Individualized Prescribing for the Elderly

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Nearly 300 years ago, Thomas Jefferson, the namesake of the institution where several coauthors of this P&T supplement work, was quoted as saying, “My only fear is that I may live too long.” Three centuries later, medical technologies (particularly pharmaceuticals) have literally changed the way people age. Thanks to therapies that have been available only over the last decade or so, our patients—and we, ourselves—live not only longer, but better lives.

Such dramatic improvements do not come easily. Until a future Ponce de Leon discovers a scientific answer to the search for the fountain of youth, there will be no cure-all for the aging of the human body. Even the interventions we currently use to lengthen and improve patients’ lives demand careful and informed attention. No matter how far we’ve come, an 82-year-old body is quite different from a 20-year-old one, and our interventions (pharmaceutical or otherwise) need to acknowledge and respect that difference. To do so, we must arm ourselves with the necessary tools—a strong foundation of knowledge, a reliance on evidence-based medicine, and dedication to continuous learning—to protect and care for our patients at an extremely vulnerable stage of life, the twilight years. That is our intent in bringing to you this publication, to provide a tool with which to build and strengthen the practice of geriatric medicine, for ourselves, for our professions, and most importantly, for our patients.

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Advances in health care and pharmaceuticals have made it possible to treat many diseases that manifest as people age. However, a “one-drug-fits-all” approach is not ideal, especially for older patients, who are exposed to unique health-related variables. When these variables interact in an older patient, individualized drug therapy is required.

Selection of pharmaceutical therapy for elderly patients 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. The presence of comorbidity underscores the necessity of optimizing multi-drug therapy to avoid possible interactions and maximize therapeutic effects.

Second, the physiological changes that accompany aging affect each patient’s response to pharmaceutical therapy: metabolism rates change, organ function declines, and sensitivity to some drugs can be altered.

Finally, drug side effects—which can be viewed as the price paid for controlling diseases associated with ever-increasing life spans—can appear unpredictably in this population because of the extreme physical heterogeneity in physiological reserve.

These three factors suggest a clear need for individualized prescribing for the elderly. Alone, a population-based approach to treatment is limited in its effectiveness. It is better to use a population-based approach as the foundation for drug therapy decision-making, and augment it with appropriate individualized treatment. This supplement describes specific clinical factors implicitly involved in determining individual drug-therapy regimens for elderly patients with multiple health concerns.
Part 1: The Complex Dynamics of Aging, Comorbidity, and Drug Therapy

OBJECTIVES

✓ Identify the unique physiological characteristics of the elderly that have an impact on prescribing decisions.
✓ Identify and discuss the factors contributing to the need for individualized, coordinated pharmaceutical care of the elderly.
✓ Examine ten principles of individualized prescribing for the elderly using case-based scenarios.

One rationale for individualized pharmaceutical treatment is the frequency of comorbidity in the elderly. The rate of comorbidity in this population has increased steadily since the early 20th century. This increase can be attributed to increased longevity; individuals are living longer with more chronic diseases. Verbrugge and colleagues determined that a person over age 65 has an average of 2.66 chronic health conditions; and Hobson cited five coexisting conditions in patients 65 years and older. Although estimates vary (most likely because of variances in reporting and methodologies), sources indicate that the number of these diseases per person increases with the age of the individual. By the seventh decade of life, three out of four people suffer from at least one chronic disease and more than half suffer from comorbidity, which often affects their well-being and functional abilities.

In the elderly, frequently occurring disease pairs that require pharmacotherapy include arthritis/hyper tension (24.1%); depression/other medical illness (15%); arthritis/heart disease (8%); hyper tension/heart disease (8%); hypertension/diabetes (5.7%); and arthritis/diabetes (5.6%). Certain disease pairs have unexpectedly significant effects that are much greater than the singular effects of the two component diseases. These synergistic effects are measured by the extent to which they adversely affect functional ability. For a patient with synergistic diseases, simply combining the standard of care for each disease might not be enough. As explained by Schellens and colleagues in a 1993 article in The Journal of Epidemiology, "As the natural course and therapeutic interventions of one disease will influence the coexisting second (or even third) disease, comorbidity diminishes the practical value of single-disease standards for treatment and management." Many drugs on the market are listed in single-disease trials and include few elderly participants with comorbidities. This underscores the need for more epidemiological research on comorbidity in the elderly population; clinically, it reinforces the mandate for individually tailored and routinely monitored drug-therapy regimens.

According to the NHANES III—a large, well-designed study sponsored by the federal government—approximately 30% of patients aged 75 or older with two or more chronic conditions take at least five prescription drugs regularly. Another study reports that the average elderly person commonly takes 4-5 prescription medications among nursing home residents; this number may be as high as seven or more drugs. Co-administered medications can often result in changes in drug effects, an occurrence that affects comorbid diseases. Similarly, taking multiple medications increases the risk of adverse drug reactions (ADRs). Patients taking five or fewer drugs have a 4% chance of developing an ADR. With six to 10 medications, the risk increases to 10%, and at 11 to 15 medications, the risk of an ADR skyrockets to 28%. Although coordinating medications among multiple physicians in most current health care systems is difficult, coordination can greatly optimize a patient's drug-therapy regimen. A coordinated approach can encourage better treatment of all coexisting illnesses and reduce the risk of ADRs. As conscientious physicians and pharmacists, we must be advocates for appropriate coordinated care for all patients, especially older ones, to circumvent untoward outcomes and optimize therapeutic effects.

The complex picture created by comorbidity when prescribing medication for the elderly is illustrated in the subsection "Depression and Comorbid Medical Disease," which provides an overview of this common condition. Following the general discussion, we look at two conditions that often exist with depression in the 65+ age group—heart disease and dementia. Following the comorbid depression discussion, we examine another disease pair with serious physical effects for seniors: heart
Disease (including hypertension) and diabetes. All three pairs—depression/dementia, depression/heart disease, and diabetes/heart disease—were selected as examples based on their prevalence in the elderly population, the seriousness of their impact on health, or both.

DEPRESSION AND COMORBID MEDICAL DISEASE

At least 15% of elders who are seriously and/or chronically ill experience concurrent depression. The true prevalence is probably greater in the medically ill elderly because depression is often underreported by patients and under-diagnosed by physicians. Nearly 50% of people with depressive symptoms do not seek treatment; of those who do, almost half are misdiagnosed. Underuse of effective antidepressant therapy can result from the perception, by both patients and doctors, that depression is an inevitable consequence of old age combined with declining health. Likewise, underutilization of beneficial antidepressant therapy can result from hesitancy to add another medication to the current treatments for comorbid physical illnesses. Especially in the era of increased attention to patient safety and medical errors, physicians often avoid prescribing multiple medications because of their fears about ADRs. However, combination drug therapy that considers all of an individual’s conditions and all potential drug effects can offer a better outcome than not treating the depression.

Because of the synergy between depression and medical illness, treating one condition effectively can encourage the improvement of the other and reduce associated disability. According to numerous, well-documented sources, morbidity and mortality increase in depressed patients with medical illnesses. The question then becomes how to treat depression in the elderly, not whether it should be treated.

Clinical trial data indicate that newer medications like selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs) offer similar efficacy (approximately 60–80% patient response rate) and improved side-effect profiles compared to older antidepressants, including tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). In rare instances, TCAs can be a superior option, depending on individual patient characteristics, which vary widely in the elderly population. Most important is the selection of the appropriate combination of antidepressant(s) and other pharmaceuticals prescribed for comorbid diseases.

DEPRESSION AND CARDIAC DISEASE

Cardiac disease affects more than 31% of Americans over the age of 65. For patients with coronary heart disease, the risk of depression increases from 15% in the general population to between 18% and 50%. Numerous researchers contend that depressed cardiac patients risk longer recovery periods, increased use of medical resources, and greater mortality, particularly for post-myocardial infarction. Effective pharmaceutical treatment can reduce these risks appreciably. However, care must be taken to select the most effective agent for individual elderly patients.

Although they are now used less frequently, TCAs (e.g., desipramine, nortriptyline) and MAOIs provide effective therapeutic relief of depression. However, data on prescription usage suggest that most physicians are choosing SSRIs over older antidepressants to treat depression. As we now know, older antidepressants, while efficacious, have a less favorable side-effect profile than newer agents. In elderly patients with cardiac disease, these drugs can pose a serious health threat. Many TCAs have unpredictable proarrhythmic effects, and high concentrations can cause ventricular arrhythmias, especially in patients with cardiacconduction disease. According to Explicit Criteria for Determining Inappropriate Medication Use, developed in 1997 by Mark H. Beers, MD, and six other national experts in cardiovascular pharmacology, TCAs are considered inappropriate for elderly patients with pre-existing arrhythmias because of their propensity to induce arrhythmic response. This panel concluded that the highest risk and severity of adverse reaction occurs within the first month of administration, highlighting the need for close monitoring, especially near the initiation or change of therapeutic regimens.

MAOIs, which reduce depression by blocking the monoamine oxidase enzyme that breaks down norepinephrine and serotonin, also raise similar concerns for cardiac patients. MAOIs can provoke hypertension to dangerous levels if taken in combination with certain foods and beverages, such as hard cheeses, aged meat, fish, and wine. Both TCAs and MAOIs have side-effect profiles that make them inappropriate for treating geriatric depression in many patients, with or without cardiac conditions. These side effects are discussed further in Part 3: Drug Variation and Side Effects in Older Patients.

