

Geriatric Pharmacology & Its Considerations

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OBJECTIVES

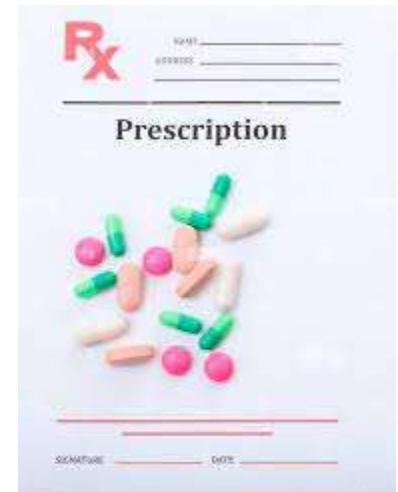
- 1) Identify the physiologic changes associated with normal aging that influence pharmacokinetics and pharmacodynamics
- 2) Avoid potentially harmful medications for older adults
- 3) Recognize Adverse Drug Events (ADEs) when an older adult presents with a new condition or complaint
- 4) Utilize strategies for evaluating starting and stopping medications

IRAN'S STATISTICS

- Rapidly changing demographic pattern
- The latest census : 10.2% of the country's population are elder
- Iran has one of the most accelerating rate of elder population in the world
- By 1420, the ratio of elder population will reach 20%

CHALLENGES OF PRESCRIBING FOR OLDER ADULTS

- Multiple medical conditions
- Multiple medications
- Multiple prescribers
- Different metabolisms and responses
- Adherence and cost
- Supplements, herbals, and OTC drugs



LOTS OF MEDICATIONS AND LITTLE EVIDENCE

- 2/3 of older adults are on regular medications
- Adults age >65 account for 33% of all prescriptions
- Older adults are frequently not included in clinical trials, which makes it difficult to predict drug metabolism or drug effects

ADVERSE DRUG EVENTS (ADE)

Adverse symptoms

Adverse clinical outcomes

- Doctor visits or hospitalizations
- Falls
- Functional decline
- Changes in cognition (delirium)
- Death

Poor adherence, poor quality of life

Increased cost



PHYSIOLOGIC CHANGES WITH NORMAL AGING

- Less Water
- More Fat
- Less muscle mass
- Slowed hepatic metabolism
- Decreased renal excretion
- Decreased responsiveness and sensitivity of the baroreceptor reflex



ABSORPTION

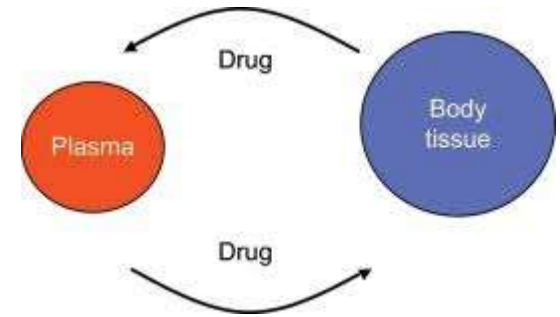
- Not affected by the normal aging process
- altered nutritional habits, greater consumption of drugs (eg, antacids and laxatives)
 - Antacids, PPIs, H2 blockers
 - Iron, Calcium, Zinc

Can be affected by disease

- Lack of intrinsic factor (B12 absorption)
- Delayed gastric emptying (e.g. diabetic gastroparesis)



DISTRIBUTION



- Less water = ↓ volume of distribution

Higher concentration of water soluble drugs

- More fat = ↑ volume of distribution

Prolonged action of fat-soluble drugs (increased half-life)

- Lower serum proteins (like albumin) increases the concentration of unbound (free or active) form of drugs

Some changes related to aging that affect pharmacokinetics of drugs.

Variable	Young Adults (20–30 years)	Older Adults (60–80 years)
Body water (% of body weight)	61	53
Lean body mass (% of body weight)	19	12
Body fat (% of body weight)	26–33 (women)	38–45
	18–20 (men)	36–38
Serum albumin (g/dL)	4.7	3.8
Kidney weight (% of young adult)	100	80
Hepatic blood flow (% of young adult)	100	55–60

METABOLISM



- Slowed Phase I, cytochrome P450, reactions
 - Oxidation, reduction, dealkylation
 - Many drugs level may be higher because of altered metabolism
- Phase II reactions are essentially unchanged
 - Conjugation, acetylation, methylation
- Drug-drug interactions
 - Increased risk with increased number of drugs

