

# Bad Drugs: It might not be dementia - It might be the medication!

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# Lecture Objectives

1. Recognize why seniors are prone to toxicity
2. Know the bad drugs that kill memory and send seniors to the emergency room
3. Describe what to do to reduce drug poisoning in seniors
4. Know that complementary & alternative drugs can also cause toxicity in older adults

# Medication Errors and Drug Toxicity

- Occur regularly in up to 59% of hospitalized patients
- Drug toxicity 4<sup>th</sup> leading cause of death: ahead of
  - » Pulmonary disease
  - » Diabetes Mellitus
  - » AIDS
  - » Pneumonia
  - » Accidents & Motor Vehicle Injuries
- ~31% of all hospital admissions in the elderly a result of adverse drug events

van den Bemt , *Drug Safety* 2000.

Raji MA. Polypharmacy. In *Encyclopedia of Health and Aging*. Markides KS, ed. Thousand Oaks, 2007.

Institute of Medicine, National Academy Press 2000.

## A 77 year-old man with urinary tract infection

- Saw his primary care doctor on a Friday
- Has been on enalapril 20 mg once daily for 5 years to control his high blood pressure
- An antibiotic was started



## A 77 year-old man with urinary tract infection

- On Monday, patient was rushed to the emergency room for irregular heart beat, dizziness, and high blood potassium ( $K=8$ )
- Admitted to the Intensive Care Unit



Which of the following antibiotics is responsible for the high potassium level-related hospitalization in this man?

- (A) Nitrofurantoin
- (B) Amoxicilin
- (C) Bactrim
- (D) Levafloxacin
- (E) Keflex



## Renal mechanism of trimethoprim-induced hyperkalemia

- Trimethoprim (in bactrim) is structurally and pharmacologically similar to the potassium-sparing diuretic amiloride
- It reduces urinary potassium excretion by approximately 40%
- Can cause high blood potassium level when used with other potassium sparing drugs

*Ann Intern Med.* 1993

## Trimethoprim-sulfamethoxazole-induced hyperkalemia in patients receiving inhibitors of the renin-angiotensin system: a population-based study

- Bactrim (trimethoprim-sulfamethoxazole) use was associated with a 7-fold increased risk of hyperkalemia-associated hospitalization in older patients on ACEIs or ARBs
- No such risk was found with the use of comparator antibiotics

Arch Intern Med. June 2010 28;170(12):1045-9.



# Hospital admission for drug toxicity

- **Hypoglycemia:** 6-fold increased risk if bactrim used in previous week in seniors already on glyburide
- **Digoxin toxicity:** 12-fold increased risk if macrolide used in previous week in those on chronic digoxin
- **Hyperkalemia:** 20-fold increased risk if potassium-sparing diuretics used within a week in patients on chronic ACE inhibitors

JAMA. 2003 Apr 2;289(13):1652-8.



# Why are seniors more prone to adverse effects of medications?

- Unable to eliminate drugs quickly
- On too many drugs
- On bad drugs or high risk drugs



# Why are elders prone to drug toxicity

- Most drugs are eliminated by liver and/or kidneys
- Kidney and liver function decrease with aging
- So older adults are unable to eliminate drugs quickly
- Drugs at normal young adult doses can result in overdose in the elderly



# Why are elders prone to drug toxicity

- Drugs need to be started at low dose in seniors
- Frequent evaluation of levels & effects of the top 3 drugs that cause a third of ER visits for drug toxicity
  - » Digoxin
  - » Coumadin
  - » Insulin



# Polypharmacy

- “Using too many drugs”
- Refers to patient being on  $> 3$  drugs
- More drugs = higher risk of drug toxicity
- 6 drugs = 27% chance of drug toxicity

# Polypharmacy

- Two types
  1. Harmful Polypharmacy – bad drugs
  2. Rational Polypharmacy – good drugs

# Rational Polypharmacy: when seniors must be on several drugs

- Plus other drugs for
  - » Hypertension
  - » Diabetes
  - » Hyperlipidemia
  - » Atrial fibrillation



# Rational Polypharmacy: when seniors must be on several drugs

- CHF
  - » Beta blocker
  - » ACE inhibitors
  - » furosemide
  - » digoxin
  - » spironolactone





# How do seniors end up being on bad drugs – bad polypharmacy?

- Prescribing cascade
- Failure to use non-drug methods
- Failure to stop a drug when initial condition no longer exists
- Seeing many MDs & pharmacists who don't talk to one another

# Prescribing cascade

Rochon & Gurwitz. *BMJ* 1997;315:1096-1099

- The clinician prescribes a 2<sup>nd</sup> drug to treat the side effects of the 1<sup>st</sup> drug whose indication is often unclear.
- Followed by a 3<sup>rd</sup> drug to treat the side effects of the 2<sup>nd</sup> drug.
- And so the cascade of incremental prescribing continues.



## Prescribing Cascade: Mr. K Age = 76 Yr

- Seen in clinic by his PCP; BP=140/85
- Receives amlodipine 5 mg once daily
- Develops feet swelling
- Receives furosemide & potassium



Raji MA. Polypharmacy. In *Encyclopedia of Health and Aging*.  
Markides KS, ed. Thousand Oaks, CA: Sage Publications, 2007.

