

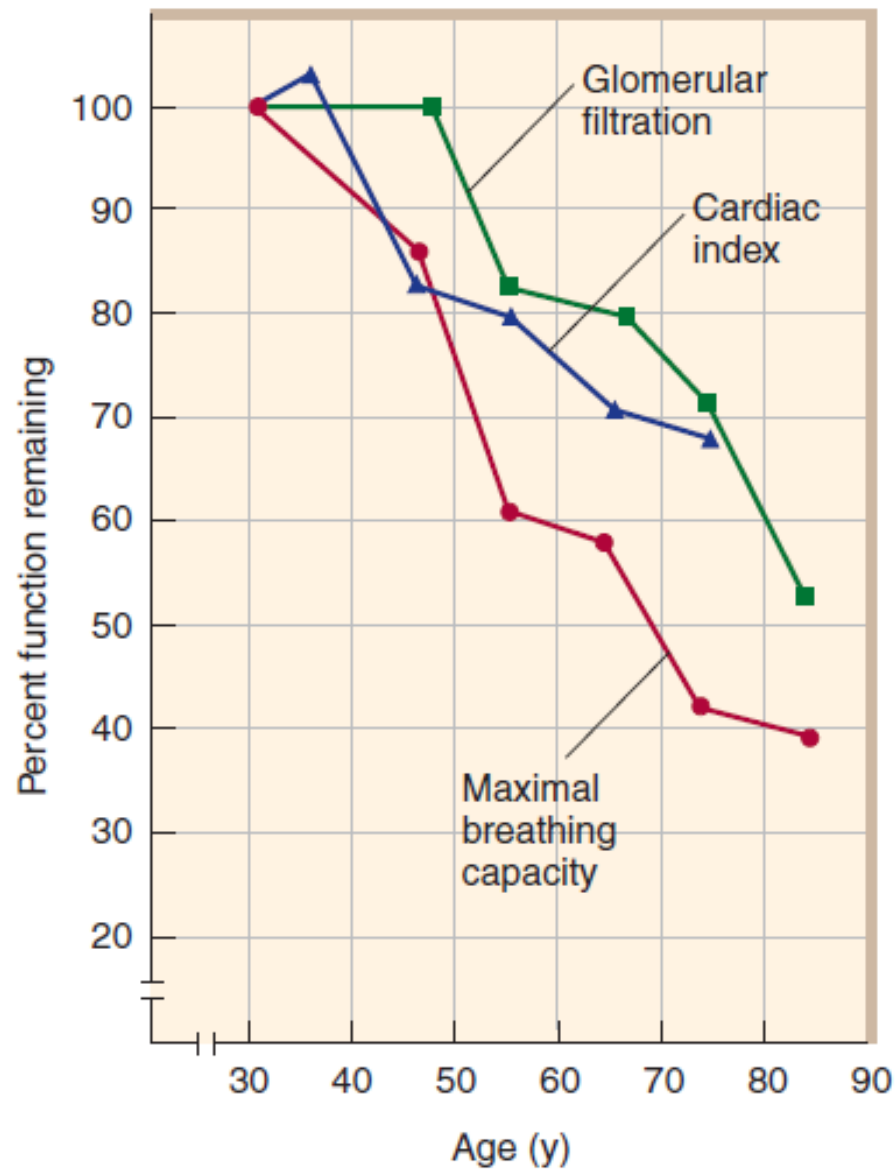
# **Drug Use in the Elderly**

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# Therapeutic Considerations in the Elderly

- **Elderly patients are those 65 years of age and older.**
- **Those who are > 65 years are NOT a one similar group.**
- **Institutionalized individuals are also different from those living in the community.**
- **Age-related changes in physiology can affect both the pharmacokinetics and the pharmacodynamics of drugs.**



**FIGURE 60-1** Effect of age on some physiologic functions.

(Modified and reproduced, with permission, from Kohn RR: *Principles of Mammalian Aging*. Prentice-Hall, 1978.)