Despite the evidence regarding TCAs and MAOIs, a few studies suggest that they are indicated (or even preferable) for elderly depressed cardiac patients under certain conditions. Because of the sleep-inducing property of most TCAs, they are effective for elders with depression-related insomnia. Selection of an agent such as nortriptyline, which engenders significantly less orthostatic hypotension than other TCAs, can help to avoid complications in cardiac patients while alleviating depression and insomnia. However, severity of cardiac illness must be a major factor in decision-making. Any patient at serious risk for ischemic heart disease should avoid the use of TCAs, because of their proarrhythmic effects on conditions caused by oxygen deprivation (i.e., during angina or myocardial infarction [MI]). The only occasion that war-
nants use of MAOIs in the elderly is when patients do not respond to other agents; even so, such cases call for review by clinicians skilled in psychopharmacology. 14

Although they are no “magic bullet”, SSRIs have considerable benefit over older agents for treating depression in elderly heart patients. 21,22 Compared to TCAs, newer antidepressants—SSRIs and SNRIs—pose minimal safety risk to elderly cardiac patients, according to the numerous studies. 13,14,16,23 A 1997 risk-benefit analysis of patients with pre-existing cardiac disease who were taking SSRIs did report a few patients developing arrhythmias, including atrial fibrillation and flutter, bradycardia, and supraventricular tachycardia. However, the study noted that these occurrences were by far the exception rather than the rule; the possibility of adverse cardiac events with the use of SSRIs is under 0.0003%. 24

If individual patient characteristics and contraindications are overlooked, however, the potential for drug-drug interactions between SSRIs and co-prescribed medications can exist. 25 SSRIs are metabolized by the cytochrome P450 system in the liver, the same site where many other medications are metabolized, including numerous cardiac agents. When adminis- tered in combination, SSRIs can increase blood levels of medications with a similar site of metabolism, escalating risks to patients. 24 This type of complication can be remedied by selecting medications for comorbid illnesses that are not metabolized by the cytochrome P450 system, or by choosing a non-SSRI antidepressant. As detailed in Table 1, medication combinations that offer optimum risk-to-benefit ratios should always be first-line therapy for patients with depression and one or more additional illnesses or conditions, particularly with heart disease, because of its inherent potential for significant morbidity and mortality.

DEPRESSION AND DEMENTIA

When depression and dementia, the two most common conditions of geriatric psychiatry, occur together, a jigsaw puzzle of overlapping symptoms and synergistic complications is formed. Although the overlap of symp- toms can obscure differential diagnoses of these disorders, accurate identification of this disease pair is crucial for improving functional ability in patients with incurable dementia. 25 The difficulty of diagnosis causes studies to vary widely in reported prevalence (0-87%); however, most research estimates that coexisting depression occurs in 30% to 40% of demented patients. 26,20 Greater disability, worsened cognitive impairment, increased resource use, and increased mortality are associated with comorbid dementia and depression, compared to either condition alone. 20

Unfortunately, although having both conditions simultaneously can exacerbate symptoms of each, effectively treating one condition does not appear to improve the primary symptoms of the other condition (unlike many other disease pairs). For that reason, concomitant therapy is almost always required. Dementia alone often calls for therapeutic treatment on two fronts: to manage behavioral symptoms and to improve cognitive performance. Concomitant antidepressant therapy considerably reduces morbidity and mortality, and effectively improves mood in demented patients, although there is no proven long-term effect on cognition. 23 Figure 1 describes the layers of treatment necessary to handle older patients with both depression and dementia.

“Pseudodementia” can sometimes be mistaken for actual dementia. Pseudodementia is a condition that mimics dementia symptoms in depressed patients, but it is reversible with antidepressant treatment. Much rarer than actual dementia, pseudodementia is believed to be an affective manifestation of somatic complaints, which are common in the depressed elderly. 20 In fact, pseudodementia can only be diagnosed using effective treatment with antidepressant therapies. If the symptoms of dementia do not resolve with antidepressant therapy, it is likely that pseudodementia is not the diagnosis and the patient will require treatment with medication for dementia as well.

Regrettably, treatments for the most common dementia, Alzheimer’s disease, are not curative at present. Palliative care is available with four FDA-approved drugs for treatment of Alzheimer’s disease — tacrine (Cognex, Parke-Davis), donepezil (Aricept, Eisai/Pfizer), galantamine (Reminyl, Jansen), and rivastigmine (Exelon, Novartis). 20 Several other agents are now in clinical trials. In addition, some clinicians treat Alzheimer’s patients with off-label drugs, such as aspirin and some nonsteroidal anti-inflammatory drugs (NSAIDs), although evidence of their effectiveness is predominantly anecdotal.

It is important to note that up to 30% of Alzheimer’s patients have at least one other psychiatric illness (such as depression) contributing to their dementia. 31 Although cognitive deterioration cannot be reversed, studies indicate that treating psychiatric comorbidities in addition to Alzheimer’s disease produces temporary functional improvement in up to 26% of patients, half of whom experience sustained improvement for at least one year. 31 Whereas medication with adverse cognitive effects (such as large, continuous doses of benzodi- azepines) should be avoided, therapies that maximize organ function by ameliorating comorbid illnesses are beneficial to Alzheimer’s patients. 27

DIABETES AND CARDIOVASCULAR DISEASE

Comorbid diabetes and cardiovascular disease (CVD)—including hypertension—frequently occur in the elderly patient population. Coronary artery disease (CAD), for example, has been documented in 31% to 83% of patients with non-insulin-dependent diabetes mellitus (NIDDM or type 2). The impact of this disease pair on
Table 1. Treatments for Depression with Comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>MAOIs*</th>
<th>Tricyclics-Tertiary Amines</th>
<th>Tricyclics-Secondary Amines</th>
<th>Tetracyclics</th>
<th>SSRIs*</th>
<th>Others</th>
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<tbody>
<tr>
<td></td>
<td>Phenelzine</td>
<td>Tranylcypromine</td>
<td>Amitriptyline</td>
<td>Clomipramine</td>
<td>Doxepin</td>
<td>Imipramine</td>
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<td>Depression Plus Disease</td>
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<td>Other Psychiatric</td>
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<td>Mixed Anxiety/Depression</td>
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<td>Psychotic Depression</td>
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<td>Cardiovascular Disease</td>
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<td>Congestive Heart Failure</td>
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<td>Cardiac Conduction Disease</td>
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<td>Ischemic Heart Disease</td>
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<td>Hypertension</td>
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<td>Dementia</td>
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<td>Epilepsy</td>
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<td>Diabetes</td>
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<td>Stroke</td>
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<td>DEPRESSION PLUS OTHER FEATURES/</td>
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<td>CONDITIONS</td>
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<td>Taking blood pressure-lowering</td>
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<td>medication</td>
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<td>Prone to Constipation</td>
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<td>Insomnia</td>
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<td>Somnolence and Lethargy</td>
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<td>Suicide Risk</td>
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<td>Frail and Underweight</td>
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X = not recommended. O = good choice under certain conditions.
*generally, MAOIs should be avoided in the elderly if possible, because of serious food interactions.
**concomitant use of certain benzodiazepines with SSRIs can be hazardous.
morbidity and mortality is astounding; the five-year post-acute MI mortality rate for type-2 diabetic patients is as high as 55%, compared to 30% in patients without diabetes. The Framingham study corroborates these findings: the risk for CAD is 2.4 times greater in diabetic men and up to 5.1 times greater in diabetic women versus the non-diabetic 45- to 75-year-old population. Having diabetes is equivalent to having any other two risk factors for CAD, such as smoking and hypertension. These facts and figures indicate that adequate management of diabetes and CAD is essential for reducing the risk of death, especially in the more vulnerable elderly population.

Although controlling both diabetes and heart disease is partly dependent upon behavioral factors such as lifestyle choices (e.g., smoking, dietary habits, and activity level) and adherence to medical treatments, physicians and pharmacists can help their elderly patients by optimizing their drug regimens. During the April 2000 annual meeting of the American College of Physicians/American Society for Internal Medicine (ACP/ASIM), physician experts identified three groups of patients who need special attention to reduce cardiovascular disease and heart-related death: people with multiple cardiovascular risk factors, people with diabetes, and the elderly. Those who are 65+ years old with comorbid diabetes and CVD fall into not one but all three of the groups mentioned, multiplying their risk of coronary events if factors such as hypertension, hyperlipidemia, and hypercholesterolemia are not well managed. Speakers at the ACP/ASIM conference cited research showing that when blood pressure is tightly controlled in diabetics, chances of developing diabetic complications, having a heart attack, and having a stroke are significantly reduced. However, it was noted that some groups, particularly the elderly, are under-treated for hypertension. Jerome D. Cohen, M.D., of the St. Louis University Health Sciences Center in Missouri, asserted that “there is no reason not to treat an otherwise healthy person in their 80s for hypertension.” Considering the additional threat diabetes poses, reducing all CVD risk factors in elderly diabetic patients is even more imperative.

Currently, treatment recommendations for reducing coronary risk in diabetic patients are more or less equivalent to those for non-diabetics. Some variances do exist, particularly when treating the 65+ year old population. Whenever possible, lipid levels should be managed primarily through dietary modifications in cases involving patients who take diabetes medications such as glucophage or injectable insulin. If this does not sufficiently control total cholesterol, LDL cholesterol, and total triglyceride levels, secondary prevention measures with antihyperlipidemics should be utilized.
When medication is required, diabetic patients with hypercholesterolemia generally receive HMGCoA reductase inhibitors, or statins, as first-line therapy to reduce cholesterol. Two secondary prevention studies, the Scandinavian Simvastatin Survival Study (the 4S study) and the Cholesterol and Recurrent Events (CARE) Study, revealed a reduction in clinical cardiac events in diabetic patients with the use of lipid-lowering therapy. The 4S trial found a 56% lower risk of coronary complications in diabetics receiving simvastatin compared to those who received a placebo. Both studies, however, were not exclusive to the elderly.

Although clinical trials have repeatedly shown the safety of statins, elderly patients with certain characteristics can respond better to one statin than another, or might require therapy with an alternative agent. Specifically, patients with diminished liver function, myopathy, and/or cancer might need individualized treatment plans. Also, patients with muscle and joint pain, a common condition in the elderly, may experience exacerbated muscle pain when taking statins. In most cases, it is recommended that patients be started on a statin and that their symptoms and blood levels be monitored. Then, if the statin is not well tolerated, an alternative agent is advised.