EFFECTS OF AGE ON HEPATIC CLEARANCE OF SOME DRUGS

Age-Related Decrease in Hepatic Clearance

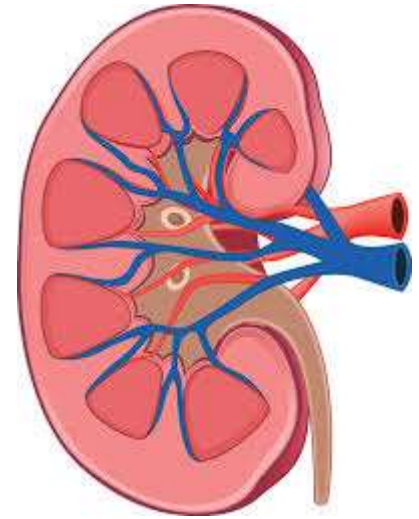
- Alprazolam
- Barbiturates
- Chlordiazepoxide
- Clobazam
- Diazepam
- Flurazepam
- Imipramine
- Meperidine
- Nortryptiline
- Propranolol
- Theophylline

EFFECTS OF AGE ON HEPATIC CLEARANCE OF SOME DRUGS

No Age-Related Difference Found

- Isoniazid
- Lidocaine
- Lorazepam
- Oxazepam
- Nitrazepam
- Prazosin
- Warfarin
- Salicylate

EXCRETION



Renal

- Renal clearance may be reduced

Drug & active drug metabolites may accumulate

- Prolonged therapeutic action
- Adverse effects

SOME PHYSIOLOGIC CHANGES ASSOCIATED WITH ALTERED DRUGS RESPONSE

➤ Cardiac Disease

- Impaired cardiac output (decreased absorption, metabolism, clearance)
- Greater susceptibility to cardiac adverse effects

➤ Kidney and Liver Disease

- Decreased drug clearance and altered metabolism

➤ Neurological Diseases

- Diminished neurotransmitter levels
- Greater susceptibility to neurological effects

Table 4. Selected High-Risk Drugs

Drug	Potential Harm	Comment
Insulin and sulfonylureas	Hypoglycemia	May often be appropriate; however, aggressive glycemic control may often yield greater harms than benefits in older adults ^{34,71,72}
Warfarin	Gastrointestinal, intracranial bleeding	Although a high-risk drug, benefits of warfarin therapy often outweigh harms; maintenance of prothrombin time international normalized ratio in therapeutic range tightly linked to risk/benefit ratio ⁷³
Digoxin	Impairment of cognition, heart block	May have a third-line role in management of systolic heart failure; suboptimal choice for rate control in atrial fibrillation
Benzodiazepines	Falls	Associated with as much as a 60% increase in fall risk ⁷⁴
Diphenhydramine, other first-generation antihistamines	Impaired cognition, urinary retention in men	Poor choice as sleep aid due to anticholinergic effects, next-day sedation, impact on performance including driving; close medication reconciliation important because patients may also obtain over-the-counter drugs
Antipsychotics	Death, pneumonia	Elevated risk of death when used to treat behavioral complications of dementia, although in selected cases, benefits may exceed risks if consistent with patient goals of care ⁷⁵

Account for
1/3 of ED
visits for
ADE

BEERS CRITERIA

- Potentially inappropriate medications for older adults.
- Originally conceived by Dr. Mark Beers
- Published in 1991, revised in 1997, 2002, and 2012.
- Consensus-based, but statistical association with adverse drug events
- Adopted for nursing home regulation.
- Does not account for the complexity of a patient's entire medication regimen.

AGS BEERS CRITERIA RESOURCES

From THE AMERICAN GERIATRICS SOCIETY

A POCKET GUIDE TO THE AGS BEERS CRITERIA

This clinical tool, based on *The AGS 2012 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (AGS 2012 Beers Criteria)*, has been developed to assist healthcare providers in improving medication safety in older adults. Our purpose is to inform clinical decision-making concerning the prescribing of medications for older adults in order to improve safety and quality of care.

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause adverse drug events in older adults due to their pharmacologic properties and the physiologic changes of aging. In 2011, the AGS undertook an update of the criteria, assembling a team of experts and funding the development of the *AGS 2012 Beers Criteria* using an enhanced, evidence-based methodology. Each criterion is rated (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document together with accompanying resources can be viewed online at www.americangeriatrics.org.

INTENDED USE

The goal of this clinical tool is to improve care of older adults by reducing their exposure to potentially inappropriate medications (PIMs).

- This should be viewed as a guide for identifying medications for which the risks of use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.
- Implicit criteria such as the STOPP/START criteria and Medication Appropriateness Index should be used in a complementary manner with the 2012 AGS Beers Criteria to guide clinicians in making decisions about safe medication use in older adults.

The criteria are not applicable in all circumstances (eg, patients receiving palliative and hospice care). If a clinician is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that the potential for an adverse drug effect can be incorporated into the medical record and prevented or detected early.