**TABLE 60–1** Some changes related to aging that affect pharmacokinetics of drugs.

| Variable                              | Young Adults<br>(20–30 years) | Older Adults<br>(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)<br>18–20 (men)  | 38–45<br>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                         |

# Therapeutic Considerations in the Elderly

- Drug-related problems in older adults are common and cause significant morbidity.
- Common medical conditions in the elderly include: hypertension, diabetes mellitus, osteoporosis, bronchial asthma, COPD, cancer, arthritis, heart diseases, Alzheimer's disease and cognitive dysfunction, and stroke.

# Therapeutic Considerations in the Elderly

- The most common sensory impairments are difficulties in hearing and vision.
- The elderly are also prone to falls.

# Human Aging & Changes in Drug Pharmacokinetics and Pharmacodynamics

**Clinical manifestations of normal aging include:**

- 1. Changes in biochemical makeup of tissues.**
  - 2. Reduced functional capacity of body systems.**
  - 3. Reduced ability to adapt to physiological stress.**
  - 4. Increased vulnerability to disease.**
  - 5. Frailty (weakness, fatigue, weight loss and functional decline). (ضعف وهشاشة)**
- Individuals experience aging at different rates.**

# Common Physiological Changes Associated with Aging

**They include:**

- a) Reduced functional reserve capacity.**
- b) Reduced ability to maintain homeostasis, making them susceptible to de-compensation in stressful situations.**



# **Common Physiological Changes Associated with Aging**

**Examples of such impaired homeostatic mechanisms:**

- 1) Postural or gait instability**
- 2) Orthostatic blood pressure responses**
- 3) Thermoregulation impairment**
- 4) Reduction of cognitive reserve**
- 5) Bowel or bladder dysfunction.**

# Age-Related Altered Drug Pharmacokinetics

## Absorption:

- Absorption of drugs may be affected by age-related changes in GIT physiology, drug-food interactions, concurrent medication, and co-morbidities affecting GI function.
- 1. The bioavailability of drugs absorbed by **passive diffusion** may not be affected significantly.
- Drugs absorbed by **active transport** (vitamin B<sub>12</sub>, calcium, iron, magnesium) may have impaired absorption.

# Age-Related Altered Drug Pharmacokinetics

2. First-pass effect is decreased, leading to an increase in bioavailability and plasma concentration of some drugs (propranolol, labetolol, chlorpromazine, diazepam, imipramine, lidocaine, midazolam, morphine), while the bioavailability of some pro-drugs is reduced (enalapril, codeine, aspirin, levodopa, valacyclovir, prednisone, sacubitril, ..).

# Age-Related Altered Drug Pharmacokinetics

3. In the presence of atrophic gastritis, or in patients taking gastric acid-lowering agents, the extent of absorption of drugs requiring an acidic environment for absorption may be reduced (conazoles, iron, aspirin, NSAIDs, penicillins, phenytoin, ..).

# Age-Related Altered Drug Pharmacokinetics

## Distribution:

Factors that influence drug distribution in the elderly:

1. Altered plasma protein concentrations.
2. Individual's body composition (body fat and intracellular fluid content).
3. Decreased muscle and tissue mass.
4. Reduced blood flow to tissues and organs.
5. Active uptake into tissues may be influenced by ageing.

# Age-Related Altered Drug Pharmacokinetics

- The volume of distribution of water-soluble drugs (**ethanol, gentamicin**) is reduced.
- Lipophilic drugs (**benzodiazepines, metronidazole, and rifampin**) exhibit an increased volume of distribution.
- **Changes in the volume of distribution affect loading doses of drugs.**

# Age-Related Altered Drug Pharmacokinetics

- The brain of elderly patients may be exposed to higher concentrations of drugs and toxins because of age-related changes in the blood-brain-barrier.

# Age-Related Altered Drug Pharmacokinetics

## Metabolism:

- Hepatic metabolism of drugs depends on liver perfusion, activity and capacity of drug metabolizing enzymes, and protein binding.
- All of these factors are affected by the aging process.



