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Rational Prescribing in the Elderly

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LEARNING OBJECTIVES

1. Identify physiologic changes that occur with aging.
2. Explain the effect of aging on absorption, distribution, metabolism, and elimination of medications.
3. Recognize additional factors that affect the choice of medications and dosing in the elderly.
4. When given a medication regimen for an elderly patient, identify medications that may be inappropriate for use.

ABSTRACT: As the number of elderly people in the United States rises, sound medication prescribing for this population with special needs becomes increasingly important. There are a number of normal physiologic changes that occur with aging that may affect a medication, its dose, or frequency of administration, when used in a geriatric patient. In particular, decline in renal function, degeneration of the musculoskeletal system, and changes in the senses (i.e., vision, hearing, etc.) that regularly occur with aging may necessitate alterations in pharmacotherapy. Pharmacokinetic parameters also change with aging, most dramatically exemplified by excretion pathways. As a result, drug dosing and scheduling of medications commonly require adjustment in the elderly. A number of additional factors should be carefully considered when prescribing for the elderly. These include adverse drug reactions, interactions of all kinds, and the general functional decline that occurs with aging. To address these concerns, Beers criteria have been used over the past 10 years to assess medication regimens for geriatric patients. His recommendations serve as a guideline for rational geriatric prescribing. According to the guidelines, certain medications should not be used beyond a maximum dose or length of therapy in elderly patients. Likewise, some medications should be avoided completely in an elderly patient since safer alternatives are available. With the increasing number of medications from which to choose, pharmacists are indispensable for both proper geriatric patient assessment and in the evaluation of medication use for appropriateness and optimal therapeutic efficacy.

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RATIONAL PRESCRIBING IN THE ELDERLY

Elderly persons are the fastest growing segment of the population in the United States. With the ever-increasing array of medications available, both over the counter and prescription, most elderly patients are prescribed more medications than in the past. There are a number of factors that occur with aging, including physiologic, sensory, and pharmacokinetic changes that affect the medications an elderly person may safely take. This article will examine such factors and consider their relationship to appropriate and optimal prescribing in this patient population. Accordingly, this discussion will outline how pharmacists can play a tremendous role in assisting physicians with rational prescribing for the elderly as one facet of providing pharmaceutical care.

Demographically, the elderly are defined as persons 65 years or older. Somewhat colloquially, those from 65-74 years of age are considered the young-old, while persons from 75-84 years of age are described as the middle-old. The fastest growing segment of the elderly population, however, are those persons 85 years and older, designated the oldest-old. Overall, the elderly population in the United States is expected to peak between 2010 and 2030, when a majority of the Baby Boomer generation reaches the age of 65.

People today live longer owing to a decrease in the mortality rates with a concurrent increase in life expectancy. Mortality rates have declined because of the development of medications for both curing illness (e.g., antibiotics for infections) and controlling chronic diseases (e.g., insulin for diabetes). Life expectancy has increased attributable to a decrease in the number of premature deaths caused by accidents and on-the-job injuries. Simultaneously, there has been a significant improvement in the diagnosis of disease (e.g., cancers) and the treatment of those diseases. Technologic advances in the areas of diagnosis, surgeries and other procedures, and development of novel medications and delivery systems have contributed to increased life expectancy. There has also been a general increase in health awareness among the American population, which has improved overall health and has contributed to the delay in the development of certain diseases such as hypertension. A complex combination of these factors provides an explanation for why people live longer than in the past.

Physiologic Changes with Aging

The aging process is not attributable to a single underlying cause. Many theories have been developed to explain the changes that occur. Over a lifetime each organ system loses some ability to function optimally and to recover from insults and injuries. In an individual patient, change can occur primarily in a single organ system, leaving other organ systems able to function relatively normally. This section discusses some major physiologic alterations by organ system in the elderly.

Cardiac System

As an individual ages, a number of hemodynamic changes manifest themselves. Peripheral vascular resistance and stroke volume increase, while decreases are noted in renal blood flow, plasma volume, and cardiac output. The Renin-Angiotensin-Aldosterone (RAA system) is also affected with decreases in plasma renin and aldosterone noted; a combination of these factors contributes to hypertension. Isolated Systolic Hypertension (ISH) is of particular interest. Many elderly patients will have

normal diastolic pressure (less than 90 mmHg) but an elevated systolic pressure (140 mmHg or more). ISH needs to be identified and treated in the same manner as primary hypertension does.