AGS THE AMERICAN GERIATRICS SOCIETY
Geriatrics Health Professionals.
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http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012

BEERS CRITERIA: ANTICHOLINERGIC MEDICATIONS

Antihistamines (1st generation)

- Diphenhydramine
- Hydroxyzine
- Promethazine

Antispasmodics

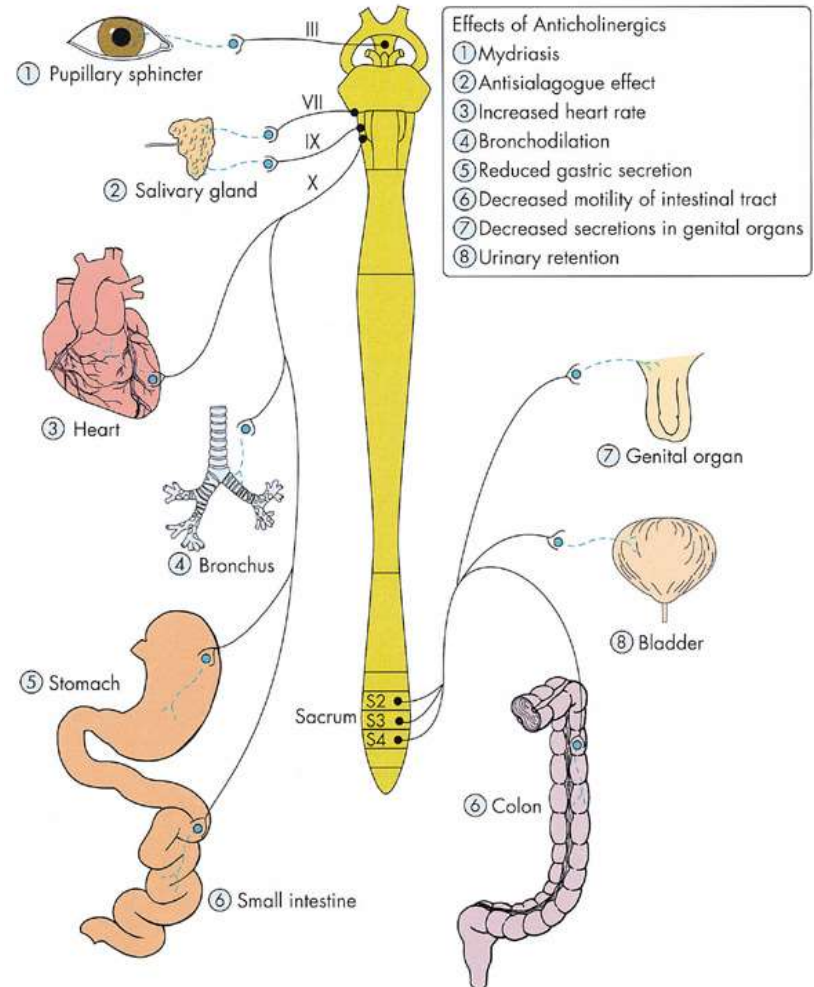
- Dicyclomine
- Hyoscine
- Scopolamine
- Propantheline

Skeletal Muscle Relaxants

- Methocarbamol (Robaxin)

Tricyclic Antidepressants

- Amitriptyline
- Imipramine
- Doxepin



BEERS CRITERIA: BENZODIAZEPINES

- **Increased sensitivity for older adults**

- Slowed metabolism, especially long-acting agents
- Similar neurocognitive effects to alcohol
- May cause a paradoxical reaction (increased agitation)

- **Increased risk of adverse clinical events**

- Falls and fractures
- Cognitive impairment
- Delirium

- **Caution: avoid if possible**

- Appropriate if being used for seizures, alcohol withdrawal, severe anxiety, or periprocedural anesthesia
- If necessary, use lowest dose possible

BEERS CRITERIA: SEDATIVE-HYPNOTICS

- **Nonbenzodiazepine Hypnotics**

- Eszopiclone (Lunesta)
- Zolpidem (Ambien)
- Zaleplon (Sonata)

- **Benzodiazepine-receptor agonists**

- **Adverse events similar to those of benzodiazepines**

- **Increased risk for delirium, falls fractures**

BEERS CRITERIA: ANTIPSYCHOTIC MEDICATIONS

- **FDA “Black Box” warning:** increased risk of death, mostly due to cardiovascular events (eg. heart failure, sudden death) and infections (eg. pneumonia)
- **Avoid using for behavioral problems associated with dementia**
 - Try non-pharmacologic interventions
 - Reserve for threat to self or others
- **Typical (First Generation, Conventional)**
 - Haloperidol (Haldol)
 - Perphenazine
 - Fluphenazine
- **Atypical (Second Generation)**
 - Risperdone (Risperdal)
 - Quetiapine (Seroquel)
 - Olanzapine (Zyprexa)
 - Ziprasidone (Geodon)
 - Aripiprazole (Abilify)
- **Adverse Effects**
 - Arrhythmias (QT prolongation)
 - Abnormal Movements (Parkinsonism, tardive dyskinesia)



