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The “How To” on Safe Prescribing Practices for the Elderly *(Patient Safety)*

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Disclosures:

Speaker has no disclosures and there are no conflicts of interest.

The speaker has attested that their presentation will be free of all commercial bias toward a specific company and its products.

The speaker indicated that the content of the presentation will not include discussion of unapproved or investigational uses of products or devices.

Geropharmacology & Safe Prescribing

{ *Paula Bordelon, DO*

Disclosures

- > Dr. Paula Bordelon has no conflict of interest, financial agreement, or working affiliation with any group or organization.

Objectives

- > Discuss pharmacokinetics and pharmacodynamics as they relate to aging process
- > Review a tool to assist providers in making "safe" prescribing choices
- > Define quality indicator tool and steps to prescribe safely

Background

- Prescribing to older adults offers special challenges
- Older adults take about 3 times as many prescription meds as younger counterparts
- Many medications need to be used with caution because of age-related changes in pharmacokinetics and pharmacodynamics



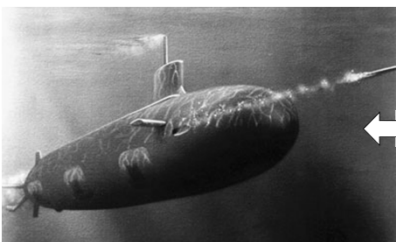
Demographic Data



- 13% of the US population is older than 65, but this group is prescribed 33% of all prescription medicines.
- More than 90% of all females over 65, take at least one prescription medicine.



Drug (*torpedo*)



Pharmacodynamics



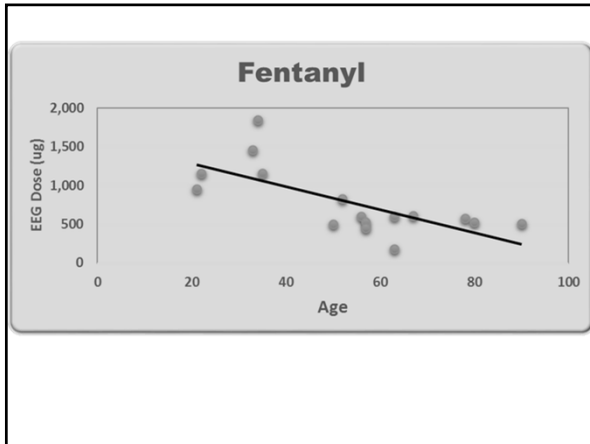
- Pharmacodynamics
 - What the drug "does" to you
 - Is the relationship between serum drug concentration and the drug's effect on the body.
- Pharmacodynamics changes with age and is less understood than pharmacokinetics
- Given genetic differences, is variable among adults
- Areas most impacted: Cardio & CNS

Pharmacodynamics-Cardio

- Reduction in cardiac and vascular B-adrenergic responsiveness
- If give IV bolus of a nonselective B-adrenoceptor agonist HR increase is reduced in seniors
- Also have reduced cAMP second messenger response to B-adrenoceptor agonists
- Older subjects less sensitive to B-adrenoceptor antagonists, less effective as initial therapy in tx HTN
- Another example is calcium channel blockers—but BP response is more marked in seniors than younger cohorts

Pharmacodynamics-CNS

- Seniors are more sensitive to sedatives and respiratory effects because brain has increased pharmacodynamic sensitivity to any given concentration (e.g. benzos, narcotics, anesthetics)
- Requires lower doses for sedative effect
- Experience more cognitive adverse effects
- Benzos:
 - Associated with more falls
 - Increased postural sway
 - Lowered SBP



Pharmacokinetics (*sub*)

- > Pharmacokinetics is the relationship between the drug input (dose, route, frequency of a drug administered), and drug concentration as it relates to four processes:
 - > Absorption
 - > Distribution
 - > Metabolism
 - > Elimination
- > One should consider each of these four processes when prescribing to older adults



Absorption

- > Absorption is not affected to a significant degree by age.
 - > That is, while rate may be slowed, bioavailability (amt absorbed) does not differ.
- > Factors that affect absorption include:
 - > Method of delivery (the way a medication is taken)
 - > What it the medication is taken with
 - > Comorbidities
 - An example of a comorbidity is when protein pump inhibitors increase gastric PH, this can:
 - increase absorption of some drugs (e.g. nifedipine, amc
 - or
 - decrease absorption (e.g. ampicillin, cyanocobalamin).