With aging, there is a decreased cardiac sensitivity to β-adrenergic stimulation. For some, this decreased sensitivity makes them unable to respond to stress with an increased heart rate. For normal adults, a change from sitting to standing position results in a transient decrease in blood pressure and the body compensates. In contrast, because the elderly have a loss of baroreceptor sensitivity, they are more prone to orthostatic hypotension. Orthostatic hypotension is defined as a 20 mmHg or more decrease in blood pressure, or a symptomatic decrease of 10 mmHg, that occurs with position changes.

With aging, structural changes occur in the myocardium, including an increase in left ventricular wall thickness and an increase in cardiac mass. Left ventricular hypertrophy (LVH) is a consequence of the increases in systolic blood pressure and peripheral vascular resistance. The cardiac valves and the aorta may enlarge and become calcified.[1] The multitude of changes with the cardiac system during aging contributes to a number of chronic problems, including hypertension and ISH, orthostatic hypotension, and heart failure.

Respiratory System

Similarly, there are a number of changes in the respiratory system that occur with aging. Reduced lung elasticity (elastic recoil), weakened respiratory muscles, and decreased cough reflex can lead to the development of aspiration pneumonia.[2] Lung volumes also may change. Forced expiratory volume in 1 second (FEV_1) may be reduced and vital capacity may decrease. Usually these changes are not clinically important unless the patient has an underlying respiratory disorder or is a smoker.

Renal System

The renal system changes in a number of important ways with aging. Most significantly, there is a decrease in renal blood flow and a decrease in glomerular filtration rate (GFR). GFR may decrease up to 7% per decade after the age of 50. It has been estimated that renal function may be 40% less at age 70 than when a patient was 30 years of age.[3] In addition, the kidney has a decreased ability to concentrate urine, which leads to a decrease in the body's ability to regulate water and electrolyte balance. Clinically, this can lead to significant dehydration. Compounding this problem, some elderly persons need to urinate more frequently owing to a decrease in bladder capacity. Coupled with increased involuntary contractions, this may lead to leaking of urine. An increased residual urine volume in the bladder can create a suitable site for bacterial overgrowth and promote the development of urinary tract infections.

Immune System

Changes in the immune system, including decreased production and activation of T cells, can leave elderly persons more susceptible to infections.[4] No decrease in the number of B cells has been detected, but it is thought that they may not function to their highest capacity. Again, the degree of clinical significance of aging on the immune system is as yet unknown.

Central Nervous System

The effects of aging on the central nervous system (CNS) include a loss of neuronal cells, cortical atrophy, and a decrease in neurotransmitters.[5] Because of this, many

patients manifest cognitive changes such as decreased ability to respond appropriately to unfamiliar material, inability to perform complicated tasks or solve problems, and loss of short-term memory.[6] Coordination, which depends on both the neurologic system and the musculoskeletal system, is also impaired. Brain mass (weight) is also reduced.

The elderly frequently have altered sleep patterns. Stage 4 sleep (deep sleep), rapid eye movement (REM) sleep, and total sleep time may be decreased. An elderly person may then awaken more during the night or get up very early in the morning;[7] this may lead to a pattern of daytime napping.

Endocrine System

The endocrine system undergoes some familiar changes with aging, particularly in women. Declining estrogen production leads to menopause and its associated vasomotor symptoms. Likewise, men experience a decrease in testosterone as they age. In addition to changes with the sex hormones, altered pancreatic and adrenal hormone production occur, leading to a decrease in glucose tolerance.[8] This accounts for the increased incidence of non–insulin-dependent diabetes mellitus (NIDDM or Type 2 diabetes) seen. Thyroid disorders are common as well, with hypothyroidism predominating, though hyperthyroidism is also seen. Osteoporosis may be a common problem with postmenopausal women, but elderly men may also develop the condition. As a person ages, a loss in bone occurs, with Vitamin D absorption and calcium intake playing a role in this process.