ANTIPSYCHOTICS CONSIDERATIONS

- There is no evidence that these drugs have any beneficial effects in Alzheimer dementia
- On theoretical grounds the antimuscarinic effects of the phenothiazines might be expected to worsen memory impairment and cognitive dysfunction
- **thioridazine** : appropriate choice when sedation is desired
- If sedation is to be avoided, haloperidol or a second generation (atypical) antipsychotic is more appropriate
- **Phenothiazines**: risk of **orthostatic hypotension**
- Evidence supporting the **benefits of olanzapine** is somewhat stronger

ANTIDEPRESSANTS CONSIDERATIONS

- Preference of selective serotonin reuptake inhibitors (SSRIs) to tricyclic antidepressants
- SSRIs have fewer autonomic adverse effects
- In tricyclics: a drug with reduced antimuscarinic effects should be selected, eg, nortriptyline or desipramine

BEERS CRITERIA: PAIN MEDICATIONS

- **Non-COX-selective NSAIDs**

- GI bleeding and peptic ulcer disease
- Avoid chronic use

- **Indomethacin and Ketorolac**

- Higher risk of GI, renal, and CNS effects

- **Meperidine**

- Can cause neurotoxicity
- Safer alternatives available

PAIN MANAGEMENT

- Unfortunately, studies show that opioids are consistently **underutilized** in patients who require **strong analgesics for chronic severely painful** conditions such as **cancer**.
- In contrast, **opioids** have been **overprescribed** in many countries for poorly documented indications, resulting in the widely reported epidemic of opioid addiction and overdose deaths

CAUTION AND WARNING FOR PRESCRIBERS

- Question the need for new medications
- Stop medications, whenever possible
- Prioritize treatments
- Weigh risks and benefits
- Avoid undertreating older patients
 - Pain
 - Systolic hypertension (stroke, renal failure, CHF)
 - Anticoagulation and atrial fibrillation (stroke)

“START LOW AND GO SLOW...”

- Start one medication at a time.
- Start with a low dose and increase gradually.
- Once daily is usually best.
- Monitor for response and adverse effects.
- Assess adherence with regimen.



“...BUT, GO ALL THE WAY!”

- Be conservative, but don't miss the target!
- What is your goal? Are you achieving it?
- Can you keep increasing the dose or are you limited by side effects?
- Are you observing a clinical benefit at lower doses?
- Consider stopping if you can't “go all the way” and the benefit is not clear.

“DEPRESCRIBING”

“Systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s care goals, current level of functioning, life expectancy, values, and preferences.”

“DEPRESCRIBING” SHOULD BE CONSIDERED

- New symptom or clinical syndrome suggestive of ADE
- Advanced disease, terminal illness
- High-risk drugs or combinations
- Preventive drugs for scenarios associated with no increased risk despite stopping drug
 - Stopping alendronate after 5 years of treatment results
 - Stopping statins for primary prevention
- Patient/family willing to participate in shared decision

“DEPRESCRIBING”

- Instruct patient to bring all medications to visit (prescription and non-prescription)
- **What Are Current Indications for Each Drug?**
- **Is the Patient Actually Taking the Drug?**
- **Does the Likely Benefit of the Drug Outweigh Its Potential for Harm?**
 - High-risk medications (see Beers Criteria)
 - Time to benefit for preventive medications

BEERS CRITERIA (2012)

Digoxin (Lanoxin) > 0.125 mg/day

- Higher dosages associated with no additional benefit and may increase risk of toxicity
- Slow renal clearance may lead to risk of toxic effects

Dronedarone (Multaq)

- Worse outcomes reported in patients with permanent atrial fibrillation or heart failure
- In general, rate control is preferred over rhythm control

Spirolactone (Aldactone) >25mg/day

- Higher risk of hyperkalemia at higher doses (especially if taking NSAID, ACE-I, ARB, or K⁺ supplement)
- Avoid in patients CrCl < 30 mL/min

A FEW PRINCIPLES IN GERIATRIC PHARMACOTHERAPY

- 1. Take a careful drug history. The disease to be treated may be drug-induced, or drugs being taken may lead to interactions with drugs to be prescribed.
- 2. Prescribe only for a specific and rational indication. Do not prescribe omeprazole for “dyspepsia.” Expert guidelines are published regularly by national organizations and websites such as UpToDate.com.
- 3. Define the goal of drug therapy. Then start with small doses and titrate to the response desired.

A FEW PRINCIPLES IN GERIATRIC PHARMACOTHERAPY

- 4. Maintain a high index of suspicion regarding drug reactions and interactions. Know what other drugs the patient is taking, including over-the counter and botanical (herbal) drugs.
- 5. Simplify the regimen as much as possible. When multiple drugs are prescribed, try to use drugs that can be taken at the same time of day.
- Whenever possible, reduce the number of drugs being taken.

