Administering Medications to Elderly Patients
Part 1: The Physiology of Aging

This course has been awarded two (2.0) contact hours.
This course will be updated or discontinued on or before August 31, 2018.

First Published: June 12, 2009
Revised: June 8, 2012
Revised: August 21, 2015

Medications and the Elderly: a 3-Part Series

This course is the first in a series of **three courses** that explore medication therapy with persons 65-years-old and older.

Administering Medications to Elderly Patients, Part 2: Administering and Monitoring Medication Therapy builds off of part 1 and addresses concerns related to administering and monitoring response to medications which elderly persons commonly receive. Administering Medications to Elderly Patients, Part 3: Discharge Planning builds off of parts 1-2 and explores issues related to patient teaching, polypharmacy, compliance, adherence and social issues that often affect elderly persons and adherence to therapy.

Each course presents **case studies** for practice in critical thinking and each course includes the **same five Appendices,** below**.**

Appendix A	Beers Criteria 1: Potentially Inappropriate Medication Use in Older Adults – High-Severity
Appendix B	Beers Criteria 1: Potentially Inappropriate Medication Use in Older Adults – Low-Severity
Appendix C	Beers Criteria 2: Drug-Disease Interactions – High-Severity Concerns
Appendix D	Beers Criteria 2: Drug-Disease Interactions – Less-Severe Concerns
Appendix E	Resources for Further Information

Acknowledgements

RN.com acknowledges the valuable contributions of…

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Purpose and Objectives

Administering Medications to Elderly Patients, Part 1: The Physiology of Aging educates healthcare professionals about the implications of medication therapy in the elderly, focusing specifically on the physiology of aging and disease conditions common among this population.

After successful completion of this course, you will be able to:

1. Describe research findings related to medication safety and the elderly.
2. Describe the implications of physical changes of aging for medication therapy.
3. Explain the metabolism and mechanism of action of selected medications in relation to disease processes that are common among the elderly.
4. Define the term Beers Criteria and explain the rationale for placement of specific medications in Beers Criteria.
5. Explain how metabolism of medications creates interactions and why the elderly are at an increased risk for medication interactions.
6. Give examples of medication interactions pertinent to common prescriptions among elderly patients.
7. Identify resources regarding medication therapy for elderly patients.

Introduction

Medications contribute to extended longevity by treating chronic conditions effectively; however, they also **create risks for elderly persons**.

This course explains how the physiological and pathophysiological effects of aging place elderly persons at risk for adverse drug events (ADEs).

Of the many factors that contribute to ADEs, the most important are the pathophysiological consequences of aging, particularly as these apply to the very old (Petrone & Katz, 2005).

This course identifies:

- Medications which researchers have declared as potentially inappropriate for elders.
- Common diseases of the elderly which create particular problems when certain commonly prescribed medications are ingested.
- The mechanism by which medications interact with one another.

Pharmacodynamics and Pharmacokinetics

Aging affects both the **pharmacodynamics** and **pharmacokinetics** of drugs.

Pharmacokinetics

The processes of drug absorption, distribution, metabolism and elimination.

Pharmacodynamics

The effect of the drug at its targeted receptor site. Altered receptor sensitivity associated with aging may cause a prolonged or more intense response to a drug.

All Elders Are Not Created Equal

The literature defines elderly to include persons aged 65 years and older; however, individuals vary in experience and the age at which changes become evident.

Biological, psychological, social, and spiritual variability has been studied in middle aged to elderly and is influenced by multiple factors.

Well-being and life satisfaction varies amongst individuals, described as "**successful aging**" (Sigelman, & Rider, 2014).

Changes of Aging

Successful aging discusses not just the social and psychological impact of aging, but the parallel with physiological and cognitive changes as well.

Usual aging discusses a normal decline in social, physical and cognitive functioning, which is seen as a minimal loss with "successful aging" (Sigelman, 2014).

Healthcare providers must assess each elderly patient carefully for signs and symptoms that indicate whether specific physical changes will influence that patient's response to medications.

Changes of aging alter the sensitivity of receptors in target organs to medications, creating a more intense or prolonged response to the medication.

Implications for Medication Therapy

Certain changes of aging have the most significant implications for medication therapy, as described here.

Changes in Body Composition

One change of aging that distresses both men and women as they grow older is the increase in body fat.

- In men, fat increases from an average of 15% in young adulthood to 36% at age 75.
- In women, fat increases from an average of 33% in young adulthood to 45% at age 75 (Rolfes, Pinna & Whitney, 2014).

This change in body composition increases the volume distribution and half-life of fat-soluble (lipophilic) drugs, including barbiturates such as secobarbital sodium (Seconal®), benzodiazepines such as diazepam (Valium®) and phenothiazines such as chlorpromazine (Thorazine®). Therefore, the elderly may require lower doses of fat-soluble drugs. In some cases, they may need alternative medications that do not present the hazards of prolonged action or adverse effects.

One of the most serious hazards of prolonged action of the fat-soluble barbiturates, benzodiazepines and phenothiazines is the **increased risk for falls and injury** that is created by sedation and cognitive impairment.

Falls contribute significantly to morbidity and mortality in the elderly. One in four elderly persons who falls and suffers a hip fracture dies within a year of the fall. Many medications, including sedatives and anticholinergics, have the potential for producing ataxia, confusion and risk for falling in elderly persons (Poole, 2015).

Changes in Proportion of Body Water

A decrease of 10% to 15% in the proportion of body water and lean mass occurs with aging (Lata & Alia, 2007; Rolfes, 2014).

Resulting in serum concentration increases for water-soluble drugs such as digoxin (Lanoxin®) that do not distribute well into adipose tissue. For this reason, lower doses are recommended for the elderly.

The dose of digoxin (Lanoxin®) for elderly patients should begin at less than or equal to 0.125 milligrams daily, except when treating atrial fibrillation, and titrated carefully based on tolerance and blood levels (Kaplan & Porter, 2011).

Dehydration frequently occurs in the elderly and compounds the problem of decreased body water. Assure that your elderly patients receive adequate amounts of water.

TEST YOURSELF
The MAXIMUM recommended daily dose of digoxin (Lanoxin®) for elderly persons in most situations is 0.15 mg.
TRUE
FALSE

Decrease in Serum Albumin

A decrease in serum albumin and protein-binding occurs in 15% to 25% of patients age 60 and older (Rosenoer, Oratz & Rothschild, 2014).

Many medications are highly-bound to plasma proteins, including:

- aspirin
- benzodiazipines such as diazepam (Valium®)
- digoxin (Lanoxin®)
- phenytoin (Dilantin®)
- propanolol (Inderal®)
- tolbutamide (Orinase®)
- tricyclic antidepressants (TCAs) such as amitriptyline (Elavil®)
- warfarin (Coumadin®)

When less serum albumin is present to bind the medication, more of the medication is circulating and exerting its effect. Therefore, the elderly may be more sensitive to protein-binding medications (Rosenoer, 2014).

TEST YOURSELF

Because phenytoin (Dilantin®) is highly protein-bound, your elderly patient who is receiving the medication may experience:

a. A need for a higher dose.
b. Greater sensitivity to the medication.
c. Increased risk for seizures.
d. Tachycardia.

Decreased Metabolic Rate

Metabolic rate begins to slow before age 65. A 45-year-old woman who eats the same number of calories that she ate to maintain her weight when she was 20 years old, will gain one pound every 12 days, or 30 pounds in a year.

Regular exercise and regular frequent meals can raise metabolic rate. However, many elderly persons do not exercise or eat nutritious meals regularly.