Gastrointestinal System

A number of changes occur within the gastrointestinal system, many of which will be discussed in consideration of absorption changes with aging. Slower esophageal motility leads to difficulty with the swallowing process, so elderly patients may need modifications to their diet. Gastric emptying time often is decreased and intestinal transit may slow. Liver mass decreases, and there is also a reduction in hepatic blood flow. Elderly persons are more prone to develop gallstones.

Musculoskeletal System

The musculoskeletal system changes that occur are demonstrated as alterations in the outward appearance of older persons. Atrophy of muscle fibers will manifest as a decrease in strength, endurance, and agility. Demineralization of the bone can lead to a decrease in bone density and an increase in the incidence of osteoporosis. Some elderly develop a shuffling or unsteady gait, or a stooped posture, making them more prone to fall. Elderly patients may "shrink" as a result of shortening of the spinal column. Such physical changes contribute to chronic pain, loss of independence, and a decreased quality of life.

Integumentary System

Changes to the integumentary system occur with aging. These skin changes include a decrease in elasticity and, thus, an increase in skin tears and ruptures.[9] Dry skin is a result of decreased moisture and sebum production on the surface of the skin. Circulation can be impaired leading to a decreased blood supply to the skin. Nails may become brittle and are subject to cracking and present a risk of developing secondary infection. Furthermore, skin may be more susceptible to infections owing to poor blood flow. This also makes it difficult in some elderly patients to do fingersticks for diabetes testing. Age spots may appear attributable to sun damage. As with the musculoskeletal system, skin changes often significantly affect the outward appearance

of an elderly person, such as wrinkling of skin and gray hair.

Special Senses

Sensory changes also occur with aging. First, visual acuity decreases, peripheral vision is lost, and the eye is less able to adapt to changes in light and dark.[10] Most patients will experience an increased sensitivity to light and decreased color sensitivity. Secondly, sound waves are not properly conducted or transmitted through the auditory system, so the elderly may have a decreased ability to hear high frequencies. Third, there is a decreased number and sensitivity of taste buds. Food might not be as appealing because of this alteration in taste, which can lead to malnutrition and weight loss. Altered or decreased smell may also contribute to this weight loss. Finally, the development of peripheral neuropathies and decreased blood flow lead to changes in the touch sensation.

Pharmacokinetic Changes with Aging

Among the pharmacokinetic processes of absorption, distribution, metabolism, and elimination (ADME), absorption is the least altered during aging. There is, however, a decrease in gastric acid production, altering the dissolution rate of some medications. Slower gastric emptying decreases the peak concentration of certain drugs and potentially increases the degradation of acid labile drugs.[11] With a slowing of intestinal transit, absorption increases owing to increased contact time with the intestinal brush border. Despite this, it may actually take longer to get a medication into the circulation because of a lessened GI blood flow. The net effect is that the rate and extent of absorption does not change in an elderly person unless a specific malabsorption syndrome exists. Currently, it is not well understood how aging and changes in the integumentary system affect absorption from transdermal medication delivery systems.

Changes in body composition that occur include decreased muscle mass, decreased total body water, and increased adipose tissue. Accordingly, lean body weight decreases owing to the loss of muscle that is replaced by adipose tissue. As a result, a prolonged effect from fat-soluble drugs (e.g., benzodiazepines) may be noted. Plasma protein binding is altered owing to a 10%-20% decrease in albumin.[12] This allows more free drug to be available, and may increase toxicities and side effects from medications. An example of this is seen with phenytoin, a highly protein-bound drug. Precise evaluation of serum phenytoin levels in the elderly is often difficult because of the decreased amount of albumin available for binding.[13]

Since drug metabolism occurs primarily hepatically, the changes that occur with the aging liver affects the metabolism of many medications. As we age, there is a decrease in liver size and a corresponding decrease in the number of hepatocytes. Liver blood flow slows, which reduces first-pass metabolism, resulting in an increased concentration of orally administered, hepatically biotransformed agents. In general, Phase I metabolism (including CYP450), which produces active metabolites, is slower and less efficient in the elderly. Grapefruit juice, a specific CYP3A4 inhibitor, may produce adverse effects when co-administered with a number of medications (statins, dihydropyridine calcium antagonists, sildenafil).[14] The aging process does not seem to affect Phase II metabolism, which usually results in the production of inactive metabolites. Phase II metabolism includes the processes of glucuronidation and sulfation. Clinically, the consequences of altered metabolism are

not well understood, but probably include increased concentration of parent drug and prolonged effects from metabolites.

