AN APPROACH TO MEDICATION MANAGEMENT IN OLDER ADULTS

Claudene J. George, MD, RPh
Assistant Professor of Medicine
Albert Einstein College of Medicine
Montefiore Medical Center

THE AMERICAN GERIATRICS SOCIETY
Geriatrics Health Professionals.
Leading change. Improving care for older adults.
OBJECTIVES

• Understand the basics of pharmacokinetics and pharmacodynamics
• Discuss age-associated changes involved in drug absorption, distribution, metabolism, and elimination
• Review common mechanisms of drug-drug interactions
• Review the cytochrome P450 system
• Discuss the Beers criteria and important medication management issues
INTRODUCTION

• More than 30 new drugs are introduced each year
• Computer software has become important in detecting potential interactions
• Software is usually limited to recognizing class effects instead of drug effects
• Clinicians who understand the mechanisms involved in drug interactions can better anticipate potential adverse drug reactions for newly introduced drugs
ADVERSE DRUG REACTIONS

• 30% of hospital admissions in elderly patients may be linked to drug-related problems or toxic effects
• Fifth leading cause of death in the US
• Linked to preventable problems such as depression, constipation, falls, immobility, confusion, and hip fracture
• Costs of medication-related problems:
  - $76.6 billion — ambulatory care
  - $20 billion — hospitals
  - $4 billion — nursing homes

DRUG-DRUG INTERACTION

Modulation of the activity of one drug (object) by the prior or concomitant administration of another (precipitant)

• Pharmacokinetic interactions
• Pharmacodynamic interactions
PHARMACOKINETIC INTERACTION

Occurs when one drug alters the absorption, distribution, metabolism, or excretion of another drug.
Site of Administration

1. Absorption

- Formation of insoluble complexes
- Altered GI pH
- Altered intestinal blood flow and mucosal damage
ABSORPTION AND AGING

- No significant change in extent of absorption = no change in bioavailability
- Time to reach peak serum concentration delayed
- Lower peak serum concentration

pp 7-86.
ABSORPTION AND DRUG INTERACTIONS

• Fluoroquinolones + antacids (Ca, Mg, Al)
  ➢ Formation of poorly soluble complexes
  ➢ Effect of antibiotic decreased

• Cholestryramine plus:
  ➢ Digoxin
  ➢ Warfarin
  ➢ Loop diuretics
  ➢ Thyroid drugs
  ➢ Corticosteroids
ABSORPTION AND DRUG-NUTRIENT INTERACTIONS

Decreased absorption with food
Penicillin       Tetracycline       Erythromycin
Digoxin          Phenytoin         Levodopa

Increased absorption with food
Spironolactone   Itraconazole      Griseofulvin

Edmunds MW. *Pharmacology for the Primary Care Provider*. 2nd ed. 2004. pp 7-86.
PHARMACOKINETICS
AND DRUG INTERACTIONS

Site of Administration

1. Absorption

2. Distribution

- Competitive binding to proteins
- Deposition into fatty stores
DISTRIBUTION AND AGING

- Decreased total body weight — ↓ volume of distribution (Vd) — ↑ water-soluble drugs
- Increased fat stores — ↑ Vd — prolonged action of fat-soluble drugs
- Decreased lean body mass — ↓ Vd
- Decreased albumin — ↑ concentration of free drug
DISTRIBUTION AND DRUG INTERACTIONS (1 of 2)

• High binding to albumin (prescribe in reduced doses)
  Phenytoin    Warfarin
  Naproxen     Theophylline
  Phenobarbital

• Lipid-soluble
  Benzodiazepines    Barbiturates

• Distributed in lean body mass
  Digoxin       Lithium       Meperidine
  Gentamycin    Phenytoin     Cimetidine
DISTRIBUTION AND DRUG INTERACTIONS (2 of 2)

- Acidic drugs
  - High affinity for proteins
  - Bind to protein and rendered inactive
  - More free drug in bloodstream
PHARMACOKINETICS AND DRUG INTERACTIONS

Site of Administration

1. Absorption

Plasma

2. Distribution

Tissue

3. Metabolism
METABOLISM (1 of 3)

• Drugs must be changed from water-soluble to lipid-soluble to cross membranes to reach their site of action

• Metabolism converts active lipid-soluble compound to inactive water-soluble substance that can be excreted primarily by kidney
METABOLISM (2 of 3)

- **Phase I**
  - Hepatic microsomal enzymes in the endothelium of liver cells oxidize, demethylate, and hydrolyze.
  - From active to more, equally, or slightly less active.
  - More clinically significant drug interactions.