Distribution



- Refers to locations in the body a drug penetrates and time required to reach said location
- Changes in body composition can alter drug distribution.
- On average, the percentage of body fat doubles between the ages of 15 and 65.
- As one ages:
 - Body H₂O ↓
 - Lean muscle mass ↓
 - Plasma volume ↓
 - Fat ↑



Distribution (cont'd)



- Hydrophilic drugs have lower volume distribution.
 - For example, alcohol, aspirin and lithium have a shorter half-life ($t_{1/2}$) and more rapid onset of action.
- Lipophilic drugs have increased volume of distribution.
 - For example, diazepam, trazadone, and hormones have a longer half-life ($t_{1/2}$).
- Extent a drug is bound impacts Vd; primary protein is serum albumin declines with age
 - This is why rec * ↓↓↓ #Etoh drinks



Distribution (cont'd)

- Albumin is the primary plasma protein that binds drugs.
 - With a decrease in albumin, a higher proportion of drug volume is free (unbound) and pharmacologically active.
 - Examples are ceftriaxone, lorazepam, valproic acid, and warfarin.
 - Age-related decreases in elimination can result in accumulation of unbound drug



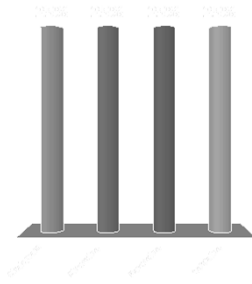
Metabolism

- > The liver is the most common site of drug metabolism.
- > Metabolism is not as significant as distribution and elimination, unless the patient has liver disease



Cytochrome 2D6 (CYP 2D6) is active in metabolizing one quarter of medications on the market. Approximately 10% of Caucasians are deficient in this enzyme. Additionally some SSRIs inhibit CYP 2D6. All of the following inhibit CYP 2D6 except:

- A. Citalopram
- B. Fluoxetine
- C. Paroxetine
- D. Sertraline



Metabolism (cont'd)

- > Phase I – cytochrome –mediated
 - > Drugs metabolized here converted to lesser, equal, greater pharmacologic metabolites
 - > Declines with aging
 - > Drugs metabolized via Phase I (e.g., diazepam)
- > Phase II – glucuronidation, conjugation, acetylation
 - > Drugs are converted to inactive compounds
 - > Not significantly affected by aging
 - > Drugs metabolized via Phase II (e.g., oxazepam, lorazepam)
 - > Preferred!



Metabolism via Cytochrome P450

- > CYP 450 is an oxidizing enzyme
- > Some decline with aging
- > CYP 3A4 & CYP 2D6 are common members

Elimination



- > gFR declines as one ages because of:
 - > decreased blood flow,
 - > decreased renal size
 - > a decrease in functioning nephrons
- > Kidney function declines 6 ml/min/1.73m² per decade beginning in the mid-30's.
- > Can't rely on serum creatinine to accurately reflect creatinine clearance (CrCl)

Estimating CrCl

1. Cock Croft-Gault

- >
$$\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight}(\text{kg})}{72 \times \text{serum Cr}(\text{mg/dL})}$$
 - * (X 0.85 for females)
- > Not all patients have significant age-related decline, CrCl can be understated.
- > Those with muscle mass reduction beyond normal aging are likely to have CrCl overestimated.

Estimating CrCl (cont'd)

2. Modification of Diet in Renal Disease (MDRD)

- This method has not been validated in patients older than 70.
- Similarly, it has not been validated in racial or ethnic groups other than white and blacks.

