Essentials of Geriatric Pharmacotherapy

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Disclosures

None to report

Poll Question
Poll Question

Pharmacist Presentation Objectives
• Describe physiologic changes associated with aging and the effects on drug metabolism
• Outline tools to evaluate appropriate medication use in elders
• Discuss factors associated with adverse drug reactions in geriatrics
• Examine sample medication lists and identify potential problems

Technician Presentation Objectives
• Describe how aging affects what the body does to drugs and what drugs do to the body
• Outline tools to evaluate appropriate medication use in elders
• Discuss ways that elders can be harmed from medication use
• Examine sample medication lists and identify potential problems
Definitions

- Functional Status – ability to live independently
- Activities of Daily Living (ADLs)
  - Dressing, bathing, transferring, feeding, toileting
- Instrumental Activities of Daily Living (IADLs)
  - Telephone, meal preparation, housework, shopping, managing money and medications

Aging Dichotomy

- Goal: maintain independence and avoid long-term care
- Disability common among elders > 75
  - Difficulty performing ADLs and IADLs
- Decreased physical function
  - Inability to lift heavy objects, walk 2-3 blocks, reach overhead

Physiological Effects of Aging
Why do we age?

**Biology**
- DNA (genetic factors)
- Telomeres - [http://www.youtube.com/watch?v=6nptuLbVPrs](http://www.youtube.com/watch?v=6nptuLbVPrs)
- Oxidative stress
- Glycation

Siegel, L. Are telomeres the key to aging and cancer? [http://learn.genetics.utah.edu/content/begin/traits/telomeres/](http://learn.genetics.utah.edu/content/begin/traits/telomeres/). Accessed Feb 2013.

As we age, what changes?

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Clinical Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body composition</strong></td>
<td></td>
</tr>
<tr>
<td>↓ Total body water</td>
<td>For water soluble drugs: ↓ Vd, ↑ Cp</td>
</tr>
<tr>
<td>↓ Lean body mass</td>
<td>↓ Creatinine production</td>
</tr>
<tr>
<td>↑ Body fat</td>
<td>For lipophilic drugs: ↑ Vd, ↑ half-life</td>
</tr>
<tr>
<td>↔ or ↓ Serum albumin</td>
<td>Protein bound drugs: ↑ free fraction, ↑ toxicity</td>
</tr>
</tbody>
</table>

From: Pharmacotherapy
### As we age, what changes?

#### Cardiovascular
- **Manifestation**
  - Decreased myocardial sensitivity to beta-adrenergic stimulation
  - Decreased baroreceptor activity
  - Decreased cardiac output
  - Increased total peripheral resistance
- **Clinical Relevance**
  - Decreased effectiveness of beta blockers
  - Lightheadedness
  - Dizziness and loss of balance with exertion
  - Increased risk of LVH

#### Central Nervous System
- **Manifestation**
  - Decreased weight and volume of the brain
  - Alterations in several aspects of cognition
- **Clinical Relevance**
  - Memory lapses
  - Forgetfulness

#### Endocrine
- **Manifestation**
  - Atrophy of thyroid gland
  - Testosterone & estrogen
- **Clinical Relevance**
  - Various

#### Gastrointestinal (GI)
- **Manifestation**
  - Increased gastric pH
  - Increased GI blood flow
  - Delayed gastric emptying
  - Slowed intestinal transit
- **Clinical Relevance**
  - Drug breakdown
  - Drug absorption
  - Drug absorption/distribution affected
  - Drug absorption

#### Immune
- **Manifestation**
  - Cell-mediated immunity
- **Clinical Relevance**
  - Risk of infections

#### Liver
- **Manifestation**
  - Increased hepatic size
  - Increased hepatic blood flow
- **Clinical Relevance**
  - Drug metabolism

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**From: Pharmacotherapy**
As we age, what changes?

**Organ System** | **Manifestation** | **Clinical Relevance**
--- | --- | ---
Oral | Altered dentition ↓ ability to detect sweet, sour, and bitter tastes | Problems chewing, ↓ enjoyment of food, ↑ risk of endocarditis
Pulmonary | ↓ Respiratory muscle strength | ↓ absorption of inhaled medications
| ↓ Maximal breathing capacity | ↓ capacity for strenuous exercise

As we age, what changes?

**Organ System** | **Manifestation** | **Clinical Relevance**
--- | --- | ---
Renal | ↓ GFR | Decreased drug elimination
| ↓ Renal blood flow | 
| ↓ Tubular secretory function | 
| ↓ Renal mass | 

As we age, what changes?