Among the pharmacokinetic phases of drug fate, excretion is the most affected process in the elderly. As noted previously, decreased renal blood flow and decreased GFR result in impaired handling of water, electrolytes, and glucose. Because there are marked inter-individual differences in estimated creatinine clearance, many drugs need to be adjusted based on renal function in the elderly population (see Table 1). Unlike other kinetic alterations that result from aging, the changes to excretion that occur have been extensively studied.[15]

Table 1
Medications that May Need to be Dose Adjusted in Elderly Patients Owing to Decreased Creatinine Clearance

ACE Inhibitors	Furosemide	Quinidine
Allopurinol	H_2 receptor antagonists	Quinolone antibiotics
Amantadine	Lithium	Spironolactone
Aminoglycoside antibiotics	Methotrexate	Sulfonamide antibiotics
Atenolol	Metoclopramide	Thiazide diuretics
Cephalosporin antibiotics	Nadolol	Trimethoprim
Chlorpropamide	Normeperidine (metabolite	Vancomycin
Digoxin	of meperidine)	
Disopyramide	Penicillin antibiotics	
Fluconazole	Procainamide	

Other Considerations

Rational medication prescribing in the elderly requires consideration of a host of other factors. These factors include complications from treatment (adverse drug reactions, drug-drug interactions, or drug-food interactions), trauma owing to accidents and falls, functional decline caused by hospitalization or prolonged bed rest, and medication misuse.

A recent study reviewed adverse drug reactions, as well as therapeutic failures and adverse drug withdrawal events in the elderly.[16] It is difficult to determine, however, if advancing age by itself is the prime factor, or how other considerations come into play. The elderly are more likely to be on several medications belonging to multiple drug classes than persons in any

other age group. Elderly people usually have more chronic illnesses and, in general, are in poorer health than young persons. Finally, many physicians do not consider the pharmacokinetic and pharmacodynamic changes that occur with aging when prescribing a medication, which are paramount with regard to the possible development of an adverse drug reaction (ADR).

Drug interactions can be considered a type of ADR. Drugs interact with other medications, nutrients, and with disease states. Drug-drug interactions are more common in the elderly because they are usually prescribed a greater number of medications. Also, in an effort to self-medicate chronic conditions, they commonly use a variety of OTC medications, herbal medications, or other alternative therapies that interact with their prescribed medications. Consequently, response to a medication may be excessive (if concurrent medications have similar actions) or diminished in one or both medications (if they have opposing actions). Sometimes, physicians take advantage of these interactions and prescribe 2 medications with similar actions to obtain a synergistic effect. This can be easily seen in the common practice of managing blood pressure by using 2 medications from different drug classes and with different mechanisms of action. This allows greater control of blood pressure without increasing side effects from either medication.

Similarly, drug-nutrient interactions are commonly overlooked in prescribing. Food in the stomach can significantly decrease the absorption of a number of medications. Additionally, there are a number of vitamin-drug interactions. As an example, folic acid therapy will increase the metabolism of phenytoin, leading to decreased serum phenytoin concentrations. Vitamin K interferes with the action of oral anticoagulants (warfarin). Some medications may alter the taste of food, so patients will stop taking the medication to enjoy their meals more, or they may begin to eat less, leading to malnutrition. A representative list of medications known to alter taste or that may produce a bad taste is given in Table 2.[17,18]

Table 2
Medications Altering Taste or Causing a Bad or Unpleasant Taste[17, 18]

Abuterol HFA aerosol	Felbamate	Pimozide
Amitriptyline	Flunisolide aerosol	Propafenone
Atovaquone	Fluvoxamine	Ribavarin
Carbenicillin oral	Ipratropium aerosol	Rifabutin
Cefuroxime oral	Miconazole	Theophylline oral solution
Clarithromycin	Penicillamine	Zinc lozenges
Docusate liquid	Penicillin liquids	

Drug-disease state interactions occur when administration of a medication causes a new disease or exacerbates an existing condition. A very simple example of this occurs when a non-specific β-blocker is given to a patient with asthma, and breathing difficulties arise. Likewise, some Angiotensin Converting Enzyme (ACE) Inhibitors produce a cough in certain patients, which leads to discontinuing that medication in affected patients.