Although numerous medications are available to control hypertension, not every agent is appropriate for diabetic heart patients. Diuretic and β-blocker therapy can reduce morbidity and mortality associated with hypertension, but they can negatively affect glucose tolerance and lipid profile. Generally, angiotensin-converting enzyme (ACE) inhibitors are considered first-line therapy because of their protective effects on the heart and kidneys. Combined therapy using two or more antihypertensive agents is frequently necessary to adequately manage blood pressure in some elderly patients. Even so, researchers contend that prospective trials are critically necessary to better compare the different classes of antihypertensive agents in this population.
Part 2: The Impact of Age-Related Physiological Changes on Pharmacokinetics and Pharmacodynamics

As a group, the elderly span the continuum from near-perfect health to extreme physiological decline. Although there is a general decline in physiological integrity with age, the health status of the elderly varies considerably from individual to individual. The greatest variation in organ function appears among the younger-old (65-75) and the oldest-old (85+). With declining organ function, the body responds differently to pharmaceuticals. The decline of organ systems is not necessarily a steady downward slope, nor is the rate of decline similar among individuals; heredity, disease, and lifestyle affect physiological aging. In fact, there is consensus that physical and medical heterogeneity increases as the population gets older; that is, this population is unique for its non-homogeneity.19

Many studies have demonstrated that age-related physiological changes affect the outcomes of drug therapy. With time, the body's organ systems decline, metabolic pathways vary, and physiology and biochemistry change. Although changes in pharmacokinetics in the elderly have been widely studied, gaps still exist in the medical literature describing alterations in pharmacodynamics. A comprehensive understanding of physiological aging and its effect on both processes is needed to optimize medications for older patients.

CHANGES IN ORGAN SYSTEMS
This section explains the age-related physiological changes occurring in the body's organs that can alter the outcomes of drug therapy. With age, the body's ability to preserve homeostasis is compromised, and older individuals are therefore less able to regulate blood glucose levels, blood pH, heart rate, blood pressure, and oxygen consumption.5 Organ systems are affected by these fluctuations, and consequently experience variable response to drugs entering the system. The organ systems that respond most variably are those most debilitated by age and/or disease, including central nervous (CNS), cardiovascular, and musculoskeletal systems. Below, we discuss the CNS and cardiovascular systems as examples. For a summary, see Table 2.

Central Nervous System
Significant age-related changes in the brain and nervous system affect pharmacodynamics significantly, with the most noticeable result being a generally increased sensitivity to CNS agents. Drug dosing might need to be reduced by up to 50% and dosing intervals can require lengthening36. Benzodiazepines are a prime example of medications that require adjustment in older patients. When administered in normal adult doses, benzodiazepines can produce ataxia, confusion, imbalance, immobility, incontinence, limited reaction time, and sedation.5 Secondary to several of these effects is an increased risk of falls and fractures.46

In pain management, specific NSAIDs result in marked variation of CNS response among older patients.5 The numerous agents available in this drug class pair with a wide range of options for the elderly. Although effective for severe pain relief, other medications (including narcotics and opioids) can cause drowsiness, sedation, nausea, and vomiting. Because of the range of idiosyncratic responses, the optimal pain agent is the one that promotes the best response for the individual with the fewest side effects.

Cardiovascular System
Changes in the cardiovascular system cause drugs to act differently in older patients. Maximum heart rate and average cardiac output decline, ventricular mass and maximum coronary blood flow decrease. Likewise, blood vessels lose elasticity and thickening of the arterioles occurs, both of which contribute to an increase in blood pressure. These and other physiological changes affect the properties of drugs that act in the cardiovascular system. Attention to drug selection, dosage, and individual response is particularly necessary when using the following drugs: β-blockers, diuretics, ß-blockers, and agents with an inotropic effect.

PHARMACOKINETICS
Simply put, pharmacokinetics involves the four processes the human body uses to handle drugs: absorption, distribution, metabolism, and elimination. Age-related physiological changes alter all of these processes, and most changes clinically alter the effects of medication. Although changes in the absorption process have little bearing on
Table 2. Medications Affected by Age-Related Changes in Drug Distribution

<table>
<thead>
<tr>
<th>Hydrophilic Drugs</th>
<th>Lipophilic Drugs</th>
<th>High-Protein Bound Drugs</th>
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<tbody>
<tr>
<td>Decreased distribution/</td>
<td>Increased distribution/</td>
<td>Increased non-bound drug/</td>
</tr>
<tr>
<td>Increased levels of drug in blood</td>
<td>Prolonged clearance time</td>
<td>Potential pronounced drug levels</td>
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<tr>
<td>digoxin</td>
<td>diazepam</td>
<td>naproxen</td>
</tr>
<tr>
<td>warfarin</td>
<td>lidocaine</td>
<td>Exceptions:</td>
</tr>
<tr>
<td>lithium</td>
<td>TCAs</td>
<td>warfarin</td>
</tr>
<tr>
<td>cimetidine</td>
<td>phenothiazines</td>
<td>lidocaine*</td>
</tr>
<tr>
<td>acetominophen</td>
<td>propranolol</td>
<td>propranolol*</td>
</tr>
<tr>
<td>theophylline</td>
<td>Exceptions:</td>
<td></td>
</tr>
<tr>
<td>aminoglycosides</td>
<td>lorazepam</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
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</tbody>
</table>

* In patients with inflammation (such as arthritis)


pharmacological effect, the three remaining processes—distribution, metabolism, and elimination—are significantly affected by age-related pharmacokinetic changes.

Absorption

Drug absorption rates fluctuate based on changes in the vascular, gastrointestinal, and other aging body systems. For example, drugs administered transdermally can be absorbed more slowly because of decreased vascularity in older patients. Likewise, orally administered drugs are absorbed less readily because of increased gastric pH, decreased intestinal motility, and delayed gastric emptying. For example, delayed gastric emptying time, which has been documented in the elderly, can cause drugs with a short half-life to fail to reach therapeutic levels in the bloodstream, thereby reducing effectiveness. Alternately, some researchers have observed an increase in the absorption of particular substances, including fat, methionine, and cysteine. The effects of altered absorption rates are so minute that they are clinically insignificant, and therefore do not usually influence drug selection for older patients.

Of all the age-related stages of the pharmacokinetic process, absorption has the smallest clinical impact. Geriatrician Robert E. Vestal, MD, his colleagues, and other researchers have conducted numerous studies to test age-related changes in bioavailability and absorption of various drugs. According to their findings, there is no evidence to suggest that age-related variances in absorption significantly alter the effects of medications.

Although physiological changes do not have a great impact on the absorption of medications, some coadministered prescription and over-the-counter drugs, such as antacids or bile acid sequestrants, can affect the absorption of certain drugs: cimetidine, digoxin, tetracycline, phenytoin, iron, quinolones, and ketocanazole, for example. Other factors are food intake and the use of some anticholinergic and cholestyramine agents.

Distribution

Unlike absorption, the altered distribution of drugs caused by physiological aging can profoundly affect the therapeutic effects of many medications. Factors that produce changes in distribution include body composition, debility, and poor nutrition. Three characteristics of elderly body composition are an increase in body fat, a decrease in lean muscle tissue, and a decrease in total body water. Because body composition affects the volume of drug distribution, each feature can potentially alter the intended effect of a given drug, depending on its chemical composition.

Hydrophilic drugs, like digoxin, distribute through the lean body mass, which is reduced in the elderly. With reduced mass, extraneous active drug remains in the blood, and drug concentrations can exceed therapeutic levels. Prescribing a lower initial dose of such water-soluble agents, and then titrating the drug to a therapeutic level is often recommended to avoid drug overload.

Other examples of hydrophilic drugs that show decreased distribution (with a corresponding increase in initial blood concentrations) in the elderly include ethanol, antipyrine, and cimetidine. There are a few important exceptions to the rule: pancuronium and tobramycin show an increased volume of distribution in older patients, despite being water-soluble (Table 2).

Lipophilic drugs, on the other hand, are stored in fatty tissue, which the elderly tend to have in greater supply than lean muscle. By distributing to areas with larger volume, lipophilic agents clear more slowly and encourage a prolonged effect. If it is unrecognized, a prolonged effect can lead to a pronounced, even toxic effect if dosing intervals are not adjusted as necessary. Benzodiazepines (i.e., diazepam) used in the elderly population can produce this effect. Because of this and other reasons, many geriatricians and the American Society of Consultant Pharmacists (ASCP) recommend that clinicians take special care when prescribing these medications for their older patients, or
Table 3. Aging Organ Systems and Prescribing Implications

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Effects of Aging</th>
<th>Prescribing Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory system</td>
<td>Increased sensitivity to certain pharmaceuticals</td>
<td>Problems with sleep apnea and periodic breathing with narcotics</td>
</tr>
<tr>
<td></td>
<td>Increasing rigidity of chest wall</td>
<td>Exacerbation of opioids</td>
</tr>
<tr>
<td></td>
<td>Reduced lung muscle strength and endurance</td>
<td>Worsened strength and endurance of lungs with some medications</td>
</tr>
<tr>
<td>Cardiac system</td>
<td>Changes of heart (stiffening, reduced muscle strength) and blood vessels</td>
<td>Weaker and slower heartbeat and worsened circulation with diuretics and narcotics</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Increased sensitivity</td>
<td>Enhanced response to CNS agents requiring lower doses of drugs such as benzodiazepines and opioids</td>
</tr>
<tr>
<td></td>
<td>Decline in receptors and pathways, fewer brain cells and decreased connection</td>
<td>Slower mobility and voluntary motor activity; carefully monitor drugs that affect motor function</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
<td>Increase in gastric emptying time Decrease in GI blood flow</td>
<td>Possible gastrointestinal (GI) bleeding with some NSAIDs</td>
</tr>
<tr>
<td>Renal System</td>
<td>Decreased blood flow in kidneys and decrease in kidney mass</td>
<td>Slower healing of drug-induced bleeding</td>
</tr>
<tr>
<td>Immune System</td>
<td>Decreased immunity to disease Greater susceptibility to infection</td>
<td>Possible increase in antibiotic use</td>
</tr>
</tbody>
</table>


Avoid them altogether.56 Surprisingly, the benzodiazepine lorazepam has the idiosyncratic feature of reduced volume of distribution that is uncharacteristic of lipophilic agents.