Elimination: The Bottom Line

- CrCl underestimates kidney function
- Use MDRD or calculated GFR.
- Age-related changes in GFR will change the prescribing of many medications, e.g.:
 - Gabapentin
 - Antibiotics (e.g., vancomycin)
 - TZD (i.e., useless because of low GFR)
 - Some sulfonylureas

Age-Related Changes in Pharmacokinetics and Drug-Drug Interactions

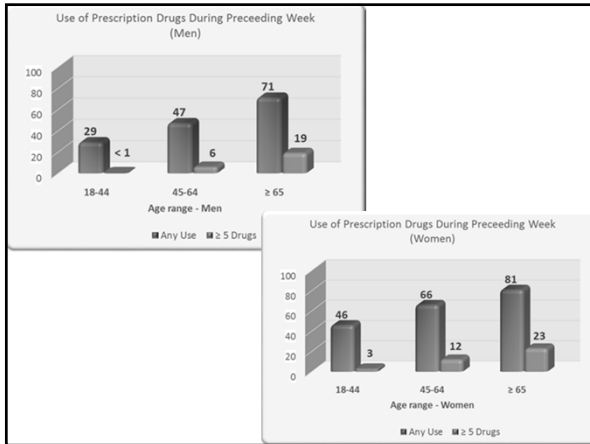
- **ACE-I**: associated with orthostasis
- **Beta-blockers**: decrease in lowering of systolic heart-rate and blood pressure
- **Diuretics**: decreased effectiveness of diuretics
- **Opioids**: increased sensitivity to sedative effects
- **Benzos**: slowed reaction time and increased postural sway
- **Bowie, MW** Am J Geriatric Pharmacotherapy 2007: -
- ⊗ ACE-I + diuretic: hypotension, hyperkalemia
- ⊗ Benzo + SSRI: confusion, sedation, falls
- ⊗ Dig + diuretic: arrhythmias
- ⊗ Diuretic + nitrate: hypotension
- ⊗ CCB + diuretic: hypotension
- ⊗ Doucet J, Chassagne P, et al. Drug-Drug interactions related to hospital admissions in older adults. J Am Geriatr Soc 1996;44(8):944-948.

Quality Measures for Safe Prescribing

- > Multiple step process
 - > Avoid "inappropriate" medications
 - > Use medication as indicated
 - > Monitor for side effects and drug levels
 - > Avoid drug-drug interactions
 - > Involve patient, recognizing his/her values

Polypharmacy

- > This number is variable, but typically use of 5 or more medications
- > Refers to both prescribed and nonprescription medications
- > Polypharmacy is an independent risk factor for adverse drug events (ADE)
- > Balance between clinical practice guidelines, safe prescribing (e.g. 85-year old new diabetic with hx HTN and COPD), goals, and appropriateness late in life



Inappropriate Medication Use

- Various criteria developed by expert panels
- Addresses "over-prescribing" and "inappropriate" use
 - Drug Burden Index
 - STOPP START Toolkit
 - Beers Criteria
- <http://www.cumbria.nhs.uk/ProfessionalZone/MedicinesManagement/Guidelines/StopstartToolkit2011.pdf>
- <http://www.americangeriatrics.org/files/documents/beers/PrintableBeersPocketCard.pdf>

Beers List

- Conceived of in 1991 by a geriatrician & targeted to frail elderly in nursing homes.
- Targeted "problematic" meds -- certain pharmacologic properties and physiologic changes
- Revised in 1997, 2003, & 2012
- In 2011, AGS undertook to update the list using evidence-based methodology.
 - This update (2012) targeted to community-dwelling elderly.

Beers List



- 53 medications on the list
- OTC medications on list; demonstrates we must begin to consider OTC
- Divided into 3 categories
 - Medications to generally avoid
 - Medications that are potentially inappropriate
 - Medications to use with caution

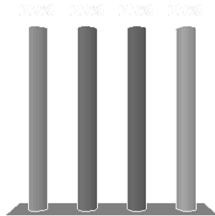
Beers List (cont'd)

- Goal is to reduce exposure to inappropriate meds
- Is a guide
- Should not be punitive
- Not meant to supplant provider judgment, patient's values, and goals of care
- Not to be used in certain groups of patients, e.g. Hospice



The 2012 Beers List includes each of the following, except:

- A. Amitriptyline
- B. Diphenhydramine
- C. Cyclobenzaprine
- D. It includes all of the above



Beers List (cont'd)

