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**GERIATRIC
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Learn@Lunch
Geriatric Education Series

Kathryn Hyer, PhD, MPP
Principal Investigator



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Polypharmacy and Common Drug Interactions in Geriatric Patients



Jasmine Cutler, Pharm.D., CPh
USF Health Byrd Alzheimer's Institute
Assistant Professor, USF College of Pharmacy
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Today's 4 Objectives

Review basic pharmacodynamics (PD) and pharmacokinetics (PK) in the elderly population

Discuss common drug interactions in the elderly population

Discuss clinical effects of common drug interactions

Discuss ways to identify and resolve common drug interactions

What is Polypharmacy?

Polypharmacy is defined as the simultaneous use of multiple medications by a single person or patient.

- Potentially inappropriate drug
- Presence of six or more concurrent medications



Geriatric Population

- In 2014, represented 14.5% of the U.S. population, totaling 46.2 million people
- Uses more than 30% of all prescription medications
- Consumes more than 40% of nonprescription medications
- More than 80% of this population has at least one chronic disease



Little Known Facts

- Florida has highest percentage of total population (19.4%) aged 65 years and over
- Sumter County has the oldest median age of any US County.



Where to First?

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PD and PK

- Pharmacodynamics (PD) deals with how the *body* handles the medication from administration to eliminations with particular emphasis on the relationship between drug concentration and effect.
- Pharmacokinetics (PK) deals with the movement of drugs within the body and concentrates on drug *absorption, distribution, metabolism, and excretion.*



Pharmacokinetic Changes



Pharmacokinetic Changes

Absorption

- **Age-related changes**
 - Increased gastric pH
 - Decreased gastric emptying
 - Decreased GI motility
- **Result**
 - Decreased absorption of acidic drugs
 - Increased “contact time” of drugs in the stomach



Pharmacokinetic Changes

Absorption

- **Age-related changes**
 - Decreased intestinal blood flow and poor blood perfusion
 - Thinning of skin
 - Reduction of muscle mass
 - Impairment of active and passive transport
- **Result**
 - Possible slowing of *rate* of absorption, but little effect on *extent* of absorption
 - Transdermal drug absorption is impaired



Pharmacokinetic Changes

Distribution

- **Age-related changes**
 - Decrease in total body water and lean body mass
 - Increase in total fat content
- **Result**
 - Decreased volume of distribution (V_d) of drugs primarily distributed in water and lean mass (higher blood levels of the drug)
 - Increased V_d of lipid-soluble drugs (delayed effect or accumulation of the drug)



Pharmacokinetic Changes

Distribution

- **Age-related changes**
 - Decrease in serum albumin concentrations, especially in malnourished or frail patients
 - Decreased circulation
- **Result**
 - Increased serum concentrations of drugs highly bound to albumin



Pharmacokinetic Changes

Metabolism

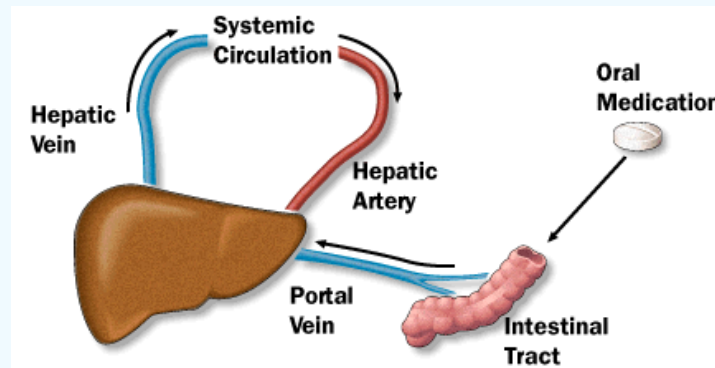
- **Age-related changes**
 - Decline in liver mass
 - Decrease in hepatic blood flow, function, and first-pass metabolism
- **Result**
 - Decreased clearance and hepatic metabolism of certain medications
 - Changes in bioavailability of certain drugs
 - Phase II metabolism *not* affected

See Table 5-2 in Murphy Text



Common Hepatically Metabolized Medications

- Morphine
- Meperidine
- Verapamil
- Amitriptyline
- Nortriptyline
- Nifedipine



Pharmacokinetic Changes

Excretion

- **Age-related changes**
 - Decreased kidney mass, renal perfusion, and glomerular filtration
 - Decline in ability to concentrate urine
 - Reduced creatinine clearance
- **Result**
 - Prolonged half-life for renally-excreted drugs, *results in more adverse events than any other age-related alteration!*



Common Renally Eliminated Medications

- Allopurinol
- Aminoglycosides
- Atenolol
- Baclofen
- Ciprofloxacin
- Digoxin
- Diltiazem
- Gabapentin
- Lithium
- Metformin
- Methotrexate
- Ranitidine
- Tetracycline



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What is a Drug Interaction?