Failure to exercise and eat regularly compounds the problem created by the declining metabolic rate. As compared with younger persons, elderly people metabolize drugs more slowly. Consequently, drugs have longer half-lives and remain active for a longer period of time.

If a younger person and an older person received the same dose of a drug, the older person would likely experience greater concentrations and more prolonged clinical effects than the younger person (Rolfes, 2014).

TEST YOURSELF

Elderly persons metabolize medications more slowly than younger adults. Therefore, as compared with younger adults, elderly patients are likely to experience:

a. Lower serum concentrations of medications.
b. Diminished effectiveness of medications.
c. A need for more frequent doses.
d. Effects of medications for a longer period of time.

Decreased Cardiac Output

Decreased cardiac output common in aging bodies interferes with the distribution of medications to the receptor organs and tissues.

Reduced blood supply that results from decreased cardiac output affects gastrointestinal function and slows absorption and distribution of medications.

Decreased cardiac output also affects blood flow to the liver and kidneys. These organs play a major role in the metabolism of medications and the excretion of end-products of medication metabolism. Slower metabolism and slower elimination of metabolites results in longer exposure to the effects of the medication.

Decreased cardiac output reduces the safe dosage of many medications.

Many elderly patients suffer from congestive heart failure (CHF) which is characterized by decreased cardiac output and sluggish circulation, and in turn affects the actions of medications (Lata & Alia, 2007).

Changes in GI Function

Changes in gastrointestinal function associated with aging affect the patient's response to oral medications. Most medications are absorbed by passive diffusion which is unaffected by age. However, older persons have reduced gastric acidity (achlorhydria) which reduces the bioavailability of medications that depend upon gastric acidity for absorption. Some tablets and capsules and some specific drugs (such as aspirin) require gastric acidity for absorption.

Risks

Decreased gastric motility can result from aging and from disease conditions common in the elderly, such as congestive heart failure (CHF). Decreased gastric motility and decreased motility in the duodenum, where most medications are absorbed, cause medications to be in contact with the gastric and intestinal mucosa for a longer time than in younger adults. This presents a risk for gastrointestinal irritation and ulceration when the patient is receiving medications that have ulcerogenic potential, such as nonsteroidal anti-inflammatory drugs (NSAIDs). Alternatives to NSAIDs such as COX-2 inhibitors are recommended.

Reduced blood flow in the gastrointestinal tract due to cardiovascular changes may decrease or delay absorption of many medications.

Duodenal diverticuli common in aging bodies increase bacterial growth in the intestine and interfere with absorption of medications (Kaplan & Porter, 2011; Hutchison & Sleeper, 2010).

TEST YOURSELF

Your elderly patient seems to be getting little or no effect from aspirin. Which change of aging is probably responsible?

a. Reduced gastric acidity
b. Reduced serum albumin
c. Increased body fat
d. Changes in liver function

Changes in Liver Function

A system of enzymes (the CYP system), located primarily in the liver, metabolizes more than 80% of medications. The activity of these enzymes decreases with age. Hepatic mass and hepatic blood flow also decrease with age. These changes have the potential for lowering the safe dosage of a number of medications.

More active medication may be circulating because a reduced amount of the medication is extracted during passage from the portal to the systemic circulation (reduced first-pass effects).

Decreased CYP activity may result in prolonged duration of action of some medications, including:

- acetaminophen (Tylenol®)
- lidocaine (Xylocaine®)
- metoprolol (Lopressor®)
- meperidine (Demerol®)
- nitrates such as nitroglycerin
- propranolol (Inderal®)
- tricyclic antidepressants such as amitriptyline (Elavil®)
- verapamil (Isoptin®)

Age-related changes in hepatic function vary greatly among individuals. In some elderly persons, liver function is not impaired. Carefully assess laboratory results and clinical signs and symptoms to identify indications of sub-therapeutic dosing or toxicity (Hutchison & Sleeper, 2010).

The CYP System

Over 300 different microsomal enzymes located primarily in the liver, and also in the brain and intestine, comprise the cytochrome P450 (CYP) system. Aging creates both a decrease in number of the cytochrome P450 enzymes and a decrease in their affinity for certain medications (Olsen, Tindall, & Clasen, 2007).

Changes in Renal Function

Depressed renal function markedly affects response to medications in the elderly. According to some authorities, in many elderly persons changes in renal elimination of medications is the most critical age-related consideration – especially for the very old (Hutchison & Sleeper, 2010).

A decline in renal blood flow and glomerular filtration rate accompanies aging. For renally-excreted medications, reduced filtration results in more active medication in the circulation. Reduced dosages may be required when renal function is impaired.

Creatinine clearance results are used as a basis for adjusting dosage of renally-excreted medications including:

- digoxin (Lanoxin®)
- chlorpropamide (Diabinese®)
- penicillin
- antihistamines
- cimetidine (Tagamet ®)
- diltiazem (Cardizem®)
- diuretics such as hydrochlorothiazide (Hydrodiuril®) and furosemide (Lasix®)
- methotrexate (Rheumatrex®)
- ranitidine (Zantac®)
- verapamil (Isoptin®)
- streptomycin
- aminoglycosides such as gentamicin (Garamycin®)

Cockroft-Gault Formula

Creatinine clearance results for elderly persons may be misleading. Since elderly persons have relatively less muscle mass and protein, laboratory values for creatinine clearance may be within normal limits despite kidney impairment. Other tests of glomerular filtration rate may be used in your facility, such as the Cockcroft-Gault Formula (Patel & Frame, 2014).

The Cockroft-Gault Formula

For **men**, calculate creatinine clearance using the following formula.

$$\frac{140 - \text{age in years} \times \text{lean body weight in kg}}{\text{serum creatinine in mg/dL} \times 72}$$

For **women**, use the same formula, but then multiply the answer by 0.85.

Between the ages of 20 and 80, there is an average decline of 40% in glomerular filtration for many medications excreted by the kidney such as penicillins, cephalosporins and aspirin (Patel & Frame, 2014).

What Do You Think?

A patient shows signs of phenytoin toxicity and yet has an acceptable total serum phenytoin concentration.

Why would this happen?

ANSWER
The total serum drug concentration includes both the bound and unbound portions of the drug. The unbound portion is the active portion.

If a drug is highly protein-bound [such as phenytoin (Dilantin®), a portion of the total serum concentration of the drug is bound to protein and therefore inactive. If a patient has less plasma protein for protein binding (as elderly persons do), a larger proportion of active drug is circulating and exerting its effect.

So, in an elderly person, total serum concentration of a drug that is highly protein-bound may be within usual acceptable therapeutic limits, yet because a larger portion of drug is unbound and active, the patient could be showing signs of toxicity.

Laboratories can test for unbound drug, but the serum concentration that is usually tested is total serum concentration. It is possible to test for an unbound drug level. However if symptoms of toxicity develop, the prescriber will probably adjust the dosage promptly.

When elderly patients receive a low dose, **assess carefully to determine if they are obtaining a therapeutic effect at the low dose** (Kaplan & Porter, 2011).

Case Study #1: Mr. Ochoa

Mr. Ochoa, 82-years-old, is hospitalized due to exacerbation of congestive heart failure.

Prior to being hospitalized he gained 17 pounds in a one week time frame, developed a moist cough and complained of increasing fatigue.

On admission you measure 4+ pitting edema in his ankles.

At home he took oral furosemide (Lasix®), but administration through the IV route is ordered during hospitalization.

In addition, he receives potassium supplements and digoxin (Lanoxin®).

