of lungs with some medications		
Cardiac system	Changes of heart (stiffening, reduced muscle strength) and blood vessels	Weaker and slower heart beat and worsened circulation with diuretics and narcotics		
Central nervous system (CNS)	Increased sensitivity	Enhanced response to CNS agents requiring lower doses of drugs such as barbiturates and opioids		
	Decline in receptors and pathways (fewer brain cells and connections)	Slower mobility and voluntary motor activity; carefully monitor drugs which affect motor function		
Gastrointestinal (GI) system	Increase in gastric emptying time	Possible GI bleeding with some NSAIDs		
	Decrease in GI blood flow	Slower healing of drug-induced bleeding		
Renal system	Decreased blood flow in kidneys and decrease in kidney mass	Prolonged effects of drugs that are eliminated by the kidneys		
Immune system	Decreased immunity to disease	Possible increase in antibiotic use		
	Greater susceptionity to intection			

promazine and thioridazine, for instance, are useful in treating agitated behavior because of their sedative effects. However, the administration of these drugs in the elderly may cause enhanced effects including over-sedation and a drop in blood pressure. For patients with pre-existing hypotension (low blood pressure), this could cause weakness and dizziness resulting in falls and fractures.¹⁷ Likewise, long-acting anti-anxiety drugs such as benzodiazepines, which may be a good choice for elderly patients with occasional insomnia, are not appropriate for long-term daily use because of their tendency to build up and increase the risks of sedation, confusion, and falls.¹⁷ To induce sleep, alternatives such as antihistamines or newer agents without these side effects could be considered.

Diminished Effects

The opposite of enhanced drug effects, diminished effects are sometimes seen in the elderly. Just as some organ systems are more sensitive to

some agents, some systems are less sensitive to particular drugs as well. For instance, the elderly tend to be less sensitive to some calcium channel blockers, which are used to treat heart disease. Older patients may require a higher dosage of a calcium channel blocker to achieve the same therapeutic effect as younger patients. This may be due to the decrease in receptor sensitivity. Interestingly, older patients are more sensitive to the secondary effects, or side effects, of some calcium channel blockers, which include decreased blood pressure and heart rate. For these reasons, calcium channel blockers may be an appropriate and cost effective choice for treating patients with comorbid heart disease and hypertension.¹⁷

Side Effects

As seen in the calcium channel blocker example, some drug side effects can be used to a patient's advantage depending on the individual and his or her particular health needs. Other side effects may not be desirable but can be tolerated, again depending on the patient's condition. Three types of drug side effects that are particularly significant for elderly patients are central nervous system (CNS) effects, anticholinergic effects, and cardiovascular effects. With younger patients, these side effects would not cause the same concern they do for older patients; in fact, in some instances younger patients would not experience them at all. Because of the increased prevalence of comorbidities and the tendency toward physiological decline, the elderly may be more susceptible to side effects. Heightened sensitivity to side effects is important in selecting drugs for individuals.

Central Nervous System

The central nervous system can be affected by particular drugs used to treat other organ systems. For example, the H_2 receptor antagonist cimeti-

The elderly may be more susceptible to side effects.

dine, used to treat gastrointestinal disorders, has been associated with reversible CNS side effects, such as confusion, psychosis, and hallucination in the elderly and the severely ill.¹⁷ For patients who have comorbid conditions or who are very old, selection of an alternative H_2 receptor antagonist with lesser side effects may be a safer choice. In addition, some NSAIDs that treat arthritis can cause confusion in elderly patients as well.

Anticholinergic

Also referred to as anticholinergic agents, drugs that block the action of acetylcholine in the body have many uses in elderly persons (e.g., glaucoma, Parkinson's disease). However, anticholinergic properties of agents used to treat other diseases can result in negative side effects. Many of the tricyclic antidepressants, for example, which are often used to treat depression in older individuals, have substantial anticholinergic activity. Importantly, anticholinergic side effects often parallel problems that are already common in the elderly, including:⁸

- Dry skin and mouth
- Tachycardia (rapid heart beat)
- Ataxia (inability to coordinate voluntary muscular movements)
- Dementia (disorientation, confusion)
- Constipation

If a patient shows signs of these conditions prior to drug selection, alternate agents that do not cause anticholinergic effects may be preferable.