- For primary prevention, use aspirin with caution with adults > 79 years old
- Sliding scale insulin should be avoided in any care setting because higher risk of hypoglycemia without improvement of hyperglycemia
- Long-acting sulfonylureas (chlorpropamide and glyburide) should be avoided because of prolonged half-life and causing SIADH
- Avoid chronic use (>90 days) of nonbenzodiazepine hypnotics because of increased risk of falls, delirium, fractures

Beers List (cont'd)

- Megestrol AVOID because of minimal effect on weight and increase of thrombotic events and death
- Avoid diphenhydramine because potential to worsen cognitive impairment, delirium, constipation
- Desiccated thyroid avoid because of cardiac concerns and there are safer alternatives

Beers List (cont'd)

- Table 2 Highlights 34 potentially inappropriate medications and classes to avoid in older adults.
- Noteworthy:
 - Desiccated thyroid
 - Megestrol
 - SSI
 - Skeletal muscle relaxants

Beers List (cont'd)

- Table 3 Potentially inappropriate medications for Drug-Disease or Drug-Syndrome
- Pairs include:
 - Heart failure pioglitazone, NSAIDS/COX-2 inhibitors
 - Dementia H2-blockers
 - Falls SSRIs, sleepers
 - Seizures bupropion, tramadol, olanzapine
 - Parkinson's anti-psychotics (except quetiapine and clozapine)

Beers List (cont'd)

- Not only used by physicians but also governing bodies (e.g. CMS) to monitor quality of care provided
- Target 8 classes of medications
 - Antidepressants Antipsychotics
 - Benzos H-2 blockers
 - CCB ACE-I
 - Digoxin NSAIDs
- Target 4 prescribing problems
 - Inappropriate dose
 - Inappropriate duration
 - Duplications
 - Potential drug-drug interactions



Underutilization of Appropriate Medication

- Optimizing therapy is achieving balance between overprescribing and underprescribing
- Can result from
 - Attempt to avoid excess medication use
 - Desire to avoid complex medication regimen
 - Belief that patient won't benefit
 - Endeavor to minimize adverse effects

Assessing Care of Vulnerable Elderly (ACOVE) Project

- Expert Panel developed nearly 400 QIs encompassing 26 ACOVE conditions common to elderly
- Each QI reflects a care process that should be performed for all eligible patients, and if not performed indicates a deficiency in care quality
- Identified quality indicators (QI) for appropriate medication use



QIs Pertaining to Pharmacotherapy

- Prescribing to older adults offers special challenges
- Older adults take about 3 times as many prescription meds as younger counterparts
- Many medications need to be used with caution because of age-related changes in pharmacokinetics and pharmacodynamics



Improving Prescribing the ACOVE Way

- Medication list – up-to-date
- Drug regimen review – TBD annually
- Drug indication – define
- Patient education – how to use; side effects
- Response to therapy – document
- Continuing a medication – note compliance, adverse events, if not started or stopped give reason



Improving Prescribing the ACOVE Way

- Antipsychotic response
 - If begun on an antipsychotic, there should be documentation of assessment of response within 1 month
- Avoid strong anticholinergics
 - No vulnerable elderly should be prescribed any medication with strong anticholinergic effects if alternative are available
- Avoid chronic or high-dose benzos
 - If using > 1 month, discuss at least annually the risks; attempt to taper to d/c benzo
- Avoid barbiturates
 - If not requiring seizure control, avoid barbiturates



Adverse Drug Event (ADE)

- ADE is defined as an injury resulting from the use of a drug, including noxious responses, administration errors, or circumstances leading to error
- ADE's are responsible for an estimated 5 – 30% of acute geriatric admissions.
- 770K hospitalized patients experience ADE, costing an estimated \$5.6 million/yr.
- Data showed annually from 2007 – 2009, over 99,000 emergency hospitalizations of seniors 2d ADE
- In nursing homes, for every \$1 spent on medicine, an estimated \$1.33 in health care resources are consumed in treating drug-related morbidity and mortality.