In addition, older bodies tend to distribute highly protein-bound medications in an unexpected way.56 Protein-bound drugs bind with serum albumin during the distribution process; however, aging reduces serum albumin levels.5 When serum albumin levels are low, there is less to bind with the ingested drug. Because the unbound drug is the active form, the effects of the drug can be exaggerated. Although lower serum albumin levels can be attributed to multiple factors (poor nutrition, coexisting disease, etc.), physiological aging might be at least partially culpable. For extremely protein-bound drugs, even a slight reduction in serum albumin levels in an older patient can produce excessive drug levels, and consequently, undesirable effects. If dosage is not appropriately adjusted for the elderly, toxicity can occur.57 Examples of highly protein-bound drugs include naproxen, warfarin, tolbutamide, phenytoin, and salicylic acid.51

Malnutrition is another concern and exacerbates the potential for untoward effects during the distribution phase of pharmacokinetics. 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%.58 These statistics indicate a need for careful dosing and monitoring of malnourished patients. Although improving diet is the best solution, this is not always possible, especially for the elderly who live alone. When malnutrition is suspected, the use of a low-dose, non-protein-bound drug might be the best choice.

Other examples of drugs that can be affected by age-related changes in distribution are gentamicin, a potentially toxic antibiotic, and lithium carbonate, a mood stabilizer indicated for manic-depressive disorder.50

Metabolism

Two age-related metabolic changes, reduced hepatic blood flow59 and impaired metabolic pathways,7 have clinically important effects on the action of medications. However, these two factors vary significantly among the elderly, and a method for determining the extent to which hepatic metabolism is impaired is not readily available. This poses a challenge to physicians prescribing for the elderly. In general, hepatic mass and the number of healthy hepatocytes decline with age. Also, diminished hepatic blood flow (reduced by 40–45% in the elderly compared to younger patients) results in crucial reductions in first-pass metabolism of drugs.53

Drugs that depend on first-pass metabolism in the liver, such as isosorbid and lidocaine, are termed perfusion-limited. Other examples include propranolol, some calcium channel blockers, and some TCAs.53 Older patients taking these medications should be carefully titrated until the desired therapeutic effect is achieved, then observed closely and/or tested for signs of drug overload.3
Likewise, because certain pathways are affected by aging, drugs that are metabolized by these pathways are less preferable than drugs that are not. Metabolic reactions such as oxidation and hydrolysis occur in the liver and are affected by aging. Therefore, drugs that depend on these processes could have altered effects in the elderly. Researchers studied another agent, antipyrine, to generalize the effects of aging on all drugs that use the oxidative pathway. Most results have shown a longer half-life and decreased clearance in elderly patients, with these effects being more pronounced in men than in women. Other similarly affected drugs include the antianxiety agent diazepam, the cardiovascular agent quinidine, and the antidepressant nortriptyline.

**Elimination**

Unlike metabolism in the liver, the rate of decline in elimination by the kidneys is fairly predictable. In elderly patients, renal blood flow can be reduced by as much as 40% and kidney function can be reduced by as much as 50% by age 75. However, the extent of decline is also heavily influenced by illnesses that further impair renal function, such as hypertension, common in the elderly. Unfortunately, it is difficult to measure the exact extent of renal decline because serum creatinine (Cr) is not as reliable an indicator of renal failure in older patients as it is with younger patients. Serum Cr levels can appear normal in an older person with substantial renal impairment because Cr is a product of muscle breakdown, which is reduced in the elderly.

Of particular concern are renally eliminated drugs with a narrow therapeutic range. If kidney function is reduced, toxicity can occur. It is recommended that physicians monitor blood plasma levels when using drugs with renal clearance and a low therapeutic index to reduce the risk of drug build-up and pronounced and/or prolonged effects. Examples of drugs that produce these effects are digoxin, cimetidine, coumadin, procainamide, vancomycin, lithium, and certain aminoglycosides. The administration of similar drugs with wider therapeutic ranges is preferable for elderly patients.

**HOW AGING ALTERS THE BIOCHEMICAL AND PHYSIOLOGICAL EFFECTS OF DRUGS**

As physiological aging occurs, pharmacodynamics (biochemical and physiological effects of drugs and their mechanisms of action) are altered. The body’s change in response to medications most often manifests itself starting at age 70 to 75. Specific pharmacodynamic changes at the receptor level include the following: changes in receptor binding, a decrease in the number of receptors, and altered biochemical reactions initiated by receptors.

Researchers have not yet constructed as complete a picture of pharmacodynamics as they have of pharmacokinetics in the elderly. Nonetheless, studies have explained how pharmacodynamic changes are implicated in the use of certain drugs. For example, decreased receptor response to beta-adrnergic agonists and beta-adrenergic blockers results in a reduced clinical effect in the elderly. Conversely, an increased receptor response occurs with opiates and benzodiazepines such as morphine and diazepam, producing an exaggerated effect. More generally, the action of stimulants can be diminished in the elderly while the action of depressants increases.

Other medications that show a pronounced pharmacodynamic effect in the central nervous systems of elderly individuals are sedatives, antihypertensives, analgesics, and H2 receptor antagonists. With narcotics, CNS effects are not only greater but also different: delirium often results, instead of over-sedation. CNS effects caused by anti-cholinergic drug properties are most likely related to the reduced cholinergic activity in the brain that accompanies aging [See page 15 for more details].
Part 3: Side Effects

In the U.S., the average person fills five prescriptions annually; in people age 65 and older, this average is as high as 18 prescriptions per year. With 260 million Americans, this equates billions of prescriptions used to manage health problems and improve quality of life every year. It would seem, then, that the number of drug problems as a percentage of overall utilization is relatively small. However, the consequences of the drug-related problems that do occur are serious—both to the health of patients and to the health care economy. Therefore, the fact that the relative risk of adverse events is small does not mean that we should stop being vigilant in following the safest and most beneficial prescribing practices, especially for older patients.

The types of side effects experienced by the elderly vary widely, from the more common minor discomforts to rarer but more serious complications. The extent and results of side effects will depend largely on the individual patient's health status, physiological integrity, illness, concomitant medications, idiosyncratic response, etc. It is the combined responsibility of physicians, pharmacists, and patients to anticipate, avoid, and manage side effects. Clinicians can anticipate side effects and make patients aware of them before therapy begins. As therapy continues, patients and caregivers should be alert and communicate all adverse drug effects to their physicians and pharmacists as soon as possible.

In some instances, clinicians can actually take advantage of side effects to treat secondary medical conditions. Of course, this is not always possible, and the best clinicians can do is to minimize the discomfort and risks side effects may pose. There are four aspects of the side-effect issue that affect older patients: 1) identifying side effects; 2) defining the most common types; 3) minimizing potential problems; and 4) optimizing potential benefits.

IDENTIFYING SIDE EFFECTS

When an older patient taking one or more medications complains of any new symptom or illness, the first step is to rule out a drug side effect as the cause of the problem. If the symptom is not drug-related, clinicians can proceed with the standard of care indicated for older patients. If the root cause is drug-related, an alternative agent can frequently alleviate uncomrortable or potentially harmful secondary effects. For many reasons, side effects are sometimes misperceived as new medical problems and treated with additional medications. This action can initiate what Gurwitz and Rochon describe as "the prescribing cascade," and can result in unwarranted polypharmacy, thereby significantly endangering the elderly.

For instance, side effects such as restlessness, drowsiness, altered speech, and irritability are sometimes observed in the medicated elderly, and misinterpreted as new conditions such as depression, dementia, or anxiety. This marks the beginning of a prescribing cascade of unnecessary medications, followed by additional side effects.

An example of the prescribing cascade relates to the use of thiazide diuretics in patients with hypertension. Although thiazide diuretics have shown good results in reducing blood pressure, their side effects sometimes manifest themselves as gout-like symptoms, such as swelling in the extremities. (Thiazide diuretics do not cause gout, but the edema they cause as a side effect has been misinterpreted as a sign of gout.) In a study involving over 9,000 New Jersey Medicaid patients over 65, the risk of beginning treatment for gout was almost double in patients who receive thiazide diuretics compared to those who received a non-thiazide treatment for hypertension. The risk of being treated for gout was much lower when thiazide was prescribed at low-dose levels (less than 25 mg/day). It is important to note that the lower dosage did not significantly reduce the antihypertensive effect of thiazide diuretics. This suggests that before physicians diagnose and prescribe for gout in patients taking thiazide diuretics, a full review and assessment for hyperuricemia should be made, and an alternate dosage and/or an alternate antihypertensive agent should be considered if these steps are not taken, a prescribing cascade can occur.

DEFINING SIDE EFFECTS COMMON AMONG THE ELDERLY

Because of the increased comorbidities among the elderly, their limited physiological compensation mechanisms, and their altered receptor responses, they are more susceptible to certain types of side effects. Three types of drug side effects that are particularly significant for elderly patients are cardiovascular effects, central nervous system (CNS) effects, and anticholinergic effects.

Cardiovascular Side Effects

Therapeutic agents for various conditions can have side effects on the cardiovascular system. For example, drugs with high sodium content, such as certain antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs), can cause an increase in sodium retention. Some psychoactive drugs, particularly triyocyclic antidepressants, can cause arrhythmia. Also, fluid and elec-
troyte disorders can result from the use of some NSAIDs or antibiotics. These side effects are a concern in patients with hypertension or congestive heart failure (CHF).

Certain drugs used to treat the cardiovascular system can cause side effects as well. Although these agents offer management of life-threatening diseases, such as CHF and myocardial infarction (MI), they can also result in serious side effects if the selected agent is not well-matched to the patient’s health status and individual characteristics. Powerful healing agents can also cause harm when the wrong dose, drug, or combination is prescribed. Especially where cardiovascular drugs are concerned, clinicians need to tailor health care to specific patient needs.