# Age-Related Altered Drug Pharmacokinetics

- For drugs that have high intrinsic clearance (high hepatic extraction ratio), hepatic clearance depends on hepatic blood flow mainly (flow-limited metabolism).
- Age-related decreases in hepatic blood flow (20-50%) can decrease significantly the metabolism of high extraction ratio drugs (propranolol, amitriptyline, diltiazem, lidocaine, metoprolol, morphine and verapamil).

# Age-Related Altered Drug Pharmacokinetics

## Elimination:

- There is age-related reductions in GFR.
- Serum creatinine is a poor indicator of renal function in the elderly because creatinine is produced by muscles and there is reduced muscle mass in the elderly.
- Accurate measurement of  $CL_{cr}$ , rather than eGFR, is required for dose adjustment in patients with reduced renal function.

# Age-Related Altered Drug Pharmacokinetics

- Dosing guidelines of drugs that are eliminated by the kidney are based on creatinine clearance.
- ✓ Some drugs should be avoided when  $CL_{cr} < 30$  mL/min: colchicine, co-trimoxazole, glyburide, nitrofurantoin, probenecid, spironolactone, triamterene...
- ✓ Some drugs need dose reduction in reduced renal function: acyclovir, amantadine, ciprofloxacin, gabapentin, ranitidine, aminoglycosides, vancomycin...

# Age-Related Altered Drug Pharmacodynamics

- **Changes in PDs are less understood in the elderly than changes in pharmacokinetics.**

**Proposed changes leading to altered pharmacodynamics of drugs may include:**

- 1. Changes in drug concentration at the receptor.**
- 2. Changes in receptor numbers.**
- 3. Changes in receptor affinity.**
- 4. Post-receptor changes.**
- 5. Age-related changes in homeostatic mechanisms.**

# Age-Related Altered Drug Pharmacodynamics

## A. Older adults are more sensitive to the CNS effects of drugs:

1. Changes in size and weight of brain.
2. Changes in the neurotransmitter systems.
3. Drugs penetrate CNS easier than in young adults.

# Age-Related Altered Drug Pharmacodynamics

- For example, in the elderly there is decreased levels of dopamine transporters, decreased number of dopaminergic neurons, and decreased density of dopamine receptors; **leading to increased sensitivity to the adverse effects of antipsychotic drugs.**

# Age-Related Altered Drug Pharmacodynamics

- There is increased sensitivity to benzodiazepines, opioids, general anesthetics antipsychotics, lithium and anticholinergic drugs.
- B. The elderly are more likely to develop orthostatic hypotension as an adverse effect of some antihypertensive drugs.**

# Age-Related Altered Drug Pharmacodynamics

## **C. There is also:**

- **Increased hypotensive and bradycardic effect to calcium channel blockers.**
- **Reduced blood pressure response to  $\beta$ -blockers.**
- **Reduced effectiveness of diuretics.**
- **Increased risk of bleeding with warfarin.**



# Drug-Related Problems in the Elderly

They include 3 important, potentially preventable, negative outcomes:

1. Withdrawal effects.
2. Therapeutic failure.
3. Adverse drug reactions.

# Drug-Related Problems in the Elderly

## Risk Factors:

1. **Polypharmacy** ( $\geq 5$  drugs) including prescription and non-prescription drugs, herbal medicines, supplements and unnecessary drugs.
- Polypharmacy has been strongly associated with ADRs, **risk of geriatric syndromes (falls, cognitive impairment)**, non-adherence, diminished functional status, and increased health care costs.

# Drug-Related Problems in the Elderly

## 2. Inappropriate Prescribing, which includes:

- a. Wrong dose and duration.
- b. Duplication.
- c. Drug interaction problem.
- d. Prescription of drugs that should be avoided in the elderly. \*\*\*\*\*

## 3. Underuse:

- Omission of drug therapy that is indicated in prevention or treatment of disease.

# Drug-Related Problems in the Elderly

## 4. Medication non-adherence:

### Causes:

- a. Adverse effects.
- b. Complex regimens.
- c. Misunderstanding of information about prescribed medications.
- d. Cost.
- e. Dys-mobility (arthritis, ..).
- f. Social factors (living alone).
- g. Dementia.