Read Mr. Ochoa's situation and the questions suggested on the next screen. As you perform this exercise, consider the following:

- Would you ask similar questions to those suggested?
- Are there other, more thought-provoking questions that should be asked?
- In addition to the questions, what orders do you think might be indicated?

Case Study #1: Questions Regarding Mr. Ochoa

What side effects and adverse effects is this patient most likely to experience?
The elderly are more prone to hypotension and electrolyte abnormalities related to furosemide (Lasix®) than are younger people.

The risk of digoxin (Lanoxin®) toxicity increases during electrolyte imbalances.

Hypotension, electrolyte imbalances and urinary urgency related to furosemide (Lasix®) increase his risk of falling.

What effects of aging have implications for the medications this patient is receiving?
Age-related decreased renal function may make the elderly more sensitive to the usual adult dose of furosemide (Lasix®).

It may also increase his risk of electrolyte imbalances.

How will this patient's care be managed and monitored after discharge?
Is this patient monitored for early signs of CHF exacerbation?

Does he know what signs to report to his healthcare provider?

What laboratory tests or other means of monitoring response to medication therapy will the patient need now and after discharge?

What laboratory tests or other means of monitoring response to medication therapy will the patient need now and after discharge?
Periodic BUN and electrolyte measurements are needed due to furosemide (Lasix®), digoxin (Lanoxin®) and potassium supplements. Daily weights.

What disease processes effect metabolism and action of medications for this patient?
Absorption of oral of furosemide (Lasix®) may be markedly reduced during an exacerbation of CHF due to edema in the bowel.

What are the implications of the dosage form the patient is receiving?
Compared to oral route, IV furosemide (Lasix®) has a much faster onset of action and shorter duration of action.

Beers Criteria: Gray List, PIMs and PIPEs

In the 1990s, Beers (Beers, et al., 1991) developed a research-based **list of medications considered inappropriate for use with elderly patients.** Researchers have used the list, formally known as Beers Criteria, to study the use of Potentially Inappropriate Medications (PIMs), also known as Potentially Inappropriate Prescribing for Elders (**PIPEs**), or the **Gray List**.

Beers first published his recommendations in the 1980s, but prescribing practice has not yet caught up with his widely endorsed recommendations.

In 2002, Beers and his associates updated Beers Criteria (Kaplan & Porter, 2011). You can view the complete list of medications presenting high-severity risks in Appendix A and those presenting low-severity risks in Appendix B. From what you have learned so far in this course, you can probably name a few medications that you will find on the list.

What Places a Medication in Beers Criteria?

Beers Criteria medications create safety risks for elderly persons. **Adverse effects increase risks** to which the elderly are particularly vulnerable, **such as injuries sustained in falls.**

Anticholinergic medications that cause ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate.

Examples include:

- The allergy medication diphenhydramine (Benadryl®)
- The antiarrhythmic disopyramide (Norpace®)
- Antihistamines
- GI antispasmodics
- Muscle relaxants
- The Parkinson's medication orphenadrine (Norflex®)
- Tricyclic antidepressants
- Urinary antispasmodics

Medications that can cause **orthostatic hypotension** such as the antihypertensive medication guanadrel (Hylorel®) and short-acting nifedipine (Procardia®, Adalat®) also given for angina.

Medications which impair **renal function** such as non-Cox NSAIDs and nitrofurantoin (Macrodantin®) which is given to treat urinary infection.

Beers Criteria Medications

- Have a **long half-life**, including chlorpropamide (Diabinese®) which exerts a long-lasting hypoglycemic effect, and long-acting benzodiazepines such as diazepam (Valium®) and selected serotonin uptake inhibitors (SSRIs) such as fluoxetine (Prozac®) because of risk of toxicity and sustained side effects, including risk for falling.
- Have **extrapyramidal effects** which include movement disorders, slowed thinking, dizziness and slurred speech. Examples include psychotropic medications such as thioridazine (Mellaril®) and trimethobenzamide (Tigan®) which is given to treat nausea and vomiting.
- **Stimulate the central nervous system or the cardiovascular system** such as amphetamines, fluoxetine (Prozac®), the NSAID indomethacin (Indocin®), cimetadine (Tagamet®) and clonidine (Catapres®).
- Can cause **confusion and hallucinations**, such as pentazocine (Talwin®)
- Can create a particular problem if **aspirated**, such as mineral oil. Mineral oil can also **interfere with absorption** of medications and nutrients.
- Cause **GI disturbances**, such as risk of GI bleeding which is a risk of NSAIDs and ketorolac (Toradol®), and constipation which is a risk associated with narcotics and anticholinergics.
- **Lack efficacy** and exert adverse effects such as ticlopidine (Ticlid®), given to prevent thrombosis, and amiodarone (Cordarone®).
- **Lead to dependence** such as barbiturates which are recommended only to control seizure activity.

Beers Criteria is a Guide for Further Investigation

Placement in the Beers Criteria simply means that a medication's adverse effects ***MAY*** outweigh its benefits for a particular elderly patient. It is a guide for further investigation, not an absolute contraindication for all elderly persons.

Questions to Assess Your Patient's Medication Profile

- What physical effects of aging have implications for the medications this patient is receiving?
- What disease processes affect metabolism and action of medications for this patient?
- Is this patient receiving any Beers Criteria medications, that is, medications considered inappropriate for persons aged 65 years and older?

If Your Elderly Patient is Receiving a PIM

Prescribers **can often avoid the use of all PIMs** in their elderly patients with safe substitutes. Yet, studies continue to show that **many elderly patients receive medications considered inappropriate for the elderly.**[1] The problem persists not only in the U.S., but worldwide.

Click the mouse icon to view a list of questions to ask yourself if you discover that your elderly patient is receiving a PIM:

- Consider how the medication earned its place in Beers Criteria. Do the risks apply to this patient?
- Is there a unique and clinically important indication for the medication?
- Are any safer substitutes available?
- Are precautions in place to alert you, the prescriber and the patient to signs of adverse effects?
- Is the patient receiving a safe low dose for an indication other than the most common use? For example, the tricyclic antidepressant amitriptyline (Elavil®) may be prescribed at a low dose for migraine prophylaxis or for neuropathic pain. The dose for migraine prophylaxis is frequently much less than a daily dose of 100 mg, which the maximum dose USP recommends for geriatric use (Lacy, Armstrong, Goldman, & Lance, 2015).

[1] Passarelli, et al., 2005; Pugh, et al., 2005; Simon, et al., 2005; Brown University, 2006; AHRQ, 2007; Gallagher, et al., 2007; Basger, et al., 2008; Wessell, et al., 2008; Ryan et al., 2009).

Cast Study #2: Mr. Peabody

At 7:00 p.m., Mr. Peabody, an 84-year-old admitted due to exacerbation of symptoms of congestive heart failure, asked for his “sleeping pill.”

He seemed mildly confused and repeatedly calls you by the wrong name.

His confusion seems to get worse as the night progresses.

His physician has ordered diazepam (Valium®) 5 mg po PRN.

He also receives a diuretic and digoxin (Lanoxin®).

Read Mr. Peabody’s situation and the questions suggested.

- Are you asking similar questions to those suggested?
- Are there other more thought-provoking questions that should be asked?
- In addition to the questions, what orders do you think might be indicated?

Case Study #2: Mr. Peabody Questions - Is this patient Receiving any PIMs?

What effects of aging have implications for the medications he is receiving?
Half-life may be prolonged due to reduced capacity of cytochrome P450 enzymes in the elderly. Expected changes in body composition, especially a relative increase in the proportion of fat, increases the duration of action and facilitates accumulation of diazepam (Valium®) in the elderly.