- **Phase II**
  - Large water-soluble substances attach to drugs.
  - Form inactive or significantly less active water-soluble metabolites (conjugation).
METABOLISM: AGE-ASSOCIATED CHANGES

- Decreased hepatic blood flow
- Decreased liver size and mass
- Decreased metabolism
METABOLISM: CYTOCHROME P450 SYSTEM (1 of 3)

• Located in hepatocytes and cells of small intestine

• Responsible for the first phase of biotransformation for many drugs

• Comprises more than 30 isoenzymes whose presence and function are genetically determined
Example: Codeine

- Individuals with CYP2D6 deficiency cannot convert codeine to its active metabolite, morphine
- They receive little if any analgesic benefit
- They are usually unable to metabolize many psychotropic agents (eg, phenothiazines)
METABOLISM: CYTOCHROME P450 SYSTEM (3 of 3)

- **Substrates**: Drugs metabolized as substrate by enzymes
- **Inhibitors**: Drugs that prevent the enzyme from metabolizing the substrate
- **Activators**: Drugs that increase the enzyme’s ability to metabolize the substrate
<table>
<thead>
<tr>
<th>Substrates</th>
<th>1A2</th>
<th>2B6</th>
<th>2C19</th>
<th>2C9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clozapine</td>
<td>Bupropion</td>
<td>Proton pump inhibitors:</td>
<td>NSAIDs:</td>
</tr>
<tr>
<td></td>
<td>Cyclobenzaprine</td>
<td>Cyclophosphamide</td>
<td>Omeprazole</td>
<td>Diclofenac</td>
</tr>
<tr>
<td></td>
<td>Imipramine</td>
<td>Efavirenz</td>
<td>Lansoprazole</td>
<td>Ibuprofen</td>
</tr>
<tr>
<td></td>
<td>Mexiletine</td>
<td>Ifosfamide</td>
<td>Pantoprazole</td>
<td>Piroxicam</td>
</tr>
<tr>
<td></td>
<td>Naproxen</td>
<td>Methadone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Riluzole</td>
<td></td>
<td>Anti-epileptics:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tacrine</td>
<td></td>
<td>Diazepam</td>
<td>Oral hypoglycemic agents:</td>
</tr>
<tr>
<td></td>
<td>Theophylline</td>
<td></td>
<td>Phenytoin</td>
<td>Tolbutamide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Phenobarbitone</td>
<td>Glipizide</td>
</tr>
<tr>
<td>2E1</td>
<td>Acetaminophen</td>
<td></td>
<td>Miscellaneous:</td>
<td>Angiotensin II blockers:</td>
</tr>
<tr>
<td></td>
<td>Chlorzoxazone</td>
<td></td>
<td>Amitriptyline</td>
<td>NOT candesartan or valsartan</td>
</tr>
<tr>
<td></td>
<td>Ethanol</td>
<td></td>
<td>Clomipramine</td>
<td>Irbesartan</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cyclophosphamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Progesterone</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Miscellaneous:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Celecoxib</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fluvastatin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Naproxen</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phenytoin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sulfamethoxazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tamoxifen</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tolbutamide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Torsemide</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Warfarin</td>
</tr>
</tbody>
</table>
## CP450 Drug Interaction Table (2 of 4)

<table>
<thead>
<tr>
<th>Substrates</th>
<th>2D6</th>
<th>3A4,5,7</th>
<th>3A4,5,7</th>
<th>3A4,5,7</th>
<th>3A4,5,7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-Blockers:</strong></td>
<td>S-metoprolol Propafenone Timolol</td>
<td><strong>Miscellaneous:</strong></td>
<td>Codeine Dextromethorphan Flecainide Mexiletine Ondansetron Tamoxifen Tramadol Venlafaxine</td>
<td><strong>Macrolide antibiotics:</strong></td>
<td>NOT azithromycin Clarithromycin Erythromycin Telithromycin</td>
</tr>
<tr>
<td><strong>Antidepressants:</strong></td>
<td>Amitriptyline Clomipramine Desipramine Imipramine Paroxetine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics:</strong></td>
<td>Haloperidol Risperidone Thioridazine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics:</strong></td>
<td>Haloperidol Risperidone Thioridazine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antihistamines:</strong></td>
<td>Astemizole Chlorpheniramine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Calcium-channel blockers:</strong></td>
<td>Amlodipine Diltiazem Felodipine Nifedipine Nisoldipine Nitrendipine Verapamil</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HMG CoA reductase inhibitors:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous:</strong></td>
<td>Buspirone Haloperidol Methadone Pimozide Quinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## CP450 Drug Interaction Table (3 of 4)