Adverse Drug Events (cont'd)

- More than 95% of ADEs experienced by older adults are considered predictable.
- To emphasize:
 - GI bleed with NSAIDs
 - Hypoglycemia due to insulin
 - Urinary retention with opioids



Risk Factors for ADE

- Age over 85
- Low BMI/frailty
- More than 6 concurrent diagnoses
- CrCl less than 50 ml/min
- More than 9 medications
- More than 12 doses of medication/day prior to ADE
- Care transitions
- Memory impairment

Prescribing Cascade

- Occurs when a new drug is prescribed to treat a symptom that resulted from an unrecognized ADE related to existing
- Example: one study looked at approximately 3500 Medicare recipients age 65 – 99; those who received an antipsychotic 90 days prior were 5.4 times more likely to receive an anti-Parkinson medication when compared to cohorts not receiving an antipsychotic
- Example: senior using ducosate for constipation associated with iron use and is begun on loperamide for diarrhea

Drug-drug Interactions

- Is pharmacologic or clinical response to the administration of a drug combo that differs from the anticipated effect when each agent is given alone
- Seniors are particularly vulnerable to drug-drug interactions because of multiple comorbidities
- Likelihood increases as number of meds increases
- Most common offenders: cardiovascular and psychotropics
- Example: on warfarin for atrial fibrillation, on sertraline for depression, tramadol for chronic pain, and see ortho who prescribes indomethacin for gout






Age-Related Changes in Pharmacokinetics and Drug-Drug Interactions

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Dose-related ADEs

- Renal impairment
 - Occurs from failure to dose-adjust for renal impairment
 - Programs available assist with dose adjustment (e.g. Epocrates and Lexi-Comp)
 - RULE: initial starting dose for new medication should be reduced for elderly and titrated up slowly
- LTC setting
 - At particular risk since frail and polypharmacy

Prevention of ADE

- Drugs associated with preventable ADEs
 - Cardiovascular 
 - Diuretics 
 - NSAIDs 
 - Hypoglycemics 
 - Anticoagulants 

Prescribing Principles for Older Adults

Basics:

- Start with low dosage
- Titrate up slowly
- Avoid starting 2 or more meds at the same time

Before starting a new med, determine:

- Are there nonpharmacologic ways to treat?
- How & when will you assess the therapy?
- Are the potential benefits greater than the risks?
- Can 1 medication be used to treat 2 conditions?
- Determine if there are drug-drug or drug-disease interactions



Prescribing Principles (cont'd)

- Do the patient and the caregiver understand:
 - the purpose of the medication
 - how to take it
 - possible adverse events
 - what to do if an ADE occurs



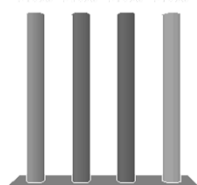
Prescribing Principles (cont'd)

Annually:

- Brown-bag all meds (RX, OTC, herbals) to office for review.
- List should contain brand and generic name, dose of tablet, dose to take, frequency, route
- Educate the patient as to combination pills (e.g. hydrocodone with acetaminophen)
- Do actual label directions match those in the chart?
- Eliminate unnecessary medications
- Simplify regimen as much as possible, with fewest meds and doses required for efficacy.
- Suggest blister packs (prefilled by pharmacist) or family filling medication organizer

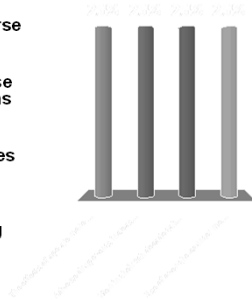
You are reviewing the medication list of an 88-year old female admitted to the hospital with CAP. She has a PMHx HTN, depression, hypothyroidism, and hyperlipidemia. Her medications from home have all been continued and include levothyroxine, atorvastatin, lisinopril, sertraline, and omeprazole. Which of the following statements is true?

- A. Use of statins increase risk of pneumonia.
- B. Her antidepressant should be held while hospitalized.
- C. 30% of patients on PPIs have no documented indication for one.
- D. The PPI will lower the gastric pH and increase absorption of antibiotic.



Mark all of the following statements that are true regarding medication use by seniors in the U.S.?