Decreases in serum proteins in the elderly may result in fewer protein-binding sites that inactivate less diazepam (Valium®) than in younger people.

Expected reduction in serum albumin may increase the likelihood and severity of sedation from diazepam (Valium®) in the elderly.

Are certain side effects particularly hazardous because of the patient's disease processes?
Reduced cardiac output may increase the likelihood of CNS side effects associated with diazepam (Valium®) in the elderly.

Urinary urgency resulting from diuretic treatment for congestive heart failure may increase the risk of falls associated with diazepam (Valium®) in the elderly.

How will this patient's medication profile change upon discharge (new medications, dosage changes, discontinuations)?
If a new hypnotic medication is prescribed at discharge, ensure that he knows to discontinue the diazepam (Valium®).

What are your resources for further information about the medications he is receiving?
The patient or family members may provide a history of the patient’s diazepam (Valium®) use.

The Pharmacy or Drug Information Center may suggest safer alternative medications for the elderly.

With whom will you collaborate to assure safety and effectiveness of this patient's medication therapy?
Long-term diazepam (Valium®) users may need drug detoxification and rehabilitation services.

How will this patient's care be managed and monitored after discharge?

If diazepam (Valium®) is discontinued following an extended period of regular use, withdrawal symptoms may not begin until 10 to 20 days after he stops taking the medication.

Medication Interactions with Diseases Commonly Seen in the Elderly

Disease conditions common in the elderly such as congestive heart failure, diabetes mellitus and hypertension impair renal blood flow which interferes with excretion of some medications and their metabolites, creating a risk of toxicity.

A complete list of drug-disease interactions is contained in **Appendix C and Appendix D.** These two lists combined are sometimes referred to as **Beers Criteria, List 2 or Beers II,** which includes medications that elderly persons who have certain conditions should avoid.

- **Anticholinergics** create problems for patients who have certain types of **glaucoma** or **urinary retention** problems.

- Patients who have **Parkinson's disease** are especially susceptible to **extrapyramidal effects** such as involuntary muscular movements, tremors, rigidity, restlessness and changes in heart rate and respiratory rate.

- **NSAIDs** block prostaglandins which the body normally produces and which boost renal circulation. NSAIDs can lead to renal failure for patients who have **compromised renal function**. This effect and GI irritation make use of NSAIDs risky for elderly persons.

- **Long-acting benzodiazepines** may further depress respiration in patients who have **COPD** (Lacy, 2015).

TEST YOURSELF

Which classification of medications creates problems for patients who have glaucoma?

Enter your answer in the box below.

Anticholinergics

Interactions Between Medications

Most interactions between medications occur because of the effect of a specific medication upon the enzymes that metabolize medications; the CYP system, located primarily in the liver, metabolizes more than 80% of medications. The effect of a medication upon a CYP enzyme may be to:

- **Induce** the enzyme, thereby enhancing the rate at which the enzyme metabolizes another medication, or
- **Inhibit** the enzyme, thereby slowing the rate at which the enzyme metabolizes another medication

Not all medications and substances have the same affinity for the enzyme and so some may produce a marked effect, while others produce little effect. Not all interactions are clinically significant. Most medications are metabolized via multiple CYP pathways and so the effects of a number of different CYP enzymes contribute to medication interactions.

Medication interactions may be used to produce a positive effect.

For example, if antibiotic A inhibits metabolism of antibiotic B, the serum level of antibiotic B will be elevated when the two antibiotics are given together. Therefore, antibiotic B may be prescribed at a lower dose to minimize adverse effects of antibiotic B, or reduce costs if antibiotic B is expensive.

Medication Interactions and Elderly Patients

- Persons aged 65 and older comprise approximately 12% of the population of the United States, yet they consume one third of all prescription medications and more than half of OTC medications.
- 74% of people 65-years-old or older confirmed recent use of prescription medication.
- Among persons aged 65 to 74 years, more than half used two or more prescription medications – and 12% used five or more prescription medications. The average number of medications for elderly is between 8 and 15.
- For those aged 75 and older, 60% used at least two prescription medications – and 16% used at least five. (Bushardt, 2005; Farrell, Szeto, & Shamji, 2011).

Click the mouse icon to view what researchers recommend as the best way to reduce the prevalence of adverse drug reactions among elderly persons

- Limit medication prescription to essential medications.
- Clearly explain use of prescribed medications to the patient.
- Give medications for as short a period as possible.
- Periodically re-evaluate all use of medications in the elderly (Hutchison & Sleeper, 2010)

Elderly persons are particularly at risk for adverse effects of medication interactions because of the number of medications they take concurrently.

Polypharmacy: A Significant Problem for Elders

Polypharmacy is defined as "**excessive or unnecessary use of prescription or nonprescription medications**" (Jones, 1997).

Other definitions include "medication not matching a diagnosis", and "inappropriate or potentially inappropriate use of medications". Some definitions place a numeric value on concurrent medications, including six or more medications. This issue is of particular concern in elderly patients.

Criteria to specify excessive or unnecessary use include:

- Use of medications without indication.
- Use of duplicate medications to treat the same condition.
- Concurrent use of interacting medications.
- Use of an inappropriate dosage.
- Use of medication therapy to treat side effects or adverse reactions of other medications.

Medication Interactions: Safe Practices

The effect of medication interactions cannot always be accurately predicted – especially when multiple medications are involved.

To practice safely with respect to medication interactions:

- Know the significant interactions associated with each medication your patient receives.
- Know the toxic effects and therapeutic effects of each medication your patient receives. If you observe either toxic effects or lack of therapeutic effects an interaction with another medication may be responsible.
- Consult with the pharmacist and physician concerning questions related to potential medication interactions.

Click the mouse icon to see the most commonly prescribed medications for elders that interact with many medications and substances.

- Antidepressants
- Phenytoin (Dilantin®)
- Warfarin (Coumadin®)
- Charcoal, grapefruit juice and caffeine in coffee, tea or chocolate and the alcohol in alcoholic beverages interact with many medications prescribed for the elderly

  (Hutchison & Sleeper, 2010).

Fatal Serotonin Syndrome

Fatal serotonin syndrome may result when a patient who is receiving a selective serotonin reuptake inhibitor (SSRI) such as fluoxetine (Prozac®) or paroxetine (Paxil®) receives another medication which enhances serotonin.

Patients who receive SSRIs are at risk for serotonin syndrome if they receive lithium, tryptophan, meperidine (Demerol®), tricyclic antidepressants such as clomipramine (Anafranil®) or electroconvulsive shock treatments (ECT).

Case Study #3: Mrs. Stewart

Mrs. Stewart, 85-years-old, was admitted after she fell at home and fractured her wrist. She lives alone and was found by a neighbor. Mrs. Stewart doesn't remember falling. She has hypertension and osteoarthritis.

Her neighbor brought in a bag full of medications including outdated prescriptions for:

- acetaminophen with 30 mg of codeine (Tylenol #3®) from 2001
- acetaminophen with 60 mg of codeine (Tylenol #4®) from 2004

There are also separate medication bottles labeled:

- Diuril® 500 mg daily
- chlorothiazide 500 mg daily
- 50 mg atenolol with 25 mg chlorthalidone (Tenoretic®) daily
- dorazasin (Cardura®) 0.5 mg daily

Mrs. Stewart explained that she takes pain medication only when the pain "gets really bad." She tells you that she took the Cardura® at night and the Tenoretic®, Diuril® and chlorothiazide in the morning because they make her "go to the bathroom so much."

The labels on the medication bottles were from three different pharmacies, including a mail order pharmacy. She stated, "When you have as little money as I do, you go where there's a bargain."