There are a number of ways to minimize the risk of drug interactions in the elderly. As a pharmacist, being aware of possible drug interactions is always a factor. In some cases, 2 drugs that are known to interact can be given together when appropriate monitoring is performed or doses are properly adjusted. Patient medication profiles should be accurate and kept up to date, and include any OTC, herbal, and alternative therapies a patient may take. To minimize the likelihood of interactions medication regimens should be kept as simple as possible. Patients should be maintained on the least number of medications necessary to appropriately manage their medical conditions. Also, patients should be encouraged to report any unusual symptoms or reactions to medications to their physician or pharmacist, especially when new medications are added to the regimen. The pharmacist should always keep in mind that when using any medication, there is a wide range of inter-patient variability seen with effectiveness and adverse reactions.

A common source of morbidity and mortality in the elderly is owing to trauma caused by accidents and falls. Patients can fall from beds, chairs, or wheelchairs. Up to one-third of community-based elderly citizens fall in their own home every year.[19] Twenty percent of hospitalized elderly patients fall during their stay. Falling can lead to fractures, head trauma, and other types of internal injuries. Besides age (over 80 years), diagnoses, and physical functional ability, medication use can play a major role in elderly patients and their risk for a fall. Any medication that affects the CNS (benzodiazepines, antidepressants), causes orthostatic hypotension (diuretics, antihypertensives), or causes a patient to be dizzy (nonsteroidal anti-inflammatory drugs, aspirin) can increase the elderly's risk for a fall. A thorough review of a patient's medication profile can help to identify offending agents.

Functional decline in the elderly can be caused by a number of factors. Immobility because of hospitalization and bedrest can lead to the development of pneumonia, thrombosis, and pressure sores. Dietary restrictions placed on a hospitalized elderly patient prior to procedures and surgery can lead to diminished nutritional reserves. Hospitalization and bedrest can lead to problems with the urinary system including acute urinary retention and incontinence. Constipation can lead to a small bowel obstruction. Finally, elderly patients placed in the unfamiliar environment of a hospital can respond with confusion and delirium.

Medication misuse includes a number of situations. Among these scenarios is a patient taking too many medications, too much of a medication, a patient with an untreated medical problem, and medication noncompliance (nonadherence). Medication noncompliance is a problem with every age group of patients. Many think that medication noncompliance is a more common problem for the elderly, but some studies show otherwise.[20,21] Considering that elderly patients use more medications

than other age groups, it might be expected that this contributes to noncompliance. Others have argued that as elderly patients are becoming more knowledgeable about their health, they are more motivated to take medications correctly, so they feel better and live longer.

Beers Criteria and Recommendations—1991 and 1997

In 1989, Beers and Ouslander published "Risk Factors in Geriatric Drug Prescribing, A Practical Guide to Avoiding Problems" in *Drugs*.[22] This article was one of the first published attempts to develop a list of medications that present problems, particularly in elderly patients. Beers and Ouslander listed "special considerations" that needed to be taken into account when prescribing both specific medications and medication classes. The list at that time included the medications listed in Table 3.

Table 3

Beers and Ouslander Drugs Posing Special Risks in the Elderly—1989[16]

Amitriptyline	Digoxin	Narcotics
Antiemetics	Diphenydramine	OTC cold medications
Antipsychotics	Disopyramide	Propoxyphene
Barbiturates	GI antispasmotics	Reserpine
β-blockers	H_2 receptor antagonists	Timolol
Chlorpropamide	Long-acting benzodiazepines	Xanthenes

In 1991, Beers and colleagues further defined this list with a publication in the *Archives of Internal Medicine*.[23] This article, entitled "Explicit Criteria for Determining Inappropriate Medication Use in Nursing Home Residents," described the survey form used to develop the criteria, presented the medications developed in the guidelines, and discussed areas where no consensus could be made among the expert panel members consulted. This list of medications and considerations was more specific than those initially presented in 1989.