Cardiovascular

Several agents used to treat diseases of the elderly have effects on the cardiovascular system, the heart and blood vessels. Powerful diuretics often used for congestive heart failure may lower blood pressure in the elderly. When blood pressure drops significantly, orthostatic hypotension, a dizziness that occurs when a person stands or sits up quickly, can occur. A common problem in the elderly, orthostatic hypotension can result in lifethreatening falls and fractures. The opposite effect, an increase in blood pressure, can be caused by some antibiotics and some NSAIDs with high sodium content. This is a cause for concern with hypertensive patients. Some psychoactive drugs, particularly tricyclic antidepressants, Drug variances should be taken into account to optimize any properties that could prove beneficial.

can cause arrhythmia, or an irregular heart beat.²⁸ Finally, fluid and electrolyte disorders can at times be attributed to the use of some NSAIDs, antibiotics, or diuretics—a consideration for patients with congestive heart failure.

In addition to the CNS, anticholinergic, and cardiovascular side effects described, other side effects may materialize during the course of drug therapy. All potential drug variances—be they side effects, enhanced effects, or diminished effects—should be taken into account during

Taking Advantage of Side Effects

Mrs.W, a 70-year-old married smoker and diabetic, cares for her husband, whose health has been in decline since his stroke a year ago. The worry about her husband's health plus the physical burden of caring for him has placed considerable stress on Mrs. W. Her doctor has warned her about long-term smoking, but she continues with the habit. Her blood pressure has recently been elevated at 140/100 mmHg, and traces of protein have been found in her urine, which indicates that Mrs. W might be developing diabetic kidney disease. Her doctor suggests a medication that could manage both the hypertension and kidney disease: an ACEinhibitor (for high blood pressure) that has the side effect of reducing the protein in Mrs. W's urine. This medication could lower her blood pressure and could possibly forestall kidney disease, thereby "killing two birds with one stone," as Mrs. W puts it.

drug decision-making for elderly patients to avoid harm and optimize any properties that could prove beneficial for an individual. An adequate choice of medications should be available for this purpose.

Obstacles to Individualized Drug Therapy for the Elderly

Considering the variation among elderly individuals and the medications they use, individually customized drug therapy makes good sense. However, external obstacles often impede this initiative. Major impediments include switching and limiting drugs. Yet, these obstacles are not all within the control of the patient and physician. As medical and economic factors collide, patient wellness and quality of care can be compromised.

Switches

A variety of circumstances can lead to a switch in an elderly patient's drug therapy regimen. Many times these switches are not based on a physician's advice, but instead are the result of factors beyond patient and physician control such as a change in insurer, formulary, or care setting. Pharmaceutical switches can occur when a patient retires from employment, which often means a change in health insurance benefits. Because drug formularies vary by insurer, patients could be forced to switch drugs when they change insurers, even if their current drug therapy regimen is working perfectly. Similarly, when patients migrate across various care settings, as the elderly are likely to do, formularies may change and drug switches may occur. From home, to hospital, to nursing facility, to hospice, the availability of specific medications to older patients will fluctuate.

Similarly, switches can occur when drugs in the same class are prescribed interchangeably as a cost-saving measure. Therapeutic interchange may result in unexpected, and unwanted, responses

due to variation among drugs of the same class, as alluded to earlier. Expert medical groups, notably the American Association for Geriatric Psychiatry (AAGP)³¹ and the American Medical Association (AMA)³² have

voiced concerns regarding the appropriateness of drug interchange in the elderly. The AAGP supports the notion that biological and physiological characteristics of the elderly, like comorbidities and changes in pharmacokinetics, may cause unexpected changes in the effects of certain medications. The AAGP also asserts that restricted choice of medications may be detrimental to the elderly individual and to the community in many ways.³¹

Therapeutic interchange—or switching—may be

... restricted choice of medications may be detrimental to the elderly used by organizations or hospital pharmacies as a cost-saving measure, and indeed cost savings are documented in some cases.³³ But often the cost savings are minimal, are offset by higher utilization costs for other services,³⁴ or are a

trade-off with reduced quality of care.³⁵ Several studies have reported negative health outcomes resulting from switches as well. Even substituting dosage forms—chewable tablets for capsules or liquid for solid medication—can present problems for older patients who may have difficulty with chewing, measuring, or pouring.³⁶ This could result in hazardous under- or over-medication. In one study, when patients who were stabilized on one of three medications for hypertension were switched to a fourth agent, there were increases in

The Aging Body, Multiple Diseases, and Medication Restriction: A Cascade of Events

Mrs. C, a small, thin woman of seventy-five, lives alone in a low-rent apartment and is often lonely and anxious. She kept her health benefits after retiring from her secretarial job ten years ago, but her plan does not cover all of her medical expenses. She suffers from atrial fibrillation, an abnormal heart rhythm that could result in dangerous blood clots. To reduce the risk of clotting, her physician has prescribed the anticoagulant drug warfarin, which she has now been taking for over a year.