Read Mrs. Stewart's situation and the questions suggested on the next screen.

- Are you asking similar questions to those suggested?
- Are there other more thought-provoking questions that should be asked?
- In addition to the questions, what orders do you think might be indicated?

Case Study #3: Mrs. Stewart Questions

Name every medication that this patient is taking. Include over-the-counter medications, herbals, alcohol, caffeine, tobacco and home remedies.
Although Mrs. Stewart's neighbor provided the prescription medications, the patient's medication profile is incomplete without details of over-the- counter medications, herbal remedies, alcohol consumption, caffeine consumption and use of tobacco.

Also assess her usual dietary habits for substances which may interact with her medications.

What is the indication for each medication Mrs. Stewart is taking? Is she benefiting from each medication she is taking?
The indication isn't clear for the analgesics, though you might assume that they are intended to treat pain of osteoarthritis. You need to inquire and validate or disprove that assumption.

It's impossible to evaluate the benefits from the antihypertensives and the diuretics when they are taken in unintended combinations.

What creates risks for drug-drug interactions for this patient?
There is a dangerous potential for hypotension, dehydration and electrolyte imbalances from the unintended use of diuretics and antihypertensives. These side effects increase the risks of cognitive impairment and falls.

There is potential for overdose of analgesics.

She is taking double doses of chlorothiazide (Diuril®).

What social issues create polypharmacy for this patient?
She is taking outdated medications, assumed by the prescriber to have been discontinued.

Her financial problems prevent her from using a single pharmacy which would help monitor and question inappropriate medications and duplications.

What actions do you take when you suspect polypharmacy?

- Notify the prescriber of her complete medication profile.
- Review her serum electrolytes results.
- Monitor her blood pressure.
- Assess her need for analgesics.

- Clarify with the prescriber the intended treatment for hypertension.
- Supervise her disposal of unnecessary medications.
- After clarifying the intended medication regimen, instruct the patient as to proper use of her medications.
- Urge the patient to transfer her prescriptions to a single pharmacy that can oversee her medication profile.
- Urge the patient to bring a neighbor, friend or relative with her to doctor's visits to help her monitor changes in her medication regimen.

What references and resources are available to you to address the problem of polypharmacy?

Explore resources to aid her in the economical and safe purchase of her medications.

Resources for Information

Appendix E contains a lengthy list of specific resources for helpful information about medications and the elderly. General categories include:

- U.S. Government Websites.
- Geriatric Care Resources.
- Professional Organizations, such as the American Geriatrics Society, the American College of Cardiology, the American Heart Association and Oncology Nurses Society (ONS).

Package inserts and drug references contain drug-specific recommendations for use, dosage and monitoring.

Medical and nursing departments in your facility may have approved practice guidelines related to the use and monitoring of specific medications.

Resources at Your Facility

Learn about resources are available at your facility and how to access them.

- If you identify a deficit in unit-based resources, make recommendations to your manager or pharmacist.
- Some facilities have networked computerized systems for flagging potential hazards, such as PIMs and drug-disease interactions when an order is entered.
- Some facilities have safety systems that automatically alert a clinical pharmacist when certain lab values, dosages or other triggers occur.
- Many facilities have placed their formularies on their intranet systems. Other facilities may rely on package inserts and reference books such as the Physician's Desk Reference.
- Make a commitment to use a comprehensive reference for reviewing information about the medications you administer frequently. **For every medication you administer, know dose range, action, side effects and toxic effects.**

The facility's pharmacy usually has the most recent annual update of two USP publications:

- Drug Information for the Healthcare Professional.
- Advice for the Patient: Drug Information in Lay Language.

Current References are Crucial

The pharmaceutical industry moves quickly. The FDA approves new medications frequently and with less scrutiny than it has previously used.

Manufacturers also withdraw medications from the market based on research-based safety information. For example, Troglitazone (Rezulin®) was withdrawn from the market in March 2000, after safety study results revealed that other medications [rosiglitazone (Avandia®) and pioglitazone (Actos®)] offered the same benefits in the treatment of type 2 diabetes without the risk of liver damage (Lacy, et al, 2011).

A medication may be withdrawn from the market and then returned, but with additional warnings as was the case with certain coxib medications.

In addition, pharmacological research produces new pharmacodynamic and pharmacokinetic information on an ongoing basis. Emerging information may indicate new safety hazards such as previously unknown drug-disease or drug-drug interactions.

Always use CURRENT drug references!

Conclusion

Safe and effective administration of medications to elderly persons requires special precautions.

This course has:

- Provided information about characteristics and common conditions among the elderly that have implications for safe and effective administration of medications to elderly patients, and

- Presented specific information about particular medications and drug-disease interactions that create risks for elderly patients.

Case situations have given you the opportunity to apply your critical thinking skills.

The appendices contain reference information to support you in administering medications safely and effectively to elderly patients.

"In addition to reductions in various organ functions, factors connected with very old age such as frailty, falls, abnormal sensitivity to medications and polypathology, all of which tend to be more common in the last years of life, all directly impact on adverse drug events (Merle, et al., 2005)."

Appendix A: Beers I, High-Severity Concerns

Adapted from The Merck manual of diagnosis and therapy, (Kaplan & Porter, 2011) and Geriatric pharmacotherapy: A guide for the helping professional (Olsen, et al., 2007).

* When a category or class of drugs is named, the precaution applies to the entire category or class and not only the example given.

Drug or Classification*	Usual Indication	Risk for Patients Age 65 and Older
Amiodarone (Cordarone®)	Arrhythmias	Lack of efficacy older adults. Risk of QT interval problems and provoking torsades de pointes.
Amitriptyline (Elavil®) and combinations e.g., with chlordiazepoxide (Limbitrol®), perphenazine-amitriptyline (Triavil®)	Depression; migraine headaches	Strong anticholinergic and sedating properties. Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate.
Amphetamines Excluding methylphenidate hydrochloride (Concerta®, Metadate®, Ritalin®) and anorexics	Narcolepsy, attention-deficit/hyperactivity disorder (ADHD), CNS depression, respiratory depression	Risk of dependence, hypertension, angina and MI. Adverse CNS stimulation effects.
Antihistamines such as chlorpheniramine in combinations such as with phenylephrine (Histatab Plus®), with acetaminophen (Coricidin®), with pseudoepheldrine (Allerest®, ChlorTrimeton®, Triaminic®) with acetaminophen and phenylephrine (Actifed®); diphenhydramine (Benadryl®), hydroxyzine (Vistaril®, Atarax®), cyproheptadine (Periactin®), promethazine (Phenergan®), tripelennamine (PBZ®), dexchlorpheniramine (Polaramine®)	Nasal and sinus congestion, colds, flu, allergies	Potent anticholinergics. Many cough and cold preparations are available without antihistamines. Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate.
Anticholinergic: muscle relaxants such as cyclobenzaprine (Flexeril®), methocarbomol (Robaxin ®), carisprodol (Soma®), chlorzoxasone (Paraflex®), metaxalone (Skelaxin®) Urinary antispasmodics such as Tolterodine (Detrol®), flavoxate	Muscle spasms	Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate. Poorly tolerated by elderly.