<table>
<thead>
<tr>
<th>Inhibitors</th>
<th>1A2</th>
<th>2B6</th>
<th>2C19</th>
<th>2C9</th>
<th>3A4,5,7</th>
<th>2D6</th>
<th>2E1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticlopidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiotepa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lansoprazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticlopidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV antivirals:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delavirdine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indinavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nelfinavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saquinavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOT azithromycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clomipramine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mibefradil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranitidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disulfiram</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOT azithromycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mibefradil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nefazodone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troleandomycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### CP450 DRUG INTERACTION TABLE (4 of 4)

<table>
<thead>
<tr>
<th>Inducers</th>
<th>1A2</th>
<th>2B6</th>
<th>2C19</th>
<th>2C9</th>
<th>2D6</th>
<th>2E1</th>
<th>3A4,5,7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td></td>
<td>Tobacco</td>
<td>Phenobarbital</td>
<td>Rifampin</td>
<td>Phenobarbital</td>
<td>Rifampin</td>
<td>St. John’s wort</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Secobarbital</td>
<td>Ethanol</td>
<td>Isoniazid</td>
<td>Troglitazone</td>
</tr>
</tbody>
</table>
ELIMINATION: AGE-ASSOCIATED CHANGES

- **Glomerular filtration rate** is decreased (6–12 mL/min per 1.73m² per decade) due to decreased:
  - Kidney size
  - Renal blood flow
  - Nephron function

- **Renal tubular secretion** decreases

- **Serum creatinine** stays the same since lean body mass decreases
CALCULATE CREATININE CLEARANCE

\[ \text{CrCl} = \frac{(140 - \text{age}) \times \text{Wt [kg]}}{72 \times \text{serum creatinine (mg/dL)}} \times 0.85 \text{ for females} \]

<table>
<thead>
<tr>
<th></th>
<th>20 years</th>
<th>80 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>72</td>
<td>72</td>
</tr>
<tr>
<td>CrCl, mL/min</td>
<td>101</td>
<td>50</td>
</tr>
</tbody>
</table>
ELIMINATION: EXAMPLE

Phenobarbital + ascorbic acid
• Acidification of urine with ascorbic acid
• Increased phenobarbital level
PHARMACODYNAMIC INTERACTIONS

• Associated with synergism, antagonism, or altered cellular transport

• Affect organ systems and/or receptor sites
Table 9. Age-associated Changes in Pharmacokinetics and Pharmacodynamics

Pharmacodynamics

Age Effect
Less predictable and often altered drug response at usual or lower concentrations

Disease, Factor Effect
Drug-drug and drug-disease interactions may alter responses

Prescribing Implications
Prolonged pain relief with opioids at lower dosages; increased sedation and postural instability to benzodiazepines; altered sensitivity to β-blockers
COMMON CHARACTERISTICS OF OLDER ADULTS WITH MEDICATION-RELATED PROBLEMS

- 85 years of age or older
- More than 6 active chronic medical diagnoses
- Decreased kidney function (estimated CrCl < 50 mL/min)
- Low body weight or body mass index
- Nine or more medications
- More than 12 doses of medication per day
- Previous adverse drug reaction

APPROACHES TO POLYPHARMACY AND DRUG INTERACTIONS

Complicating issues

• Continuous arrival of new drugs
• Changing information about existing medications
• Limited available data in older adults with multiple comorbidities

What are we doing?

• “Starting low, going slow”
• Minimizing number of medications
• Brown-bag approach
• Computer programs
• Beers criteria
BEERS CRITERIA

- Consensus criteria for drugs generally considered inappropriate for use in elderly
- Literature search and questionnaires completed by experts in geriatrics, clinical pharmacology, and psychopharmacology
- Evaluated new medications and conditions, rated severity of interactions, and removed medications that were no longer contraindicated
- Used in literature to evaluate prescribing patterns, educate clinicians, and evaluate healthcare cost and utilization

UPDATE TO BEERS CRITERIA
Medications Added Since 1997, Independent of Diagnosis

- Ketorolac (Toradol)
- Doxazosin (Cardura)
- Clonidine (Catapres)
- Mineral oil
- Cimetidine (Tagamet)
- Ferrous sulfate > 325 mg
- Short-acting nifedipine
- Daily fluoxetine (Prozac)
- Stimulant laxatives if not for chronic pain/opioid tx
- Amiodarone (Cordarone)