**Organ System** | **Manifestation** | **Clinical Relevance**
--- | --- | ---
Sensory | ↓ Accommodation of the lens of the eye (farsighted) | Difficulty reading prescription bottles
| Loss of auditory acuity | Difficulty in communication
Skeletal | Osteopenia | Falls
Skin/hair | Dryness, wrinkling, pigment change, thin skin, loss of dermal thickness | ↓ Drug absorption
| ↓ Number of hair follicles, melanocytes in hair bulbs | Bald and gray
Fr | 

From: *Pharmacotherapy*
Drug Effects based on

• Pharmacokinetics (PK)
  – What body does to the drug
  – Cp = plasma concentration
  – Vd = volume of distribution
  – t ½ = half-life

• Pharmacodynamics (PD)
  – What drug does to the body

Altered PK/PD

• PK/PD influenced by:
  – Acute and chronic illnesses
  – Concomitant medications
  – Co-morbidities
  – Nutritional status

• Differences in ADME
**Pharmacokinetics - Absorption**

<table>
<thead>
<tr>
<th>Effect of Aging</th>
<th>Medication Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-pass extraction and ↑ Bioavailability for some drugs</td>
<td>Propranolol and morphine</td>
</tr>
</tbody>
</table>

Chemical reaction:

\[
CaCO_3 + 2HCl \rightarrow CaCl_2 + CO_2 + H_2O
\]

**Pharmacokinetics - Distribution**

<table>
<thead>
<tr>
<th>Effect of Aging</th>
<th>Medication Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water soluble drugs: ↑ Vd and ↑ Cp</td>
<td>Aspirin, famotidine, lithium, ethanol</td>
</tr>
<tr>
<td>Fat soluble drugs: ↑ Vd &amp; ↑ half-life</td>
<td>Amiodarone, diazepam, verapamil</td>
</tr>
</tbody>
</table>

**Pharmacokinetics - Metabolism**

<table>
<thead>
<tr>
<th>Effect of Aging</th>
<th>Medication Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Hepatic blood flow</td>
<td>Morphine, lidocaine, verapamil, propranolol, nitroglycerin</td>
</tr>
<tr>
<td>↓ Clearance for drugs with high hepatic extraction ratio</td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>Phenytoin</td>
</tr>
</tbody>
</table>
Pharmacokinetics - Elimination

<table>
<thead>
<tr>
<th>Effect of Aging</th>
<th>Medication Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced clearance of drugs</td>
<td>famotidine, enoxaparin, antibiotics, hydrochlorothiazide</td>
</tr>
</tbody>
</table>

For renally excreted drugs, adjust dose based on CrCl

- Cockcroft-Gault equation most common:
  
  \[
  \frac{\text{Ideal weight in kg} \times (140 - \text{age}) \times 0.85 \text{ if female}}{\text{serum creatinine in mg/dL}} \times 72
  \]

Pharmacodynamic Changes

- Altered drug response/sensitivity in seniors
  - More sensitive to CNS effects of benzodiazepines
  - Greater analgesic response to opioids
  - Enhanced responsiveness to warfarin and heparin
  - Decreased responsiveness to beta agonists and beta blockers

Poll Question
TOOLS TO EVALUATE MEDICATION THERAPY

Beers Criteria
History and Utilization

• Created in 1991 by Dr. Mark Beers
• Focus: nursing home residents
• Identified medications where risks > benefits in older adults
• Potentially Inappropriate Medications (PIMs)

Beers Criteria
History and Utilization

• Beers list updated in 1997 and 2003
  – Included all adults ≥ 65 years
  – 2011: AGS sponsored an update and expert panel identified
  – PIMs
  – Problematic drug-disease combinations
  – Medications that should be used with caution
**Intent of the Criteria**

- Improve drug selection
- Assist with evaluating patterns of drug use
- Educate clinicians and patients on potentially problematic medications in older adults
- Evaluate health outcome, quality of care, cost, and other utilization data

**Beers Criteria 2012**

- Medications or medication classes that *should generally be avoided* in persons 65 years or older

**Medications to Avoid**

- Notable mentions:
  - Sliding scale insulin
  - Antipsychotics for behavioral issues associated with dementia
  - Use of nonbenzodiazepine hypnotics for > 90 days
  - Megestrol
Beers Criteria 2012

- Medications that should not be used in older persons known to have specific medical conditions

<table>
<thead>
<tr>
<th>Disease or Syndrome</th>
<th>Drug/Drug Class</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>NSAIDs and COX-2 inhibitors</td>
<td>Potential to promote fluid retention and/or heart failure</td>
</tr>
<tr>
<td></td>
<td>Nondihydropyridine CCBs (avoid only for systolic heart failure)</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td>Acetylcholinesterase inhibitors</td>
<td>Increased risk of orthostatic hypotension or bradycardia</td>
</tr>
<tr>
<td></td>
<td>Peripheral alpha blockers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tertiary TCAs</td>
<td>Chlorpromazine, thioridazine, and olanzapine</td>
</tr>
</tbody>
</table>
### Drug-Disease Combinations to Avoid Notable Mentions