A drug interaction occurs when a substance affects the activity of a drug when both are administered concomitantly. It can lead to a ***beneficial, synergistic, or detrimental clinical outcome.***



Drug-Drug Interactions

- Cytochrome P450 system
 - Isoenzymes: 1A2, 2C19, 3A4, 2C9
 - Drugs are either substrates, inducers, or inhibitors of these isoenzymes
- Antagonistic
- Additive or synergistic



Factors Influencing Cytochrome P450 System

- Age
- Gender
- Ethnicity/race
- Liver function
- Circadian rhythms
- Comorbid conditions



Modifiable Factors Influencing Cytochrome P450 System

- Diet
- Weight
- Physical activity
- Cigarette smoking
- Alcohol abuse



Knowledge Check

In relation to the cytochrome P450 system, cigarettes act as an:

- A. Inducer
- B. Inhibitor
- C. Substrate
- D. Has no effect



Knowledge Check

In relation to the cytochrome P450 system, cigarettes act as an:

- A. Inducer**
- B. Inhibitor
- C. Substrate
- D. Has no effect



Common Inducers

- Anticonvulsants
 - Phenytoin
 - Phenobarbital
 - Carbamazepine
- Barbiturates
- Carbamazepine
- Cigarettes
- Ethanol
- Glucocorticoids
- Primidone
- Rifampin
- St. John's Wort



Common Inhibitors

- Amiodarone
- Antibiotics
 - Ciprofloxacin
 - Erythromycin
 - Metronidazole
- Antidepressants
 - Fluoxetine
- Antihypertensives
 - Verapamil
- Clopidogrel
- Grapefruit juice
- Antifungals
 - Ketoconazole
 - Itraconazole

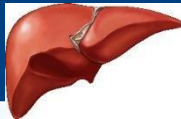


Effects of Grapefruit Juice

Contains
furanocoumarins



Irreversibly inhibits
intestinal CYP-450
3A4



Increase plasma
serum levels of drugs
with high first-pass
metabolism



Common Medications with Significant Interactions with Grapefruit Juice

Felodipine

Carbamazepine

Amiodarone

Oxycodone

Simvastatin

Sildenafil



“Red Flag” Medications

- First generation anticonvulsants (carbamazepine, phenytoin, phenobarbital)
- Selective serotonin reuptake inhibitors (SSRIs)
- Antifungals (ketoconazole)



“Red Flag” Medications

- Digoxin
- Erythromycin/Clarithromycin
- Hormones
- Lithium
- Theophylline
- Warfarin



Over-the-Counter Medications and Drug Interactions

- Antacids/laxatives
- Cimetidine
- Vitamin K
- Iron
- Cranberry
- Herbals
 - St. John's Wort
 - Ginkgo biloba
- Sleep aids
- Cough/cold products
- Diet aids



Drug-Food Interactions

- Caffeine
- Charbroiled foods
- Cheeses
- Cranberry juice
- Dairy
- Grapefruit juice
- Green, leafy vegetables
- Salt substitutes
- Tyramine-containing foods



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Consequences of Drug Interactions



- Drug toxicity
- Therapeutic failure
- Additive effects



Drugs that Increase QT Interval

- Amiodarone
- Amitriptyline
- Diphenhydramine
- Dofetilide (Tikosyn)
- Citalopram
- Clarithromycin
- Droperidol (Inapsine)
- Haloperidol
- Quinidine
- Mirtazapine
- Trazodone
- Vandetanib (Caprelsa)



Knowledge Check

Which of the following medication(s) interact with warfarin? (Select all that apply)

- A. Bactrim DS
- B. Cephalexin
- C. Ibuprofen
- D. Vodka



Knowledge Check

Which of the following medication(s) interact with warfarin? (Select all that apply)

A. Bactrim DS

B. Cephalexin

C. Ibuprofen

D. Vodka



Knowledge Check

Which of the following medication(s) can cause photosensitivity?