When Mrs. C reports that she is depressed and anxious, her physician prescribes an antidepressant medication. But she is told at the pharmacy that the prescribed drug is not covered by her health insurance and is given an alternate antidepressant with the same mechanism of action. After two months on this medication her depression and anxiety have improved. But her clothes feel bigger and she is eating less, and the slightest pressure seems to result in a black and blue bruise on her body.

The next time Mrs. C visits her doctor, her weight has dropped ten pounds and she shows signs of malnutrition. She shows him the bruising. When the doctor asks how she is doing on the medication he prescribed for depression, she tells him about the replacement. The doctor then is able to understand the unfortunate cascade of events that have occurred. He explains that a side effect of the replacement drug is appetite suppression, and this has reduced Mrs. C's already small appetite to almost nothing. Without a healthy diet, the anticoagulant effects of the warfarin she takes for her heart condition have become exaggerated. The excess anticoagulant in her blood has caused the bruising. The doctor says he is glad she brought these symptoms to his attention because with time a more serious problem such as stroke could have developed.

Under use of beneficial drug therapy by seniors has been associated with increased morbidity, mortality, and reduced quality of life.

clinic visits, laboratory services, and side-effects management, even though all four drugs were of the same class.³⁷ Although the scope of this paper precludes a detailed account of all the negative outcomes of pharmaceutical switches, numerous studies show similar findings.³⁸

Limits

As with drug switching, some policy-makers and drug benefit managers have sought to manage costs by limiting the number or range of drugs available for reimbursement. Limits have also been suggested as a way to promote appropriate prescribing in nursing homes.³⁹ Studies have demonstrated, however, that limits can result in negative outcomes for elderly patients: "Under use of beneficial drug therapy by seniors has been associated with increased morbidity, mortality, and reduced quality of life."⁴⁰

For example, a Medicaid study revealed that the number of gastrointestinal surgeries increased after an important drug for peptic ulcers was removed from the formulary.⁴¹ In another study, when caps were placed on the drug benefit of Medicaid beneficiaries, nursing home admissions increased.⁴² In the latest nursing home guidelines, however, the Health Care Financing Administration (HCFA) suggested that patients taking nine or more drugs might be receiving

inappropriate care. The American Society for Consultant Pharmacists opposes this claim, responding, "The number of medications ordered per resident per month is not a meaningful measure of quality. The correct number of medications must be determined individually for each patient."³⁹ Yet, individualization of pharmaceutical regimens for the elderly is challenging if switches and limits occur without regard to the specific health status of the patient, as with routine therapeutic interchange and some restrictive drug policies.

In addition to the potential for counterproductive effects on treatment outcomes, limiting drug benefits is not always a cost-saving measure because of the possible negative economic outcomes associated with under-utilization and other inappropriate prescribing practices.⁴³ Numerous studies have documented a cost shift rather than cost savings when drug limits are used as a cost containment strategy; drug costs may be reduced, but utilization of services increases.³⁸ Focus should be on appropriate prescribing practices rather than savings strategies that could compromise care. To ensure a stable balance between quality therapy and cost-minimization, simply limiting drugs will not work. A coordinated approach to pharmaceutical care in which elderly patients have access to much-needed pharmaceutical options may reduce money spent on complications while enhancing quality of care.44

The number of medications is not a meaningful measure of quality for each patient.

Conclusions: The Need for Coordinated Pharmaceutical Care

The elderly can benefit most from customdesigned, coordinated pharmaceutical therapy, but they are also the population at greatest risk for receiving sub-optimal drug therapy if their unique needs are overlooked. The special risks that older Americans face—due to comorbidities, age-related physiological changes, and variation of drug effects—call for individually tailored drug therapy programs and a coordinated approach. As the pace of innovation in pharmaceuticals, diagnostics, and medical practice quickens, the "practice gap" between the availability of important innovations and their most effective use is widening. The advent of "disease management," which has brought many important advances beyond episodic and uncoordinated care, has resulted in increased cooperation and information-sharing among providers.

Still, additional coordination of pharmaceutical care is often required because disease-by-disease approaches may neglect interactions among diseases and their treatments.⁴⁵ The rise of medical specialists and sub-specialists coupled with the

The next step in the evolution of geriatric pharmaceutical care will be to improve the coordination of treatments. increase in fragile elderly with chronic, comorbid diseases demands greater coordination of care. Older patients often see several prescribing physicians, who may not be aware of all the medications patients are taking. Such disconnected care can result in poor outcomes including medication errors and adverse events, as illustrated in the vignettes included in this article. Similarly, the increasing number of health system mergers has resulted in increased shifting of patients among treatment sites, a practice that can disrupt the continuum of care so necessary for the proper treatment of the frail elderly.