Drug or Classification*	Usual Indication	Risk for Patients Age 65 and Older
(Urispas®), oxybutynin (Ditropan®), not including extended release (Ditropan-XL®)	Urinary spasms, urinary frequency, urgency, urge incontinence	Weakness and sedation. Questionable effectiveness at doses tolerated by elderly.
GI antispasmodics such as dicyclomine (Bentyl®, Antispas®), hyoscyamine (Anaspaz®), propantheline (ProBanthine®), belladonna alkaloids (Donnatal®), belladonna alkaloids with opium (B&O supprettes®), clidinium with chlordiazepoxide (Librax®)	Disturbances of GI motility such as irritable bowel syndrome	Highly anticholinergic; questionable effectiveness; especially avoid long-term use.
Barbiturates such as pentobarbital (Nembutal®) except phenobarbital and except to control seizures	Seizures; need for sedation	Cause more side effects than most other sedatives and hypnotics. Should be used only to control seizures. Highly addictive.
Chlordiazepoxide (Librium®) and combinations such as chlordiazepoxideamitriptyline (Limbitrol®); also Long-acting benzodiazepines: clidinium-chlordiazepoxide (Librax®), diazepam (Valium®), quazepam (Doral®), halazepam (Paxipam®), chlorazapate (Tranxene®)	Anxiety; chlordiazepoxide for alcohol withdrawal in acute alcoholism	Long half-life in the elderly (often days), produces sedation and increased incidence of falls. Short- or intermediateacting benzodiazepines are preferred if benzodiazepines are required.
Chlorpropamide (Diabinese®)	Type II diabetes	Prolonged half-life; can cause prolonged, serious hypoglycemia. Only hypoglycemic causing inappropriate secretion of antidiuretic hormone.
Diphenhydramine (Benadryl®)	Allergic reaction; sometimes used to produce sedation.	Potent anticholinergic, confusion and sedation. For allergic reaction use lowest dose. Additional anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, increased temperature and heart rate.
Disopyramide (Norpace®), not including extended release formulation	Arrhythmias	Most potent negative inotrope of all antiarrhythmics, which may induce heart failure in the elderly. Also, strong anticholinergic. Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus

Drug or Classification*	Usual Indication	Risk for Patients Age 65 and Older
		membranes, visual disturbances, confusion, increased temperature and heart rate.
Doxepin (Sinequan®)	Anxiety; depression	Strong anticholinergic and sedating properties. Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate.
Fluoxetine (daily) (Prozac®)	Depression	Long half-life; risk of CNS stimulation, sleep disturbance, increasing agitation.
Flurazepam (Dalmane®)	Need for sedation	Extremely long half-life in the elderly (often days), produces sedation and increased incidence of falls. Short- or intermediate-acting benzodiazepine preferred.
Guanadrel (Hylorel®)	Hypertension	Risk for orthostatic hypotension
Guanethedine (Ismelin®) – no longer available in the USA	Hypertension	Risk for orthostatic hypotension, dizziness, fainting.
Indomethacin (Indocin®)	Inflammatory diseases and rheumatoid disorders, arthritis; pain	Most CNS side effects of any NSAID.
Ketorolac (Toradol®)	Pain	GI effects – many elderly persons have asymptomatic GI pathology
Long-term use of stimulant Laxatives such as bisacodyl (Dulcolax®), cascara sagrada (herbal), castor oil preparations such as Neoloid® - except with opioid therapy	Constipation	May exacerbate bowel dysfunction
Lorazepam (Ativan®) 3 mg, oxazepam (Serax®) 60 mg, alprazolam (Xanax®) 2 mg, temazapam (Restoril®) 15 mg, triazolam (Halcion®) 0.25 mg	Anxiety, need for sedation	Total daily doses should not exceed these recommendations. Smaller doses may be effective as well as safer due to increased sensitivity of the elderly to benzodiazepines.
Meperidine (Demerol®)	Pain	Not effective orally; more disadvantages than other narcotics. Causes confusion.
Meprobamate (Miltown®, Equanil®)	Anxiety	Addictive, sedation.
Mesoridazine (Serentil®)	Schizophrenia, psychosis	CNS and extrapyramidal adverse effects.

Drug or Classification*	Usual Indication	Risk for Patients Age 65 and Older
Methyldopa (Aldomet®) and combinations [e.g., with hydrochlorothiazide (Aldoril®)]	Hypertension	May cause bradycardia and exacerbate depression in the elderly.
Methyltestosterone (Adroid®, Virilon®, Terstrad®)	Male: Impotence, climacteric symptoms Female: Palliative in metastatic breast cancer	Potential for prostatic hypertrophy and cardiac problems.
Mineral oil	Constipation	Potential for aspiration, may interfere with absorption of drugs and nutrients.
Long-term use of full dose of longer half-life, non-Cox NSAIDS, such as naproxen (Naprosyn®, Avaprox®, Aleve®), oxaprosin (Daypro®), piroxicam (Feldene®)	Inflammatory diseases, arthritis; pain	Risk of GI bleeding, renal failure, hypertension, heart failure.
Short-acting nifedipine (Procardia®, Adalat®)	Angina, hypertension, pulmonary hypertension	Risk for hypotension and constipation.
Nitrofurantoin (Macrodantin®)	Urinary tract infection	Potential for renal impairment.
Orphenadrine (Norflex®)	Muscle spasm, Parkinson's disease	More anticholinergic effects and sedation than alternatives. Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate.
Pentazocine (Talwin®)	Pain, need for sedation	Mixed narcotic agonist/antagonist; Causes confusion, hallucinations more commonly than other narcotics.
Thioridazine (Mellaril®)	Schizophrenia, psychosis	Increased risk for adverse CNS and extrapyramidal effects.
Dessicated thyroid (natural thyroid), not the synthetic preparations such as levothyroxine (Synthroid®)	hypothyroidism	Risk for cardiac effects.
Ticlopidine (Ticlid®)	Thrombosis, stroke and stroke prevention	No better than aspirin to reduce clotting, but more toxic.
Trimethobenzamide (Tigan®)	Nausea and vomiting	One of least effective antiemetics, but can cause extrapyramidal side effects such as drowsiness and dizziness.

Appendix B: Beers I, Low-Severity Concerns

Adapted from The Merck manual of diagnosis and therapy, (Kaplan & Porter, 2011) and Geriatric pharmacotherapy: A guide for the helping professional (Olsen, et al., 2007).

* When a category or class of drugs is named, the precaution applies to the entire category or class and not only the example given.

Drug or Classification*	Usual Indication	Risk for Patients Age 65 and Older
Cimetidine (Tagamet®)	Gastric hypersecretory states, including gastric ulcers, gastroesophageal reflux disease	Adverse CNS effects, including confusion.
Clonidine (Catapres®)	Hypertension; migraine headache prophylaxis	Risk for orthostatic hypotension and adverse CNS effects including drowsiness and dizziness.
Digoxin (Lanoxin®)	Congestive heart failure, arrhythmias	Decreased renal clearance of digoxin in the elderly may lead to toxic effects. Doses should rarely exceed 0.125 mg daily, except in treating atrial arrhythmias.
Short-acting dipyridamole (Persantine®), not including long-acting. Exception: patients who have artificial heart valves.	Thrombosis. Used with warfarin post-heart valve replacement.	Causes orthostatic hypotension in the elderly. Proven beneficial only in patients who have artificial heart valves.
Doxazosin (Cardura®)	Hypertension	Risk for hypotension, dry mouth and urinary problems.
Ergoloid mesylates With caffeine (Cafergot®) (Hydergine®) cyclandelate (Cyclospasmol®) not commercially available in the USA	Migraine headache Cerebrovascular insufficiency Peripheral vascular disease	Have not been shown effective in the doses studied for the treatment of dementia or any other condition. Lack of efficacy. Risk for dizziness.
Estrogens, only (that is, not estrogen in combination with progesterone) oral (Cinestin®)	Menopause	Evidence of carcinogenic (breast and endometrial cancer) in women and lack of cardioprotective effect in older women
Ethacrynic acid (Edecrin®)	Edema associated with congestive heart failure, hepatic cirrhosis, renal disease and other conditions	Risk for hypertension, fluid imbalance. Safer alternatives available.
Iron supplements, e.g. ferrous sulfate (Feosol®)	Iron-deficiency anemia	Doses >325 mg rarely needed. At higher doses, absorption not substantially increased, but constipation is more likely.
Isoxsurpine (Vasodilan®)	Peripheral vascular disease	Lack of efficacy.
Reserpine (Serpasil®) at doses greater than 0.25 mg/day and combinations [with chlorothiazide (Diupres®)]	Hypertension	Risk for depression, impotence, sedation, and orthostatic hypotension.