Based on the 1991 article, medications that affect the CNS should be avoided in the elderly; they may produce excess drowsiness, dizziness, and sedation. When considering the sedative-hypnotic class of medications, Beers and colleagues developed the following guidelines regarding benzodiazepines, barbiturates, and sedative-hypnotics: all use of long-acting benzodiazepines, meprobamate, and short-duration barbiturates should be avoided. Dose limits were set for several agents: oxazepam should not be used in doses greater than 30 mg and triazolam should not be used in doses greater than 0.25 mg per

day. Nightly use of short-acting benzodiazepines for sleep should be avoided after 4 weeks. More recent Health Care Financing Administration (HCFA) guidelines regarding the use of hypnotic agents in long-term care facilities have set the maximum dose for oxazepam at 15 mg and triazolam at 0.125 mg per day.[24]

The use of antidepressants and antipsychotics in the elderly should be carefully considered because of their effects on the CNS. Beers and colleagues recommended that all use of amitriptyline be avoided, as an individual agent, as well as in combination with antipsychotics. Any other use of antidepressant-antipsychotic combination agents should be avoided. Beers and colleagues felt it better to use single agents as opposed to combination agents. Haloperidol doses greater than 3 mg per dose and thioridazine greater than 30 mg per day were listed as maximum doses for the elderly. In practice, some elderly patients need to be on combination products for optimal control. Low doses of the newer, atypical antipsychotics medications (e.g., olanzapine, risperidone) are being investigated for use in elderly patients, as well as their combination with antidepressants.

Certain antihypertensives seem to pose particular problems in the elderly. Beers and colleagues determined that all use of reserpine, propranolol, and methyldopa should be avoided. Reserpine and methyldopa can produce depression as a significant side effect. Propranolol has increased CNS penetration and is a non-selective β-blocker. Use of these agents for hypertension has declined over the years as newer agents have been developed. Beers and colleagues suggested that hydrochlorothiazide not be dosed over 50 mg per day owing to its effect on water and electrolytes. With consideration for the dose limit on hydrochlorothiazide, the Joint National Committee report on hypertension (JNC-VI) concluded that diuretics (hydrochlorothiazide included) are the agents of choice for ISH, and long-acting dihydropyridine calcium antagonists are a second option.[25]

Beers and colleagues list indomethacin specifically as an inappropriate agent for the elderly because of the CNS side effects. Indomethacin also has a high occurrence of gastrointestinal (GI) side effects. But in general, nonsteroidal anti-inflammatory drugs (NSAIDs) as a class have a high incidence of GI adverse effects in the elderly (peptic ulcer, hemorrhage). Cox II agents at present are safer than NSAIDs, but still carry a potential for gastric problems. In addition, NSAIDs may cause sodium and water retention in the elderly. Many practitioners today would say that acetaminophen should be the first choice for chronic treatment of mild to moderate pain in the elderly, provided it is dosed appropriately at not more than 4 grams per day (1 gram QID). For patients with severe renal impairment, acetaminophen should be dosed every 8 hours.

Beers and colleagues noted that prescribing propoxyphene or pentazocine to an elderly person can also pose a number of problems. Pentazocine may cause delirium and agitation. Propoxyphene may cause CNS depression, and has potential for addiction. Beers and colleagues suggested that other alternative agents are safer and more effective in the elderly. All narcotic agents have the potential for addiction, as well as the potential to cause CNS depression and agitation. Chronic use of meperidine in particular has been singled out to avoid in the elderly because of its potential for accumulation of its metabolite

normeperidine. Even morphine poses some particular problems for geriatric patients, including CNS depression and constipation. But for severe pain, needing chronic therapy, morphine is preferred over meperidine and methadone. The use of narcotic-acetaminophen combination agents for moderate to severe pain remains an option, as long as the total daily dose of acetaminophen is considered.

Chlorpropamide may cause syndrome of inappropriate antidiuretic hormone secretion (SIADH), in which hyponatremia may occur. Chlorpropamide also has a half-life greater than 24 hours. For these reasons, Beers and colleagues suggested use of other oral hypoglycemic agents with shorter half-lives. Today, the use of second-generation sulfonylureas (glyburide, glipizide) for NIDDM has overtaken the use of the first-generation agents in most cases.