- A. The effects of age are more highly associated with adverse events than the number of medications taken.
- B. Adverse drug events increase as the number of medications taken increase.
- C. Men in their 9th decade take more medication than females in the same decade.
- D. Use of over-the-counter medications should be considered when discussing polypharmacy



Transdermal Fentanyl

- Never a "new start" medication
- 12.5 mcg patch equivalent to 30 mg morphine
- Ratio of oral morphine mg: fentanyl mcg/hr patch is 2:1
- Adjust by 25 – 50% for "incomplete cross tolerance"



Incomplete Cross Tolerance

- Relates to tolerance to a currently used opioid that does not extend to other opioids
- This will lower the dose of the second opioid
- This incomplete tolerance exists between all opioids and the difference between 2 opioids could vary widely
- Hence, RECOGNIZE the danger of using equianalgesic conversions without making adjustments and approximations
- Reduce by 25 – 50%

Disposing the Patch

- Since 1997 FDA reports approximately 35 exposures (mostly children), 12 deaths, 12 hospitalizations
- Wear gloves
- Fold patch in half with sticky sides together
- Flush



Other Considerations: Hepatic Dysfunction

- NOT RECOMMENDED:
 - Meperidine
 - Methadone
 - Codeine
- USE WITH CAUTION:
 - Morphine
 - Oxycodone
 - Hydromorphone
 - Hydrocodone
- SAFEST:
 - Fentanyl



Murphy E.J. Acute pain management pharmacology for the patient with concurrent renal or hepatic disease. Anaesth Intensive Care. 2005;33:311-2

Other Considerations: Renal Dysfunction

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*Broadbent A, et al. Progress in Palliative Care. 2003;11(4):183-190.
EPERC Fast Fact #161 at
http://www.eperc.mcw.edu/EPERC/FastFacts/Index/ff_161.htm*

Other Considerations: Titration

- Dose escalation of opioids should be done on a percentage increase.
 - For ongoing mild to moderate pain, increase by 25-50%
 - For ongoing moderate to severe pain, increase by 50-100%
- Frequency of dose escalation depends on drug half-life
 - Short-acting oral single agents: every 2 hours (e.g. morphine, oxycodone, hydromorphone)
 - Sustained release orals: every 24 hours
 - For methadone or transdermal fentanyl: no more than every 72 hours

EPERC Fast Fact #20

If Allergies To One...

Morphine	Phenylpiperidines	Diphenylheptanes
Codeine	Meperidine	Methadone
Morphine	Fentanyl	
Hydrocodone*	Sufentanil	
Hydromorphone*	Remifentanil	
Oxycodone*		

Pharmacist's Letter; Feb. 2006; 22

In Summary

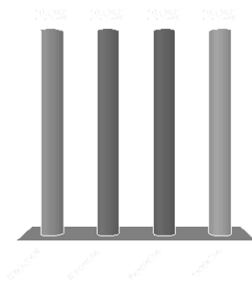
- Pharmacodynamic changes lead to increased sensitivity, especially cardiac and neurologic, to medications
- Pharmacokinetic changes lead to increased serum concentration levels of medications
- ADE are common in elderly; any new symptom should be considered drug-related until proven otherwise
- Various expert opinions and criteria exists to guide physicians as to medications that should not be prescribed or used with great caution. Physician compliance is important

In Summary

- > Preventable ADEs include drug-drug interactions, dose-related, and prescribing cascades.
- > CDC considers folding the Fentanyl patch (sticky sides together) and flushing it a reliable means of disposal
- > Mepiridine is on the Beers List and should not be used in seniors
- > Having an allergy to morphine precludes using of narcotics in the same class: codeine, hydrocodone, hydromorphone, and oxycodone

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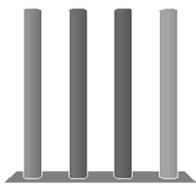
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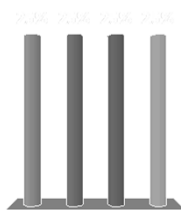
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Additional Resources

- ↳ 2012 "Special Article" published in the Journal of American Geriatrics. Please see <https://www.americanphysicianlogin.com/Upload/ItemPartDocs/3/11390-2012-BEERS-Criteria.pdf>
- ↳ AGS Beers Criteria Quick Reference Clinical Tool.
 - ⌘ There is a cost associated; 25 cards for \$20 (member.)
