Perilous Polypharmacy

Kevin L. Wallace, MD, FACMT
College of Pharmacy
Dept. of Pharmacy Practice
Presentation Objectives

- Increase awareness of risks and impact of medication overuse and underuse.
- Promote use of safe and cost-effective pharmacotherapeutic tools and strategies.
- Remain available for comments and questions.
Figure 1: Rate of unintentional drug overdose death in the United States, 1970-2006

Source: National Vital Statistics System
Figure 2: Unintentional drug overdose deaths by major type of drug, United States, 1999-2006

Source: National Vital Statistics System
Major Risk Determinant: Drug Provision

Adverse Drug Events (ADE)

- ADE = medication-related injury
- Highly vulnerable groups include:
  - Elderly (>65 yrs)
  - Younger adults/adolescents with psychobehavioral disorders
  - Infants/toddlers

“Collateral Damage”
ADE Impact

- **Patient**
  - ↓ quality of living
  - ↑ cost of care

- **Population**
  - Approx. 500,000 Medicare patient ADEs/yr in outpatient setting
  - 5\textsuperscript{th} leading cause of death
  - Cost: \$300 billion/year

Gurwitz et al 2003; NEHI 2009
Primary ADE Risk Factors

- **Exposure-related**
  - Drug(s), formulation(s), route(s)
  - Dose, frequency and duration of treatment
  - Nonpharmaceuticals (e.g., herbal supplements)

- **Patient-related**
  - Age
  - Genetic makeup
  - Comorbid disorders(s)

Number of drugs in regimen = most potent ADE risk factor!
Secondary Risk: Interactions

Drug-drug

Drug-disease
Polypharmacy – Definition?

- >4-drug regimen
- May/may not include nonprescription (OTC) medications and other supplements
Elderly Polypharmacy

- Seniors (13% total population) consume:
  - 40% of all prescription drugs
  - 35% of all OTC drugs

- Average # Rx meds/yr (OTC excluded)
  - 65-69 yrs: >13
  - 80-84 yrs: ~18

Am. Soc. Consultant Pharmacists 2004
# Geriatric Pharmacokinetics

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>AGE-RELATED CHANGE</th>
<th>IMPACT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absorption</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric pH</td>
<td>Increased</td>
<td>Reduced absorption (e.g., itraconazole)</td>
</tr>
<tr>
<td>Gastric emptying</td>
<td>Reduced</td>
<td>Reduced rate of absorption</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body fat</td>
<td>Increased</td>
<td>Increased Vd for lipophilic agents (e.g., diazepam)</td>
</tr>
<tr>
<td>Body water</td>
<td>Reduced</td>
<td>Reduced Vd for hydrophilic agents (e.g., lithium)</td>
</tr>
<tr>
<td>Plasma protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>Reduced</td>
<td>Increased free fraction (e.g., phenytoin)</td>
</tr>
<tr>
<td>α-Glycoprotein</td>
<td>Increased (illness)</td>
<td>Reduced free fraction (e.g., lidocaine)</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic mass/blood flow</td>
<td>Reduced</td>
<td>Reduced clearance (e.g., lidocaine)</td>
</tr>
<tr>
<td>Phase I enzyme activity</td>
<td>Reduced</td>
<td>Reduced clearance (e.g., diazepam, meperidine)</td>
</tr>
<tr>
<td><strong>Elimination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver metabolism</td>
<td>Reduced</td>
<td>Reduced elimination rate</td>
</tr>
<tr>
<td>Renal excretion</td>
<td>Reduced</td>
<td>Reduced elimination rate</td>
</tr>
<tr>
<td>GFR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Wallace & Morkunas 2005
Overarching Principle

Inter- AND Intraindividual Variability!
ADE Causal Determinants

- Treatment nonadherence
  - underuse
  - overuse
- Uncommon/unrecognized drug interactions (other drugs, diseases, diet, etc.)
- Inappropriate prescribing (IP)
  - overuse
  - underuse
IP Distribution by Type

(1989/90) →

Drug indication?

“More is Less”

Ira Glass, “This American Life” (NPR)
Drug- or Non-drug related?

- Balance/gait problems
- Dizziness
- Confusion
- Irritability
- Depressed mood
- Insomnia
- Sleepiness
- Fatigue
- Incontinence
- Heart rhythm problem
### Geriatric “Delerirotropics”

<table>
<thead>
<tr>
<th>CLASS</th>
<th>SPECIFIC DRUGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmics</td>
<td>Digoxin, lidocaine, procainamide, phenytoin, carbamazepine, valproic acid</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Amitriptyline, fluoxetine, phenytoin, carbamazepine, valproic acid</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Promethazine, metoclopramide, clonidine, propranolol, verapamil, amitriptyline</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>Clonidine, propranolol, verapamil, promethazine, metoclopramide</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Penicillin, ciprofloxacin, isoniazid, levodopa, amantadine</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td></td>
</tr>
<tr>
<td>Antiparkinsonians</td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td></td>
</tr>
<tr>
<td>Bronchodilators</td>
<td></td>
</tr>
<tr>
<td>Antineoplastics</td>
<td></td>
</tr>
</tbody>
</table>

- Histamine receptor
  - \( H_1 \) and \( H_2 \) antagonists
- Immunosuppressants
- Mood stabilizers
- Muscle relaxants
- Nonsteroidal anti-inflammatory drugs
- Opioid analgesics
- Sedative-hypnotics

---

Consider other triggers!

Wallace & Morkunas 2005
Other ADE Determinants

- Critical transition point (e.g., “H2H”) errors (“Falling Through the Cracks”)
- Number of prescribers per patient
- Patient-related:
  - ↓ functional status
  - ↓ support (family, finance)
ADE Primary Prevention

- Reduce IP (overuse AND underuse)
- Increase patient adherence
- Improve practice safety and outcome monitoring

Collaborative approach!!!
Cost-Saving?
Error Prevention
MTM Home Model Flow Diagram

PCP = primary care
Ph = pharmacy
A = assessment
I = intervention

EMR = electronic med. records
EPR = electronic pharm. records

EMR → PC → Patient → Ph → EPR
A1, 5
I1-3, 5, 7
A7

EMR ← PC ← Patient ← Ph ← EPR
A7
I2, 5-7

EMR → EMR
A7

EMR ← EMR
A7
Medication Review

“The single most effective and necessary step to ensure appropriate prescribing is to assess all medications prescribed at every visit.”

Ballentine 2008
SAFE Provider Practice

- **Search for ADE:**
  - Symptoms/signs
  - Risk factors (e.g., IP, nonadherence)

- **Avoid:**
  - IP (e.g., inappropriate drug, dose, frequency, duration)
  - Automatic refills
SAFE Provider Practice

- **Find cost-effective treatment:**
  - Simpler/lower-cost regimen
  - Close monitoring (med. use, outcomes)
  - Synchronized refills

- **Educate/inform:**
  - Patient/family
  - Providers
Rule of thumb

“Start low, go slow, watch closely!”
“As lay people and physicians increase their demands for coherent, evidence-based, unbiased drug information, we would all be well served by a comprehensive program to replace our current patchwork of bad communication and excessive promotion with a responsible national system of balanced, evidence-based, and user-friendly drug information.”

Avorn & Shrank 2009