UPDATE TO BEERS CRITERIA
Medications Added Since 1997, Diagnosis-Dependent

- Metoclopramide (Reglan) with Parkinson’s disease
- Olanzapine (Zyprexa) with obesity
- Calcium-channel blockers with constipation
- Clopidogrel (Plavix) for patients with blood-clotting disorders receiving anticoagulant therapy
- Propranolol with COPD/asthma
- Tricyclic antidepressant with syncope, falls, or stress incontinence

### DRUGS AND CLASSES POTENTIALLY INAPPROPRIATE FOR USE IN THE ELDERLY

- **Amiodarone**
- **Amitriptyline (H)**
- **Amphetamines (excluding methylphenidate hydrochloride and anorexics)**
- **Barbiturates**
- **Benzodiazepines, long acting (chlordiazepoxide (H), diazepam (H), flurazepam (H), oxazepam (H), temazepam)**
- **Chlorpheniramine**
- **Cimetidine**
- **Clonidine**
- **Clorazepate**
- **Cyproheptadine**
- **Desiccated thyroid**
- **Digoxin >0.125 mg/day (H)**
- **Diphenhydramine (H)**
- **Dipyridamole, short-acting (L)**
- **Disopyramide (H)**
- **Doxazosin**
- **Ergot myeloids (L)**
- **Estrogens**
- **Ethacrynic acid**
- **Ferrous sulfate .325 mg/day**
- **Fluoxetine**
- **Gastrointestinal antispasmodics (belladonna alkaloids, clidinium-chlordiazepoxide, dicyclomine, propantheline – all (H))**
- **Guanethidine**
- **Hydroxyzine**
- **Indomethacin (L)**
- **Ketorolac**
- **Meperidine (H)**

H = high severity; L = low severity

DRUGS AND CLASSES POTENTIALLY INAPPROPRIATE FOR USE IN THE ELDERLY

- Meprobamate
- Mesoridazine
- Methyldopa and methyldopa/hydrochlorothiazide
- Methyltestosterone
- Mineral oil
- Muscle relaxants (carisoprodol, chlorzoxazone, cyclobenzaprine, dantrolene, methocarbamol, orphenadrine – all (L)
- Nifedipine, short-acting
- Nitrofurantoin
- NSAIDs, long-term use of full-dose, longer half-life, non-COX-selective types (naproxen, oxaprozin, and piroxicam)
- Oxybutynin, short-acting
- Pentazocine (H)
- Perphenazine-amitriptyline
- Promethazine
- Propoxyphene
- Reserpine (L)
- Stimulant laxatives, long-term use except with opiate analgesics (bisacodyl, cascara sagrada, and Neoloid)
- Thioridazine
- Ticlopidine (H)
- Trimethobenzamide (H)
- Tripelennamine

H = high severity; L = low severity

10 STEPS TO REDUCING POLYPHARMACY

1. “Brown-bagging”: Ask patients to bring all their medications at each visit, keep accurate record, and include OTC drugs and herbs
2. Identify all drugs by generic name and drug class
3. Confirm clinical indication
4. Know side-effect profiles
5. Understand how the pharmacokinetics and pharmacodynamics of aging increase the risk of adverse drug events
6. Stop drugs without known benefit
7. Stop drugs without clinical indication
8. Attempt to substitute a less toxic drug
9. Avoid the prescribing cascade
10. Use the motto “one disease, one drug, once a day”
PREFERRED MEDICATIONS FOR THE ELDERLY

• Lipid-lowering agent
  ➢ Pravastatin (Pravachol)

• Depression: SSRIs
  ➢ Escitalopram (Lexapro), sertraline (Zoloft), Citalopram (Celexa)

• Pain management
  ➢ Tylenol (in absence of liver disease, and maximum of 3 g/day)

• Itching
  ➢ Emollients, topical antihistamines
SUMMARY: APPROACH TO MEDICATION MANAGEMENT

- Understand basics of pharmacokinetics
- Consider creatinine clearance
- Reduce polypharmacy
- Consider reasons for nonadherence
  - Cost, beliefs, comprehension, size of pills, visual and cognitive impairments
OTHER REFERENCES


THANK YOU FOR YOUR TIME!

Visit us at:
www.americangeriatrics.org

Facebook.com/AmericanGeriatricsSociety
Twitter.com/AmerGeriatrics
linkedin.com/company/american-geriatrics-society