Appendix C: Beers II, High-Severity Concerns in Drug-Disease Interaction and the Elderly

Adapted from The Merck manual of diagnosis and therapy, (Kaplan & Porter, 2011) and Geriatric pharmacotherapy: A guide for the helping professional (Olsen, et al., 2007).

* When a category or class of drugs is named, the precaution applies to the entire category or class and not only the example given.

Disease or Condition	Drug or Classification	Usual Indication	Risk for Patients 65 or Older
Anorexia and malnutrition	CNS stimulants such as dextroamphetamine +Amphetamine (Adderall®), methylphenidate (Ritalin®), methamphetamine (Desoxyn®) Non-amphetamine stimulants, such as pemoline (Cylert®) Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac®)	Narcolepsy, attentiondeficit/hyperactivitydisorder (ADHD), CNS depression, respiratory depression Depression	Further suppression of appetite
Arrhythmias	Tricyclic antidepressants: imipramine hydrochloride (Tofranil®), doxepin hydrochloride (Sinequan®), amitriptyline hydrochloride (Elavil®)	Depression, Migraine headaches	Proarrhythmic effects and may produce QT interval changes
Bladder outflow problems, including benign prostatic hypertrophy (BPH)	Anticholinergic: Muscle relaxants such as cyclobenzaprine (Flexeril®) Urinary antispasmodics such as Tolterodine (Detrol®), oxybutynin (Ditropan®), flavoxate (Urispas®) Antidepressants such as amitriptyline (Elavil®) Antihistamines and decongestants such as pseudoephedrine (Actifed®) Gastrointestinal antispasmodic drugs such as dicyclomine (Bentyl®)	Muscle spasms Urinary frequency, incontinence Depression Nasal, sinus and lung congestion Disturbances of GI motility such as irritable bowel syndrome	Anticholinergic effects include ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate.
Blood-clotting disorders or receive anticoagulant therapy	Anti-platelet agents such as clopidogrel (Plavix®), dipyridamole (Persantine®), ticlopidine (Ticlid®)	Atherosclerosis, thrombosis, and to prevent second thrombotic event (MI, CVA)	May cause bleeding due to anti-platelet activity. May prolong clotting

Disease or Condition	Drug or Classification	Usual Indication	Risk for Patients 65 or Older
	Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Advil®) and aspirin		time and elevate INR. Increased risk of GI bleeding.
Chronic obstructive pulmonary disease (COPD) COPD, asthma	Long-acting benzodiazepines: chlordiazepoxide (Librium®), chlordiazepoxide-amitriptyline (Limbitrol®), clidinium-chlordiazepoxide (Librax®), diazepam (Valium®), quazepam (Doral®), halazepam (Paxipam®), chlorazapate (Tranxene®) Beta blockers such as propranolol (Inderal®)	Anxiety, need for sedation Hypertension; arrhythmias	CNS adverse effects; May induce, cause, or exacerbate respiratory depression. May slow respirations and increase CO_2 retention. May produce bronchospasm, respiratory distress.
Cognitive impairment	Barbiturates such as pentobarbital (Nembutal®) except phenobarbital for seizures Antispasmodics drugs such as dicyclomine (Bentyl®), Tolterodine (Detrol®) Muscle relaxants such as cyclobenzaprine (Flexeril®) CNS stimulants such as dextroamphetamine +Amphetamine (Adderall®), methylphenidate (Ritalin®), methamphetamine (Desoxyn®), pemoline (Cylert®)	Need for sedation GI, urinary spasms Muscle spasms Attention-deficit/hyperactivity disorder; narcolepsy	CNS-altering effects.
Constipation	Calcium channel blockers verapamil (Isoptin®)	Hypertension	May exacerbate constipation.
	Tricyclic antidepressants (TCAs): imipramine hydrochloride (Tofranil®), doxepin hydrochloride (Sinequan®), amitriptyline hydrochloride (Elavil®)	Depression	
Depression	Long-term benzodiazepine use - Long-acting benzodiazepines: chlordiazepoxide (Librium®), chlordiazepoxide-amitriptyline (Limbitrol®), clidinium-chlordiazepoxide (Librax®), diazepam (Valium®), quazepam	Anxiety, insomnia	May produce or exacerbate depression. Long-term use interferes with balance, alertness, energy level and

Disease or Condition	Drug or Classification	Usual Indication	Risk for Patients 65 or Older
	(Doral®), halazepam (Paxipam®), chlorazapate (Tranxene®) and short- and intermediate-acting such as estazolam (ProSom®), flurazepam (Dalmane®), temazepam (Restoril®), and triazolam (Halcion®) Sympatholytic agents: methyldopa (Aldomet®), reserpine (Serpasil®) at doses greater than 0.25 mg/day, guanethidine (Ismelin®), Guanethidine no longer available in USA	Hypertension	produces tolerance to the drugs. May produce or exacerbate depression.
Heart failure	Disopyramide (Norpace®), not including extended release formulation High sodium-content drugs such as drugs containing sodium salts, including sodium -alginate -bicarbonate, -biphosphate, citrate, -phosphate, -salicylate, and -sulfate	Arrhythmias Variety of uses including electrolyte and metabolic disturbances; selected salts are antidotes for specific overdoses; GI disturbances and constipation	Negative inotropic effect. Potential fluid retention and exacerbation of heart failure.
Hypertension	Phenylpropanolamine HCl (Dexitrim®) and a variety of cold remedies), off the market in 2001; pseudoephedrine, diet pills: amphetamines, dextroamphetamine (Dexedrine®)	Desire to increase metabolism for weight loss or increased alertness	Elevation of blood pressure secondary to increased sympathomimeti c activity.
Insomnia	Decongestants Theophylline (Theodur®), Methylphenidate (Ritalin®) Monoamine oxidase inhibitors (MAOIs) such as phenalzine (Nardil®) Amphetamines such as dextroamphetamine (Dexedrine®)	Nasal or lung congestion Asthma Attention-deficit/hyperactivity disorder Depression Desire to increase metabolism for weight loss	CNS stimulation will aggravate insomnia.
Parkinson's disease	Metoclopramide (Reglan®)	Gastroesophageal reflux disease, diabetic gastric stasis	Antidopaminergi c and anticholinergic effects Anticholinergic effects include