<table>
<thead>
<tr>
<th>Disease/Syndrome</th>
<th>Drug/Drug Class</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of falls or fractures</td>
<td>Anticonvulsants</td>
<td>Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics, Benzodiazepines, Nonbenzodiazepine hypnotics, Eszopiclone, Zaleplon, Zolpidem</td>
<td></td>
</tr>
<tr>
<td>Delirium</td>
<td>All TCAs</td>
<td>May induce or worsen delirium. If discontinuing drugs used chronically, taper to avoid withdrawal symptoms</td>
</tr>
<tr>
<td></td>
<td>Anticholinergics, Benzodiazepines, Chlorpromazine, Corticosteroids, H2 Blockers</td>
<td></td>
</tr>
</tbody>
</table>

### Beers Criteria 2012

- Medications to be used with caution

### Drugs to Use with Caution Notable Mentions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rationale</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA for primary prevention of cardiac events</td>
<td>Limited data in patients ≥ 80 years of age (yoa)</td>
<td>Use caution in adults ≥ 80 yoa</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Increased risk of bleeding compared with warfarin in adults ≥ 75 yoa; lack of evidence and safety when CrCl &lt; 30 ml/min</td>
<td>Use with caution in adults ≥ 75 yoa or if CrCl = 30 ml/min</td>
</tr>
<tr>
<td>Antipsychotics, Carbamazepine, Lorazepam, SSRIs, SNRIs, TCAs</td>
<td>May exacerbate or cause SIADH or hyponatremia; monitor sodium level closely when starting or changing dosages in older adults</td>
<td>Use with caution</td>
</tr>
</tbody>
</table>
**Use the Beers Criteria...**

- As a reference when prescribing medications for elders
- To help improve medication safety and awareness
- As a guide to help identify PIMs
- To help prevent adverse drug events in elders

**Beers Criteria is NOT...**

- A substitute for professional judgment
- Applicable in all situations
- Appropriate for patients receiving palliative or hospice care
- To be used in punitively
- A sole source formulary guide

**Beers Criteria 2012 Limitations**

- Other PIMs not addressed
  - Dose adjustment with renal dysfunction
  - Drug-drug interactions
  - Therapeutic duplications
- Alternatives to PIMs not routinely provided
  - Megestrol
- Use of obscure terms
  - Peripheral alpha blockers
  - Theobromines
  - Tertiary TCAs
Poll Question

Poll Question

START/STOPP

• **START** – Screening Tool to Alert doctors to Right Treatment
  – 6 categories
  – Describes prescribing omissions
START Example

• Endocrine Medications
  – Consider STARTing the following, assuming no contraindication:
• Bisphosphonate for patients on chronic systemic glucocorticoids
• Calcium and vitamin D for patients with osteoporosis
• Metformin for patients with type 2 diabetes

START/STOPP

• STOPP - Screening Tool of Older Persons’ Prescriptions
  – 10 categories
  – Broad in clinical scope
  – Emphasizes drug-disease interactions
  – Appropriate for inpatient setting, skilled nursing, and community

STOPP examples

<table>
<thead>
<tr>
<th>Drug/Drug Class</th>
<th>PIM in elderly</th>
<th>Clinical Concern</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glyburide</td>
<td>Type 2 diabetes</td>
<td>Prolonged hypoglycemia</td>
<td>glipizide, glimepiride</td>
</tr>
<tr>
<td>SSRIs</td>
<td>History of low sodium &lt; 130 mEq/L within past two months</td>
<td>Hyponatremia</td>
<td>trazodone, mirtazapine, bupropion</td>
</tr>
<tr>
<td>Urinary anticholinergics, e.g. oxybutynin</td>
<td>With dementia</td>
<td>Increased agitation, confusion</td>
<td>For urge incontinence: scheduled toileting</td>
</tr>
<tr>
<td></td>
<td>With constipation</td>
<td>Worsening constipation</td>
<td>For constipation, increase fluids, fiber, polyethylene glycol (PEG), stool softeners</td>
</tr>
</tbody>
</table>
### STOPP examples

<table>
<thead>
<tr>
<th>Drug/Drug Class</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>Doses &gt; 0.25 mg daily, GFR &lt; 50 mL/min</td>
<td>Toxicity</td>
<td>Dose reduction, monitoring</td>
</tr>
<tr>
<td>Calcium channel blockers (CCB)</td>
<td>With chronic constipation</td>
<td>Worsening constipation</td>
<td>Change CCB to ACE inhibitor, beta blocker, diuretic For constipation, increase fluids, fiber, PEG, stool softeners</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Doses &gt; 150 mg</td>
<td>Increased risk of bleeding; no additional benefit</td>
<td>Reduce dose to 81 mg daily</td>
</tr>
</tbody>
</table>

### Poll Question

**ADVERSE DRUG REACTIONS (ADR)**
ADR Definitions

- World Health Organization
  “Any response to a drug that is noxious and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiologic function.”