## Prescribing Cascade: Mr. K Age = 76 Yr

- Potassium pills aggravates his heartburn
- Receives omeprazole, develops diarrhea
- Receives lomotil (atropine/diphenoxylate)
- Dizzy, delirious, fell & sustained hip fracture

- Raji MA. Polypharmacy. In *Encyclopedia of Health and Aging*. Markides KS, ed. Thousand Oaks, CA: Sage Publications, 2007.



## Examples of prescribing cascade

- » Dizziness from anti-hypertensive treated with meclizine
- » Feet swelling from a calcium-channel blocker treated with furosemide and KCL
- » Parkinson tremors from metoclopramide treated with drugs for Parkinson's disease
- » Hypertension from NSAID's (e.g. ibuprofen or naproxen) treated with antihypertensives

*“Any symptom in an elderly may be a drug side effect until proven otherwise”*

(Gurwitz)

## Poor communication contributes to the high rates of drug poisoning in seniors

- **Doctors' failure** to recognize and respond to drug toxicity symptoms reported by patients
- **Patients' failure** to recognize and report drug toxicity symptoms to doctors

Gandhi et al. Adverse drug events in ambulatory care. *N Engl J Med* 2003;348:1556-64.

Bates et al. Incidence of adverse drug events and potential adverse drug events: implications for prevention. *JAMA* 1995;274:29-34.

# Common symptoms of drug toxicity in the elderly

Deconditioning	Weight loss
Dizziness,	Memory loss
Dysmobility	Insomnia
Drowsiness	Incontinence
Delirium	Constipation
Dehydration	Fatigue
Depression	Nausea & Vertigo
Diarrhea	Sedation
Death	Falls and poor balance





## Electronic prescribing systems improves patient safety by offering drug allergy and drug interaction alerts

- Computerized clinician order entry reduces medication errors among inpatients & outpatients *if the warnings are heeded*



*Arch Intern Med* 2009 ;169(3):305-11.

*Arch Intern Med* 2003;163(21):2625-31.

# Reducing Polypharmacy

Use one drug to treat multiple symptoms:

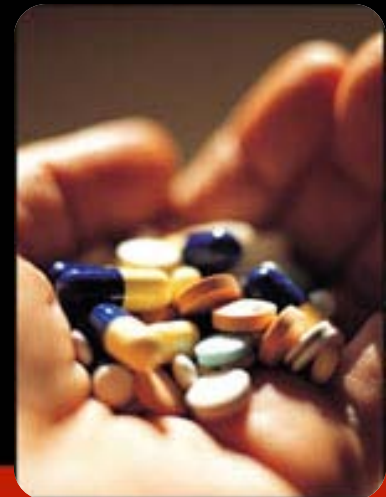
- Mirtazapine (remeron): depression, weight loss\*, insomnia, anxiety, nausea\*, emesis\*, tremors\*, diarrhea\* & pruritus\*
- Duloxetine (cymbalta): diabetic neuropathic pain, depression, anxiety & incontinence\*

Raji M. *Lancet Oncol* 2005.

Raji M. *Chest* 2006.

Raji M, et al. *Ann Pharmacother* 2007.

\* *Off label use*



# Improving patient understanding of prescription drug label instructions

Seniors with Low Health Literacy on Glipizide, 5 mg

Times per day	Take 2 pills by mouth 2 times daily	<b>33% follow instructions</b>
Time periods	Take 2 pills in the morning and 2 pills in the evening	<b>76% follow instructions</b>
Specific times	Take 2 pills by mouth at 8 a.m. and 2 pills at 6 p.m.	<b>70% follow instructions</b>

Use *explicit times periods* (i.e., morning) or *precise times of day* versus instructions with times per day (i.e., twice) or hourly intervals

# Medications associated with adverse symptoms when stopped suddenly

- Chronic Anti-Epileptic Drugs
- Chronic Corticosteroids
- Chronic Clonidine
- Chronic Beta Blockers, e.g., toprol
- Chronic Benzodiazepine, e.g. ativan

Graves et al. *Arch Intern Med* 1997.

# Avoid drugs on the Beers' list of bad drugs “inappropriate drugs in the elderly”

- These have higher potential for bad outcomes than benefits in elders



Beers MH. *Arch Intern Med* 1997;157:1531-36.

Ficks et al. *Arch Intern Med* 2003;163:2716-24.

Raji et al. *Ann Pharmacother* 37:1197-1202, 2003.

# Avoid drugs on the Beers' list of bad drugs “inappropriate drugs in the elderly”

- Most are ineffective or have very high toxicity, e.g., muscle relaxants e.g., carisoprodol



Beers MH. *Arch Intern Med* 1997;157:1531-36.

Ficks et al. *Arch Intern Med* 2003;163:2716-24.

Raji et al. *Ann Pharmacother* 37:1197-1202, 2003.