- A. Aspirin
- B. Furosemide
- C. Meloxicam
- D. B & C only
- E. All of the above



Knowledge Check

Which of the following medication(s) can cause photosensitivity?

- A. Aspirin
- B. Furosemide
- C. Meloxicam
- D. B & C only**
- E. All of the above



Case Scenario

Mr. N.B. is a 80-year old African-American male. His medical conditions include hypertension, angina pectoris, GERD, diabetes mellitus, hyperlipidemia, and occasional migraine headaches. He is currently on the following medications:

Medication List	
chlorothiazide 500 mg daily	K-Dur 10 10 mEQ daily
amlodipine 5 mg daily	ranitidine 150 mg daily
metoprolol succinate XL 50 mg daily	glyburide 2.5 mg
simvastatin 20 mg every night	Imitrex 25 mg tablet as needed
Nitrostat 0.3 sublingual tablet as needed	OTC Ibuprofen as needed
Aspirin 81 mg daily	Unisom as needed

You May Ask...

How Do We
Avoid Drug
Interactions?



...Perfect Question

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Healthcare Professional's Role

- First, do no HARM
- Patient-centered care and education
- Ensure each medication has an indication



Healthcare Professional's Role

- Advantage of an interdisciplinary health team approach
- Importance of patient follow-up and transitions of care
- Assess for mental health conditions
- Screen for use of multiple pharmacies and prescribers



Healthcare Professional's Role

- Screen for potential differential diagnosis
- Make one medication change at a time
- Start slow and titrate dosages
- Inquire about non-prescription and herbal medication use
- Be familiar with indications, side effects, properties, and formulations of each medication



Healthcare Professional's Role

Be familiar with the monitoring parameters associated with each medication

- K⁺ levels
- Na⁺ levels
- GFR and sCr
- LFTs
- GI bleeding
- TSH/T3/T4
- Behavioral changes



Healthcare Professional's Role

- Identify and eliminate duplicate therapies
- Assess medication adherence
- Ensure medications are taken properly and adverse drug events are avoided
- Use appropriate doses and be aware of best timing of administration
- Some medications should be taken with or without food



In Practice: Drug Reactions Similar to Common Complaints of Elderly

- Unsteadiness
- Dizziness
- Drowsiness
- Falls
- Dysphagia
- Anorexia
- Fatigue
- Malaise
- Incontinence
- Insomnia
- Depression



Suggested Administration Times for Select Medications

Drug Categories	Ideal Time of Administration
Blood pressure lowering agents	Morning
Lipid lowering agents	Evening
Bisphosphonates (ex. Actonel, Fosamax, Boniva)	Morning, on an empty stomach >30/60 minutes away from other medications and food with a full glass of plain water; swallow tablet whole; remain in upright position
Synthroid	Morning, on an empty stomach >30 minutes away from other medications and food with a full glass of water
Sex Hormones	Morning
Antiplatelets (not Coumadin)	Morning
Acid Secretion inhibitors	Evening
Sedating agents/Sleep aids	Evening
Diuretics (ex. HCTZ)	Morning
Stimulating Drugs	Morning
Coumadin	Evening

Resources

- Beers Criteria
- Screening Tool to Alert Doctors to Right Treatment (START)
- Screening Tool of Older Persons' Prescriptions (STOPP)
- Appropriate Medication Use in Vulnerable Elders (ACOVE)



Recent Literature

- Feasibility Trial (DEFEAT-polypharmacy)
- Development of the Tool to Reduce Inappropriate Medications (TRIM)
- Reducing Inappropriate Polypharmacy: The Process of Deprescribing



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Questions?

“The more I live,
the more I learn.
The more I learn,
the more I realize,
the less I know.”

--Michel Legrand



Contact Information

Jasmine Cutler, Pharm.D., CPh

USF College of Pharmacy (813) 974-3935

Byrd Alzheimer's Institute (813) 396-0623

Jcutler@health.usf.edu



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Jasmine Cutler, Pharm.D., CPh

Pharmacists, USF Health Byrd Alzheimer's Institute

Assistant Professor, USF College of Pharmacy

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