Definition of Serious Adverse Event

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability or Permanent Damage
- Congenital Anomaly/Birth Defect
- Required Intervention to Prevent Permanent Impairment or Damage (Devices)
- Other Serious (Important Medical Events)

Factors associated with ADRs in Geriatric Patients

- PK/PD changes
- Inappropriate prescribing
- Polypharmacy
- Drug interactions
- Poor medication adherence
- Age?
Polypharmacy

- Definitions - varied
- Examples
  - Use of medications that are not clinically indicated
  - Treating the ADR of one drug with another drug
  - Duplication of therapy
  - Use of a drug that worsens patient’s other diseases
  - Inappropriate dosing schedule
  - Inadequate dose

Risk Factors for Polypharmacy

- Demographic
  - Age
  - Race
  - Education
- Health Status
  - Poorer health
  - Chronic disease (i.e. depression, hypertension, diabetes)
  - Use of ≥ 9 medications

Consequences of Polypharmacy

- ADRs
- Geriatric syndromes
  - Falls, urinary incontinence, cognitive impairment
- Decreased adherence
- Increased cost
- Drug interactions
- Increased morbidity/mortality

Drug Interactions

- Up to 22% of all ADRs are due to drug-drug interactions
- Drugs frequently involved in drug interactions
  - Narrow therapeutic index drugs, e.g. anticoagulants, anticonvulsants, digoxin, chemotherapy agents
  - Psychotropics, analgesics, cardiovascular agents

Top Ten Dangerous Drug Interactions in Long-Term Care

1. Warfarin-NSAIDs
2. Warfarin-Sulfa drugs
3. Warfarin-Macrolide
4. Warfarin-Quinolones
5. Warfarin-Phenytoin
6. ACE inhibitors-Potassium supplements
7. ACE inhibitors-Spironolactone
8. Digoxin-Amiodarone
9. Digoxin-Verapamil
10. Theophylline-Quinolones

Medication Adherence - LTC

- ~25% of all nursing home admissions result from inability to take drugs properly
- Barriers to adherence
  - Regimen complexity
  - Miscommunication/unresolved patient concerns
  - Physical disabilities
  - Cost
Medication Adherence

- 42% of patients in an AARP survey failed to adhere to their medication regimen
  - Stopped medication before it was gone (29%)
  - Took less than prescribed amount (22%)
  - Never filled prescription (14%)
  - Filled medication but never took it (13%)

AARP 6/92; study #9185
http://www.adultmeducation.com/OverviewofMedicationAdherence_4.html

Age

- Unknown if age is an independent risk factor or if other factors associated with aging increase risk
- Geriatric patients often have several chronic illnesses and seek care from multiple providers and multiple pharmacies
- Elderly often excluded from premarketing clinical trials

Poll Question
Poll Question

How to Decrease the Risk of ADRs in the Elderly

• Prior to writing/recommending prescription, consider:
  – Is medication necessary?
  – What are the therapeutic endpoints?
  – Do the benefits outweigh the risks?
  – Is the new drug needed to treat side effects of another drug?
  – Could one drug be used to treat two conditions?
  – Could new drug interact with current drugs or diseases?
  – Does patient know indication of new medication, how to take it, what side effects to anticipate?

How to Decrease the Risk of ADRs in the Elderly

• When reviewing a patient’s medication profile, consider:
  – Does each medication have an indication?
  – What side effects should be asked about?
  – Does therapeutic duplication exist?
  – What drug-drug/drug-disease interactions need further exploration?
  – What other ‘drugs’ is the patient taking, e.g. OTCs, social drugs, and herbal products?
  – Which medications are candidates for discontinuation?
Conclusions – It is Essential to

- Monitor for changes in ADME and effects of medications in the elderly population
- Detect/prevent ADRs
  - Utilize the Beers Criteria and START/STOPP criteria to guide recommendations
  - Identify individuals at high-risk for ADRs
  - Determine which medications may need intervention

Questions?

Recommended References

- American Geriatrics Society
  - [www.americangeriatrics.org](http://www.americangeriatrics.org)
- “Geriatrics at Your Fingertips”
  - [www.geriathristsatyourfingertips.org](http://www.geriathristsatyourfingertips.org)
- American Society of Consultant Pharmacists
  - [www.ascp.com](http://www.ascp.com)