Disease or Condition	Drug or Classification	Usual Indication	Risk for Patients 65 or Older
	Conventional antipsychotics such as fluphenazine (Prolixin®), haloperidol (Haldol®), chlorpromazine (Thorazine®) Tacrine (Cognex®)	Schizophrenia, psychosis Haloperidol – also Tourette's disorder Chlorpromazine – also nausea and vomiting; mania Mild to moderate dementia of Alzheimer's type	ataxia, urinary retention, constipation, dry mucus membranes, visual disturbances, confusion, increased temperature and heart rate. Extrapyramidal effects. May produce ataxia.
Seizures, seizure disorder, epilepsy	Bupropion (Wellbutrin®), clozapine (Clozaril®), chlorpromazine (Thorazine®), thioridazine (Mellaril®), thiothixene (Navane®)	Depression, Schizophrenia, psychosis Thorazine also antiemetic, mania	May lower seizure thresholds.
Stress incontinence	Long-acting benzodiazepines: chlordiazepoxide (Librium®), chlordiazepoxide-amitriptyline (Limbitrol®), clidinium-chlordiazepoxide (Librax®), diazepam (Valium®), quazepam (Doral®), halazepam (Paxipam®), chlorazapate (Tranxene®) Anti-cholinergics (see Bladder outflow listing above) Alpha-blockers, doxazosin (Cardura®), prazosin (Minipress®), terazosin (Hytrin®) Tricyclic antidepressants: imipramine hydrochloride (Tofranil®), doxepin	Anxiety, need for sedation Nasal congestion associated with allergy, cold or prevent respiratory complications of anesthesia; disturbances of GI motility Hypertension Depression; Migraine headache	May produce polyuria and worsening of incontinence

Disease or Condition	Drug or Classification	Usual Indication	Risk for Patients 65 or Older
	hydrochloride (Sinequan®), amitriptyline hydrochloride (Elavil®)		
Syncope or falls	Long-acting benzodiazepines: chlordiazepoxide (Librium®), chlordiazepoxide-amitriptyline (Limbitrol®), clidinium-chlordiazepoxide (Librax®), diazepam (Valium®), quazepam (Doral®), halazepam (Paxipam®), chlorazapate (Tranxene®) Short- to intermediate-acting benzodiazepines: alprazolam (Xanax®), lorazepam (Ativan®), oxazepam (Serax®) Tricyclic antidepressants (TCAs): imipramine hydrochloride (Tofranil®), doxepin hydrochloride (Sinequan®), amitriptyline hydrochloride (Elavil®)		May produce ataxia, impaired psychomotor function, syncope, and additional falls.
Ulcer disease, gastritis, gastroesophageal reflux disease (GERD)	Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Advil®) and aspirin (ASA) greater than 325 mg/day. Coxibs excluded, such as celecoxib (Celebrex®)	Pain; arthritis	GI irritation can exacerbate GI problems and lead to GI bleeding.

Appendix D: Beers II, Less Severe Concerns in Drug-Disease Interaction and the Elderly

Adapted from The Merck manual of diagnosis and therapy, (Kaplan & Porter, 2011) and Geriatric pharmacotherapy: A guide for the helping professional (Olsen, et al., 2007).

* When a category or class of drugs is named, the precaution applies to the entire category or class and not only the example given.

Disease or Condition	Drug or Classification	Usual Indication	Risk for Patients 65 or Older
Obesity	Olanzapine (Zyprexa®)	Schizophrenia, bipolar mania, psychosis	May stimulate appetite and increase weight gain
Secretion of syndrome of inappropriate antidiuretic hormone secretion (SIADH)/ hyponatremia	Selective serotonin uptake inhibitors (SSRIs): fluoxetine (Prozac®), citalopram (Celexa®), fluvoxamine (Luvox®), paroxetine (Paxil®), sertraline (Zoloft®)	Depression	May cause or exacerbate SIADH

Appendix E: Resources for Further Information

New resources continually become available and Web addresses may change. Search the Internet for new credible resources for care of the elderly and for particular medications and conditions that are pertinent in the care of your patients.

Government Resources

- The Agency for Healthcare Research and Quality (AHRQ), a federal agency, has published many clinical practice guidelines, including disease-specific guidelines and the guideline, Improving Medication Management for Older Adult Clients, which grades the quality of the available evidence supporting use of the Beers criteria and lists strategies to improve medication management. http://www.guideline.gov/.
- USFDA (nd) Medicines and older adults. http://www.fda.gov/opacom/lowlit/medold.html

Professional Organizations: Clinical Practice Guidelines and Recommendations

- The American Geriatrics Society has published clinical practice guidelines and clinical practice recommendations. http://www.americangeriatrics.org/
- The American College of Cardiology and the American Heart Association have established guidelines jointly. http://www.acc.org/
- The American Diabetes Association http://www.diabetes.org/home.jsp
- The American College of Rheumatology http://www.rheumatology.org/

Professional Nursing Societies' Clinical Guidelines such as:

- Wound, Ostomy, and Continence Nurses Society (WOCN) http://www.wocn.org/
- American Association of Critical Care Nurses (AACN) http://www.aacn.org/
- Oncology Nurses Society (ONS) http://www.ons.org/

Geriatric Nursing Resources

- Assessing the Care of Vulnerable Elders (ACOVE) Indicators. 22 indicators of quality of care for the elderly. http://www.rand.org/pubs/research_briefs/2005/RB4545-1.pdf
- Hartford Foundation: http://www.hartfordign.org/ ; http://www.ConsultGeriRN.org
- Nurses Improving Care for Healthsystem Elders (NICHE) program. http://www.nicheprogram.org
- University of Minnesota http://www.nursing.umn.edu/CGN/ResearchPractice/
- University of Iowa http://www.nursing.uiowa.edu/excellence/gerontology/

Medication-Related Resources

- Decreasing Anti-cholinergic Drugs in the Elderly (DADE) resources and a clinical tool targeting PIMs are available at no charge. Materials include resources for both clinicians and patients. http://providers.ipro.org/index/pres-drug-plan-prescribers
- Medication Management Improvement System, a model which includes software and a pharmacist consultant to manage medications in the home care setting. http://www.homemeds.org

Assessment and Research Tools

Medication Appropriateness Index. A valid and reliable tool for assessing drug indication, effectiveness, dosage, correct and practical directions, drug–drug interactions, drug–disease interactions, duplication, duration and cost. See:

Spinewine, A., et al. (2007). Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: A randomized, controlled trial. Journal of the American Geriatric Society, 55(5), 658 – 665.

Lata, H., & Alia, L. (2007). Aging: Physiological aspects. JK Science, 9(3), 111-115.

Drug Burden Index. Specific to sedating and anticholinergic agents, this index considers frequency and dosage as well as mechanism of action. Useful to predict adverse effects. See:

Hilmer, S.N., et al. (2007). A drug burden index to define the functional burden of medications in older people. Archives of Internal Medicine, 167(8), 781 – 787.

Drug Regimen Unassisted Grading Scale (DRUGS). A standardized assessment of medication-related function that predicts the need for focused nursing intervention or increased support. See:

Farris, K.B. & Phillips, B.B. (2008). Instruments assessing capacity to manage medications. Annals of Pharmacotherapy, 42(7), 1026 – 1036.

Kripalani, S., et al. (2006). Predictors of medication self-management skill in a low-literacy population. Journal of General Internal Medicine, 21(8), 852 – 856.

Ryan, C., O'Mahony, D., Kennedy, J., Weedle, P., Gallagher, P., & Byrne, S. (2009)._ Appropriate prescribing in the elderly: An investigation of two screening tools, Beers criteria considering diagnosis and independent of diagnosis and improved prescribing in the elderly tool to identify inappropriate use of medicines in the elderly in primary care in Ireland. Journal of Clinical Pharmacy and Therapeutics, 34, 369–376.

Olsen, C.G., Tindall, W.N., & Clasen, M.E. (2007). Geriatric pharmacotherapy: A

guide for the helping professional. Washington, DC: American Pharmacists Association.

Expert panels frequently create targeted recommendations, such as:

- The Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults recently updated practice guidelines to expand the indications for intensive therapy with lipid lowering agents. http://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf

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