For example, strong diuretics can be vital for patients with CHF or MI; but these drugs can also lower blood pressure in the elderly, resulting in orthostatic hypotension. Orthostatic hypotension can result in falls and fractures, which can precipitate a significant decline in health, especially for the oldest patients who might not be able to fully recover from bone injuries such as hip fractures. In such cases, the benefit-to-risk ratio should be considered before therapy is initiated, and precautions should be taken to minimize the hazards associated with side effects. For instance, patients should be warned that they might experience dizziness or disorientation, and caregivers should monitor them closely when they are standing, walking, or climbing to reduce the risk of imbalance and falls.

Central Nervous System Side Effects

Drugs used to treat various organ systems have side effects in the central nervous system (CNS). Generally, lipophilic agents cross the blood-brain barrier more easily than their hydrophilic counterparts; therefore, if a highly lipophilic agent is prescribed, physicians and pharmacists should be attuned to potential CNS effects.

For example, the H₂-receptor antagonist cimetidine, 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. For patients who have comorbid conditions or are very old, selection of an alternative H₂-receptor antagonist with lesser side effects (or even another class of drugs) might be a safer choice. An example from among the β-blockers is propranolol. Propranolol is the most lipophilic of all the β-blockers. If CNS effects are problematic, a good alternative is atenolol, which is less lipophilic. Finally, some NSAIDs can cause confusion in elderly patients, specifically an older NSAID (indomethacin) that causes the most CNS effects and therefore is not recommended for use with older patients. Newer NSAIDs, particularly the COX-2 inhibitors, are safer and more efficacious in terms of CNS side effects, and offer the added benefit of fewer gastrointestinal side effects than older NSAIDs.

Anticholinergic Side Effects

Many drugs that are essential to providing quality care for the elderly have anticholinergic properties (e.g., they block the action of acetylcholine). Medications with anticholinergic properties include drugs for Parkinson’s disease, antihistamines, tricyclic antidepressants, bronchodilators, and antispasmodics. Sometimes, drugs with anticholinergic activity are used to minimize the extrapyramidal symptoms caused by typical antipsychotics and to reduce urinary incontinence. Although the therapeutic effects of these drugs are beneficial, their anticholinergic side effects warrant consideration.

- Dry skin and mouth
- Tachycardia (rapid heart rate)
- Ataxia (inability to coordinate voluntary muscular movements)
- Chronic pseudodementia (low-level, drug-induced disorientation and confusion)
- Acute delirium (intense instances of incoherent delusion)
- Constipation
- Urinary retention

It is important to note that some of these anticholinergic side effects often parallel problems that are already common in the elderly. If a patient shows signs of these conditions prior to drug selection, or if a medication is known to have strong anticholinergic properties, alternate agents might be preferable.

In addition to the CNS, anticholinergic, and cardiovascular side effects described, others can materialize during the course of drug therapy. All potential drug effects should be taken into account during decision-making to avoid harm and to optimize beneficial effects for elderly individuals. An adequate choice of medications should be available for this purpose.

MINIMIZING POTENTIAL RISKS

This section discusses selected key examples of prescribing practices that could lead to important drug side effects that are problematic for the elderly. Categorized by important diseases common in the elderly, these summaries, while not all-inclusive, serve as a reminder that side effects are especially significant for this special population, and that alternative therapies are available to meet specific patient needs.

Arthritis

Forty-nine percent of the elderly suffer from arthritis. The major symptoms (pain and mobility problems) are frequently treated with NSAIDs. Although effective, NSAIDs have been associated with several types of untoward side effects. Gastrointestinal (GI) effects (from stomach upset to bleeding and ulceration) and some CNS effects have been well-documented. As highlighted earlier, indomethacin should be avoided in the elderly because it results in the most CNS effects of all the NSAIDs. Newer agents that
selectively inhibit the COX-2 enzyme are generally considered preferable because they produce fewer GI side effects than many older NSAIDs. For long-term treatment to alleviate arthritis pain, acetaminophen might be preferable to prescription analgesics to avoid potential renal, hepatic, gastrointestinal, and cardiovascular effects that could occur over time. For arthritic patients with chronic renal failure, non-drug therapy might be the safest choice for managing pain.

Hypertension
The wide variety of antihypertensive agents allows the selection of a medication with a tolerable side-effect profile. The key is to minimize risks by matching the right drug to an individual patient’s symptoms and characteristics. In these cases, hypertension agents with tolerable profiles are preferable; these might include diuretics, ACE inhibitors, or another class of antihypertensive drug. Conversely, β-blockers might be a good alternative to powerful diuretics in patients suffering from hyperuricemia.

Heart Disease
Digoxin is a clinically important drug that is frequently used to manage heart failure or atrial fibrillation in the elderly. However, caution is warranted with the use of digoxin because of its narrow therapeutic range and side effects, which include cardiac arrhythmia and conduction disturbances, nausea, anorexia, and vision problems. These side effects are essentially dose-dependent. The elderly are more sensitive to digoxin, requiring a lower dose to achieve a therapeutic response without adverse reactions. But determining a safe and effective dose can be challenging because of digoxin’s narrow therapeutic range in the elderly. For example, digoxin-induced anorexia can manifest at below therapeutic levels in older patients, so monitoring for malnutrition is essential. Regular monitoring through blood drug levels, patient responses, and/or EKG should be standard protocol for older patients taking digoxin. The use of digoxin in older patients is controversial because it has substantial therapeutic value for some patients, but can induce toxic, dose-related side effects. Some researchers suggest limiting or even discontinuing its use in older patients because of the potential for dose-related toxicity.

β-blockers, which treat unstable angina and cardiovascular disease (CVD), have repeatedly been shown to reduce mortality risk when given to patients post-myocardial infarction. However, all β-blockers are not equivalent in terms of side effects, an important consideration for the elderly. Lipophilic agents, such as propranolol and metoprolol, can produce greater CNS effects (such as vivid dreams, depression, and fatigue) because they cross the blood-brain barrier. These effects are less frequent in hydrophilic β-blockers, such as atenolol and nadolol. Differentiation between agents of the same class is critical: an older patient with a history of dementia or depression would clearly be at reduced risk for adverse effects if prescribed a water-soluble β-blocker rather than a lipid-soluble one. Additionally, the elderly can be less sensitive to the therapeutic effects of β-blockers because of decreases in receptor response occurring with age. Increased dosages might be warranted for therapeutic reasons; however, some patients cannot tolerate the side effects that occur at higher doses. For example, at normal doses, the β-blockers atenolol and metoprolol are cardioselective, and thus less likely to induce bronchospasm. But as doses increase, their cardioselectivity is eliminated and respiratory side effects can occur. So for patients with asthma or chronic obstructive pulmonary disease (COPD), doses and drug selection must be decided with careful consideration paid to side effects of specific agents and individual patient characteristics.

Depression
Historically, the practice of identifying and treating geriatric depression has been only moderately successful at best. In the past, depression was perceived as an integral part of old age, and even today it is under-diagnosed and under-treated. Also, the pharmacological treatments available before the mid-1990s carried considerable drawbacks. Older agents like TCAs and MAOIs, although efficacious, can cause serious side effects that pose particular problems for the elderly. TCAs inhibit acetylcholine, resulting in anticholinergic side effects; MAOIs can cause adverse events through certain drug-food interactions. Since the introduction of selective serotonin reuptake inhibitors (SSRIs) less than a decade ago, the ability to treat geriatric depression without incurring major side effects has improved. Though SSRIs are equally as efficacious as their predecessors, they are less likely to cause dangerous side effects. For older patients, side effects from SSRIs can be uncomfortable or irritating, but they are generally less serious than side effects of the older antidepressants. SSRIs can include nausea, GI problems, anxiety, drowsiness, sweating, headaches, diminished libido, difficulty sleeping, and mild tremors. However, these effects are usually mild and wear off over time. Also, these effects may be avoided in the elderly by using the lowest dose possible to achieve a therapeutic effect.

Early in the history of SSRIs, there was a notion that these agents would reduce falls and fractures associated with other antidepressants like TCAs, which can cause orthostasis and other psychomotor impairment. At least two studies, however, have failed to support this theory, showing little difference in the number of falls per nursing home resident taking either an SSRI or a TCA. Dr. Jerry Avorn suggests in the New England Journal of Medicine that the methodological limitations
of observational studies such as these have the potential to skew outcomes. Since the current research is inconclusive, special care should be taken to prevent falls in elderly patients taking antidepressants of any kind.

Anxiety

Anxiety and agitation in elderly patients require medications that can have greater side effects than antidepressants. Benzodiazepines have been shown to encourage side effects such as confusion and other CNS effects, which can lead to falls. In a study on the relationship between specific medications and the incidence of falls, Gales and Menard found that the use of long-acting benzodiazepines was associated with twice the likelihood of falling, the highest association of all medications examined. Similar studies with larger patient populations have revealed that the incidence of falls is related to dosage or half-life of the benzodiazepine. If benzodiazepines are necessary, shorter-acting agents such as oxazepam (Serax) or lorazepam (Ativan), and lower doses are warranted with the elderly. Alternatively, newer anxiolytic agents such as buspirone (BuSpar) and venlafaxine (Effexor) can be another option for those with anxiety or mixed anxiety and depression.

Psychosis Resulting from Dementia or Late-Onset Schizophrenia

Psychosis in the elderly requires special treatment, depending on several factors: 1) cause; 2) degree of severity; and 3) individual patient characteristics. Psychosis can arise secondary to dementia or late-onset schizophrenia. For treating behavioral complications of dementia, neuroleptics (also termed antipsychotics or major tranquilizers) are used most often. These agents manage the symptoms of psychosis such as agitation, aggressiveness, paranoia, and hallucinations. The side effects of these therapeutic agents vary considerably.