Beers and colleagues suggest that the use of muscle relaxants (carisoprodol, chlorzoxazone, cyclobenzaprine, methocarbamol) should be avoided in the elderly. They have anticholinergic side effects that can lead to constipation and dizziness. The dizziness, coupled with the possibility of orthostatic hypotension from these agents, can lead to falls. CNS depression is also seen in the elderly.

GI antispasmotics (dicyclomine, hyoscyamine, propantheline), like the skeletal muscle relaxants, have anticholinergic side effects. These side effects may manifest in the elderly as confusion and hallucinations, as well as the traditional anticholinergic effects of dry mouth, difficulty with urination, and constipation.

Beers and colleagues listed trimethobenzamide as an antiemetic to avoid in the elderly; extrapyramidal (EPS) side effects and confusion are potential adverse effects seen with this agent. EPS side effects include tremor, rigidity, akinesia, and drooling. Other antiemetic agents including promethazine, hydroxyzine, and prochlorperazine may also cause these effects. Serotonin receptor antagonists like ondansetron may be the preferred antiemetic agents in the elderly.

Beers and colleagues list aspirin as a more effective alternative than dipyridamole for platelet aggregation. Today, the combination product of dipyridamole/aspirin (Aggrenox®) is available for use in platelet inhibition. Clopidogrel is also more commonly used for this indication.

Beers and colleagues suggested that cimetidine at doses greater than 900 mg per day, ranitidine at doses greater than 300 mg per day, and either over 12 weeks of therapy should be avoided in the elderly. In addition, cimetidine has a number of drug-drug interactions that limit its use for elderly patients. Though Beers did not include nizatidine and famotidine at the time of the article (they were not released at that time), those agents can also be considered in this category. All H_2 receptor antagonists need to be dosed carefully in patients with decreased renal and/or hepatic function. Elderly patients are commonly treated with ranitidine, famotidine, and nizatidine for chronic treatment of gastroesophageal reflux disease (GERD), and they can be safely used if appropriate dosing and drug interactions are considered.

According to Beers and colleagues, oral antibiotics should not be used continuously for more than 4 weeks except when the specific diagnosis dictates (e.g., osteomyelitis). Antibiotic doses or regimen frequency may also need to be adjusted in

elderly patients with impaired renal or hepatic function.

Daily use of decongestants (i.e., phenylephrine, oxymetazoline, and pseudoephedrine) should be avoided, since rebound congestion from decongestant nasal sprays can occur quickly. Use of oral pseudoephedrine can be a problem for elderly patients, in that it can cause hypertension and tachycardia. The non-sedating antihistamines such as fexofenadine may be quite useful for the long-term management of allergic or seasonal rhinitis in the elderly.

Other medications mentioned by Beers and colleagues in 1991 included cyclandelate (no longer available) and isoxsuprine for use as treatment for dementia. Atypical antispychotics are now used for the elderly in this area. Phenylbutazone is no longer on the market. Oral iron, for those elderly patients with iron deficiency anemia, can be dosed up to 325 mg 3 times a day, as tolerated by the patient.

Beers updated his criteria in 1997.[26] New guidelines were added for disopyramide, digoxin, doxepin, ergoloid mesylates, cyclospasmol, and ticlopidine. Disopyramide was added owing to its anticholinergic side effects and its potential to induce heart failure. Digoxin doses commonly need to be adjusted in the elderly because of poor renal function. The recommendation suggests that doses greater than 0.125 mg are probably too high for an elderly person and would predispose that patient to additional side effects. Doxepin, like amitriptyline, has a high potential to cause anticholinergic side effects in the elderly, in addition to the high degree of sedation it may induce. Selective serotonin reuptake inhibitors (SSRIs) like paroxetine, fluoxetine, sertraline, and citalopram have replaced the older agents as first-line therapy for treating depression in the elderly. Ergoloid mesylates (Hydergine®) and cyclospasmol should be avoided, considering their effectiveness has not been shown in the treatment of geriatric dementias. Ticlopidine has a number of serious adverse effects (neutropenia, thrombocytopenia,) that may occur, and these should be considered prior to use. Ticlopidine, in fact, is rarely used today. Low-dose aspirin and clopidogrel are the more commonly prescribed alternatives.