## Bad medications that seniors should avoid – See your doctor

- Barbiturates
- Meprobamate
- Belladonna alkaloids
- Dicyclomine
- Hyoscyamine
- Carisoprodol
- Chlorzoxazone
- Cyclobenzaprine
- Metaxalone
- Methocarbamol
- Atropine (in lomotil)

Beers MH. *Arch Intern Med* 1997;157:1531-36; Ficks et al. *Arch Intern Med* 2003;163:2716-24;  
Raji et al. *Ann Pharmacother* 37:1197-1202, 2003

## Medications that can kill your memory

- Long-acting benzodiazepine: diazepam (valium), chlordiazepoxide (librium)
- Narcotics: meperidine & propoxyphine

Iwagwu CU, Steiner V, Raji MA. Medication-related cognitive impairments in the elderly. *Clinical Geriatrics* 2008;16;8:11-14.

Raji MA. Polypharmacy. In *Encyclopedia of Health and Aging*. Markides KS, ed. Thousand Oaks, CA: Sage Publications, 2007.



## Medications that can kill your memory

- Anticholinergics: high dose amitryptiline for depression, chronic use of diphenhydramine for insomnia (many brands)

Iwagwu CU, Steiner V, Raji MA. Medication-related cognitive impairments in the elderly. *Clinical Geriatrics* 2008;16;8:11-14.

Raji MA. Polypharmacy. In *Encyclopedia of Health and Aging*. Markides KS, ed. Thousand Oaks, CA: Sage Publications, 2007.

# Never prescribe diphenhydramine for insomnia in the elderly

- Benadryl®
- Benadryl® Allergy
- Benadryl® Allergy Ultratab®
- Benadryl® Dye-Free Allergy Children's
- Diphenhist®
- Diphenhydramine Hydrochloride Caplets®
- Nytol® QuickCaps® Caplets®
- Excedrin P.M.® Tablets
- Bayer® PM
- Tylenol® PM
- Goody's® PM Powder
- Simply Sleep® Nighttime Sleep Aid
- Sleepinal® Night-time Sleep Aid Softgels®
- Unisom® SleepGels® Maximum
- Diphen® AF Elixir

## Medications That May Impair Cognitive Function in the Elderly

Impact	Drug Category	Examples
Learning, memory, and attention	Tricyclic antidepressants	Amitriptyline, doxepin
	Antispasmodics, gastrointestinal	Belladonna alkaloids, dicyclomine
	Antispasmodics, genitourinary	Short-acting oxybutynin chloride
	Muscle relaxants	Cyclobenzaprine, methocarbamol
	Antihistamines	Diphenhydramine
Wakefulness and alertness	Benzodiazepines	Chlordiazepoxide, diazepam
	Antiepileptics	Long-acting barbiturates
	Antipsychotics	Thioridazine, mesoridazine, chlorpromazine
Orientation and reality awareness	Narcotics	Propoxyphene, meperidine
	Nonsteroidal anti-inflammatory drugs	Indomethacin, piroxicam
	Corticosteroids	Prednisolone
	Antidiarrheals	Diphenoxylate and atropine
	Histamine-2 receptor antagonists	Cimetidine
	Antihypertensive agents	Clonidine

*Contains information from references 10, 13, 16-21.*

# Complementary Meds & Toxicity

- Alternative and Complementary Medications can also harm or kill
- Never use Kava Kava – causes liver failure, sometimes requiring liver transplantation
- Never use grapefruit juice to take your pills – it raises levels of drugs
  - » Statins
  - » Verapamil
  - » Viagra
  - » felodipine



## Seniors on any prescription medications should avoid using St. John's Wort

- Used for mild depression
- St John's Wort induces the activity of liver enzymes
- Leads to reduced effectiveness of 50% of all marketed drugs

*JAMA*. 2003;290:1500-4

# Seniors on any blood thinner must avoid *Ginkgo biloba*

- *Ginkgo biloba* extract (EGb 761) used for memory loss
- Ginkgo increases the risk of bleeding in patients on
  - » Plavix
  - » coumadin or any blood thinner



Ginkgo Biloba

Ginkgo Biloba

**Summary:**  
**How to avoid drug  
poisoning in older adults**

## Preventing drug poisoning in seniors

# Just Say No

- No meperidine as analgesic, *ever!*
- No Kava Kava, *ever!*
- No grapefruit juice with your pills, *ever!*
- No bactrim with chronic ACEI or ARBs
- No bactrim with glyburide
- No Gingko with blood thinners
- No St Johns Wort with prescription drugs



# Preventing drug poisoning in seniors

- Review all medications including non-prescription and herbal preparations
- Check for interactions (drug, dx & food)
- Start seniors on low drug dose, then go slow with dose increase based on response & safety

# Preventing drug poisoning in seniors

- Simplify therapeutic regimen
- Use instructions with explicit times periods (i.e., morning) or precise times of day
- All drugs may cause illness

*“Any symptom in an elderly may be a drug side effect until proven otherwise”*

(Gurwitz)

*“All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy”*

*Paracelsus (1493-1541)*



# Thank you



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