The traditional antipsychotics—phenothiazines (which have a lower potency), thioanthenes, and butyrophenones (which have a higher potency)—have variable effects. Phenothiazines, such as chlorpromazine and thioridazine cause sedative and anticholinergic side effects. Although these features reduce agitation, phenothiazines are not administered parenterally, delaying their therapeutic effect and making them less effective for acute episodes of psychosis. Phenothiazines also increase the risk of orthostatic hypotension, which is cause for concern about the risk of falls in elderly patients, but phenothiazines have few extrapyramidal side effects (EPS) typically associated with stronger antipsychotics.

On the other hand, thioanthenes and butyrophenones (e.g., thiothixene and haloperidol, respectively) have no anticholinergic properties, but they do incite EPS effects, such as restlessness, tremors, and motor complications.

To compensate for these side effects, patients are sometimes prescribed anticholinergic agents. Not surprisingly, some clinicians warn against this practice. A 32-member Canadian national consensus panel states that the “prescription of anticholinergic drugs to prevent extrapyramidal effects of antipsychotic drugs” should be avoided in the elderly. The panel instead suggests decreasing the dosage and/or reassessing the need for the antipsychotic agent. A third possibility would be to consider an alternative antipsychotic drug with fewer EPS effects. The intentional choice to use anticholinergic drugs to reduce EPS effects is not an example of the prescribing cascade discussed earlier. At one time, this was the best option for managing acute psychosis; however, newer antipsychotics (the atypicals, discussed later in this section) have offered another, potentially better alternative.

Atypical antipsychotics offer an additional possibility for treatment. The term “atypical” was originally used to describe the relative lack of EPS effects in patients treated with the first atypical antipsychotic, clozapine. As more agents are developed, usage of the term “atypical antipsychotic” is changing, as evidenced by difference in EPS effects, even among the atypical agents themselves.

In general, however, the newer antipsychotics offer advantages to elderly patients. The features of atypical antipsychotics that are desirable for the treatment dementia-related psychosis include the following: 1) a low propensity to cause EPS or movement disorders; 2) greater efficacy against both positive (i.e., paranoia, delusions) and negative symptoms (emotional blunting, loss of energy and motivation); 3) efficacy in patients who do not respond to traditional antipsychotics; 4) a lack of effect on prolactin levels; 5) reduced cardiac effects; 6) reduced sedative effects.

All of the newer antipsychotics share one or more of the above characteristics. Despite the variances among traditional and atypical antipsychotics, these medications are sometimes used interchangeably, a practice that is not in the best interest of elderly individuals.

OPTIMIZING POTENTIAL BENEFITS

Sometimes clinicians can choose a drug with a particular side effect to encourage a specific medical response. For example, carbamazepine (Tegretol, Ciba-Geigy), which is used for seizures, can also help manage behavioral symptoms in an older individual with dementia. Similarly, mirtazapine (Remeron, Organon) can work well for depressed patients who also have severe insomnia because of the drug’s sedative effects. However, mirtazapine is only appropriate for use in physiologically robust elderly patients because of its association with renal dysfunction and anticholinergic effects. Other antidepressants (e.g., amitryptyline) are sedating as well, but have too many other side effects to be used as first-line
therapy for older patients. Trazodone can be helpful in treating depression with insomnia in older patients because it does not have the anticholinergic effects of TCAs, but does have sleep-inducing properties.31

Prescribing to take advantage of a side effect is less common than prescribing a drug with more than one beneficial effect. There is still debate about this, but at least some studies suggest that hydrochlorothiazide (HTCZ) might have a protective effect on bone, making it a good choice for elderly hypertensive patients at risk for osteoporosis. Also, certain β-blockers might be optimal for hypertensive patients with migraine headaches, coronary artery disease, or congestive heart failure, because they have beneficial effects for these diseases as well.
Part 4: Maximizing Pharmacological Outcomes as the Effects of Aging Converge

The effects of aging discussed in parts 1 through 3 do not exist in a vacuum; rather, they collide and interact to pose special risks. To minimize these risks, we propose a three-fold action plan to encourage the best possible outcomes for older patients receiving pharmacological therapy.

**Action One: Individualized, Evidence-Based Prescribing**

First, prescribing for the elderly should be tailored to individual patient characteristics and guided by evidence-based medicine. These two initiatives are not mutually exclusive. Evidence-based medicine is founded on a population approach to clinical studies. Studies that include patients over 65 should be considered as the best potential source of information about how older patients will respond to pharmacotherapy. Applying relevant findings in treatment protocols should be a top priority in care for older patients.

As this population grows, clinical trials and post-market studies of new pharmaceuticals will need to include more elderly patients. More studies are needed, particularly to determine optimal drug treatment for the oldest elderly. But recruitment, informed consent, and retention in randomized clinical trials are extremely difficult for physically frail elderly patients, who often have cognitive impairment as well. In addition, randomized trials to determine the best combination of therapies in patients with comorbidities might require prohibitively large study samples. Naturalistic, observational studies of the relative effectiveness of specific medications and combinations in a real-world setting, using carefully controlled experimental conditions, might be more feasible and more relevant to the realities of clinical practice.

**Action Two: Coordinated Pharmaceutical Care**

The rise of medical specialists and sub-specialists—coupled with the increase in the number of elderly people with chronic, comorbid diseases—demands greater efforts at harmonization. Older patients often see several prescribing physicians, who may be unaware of all of the patients’ medications. Such disconnected care can result in poor outcomes, including medication errors and adverse events. Similarly, mergers among health care organizations have resulted in increased shifting of patients among treatment sites, a practice that can disrupt the continuum of care that is so necessary for the proper treatment of the frail elderly.

The advent of “disease management” (DM), which extends beyond episodic and uncoordinated care, has resulted in increased cooperation and information-sharing among providers. But the DM framework is relatively recent and needs additional support from individuals and institutions. The various models of DM programs require evaluation to determine which programs work in specific settings and for specific patient populations. Outcomes research can be used to assess the success of DM programs with elderly patients in terms of impact on patient compliance, effect on physician prescribing behaviors, improvements in response to treatment, and overall success.

Still, additional coordination of pharmaceutical care beyond disease management is often required because disease-by-disease approaches can neglect interactions among diseases and their treatments. While some DM programs have evolved to address this issue (for instance, programs that co-manage diabetes and heart disease), individual providers need to be mindful of the need for coordinated care of the elderly.

Several organizations have been striving to improve coordination of care, and to enhance the role of pharmacists in the care process. The American Society of Consultant Pharmacists has led significant efforts in both areas. For more information about ASCP, see the shaded box on page 20.

**Action Three: A 10-Step System to Guide Prescribing Decisions**

The third component of providing quality pharmaceutical care for the older population is to use safe and
sound prescribing practices with every patient. This section outlines 10 guiding principles (listed in Table 4) that are especially applicable when prescribing for older individuals. Each principle is exemplified as a case scenario, which includes a prescribing dilemma and a treatment resolution. Each case is followed by a discussion of the prescribing principle it represents. These fictionalized case studies are based on the authors’ own experiences as physicians and pharmacists. Although they do not represent actual individuals, the stories reflect composites of scenarios that we and our colleagues have encountered. Although decisions and recommendations are included, there may be alternative ways to manage these complex situations. Our intention is to emphasize the prescribing principle applicable to each case.

**Prescribing Principle #1**

**Determine whether or not drug therapy is truly necessary. Is there a better, non-drug alternative to try first?**

**Dilemma:** Mrs. F, 67, visited her doctor after several weeks of progressively worsening sleep problems. She has been restless, has difficulty falling asleep, and awakens several times during the night. She has never before experienced disrupted sleep. There is one additional note, however. About a month ago, her older sister, with whom she has resided for the past 10 years, was placed in a nursing facility. Now, Mrs. F is living alone for the first time. How should treatment begin in Mrs. F’s case of insomnia?

**Resolution:** Mrs. F’s physician tells her that this problem might be an episodic response to a major life change and could resolve once she is more comfortable with her new living situation. He outlines several non-drug practices for her to try over the next two to three weeks, at which time she should schedule a follow-up visit if her symptoms have not improved.

**Discussion:** The first course of action in most cases of insomnia should be non-pharmacologic. Older patients might already be taking other medications that prohibit or discourage prescription sleep aids. Improving sleep hygiene practices and employing special relaxation techniques can sometimes obviate the need for insomnia drugs. Diet, exercise, and relaxation techniques should be attempted before drug therapy is initiated. If these interventions are not successful, pharmacotherapy might be necessary, but it is important to establish the cause of the sleeplessness first so that the appropriate medication can be selected. If the insomnia is a symptom of depression, an antidepressant might be more effective than a sleep aid. If the insomnia is a side effect of another drug, changing or stopping that agent might be necessary. In any case, the first course of action should be non-drug therapy if at all possible.

**Prescribing Principle #2**

**Assess the patient’s current drug regimen (including prescription, over-the-counter, and complementary medicines) before prescribing a new drug.**

**Dilemma:** Mrs. J is a 77-year-old widow in good general health except for hypertension. None of the three antihypertensive medicines she has tried has been effective. Mrs. J’s medical history and physical exam offer no clues as to why her blood pressure is still elevated. She is not taking any other prescriptions, and she has adhered to the regimen for each of the antihypertensive agents. Why isn’t Mrs. J responding to antihypertensive therapy?

**Resolution:** The pharmacy resident recently reviewed the drug history and inquired about all of her concurrent medications, prescribed or self-selected. During this interview, Mrs. J revealed that she takes pseudoephedrine 60 mg, every six hours for her chronic nasal congestion. Mrs. J never mentioned it before because it is not a prescription drug, and she believed it was irrelevant to her cardiovascular problem.

**Discussion:** A conscientious decision to initiate new drug therapy requires an inventory of current medications. With the recent increase in the use of complementary medicine, plus the increase in prescription
drugs going over-the-counter (OTC), patients are self-medicating more often. Physicians and pharmacists must be aware of the many kinds of drugs their patients are taking. Likewise, patients should be (and are becoming in this age of health care consumerism) self-advocates by informing their doctors about the details of all their medications.