Other authors have added medications to those needing special consideration in the elderly. In 1997, an article published by McLeod and colleagues added several other medications to the list.[27] These included pentoxyphylline, imipramine, methylphenidate, diphenoxylate, and piroxicam. The effectiveness of pentoxyphylline for peripheral vascular diseases has not been shown. Newer SSRI antidepressants would be preferred over imipramine, which may produce orthostatic hypotension in the elderly, as well as anticholinergic side effects. Methylphenidate needs to be dosed with extreme caution in the elderly owing to its CNS stimulant and cardiac stimulant (i.e., hypertension, tachycardia) effects. Loperamide is a better agent than diphenoxylate for diarrhea. Piroxicam, like other NSAIDs, may pose a special risk to elderly patients in regard to GI adverse events and edema.

A recent review of inappropriate prescribing found that, despite Beers and others' work in the late 1980s and 1990s, the problem of inappropriate prescribing in the elderly remains.[28] As new medications become available, their potential for problems in the elderly needs to be considered and closely monitored. It has been suggested that more

research needs to be done in this area, particularly in consideration of the impact of inappropriate medication use in the elderly on health care costs.

Role of the Pharmacist

Pharmacists can play an important role in geriatric medication evaluation and assessment. They work with geriatric patients in a number of settings, including the community drug store, ambulatory clinic, hospital, or long-term care facility. A pharmacist can review the elderly patient's medication history and act as a drug information specialist regarding needed medication adjustments in renal or hepatic impairment, adverse drug effects, and drug interactions. The pharmacist can also function as a therapeutic problem solver, providing the physician alternatives and options for treatment.

The pharmacist should proceed, in a systematic and organized fashion, to review the medication regimen of an elderly patient. A patient-specific database should be developed, which contains the patient's medication history (including prescription, non-prescription, and alternative therapies), history, physical data, and laboratory results. The pharmacist can then create a patient-specific problem list, matching medications prescribed with their indication for use. Finally, the pharmacist evaluates the patient's medication regimen, formulating a plan and making recommendations to the prescriber when necessary. These recommendations can take many forms, and may include the following:

- Suggesting better alternative agents or more effective agents. This can include recommendations for alternative dosage forms, which may be more easily administered to the elderly patient.
- Recommending discontinuation of a medication that is no longer needed or is an unnecessary duplication of therapy.
- Suggesting a modification of a drug dose or medication frequency owing to the renal or hepatic function of a patient. The pharmacist also plays a critical role in interpreting serum drug levels and recommending dosage changes based on those levels.
- Recommending a change in the route of administration for better patient compliance.
- Suggesting a change in the medication administration schedule for individual patients to better suit their lifestyle and to improve compliance.
- Requesting laboratory tests or serum drug levels to evaluate the therapy and to maximize medication effectiveness. These test and drug levels can also play a role in evaluating adverse effects a patient may be experiencing.
- Recommending a change in the elderly patient's diet. This, in most cases would be done with the input of a dietician. These suggestions can serve to allow for better control of a chronic disease state (e.g., avoiding salt in a congestive heart failure patient or hypertensive patient).
- Suggesting other means of monitoring medication therapy. This may include taking daily weights, having frequent blood pressure checks, or monitoring daily heart rate.
- Evaluating and making recommendations regarding an elderly person's non-prescription and herbal drug use.

CONCLUSION

General Rules for Geriatric Prescribing

1. Start each new medication at a low dose and increase slowly. If no other guidelines are given, it may be safest to

start an elderly patient at half the normal adult dose.
2. The half-life of drugs is often prolonged in the elderly. It is usually safe to extend the dosing interval.
3. Rapid dose increases may not allow for an appropriate patient evaluation owing to the prolonged half-life. Wait until you are sure the patient has achieved steady-state drug concentrations before making further adjustments to the dose or interval.
4. Always use the fewest number of medications possible. This will help to avoid drug-drug interactions.
5. It is important to frequently reassess the medication regimen for an elderly person. You need to consider if the responses that a patient experiences are because of a side effect of one of his or her medications.
6. Carefully consider new medications as they become available before prescribing them. Look for specific side effects that may pose particular problems in elderly patients. Monitor patients carefully when new medications are added to a regimen.

With appropriate monitoring by a pharmacist, elderly patients can achieve successful outcomes from their medication therapy. This type of rational prescribing in the elderly will ultimately improve the quality of life of our elders.

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