To address these issues, the next step in the evolution of geriatric pharmaceutical care will be to improve the coordination of pharmaceutical treatments, including the identification of patients with undiagnosed, untreated, or under-treated disease. While the ability to select drug therapy for a given disease from a full bank of pharmaceutical options is important, every provider involved in a patient's care—including primary care physicians, specialists, pharmacists, nurses, and others—also needs a complete picture of the therapy plan.

Recent strategies to coordinate pharmaceutical care include the use of technologies such as prescription tracking software and computer algorithms to spot patients at risk for sub-optimal use of medications. Moreover, the use of highly trained clinical pharmacists is increasing, as is the streamlining of standard processes for getting the right drugs to patients. While these strategies have improved the coordination of care in some settings, most elderly patients have yet to benefit from these innovations because implementation has not been system-wide.⁴⁴ The vision for the future is a more complete and cohesive coordination of all aspects of care—including pharmaceutical care—in all healthcare settings.

Appendix: Diseases of the Elderly

Only a handful of diseases account for most of the healthcare utilization and costs incurred by the elderly population. In order to provide a more complete illustration of the healthcare needs of seniors, descriptions of some of their most prevalent diseases are provided below.

As medical and economic factors collide, patient wellness and quality of care can be compromised.

Arthritis affects over 49% of older Americans, according to a 1995 National Center for Health Statistics report.¹ A disease with more than 100 forms, arthritis is a debilitating and painful inflammation of the joints. Although arthritis affects people of all ages, the elderly are particularly at risk for its most common form, osteoarthritis. The total cost of arthritis care to the U.S. is more than \$65 million annually. Although many older people believe that arthritis and its accompanying pain is just a simple fact of aging, Dr. Steven Abramson of the Arthritis Foundation contends that early diagnosis and treatment of arthritis can forestall serious joint damage. He encourages patients to seek treatment from their physician when early signs strike rather than relying only on over-the-counter products that provide minor pain relief.²

Heart Disease, the leading cause of death among older Americans, manifests in many forms, including coronary artery disease and congestive heart failure (CHF).³ *Coronary artery disease*, or atherosclerosis, occurs when the inner walls of arteries become narrow due to an accumulation of cells, fat, and cholesterol. This makes it difficult for blood to pass through the heart, and can cause a heart attack. A second major disease of the heart, *congestive*

heart failure, occurs when the heart is not pumping fast or strongly enough to deliver the required amount of blood and oxygen to the body. The causes of CHF can include high blood pressure, coronary artery disease, past heart attack, or disease of the heart muscle itself. Two other diseases of the elderly, hypertension and stroke, are very closely tied to heart disease, but are significant enough in their singular impact as to warrant a separate description.

Hypertension, more commonly known as high blood pressure, means that the pressure in the heart's arteries is above the normal level, approximately 120/80 mmHg.³ The top number (systolic pressure) describes the pressure while the heart is beating; the bottom number (diastolic pressure) indicates the pressure when the heart is at rest. Hypertension can be an early warning sign for other life-threatening heart diseases. While a healthy diet and regular exercise can help, medication is often necessary to reduce high blood pressure, especially in older patients.

Diabetes, a chronic disease for which there is no cure, affects approximately 13% of the age 65+ population.¹ It is possible that this estimate is lower than the actual number of diabetes cases because many people remain unaware of their illness until it reaches advanced stages. Diabetes is the result of the body's inability to properly produce or use insulin, a hormone necessary for converting food into energy. **Type II diabetes,** the most common form of the disease, affects older Americans most often because of increased longevity, obesity, and lack of exercise.

When a blood vessel to the brain gets clogged or bursts, a *stroke* occurs. As a result, the portion of

As pharmaceutical innovation continues, the number of drugs that exist to treat diseases of the elderly will increase. the brain supplied by that vessel shuts down, as does any part of the body it controls. Affecting 7% of the seniors over age 65, stroke can be caused by smoking, uncontrolled hypertension, or heart disease.³

Depression is characterized by four main groups of symptoms: anxiety, a depressed mood, slower mental and physical functioning, and various physical complaints. In the elderly compared to younger patients, however, different symptoms are emphasized. Anxiety, for instance, is more common in older patients. In addition, older patients tend to report symptoms of depression less often, viewing them as just the effects of old age.⁵ This underreporting suggests that there may be even greater numbers of depressed seniors than the 10% cited in Chart 1.

Alzheimer's Disease, the most widespread type of dementia, is a progressive, degenerative brain disease that causes confusion, memory loss, and

diminished cognitive abilities. Almost all of the 4 million Americans who currently suffer from Alzheimer's disease are older people. As the elderly population grows, 14 million Americans will have Alzheimer's by 2050 unless a cure is found.⁶

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