**Prescribing Principle #3**

**Choose a drug that considers individual patient characteristics and encourages compliance.**

**Dilemma:** Mr. B is an 80-year-old with prostatism (BPH), high blood pressure, and mild dementia. He lives alone, but his son phones daily to remind him to take his medicines, a total of seven pills per day. What medication(s) might be a good choice to treat these conditions, encourage compliance, and minimize the complexity of the regimen?

**Resolution:** A drug such as terazosin would be a good choice for this patient. This drug administered once daily would treat both Mr. B’s prostatism and high blood pressure. A weekly pillbox might also help this patient to improve compliance.

**Discussion:** Adherence to medication regimens is a major issue facing the elderly; estimated rates of non-compliance in the older population range from 30% to 75%. Numerous factors affect a patient’s ability and commitment to take medications consistently. Factors include side effects; perceived improvement in health status (i.e., patients feel better after taking medication for awhile, so they think that they can stop); problems with dosage forms (i.e., difficulty swallowing pills or tablets, measuring liquids); forgetfulness or confusion (especially when many drugs or multiple daily doses are required); vision problems (patients cannot read the labels on pill bottles); and problems with access (patients cannot get to the pharmacy; they have financial issues, or a lack of insurance, etc.). When physicians and pharmacists are attuned to these issues, they can avoid compliance problems by prescribing drugs that best match the individual patients.

**Prescribing Principle #4**

**Begin with a low dose and increase as necessary until the desired therapeutic effect is achieved.**

**Dilemma:** Miss H is an 84-year-old woman who suffers from depression and chronic pain secondary to a herpes zoster infection one year ago. Her physician decides that a tricyclic antidepressant is a good choice for treating both of her conditions, as this class of antidepressants is indicated for chronic pain as well. She chooses nortriptyline because it has lower anticholinergic and other adverse effects compared to other TCAs. What would be a good dosing plan for Miss H?

**Resolution:** Miss H’s doctor prescribes 10 mg of nortriptyline daily, which is the usual starting dose for the elderly but still far below the dose recommended by the Physician’s Desk Reference (60 mg titrated to 150–200 mg). Knowing that six to eight weeks of each dose is necessary to assess efficacy for this class of drug, the doctor schedules follow-up appointments every eight weeks, at which time she increases her dosage as necessary. Miss H is likely to experience improvement with 20- or 30-mg doses, but is unlikely to have significant side effects at this low dosage.

**Discussion:** The general rule of thumb in treating the elderly is “start low, go slow”. In choosing an initial dose of medicine for an older patient, it is often best to use half the lowest dosage form available. However, with dosages this low, it is extremely important to assure that a therapeutic effect is achieved. Patients must avoid missing doses, and physicians must follow-up with slow titration to a safe and effective level.

**Prescribing Principle #5**

**Prescribe the fewest number of drugs possible, and eliminate any that are not useful.**

**Dilemma:** Mr. P is 76 years old, with high blood pressure (originally 180/90 mmHg), arthritis, and periodic
heartburn. His medications include atenolol 25 mg daily, hydrochlorothiazide 25 mg daily, amiodipine 2.5 mg daily, naproxen sodium 250 mg twice a day, and omeprazole 20 mg daily. Upon careful review of his chart and history, the physician finds that the addition of both hydrochlorothiazide and amiodipine helped lower his blood pressure somewhat (150/85 mm Hg) but not as much as desired. The atenolol was then added to help reduce blood pressure further, but the charts indicate pressure stayed at 150/85 mm Hg. She also sees that naproxen was prescribed for an episodic, weather-related arthritis flare-up, which Mr. P says has since resolved. After taking this history and reviewing the charts, what course of action seems appropriate?

Resolution: Appropriate management of this patient would include discontinuing the atenolol, because it did not improve blood pressure; eliminating naproxen, because the arthritis flare-ups have subsided; and removing omeprazole if Mr. P can manage his heartburn through dietary changes. Then the physician should observe Mr. P for recurrence of symptoms or elevation of blood pressure. One note: Mr. P’s blood pressure might improve because of the discontinuation of the NSAID, naproxen. Non-pharmacologic measures, such as diet, exercise, and smoking cessation, should be tried for all of his conditions.69

Discussion: Medication, the most common medical intervention for patients over 65, offers substantial health benefits, but the use of unnecessary medications has been associated with adverse events, which increase in number and severity with the number of medications taken.67,68 The appropriate use of concomitant medications is a valuable strategy in managing the health of older patients, but it requires periodic reviews of the total drug therapy plan to eliminate any unnecessary drugs.67,69

Prescribing Principle #6

When prescribing a new drug, tell the patient what side effects to expect and to report serious problems immediately.

Dilemma: Ms. N is an 85-year-old independent, elderly woman, who was recently diagnosed with rheumatoid arthritis. Her physician wants to prescribe a COX-2 inhibitor for her minor aches and pains, but her insurance plan requires a prior authorization for this type of drug. While processing the approval, he prescribes ibuprofen to ease Ms. N’s symptoms. The physician warns Ms. N and her family of a slight bleeding risk from the ibuprofen. He explains that the first signs are fatigue, weakness, and possible stomach pain. He calls two days later with a prescription for a COX-2 inhibitor, but Ms. N is feeling better and has already paid for a month’s worth of ibuprofen. She says she’ll stick with that until next month. But two weeks later, she is marked weak-

Resolution: Concerned that this is related to the doctor’s warnings, Ms. N visits the ER, where doctors identify anemia (Hgb 6.0) and blood in her stool, a possible sign of erosive gastritis. Identifying her symptoms as potential side effects signaled Ms. N to stop taking the ibuprofen immediately and get to the hospital right away. For her pain, her doctor switches her to COX-2, which is more selective and has fewer risks of gastrointestinal effects.

Discussion: Informing patients about the potential side effects of their medications serves two important purposes. First, if the side effect is something that could lead to a serious complication (in this case, internal bleeding), then patients will be capable of identifying the first signs of the side effect, stopping their medications, and getting to their doctors quickly to avoid adverse effects. Second, if patients are informed about possible minor side effects, they are less likely to overreact or become noncompliant. For example, if a patient knows to expect a dry mouth from her antidepressants, and if she knows that this side effect is usually not dangerous and often disappears after the first couple of weeks of therapy, she will be more likely to adhere to her medication regimen and tolerate the minor discomfort.

Prescribing Principle #7

Consider the possibility that any new symptoms could represent drug side effects or drug withdrawal symptoms.

Dilemma: Mr. D, a 78-year-old widowed male who lives with his daughter, is frail, listless, and has been experiencing insomnia. His physician started him on an SSRI agent for symptoms of depression. At a six-month follow-up visit, Mr. D presents with a 20-pound weight loss and a loss of appetite. His depressive symptoms have improved but have not resolved. What might the clinician do at this point?

Resolution: A careful chart review and medical history could inform further clinical decisions. Mr. D’s charts and history showed that weight loss began after the medication was started. His family thought his depression was responsible for the weight loss, which was why they did not contact the doctor sooner. They were unaware that anorexia can be a side effect of some SSRI agents. Because the symptoms of depression did not fully resolve and anorexia occurred, the medication was discontinued until Mr. D’s appetite returned. Then, a different antidepressant could be administered if symptoms of depression persisted.

Discussion: As discussed in Part 3, it is important to determine the cause of new symptoms before prescribing new drugs to manage them. In this way, the “prescribing cascade” described by Rochon and Gurwitz can be avoided.62
Prescribing Principle #8

Encourage frail or incompetent older patients to have a close friend, relative, or caregiver accompany them to appointments, and apprise this person of changes in drug therapy regimens.

Dilemma: Mr. W, 81 years old, is usually driven to his doctors by his son. A week ago, his cardiologist prescribed the ACE inhibitor enalapril for blood-pressure management because of mild congestive heart failure, which developed after his recent myocardial infarction. Today, Mr. W has an appointment with his primary care physician, but his son is sick so he goes alone, taking the bus to the doctor’s office. This doctor has not yet received information from the cardiologist and decides to start lisinopril, another ACE inhibitor, for the same indication. Mr. W fills the second prescription at a different pharmacy from his usual one, because he doesn’t have his son’s car and his regular pharmacy is not on the bus route. Therefore, the pharmacist does not realize this is a duplicate prescription.

Resolution: Two weeks later Mr. W is at a follow-up visit with his cardiologist, and his blood pressure is very low. The cardiologist reviews the chart and asks if he started any other medicines recently. He responds that yes, he has, but he can’t remember the name. The cardiologist calls the primary care doctor; together they discover the problem.

Discussion: Patients who have trouble understanding or who might not remember what the doctor tells them need to have support from family, friends, and/or caregivers at the point of care. Although many older people are fully capable of seeing their doctors independently, there are others who will benefit from the extra involvement of the caregiver.

Prescribing Principle #9

Provide a portable prescription record that can be taken to other physicians and pharmacists.

Dilemma: Mr. G is in his early 70s and takes six prescriptions regularly. When he switches to a new primary care physician, Mr. G is asked to fill out a form listing all current medications as well as those used in the past year. Although Mr. G agrees that such a record would be helpful, he is discouraged by the complexity of this task. However, the new doctor is hesitant to write any new prescriptions or refills until he is sure of Mr. G’s concomitant medications. What are some possible solutions to Mr. G’s problem? Who can facilitate such solutions?

Resolution: Mr. G’s new physician asks him to schedule a return visit next week and to bring in all of his pill bottles, whether empty or full, whether he is taking the pills or not. At the return visit, he is given a small booklet that he can use to write down all the important information about his prescriptions. Then, a nurse and Mr. G begin filling in the book together. Their review of the medications provides an opportunity to discuss Mr. G’s drug therapy and to teach him to use his new portable prescription record.

Discussion: Keeping track of personal medical information is a challenge for every patient, and especially for the elderly. But an effective, patient-carried drug record of some kind will go a long way to ensure optimal drug therapy. A more advanced version of a written drug record is the “smart card,” a credit card look-alike with an embedded memory chip that electronically stores a person’s entire medical history. Electronic medical cards are being used today in some countries (e.g., Germany). Until a device like this is widely available in the U.S., a small folding card can suffice.

Another solution might be a dynamic, Web-based application that allows the patient access to his individual practitioner, and which can be accessed and updated at any care site. This eliminates the need for the patient to carry the record. Of course, not all seniors have access to the Internet, and some resist the new technology. But the elderly, who are the fastest growing group of Internet users today, will be ready for technology-based health care in the very near future. Baby boomers use the Internet now and will enter the ranks of the elderly in just 10 years. By then, we will see a significant acceptance of information technology as a health care tool. The ultimate solution might be a combination of these three approaches (written, smart-card, and Web-based), depending on physician and patient preferences.

Prescribing Principle #10

Stay informed about pharmaceutical innovations (novel drugs, new diagnostics for predicting drug response, etc.) relevant to diseases of the elderly.

Dilemma: Mrs. S, a 69-year-old woman, has had mild asthma throughout her life, but it has never been severe enough to warrant medication. Recently, her symptoms have worsened. As prescribed by her doctor, she has been using a different drug by inhalation every week for the past month, trying to find something to help her continue her fairly active lifestyle without having a full-blown asthma attack. Mrs. S is not ready to slow down and she insists that her doctor keep trying to find a medication that will work for her.

Resolution: In a few short years or less, the resolution to Mrs. S’s case might look like this: A new, gene-based technology is available to help predict Mrs. S’s response to her asthma medication without trial and error. A genetic test has been developed to predict a patient’s response to the asthma drug albuterol. With a fairly simple test, doctors could determine whether albuterol will work well, somewhat, or not at all for Mrs. S.
Discussion: Tests that predict drug responses could save patients the time, trouble, and potential complications of experimenting with medications until they find the right one. The albuterol response test is currently in development, and many similar gene-based drug response tests are sure to follow. Such tests will identify genetic markers to predict drug response for hundreds of other medications. Eventually, a patient will be able to get a routine screening for genetic markers that predicts their individual response to commonly utilized drugs for a particular disease. For the elderly, such innovations are essential to improved pharmacological care. Because the elderly experience greater medication side effects than younger patients, genetic tests that can predict side effects will be extremely beneficial to older patients. Today, many pharmaceutical and biotechnology firms are using genetic and bioinformatic resources to develop predictors, diagnostics, and treatments for the elderly; at least 20 of these corporations are focused almost solely on developments in what has been coined “gero-technology.” As these firms grow, advances in biotechnology and gene-based strategies will broaden care in the coming decades. Therefore, physicians and pharmacists who stay current with medical literature will be the first to be able to offer effective new interventions to their patients.

The use of anticholinergic agents to minimize the extrapyramidal side effects of traditional antipsychotic drugs was at one time an acceptable treatment, even though this course of treatment could be considered a “prescribing cascade.” Now, atypical antipsychotics, which have fewer side effects, are available.


79. Aids International Limited. Newer antipsychotics play an important role in the management of late-onset schizophrenia. Drugs & Therapy Perspectives. 2000; 16(8):7-12.
CE Test

DIRECTIONS: Choose the best answer.

PART 1: COMORBIDITY AND MEDICATION USE

1. What is NOT a factor that suggests the need for individualized pharmaceutical care for the elderly?
   a. greater physiological homogeneity
   b. increased risk of side effects
   c. prevalence of comorbidity
   d. age-related physiological changes

2. Which of the following statements is NOT true?
   a. Most people over 65 years of age have two or more chronic diseases.
   b. The rate of comorbidity has decreased over the last 100 years.
   c. Depression is a common comorbidity among the medically ill elderly.
   d. The synergy of comorbid diseases causes more detrimental effects than the combined singular effects of each component disease.

3. Put the following pairs of comorbid diseases in order from most common to least common among the elderly:
   1. hyper tension/diabetes
   2. arthritis/hyper tension
   3. arthritis/heart disease
   4. depression/other medical illness
   a. 1, 4, 2, 3
   b. 3, 2, 4, 1
   c. 2, 4, 3, 1
   d. 4, 3, 1, 2

4. Which of the following is NOT true: “The risk of an adverse drug reaction a. increases with number of comorbidities.”
   b. decreases with age.”
   c. increases with age.”
   d. increases with number of medications.”

5. Which statement is NOT true about depression among the elderly?
   a. Nearly 50% of people with depressive symptoms do not seek treatment.
   b. Comorbid depression increases mortality rates.
   c. Depression is more likely to be diagnosed if the patient has comorbid medical disease(s) as well.
   d. Antidepressants are underutilized.

6. Which class of antidepressants is generally considered preferable for elderly patients?
   a. tricyclic antidepressants
   b. selective serotonin reuptake inhibitors
   c. monoamine oxidase inhibitors
   d. serotonin and norepinephrine reuptake inhibitors

7. Compared to elderly cardiac patients without depression, elderly cardiac patients with depression are at greater risk for all EXCEPT
   a. longer recovery periods.
   b. increased medical resource use.
   c. increased mortality.
   d. increased myocardial infarction.

8. The primary concern with the use of TCAs in elderly cardiac patients is
   a. their anticholinergic properties.
   b. their potential proarrhythmic effect.
   c. their potential for drug-food interaction.
   d. their complicated dosing regimens.

9. Which of the following is a concern regarding the use of MAOIs in elderly cardiac patients?
   a. their anticholinergic properties.
   b. their potential proarrhythmic effect.
   c. their potential for drug-food interaction.
   d. their complicated dosing regimens.

PART 2: AGE-RELATED PHYSIOLOGICAL CHANGES

10. What is NOT a pharmacokinetic process?
    a. metabolism
    b. absorption
    c. elimination
    d. utilization

11. As aging occurs, which is the least clinically significant change?
    a. metabolism
    b. absorption
    c. elimination
    d. distribution
12. Which of the following body systems is LEAST affected by age-related physiological changes that could affect drug response?
   a. central nervous system
   b. cardiovascular system
   c. musculoskeletal system
   d. autoimmune system

13. Which type of drug is most likely to increase the risk of falls in older adults if the dosage is not adjusted accordingly?
   a. NSAIDs
   b. benzodiazepines
   c. β-blockers
   d. hydrophilic drugs

14. Which type of drug generally crosses the blood-brain barrier more easily, posing special concerns for older adults?
   a. lipophilic drugs
   b. hydrophilic drugs
   c. protein-bound drugs
   d. none of the above cross the blood-brain barrier

15. Which is most likely to be an unintended effect of a drug crossing the blood-brain barrier?
   a. increased heart rate
   b. confusion
   c. GI bleeding
   d. none of the above

16. Age-related changes in pharmacodynamics occurring at the receptor level include
   a. a decrease in number of receptors.
   b. altered biochemical reactions.
   c. a change in binding at the receptor site.
   d. all of the above.

17. Which of the following drugs usually shows a reduced effect in the elderly as a result of pharmacodynamics changes?
   a. β-adrenergic blockers
   b. analgesics
   c. sedatives
   d. antihypertensive agents

**PART 3: SIDE EFFECTS**

18. Which of the following might be an example of the prescribing cascade?
   a. Prescribing anticholinergic agents to control extrapyramidal side effects of traditional antipsychotic drugs.
   b. Prescribing medication for gout to a patient who presents with edema shortly after initiation of thiazide diuretic therapy.
   c. Prescribing with multiple antihypertensive drugs to control blood pressure.
   d. Prescribing an older patient a drug at half the recommended dose, then titrating it until the desired therapeutic effect is achieved.

19. When an older patient taking one or more medications complains of any new symptom or illness, the first step is to
   a. prescribe a safe drug to treat the symptom.
   b. stop all drug therapy to see if the new symptom resolves.
   c. rule out a drug side effect as the cause of the symptom.
   d. none of the above.

20. Which agents have the most potential to induce side effects related to blood pressure in the elderly?
   a. some diuretics
   b. some NSAIDs
   c. some TCAs
   d. a and b only

21. Which side effects have the potential to encourage falls and fractures in the elderly?
   a. anticholinergic effects
   b. extrapyramidal effects
   c. central nervous system effects
   d. all of the above

22. Which of the following is NOT an anticholinergic side effect?
   a. diarrhea
   b. ataxia
   c. dry skin and mouth
   d. tachycardia

23. Which of the following is NOT a benefit of the new atypical antipsychotics compared to traditional antipsychotics?
   a. a lower propensity to cause extrapyramidal or movement disorders
   b. greater efficacy against negative symptoms (emotional blunting, loss of energy and motivation) and equal efficacy against positive symptoms (i.e., paranoia, delusions)
   c. efficacy in patients who do not respond to traditional antipsychotics
   d. reduced cardiac effects

24. Which of the following factors contributes to problems with coordinated care for older patients?
   a. the number of medical specialists and sub-specialists
   b. mergers among health care organizations
   c. changes in insurer/benefit status
   d. all of the above

25. In order to optimize clinical outcomes, pharmaceutical therapy for the elderly should be
   a. tailored to individual patient characteristics.
   b. guided by evidence-based medicine.
   c. administered by all clinicians treating the patient.
   d. all of the above.
CE Examination Answer Sheet

Program #079-999-01-032-H04
Expiration Date: September 30, 2002

Complete this answer sheet (including the questions and information requested below), detach, and mail to:

Office of Health Policy and Clinical Outcomes
Thomas Jefferson University Hospital
attn: Continuing Pharmacy Education
1015 Walnut St, Suite 115
Philadelphia, PA 19107

Directions
Select the one best answer to each question and darken the appropriate circle.

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Program Evaluation
(Circle the appropriate response):

Excellent..............Poor

General quality of article  1  2  3  4  5
Applicability to practice  1  2  3  4  5
Objectives met  1  2  3  4  5
Ease of comprehension  1  2  3  4  5

Time (in hours) to read the article and complete the exam:

________________________

Suggested topics for future consideration:

________________________

________________________

I certify that I have completed this course independently:

________________________
(Signature)

Name (print) __________________________
Date Completed ________________________
Social Security Number __________________
Address __________________________________
City ____________________________
State ___________ Zip __________
Phone __________________________
Email __________________________