# Assessing and Monitoring Drug Therapy

## 1. Compare the patient's problem list with drug list:

**A drug may be considered unnecessary if:**

- a. It does NOT have indication per the problem list.**
- b. Is NOT effective.**
- c. The risk of its use outweighs the benefits.**
- d. There is therapeutic duplication.**

# Assessing and Monitoring Drug Therapy

2. Determine if the patient is having a chronic condition but is NOT receiving an evidence-based medication to improve outcome.
3. Monitor effectiveness and toxicity of drugs by clinical assessment and lab tests.
  - **Examples:**

|                |                            |
|----------------|----------------------------|
| Amiodarone     | hepatic function tests     |
| Antiepileptics | Drug level                 |
| ACEi & ARBs    | Serum K <sup>+</sup> level |

# Assessing and Monitoring Drug Therapy

**Antipsychotics**

**Extrapyramidal ADRs**

**Diuretics**

**Serum K<sup>+</sup> level**

**Hypoglycemics**

**Glucose and glycated Hb**

**Lithium**

**Serum level**

**Warfarin**

**PT or INR**

**etc..**

# Assessing and Monitoring Drug Therapy

## 4. Documenting problems and formulating a therapeutic Plan:

- A reasonable clinical outcome for a 40-year-old patient may NOT be reasonable for an 80-year-old patient.
- **Take into account:** time until therapeutic benefit, treatment target, medication regimen complexity and goals of care, when deciding on prescribing rationally.



# Assessing and Monitoring Drug Therapy

5. Implement a team-based management approach and develop strategies to avoid prescribing errors.
6. Take measures to enhance adherence to medications:
  - a. Modify medication schedule to fit patient's life-style.
  - b. Prescribe generic agents to reduce cost.

# Assessing and Monitoring Drug Therapy

- c. Offer easy-to-open bottles.
- d. Offer easy-to-swallow dosage forms.
- e. Provide both written and verbal drug information.
- f. Involve caregivers stressing the importance of adherence.

# Assessing and Monitoring Drug Therapy

## **7. Assess the presence of drug-disease interaction:**

### **Examples:**

- a. Anticholinergics: benign prostatic hyperplasia & dementia or cognitive impairment.**
- b. Antipsychotics: history of falls and Parkinson's disease.**
- c. Aspirin: peptic ulcer disease.**

# **Assessing and Monitoring Drug Therapy**

- d. Calcium channel blockers: heart failure.**
- e. Metoclopramide: Parkinson's disease.**
- f. NSAIDs: peptic ulcer disease, heart failure and renal failure**

Table 2. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

| Organ System, Therapeutic Category, Drug(s)   | Rationale   | Recommendation | Quality of Evidence | Strength of Recommendation | Evidence  |
|---|---|----------------|---------------------|----------------------------|---|
| <b>Anticholinergics</b>   |   |                |                     |                            |   |
| First-generation antihistamines:<br>Brompheniramine<br>Carbinoxamine<br>Chlorpheniramine<br>Clemastine<br>Cyproheptadine<br>Dexbrompheniramine<br>Dexchlorpheniramine<br>Dimenhydrinate<br>Diphenhydramine (oral)<br>Doxylamine<br>Hydroxyzine<br>Meclizine<br>Promethazine<br>Triprolidine | Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity<br><br>Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate | Avoid          | Moderate            | Strong                     | 2015 Criteria:<br>Duran 2013<br>Fox 2014<br>Kalisch Ellet 2014<br><br>From previous criteria:<br><a href="#">Agostini 2001</a><br><a href="#">Boustani 2007</a><br><a href="#">Guaiana 2010</a><br><a href="#">Han 2001</a><br><a href="#">Rudolph 2008</a> |
| Antiparkinsonian agents<br>Benztropine (oral)<br>Trihexyphenidyl  | Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease   | Avoid          | Moderate            | Strong                     | <a href="#">Rudolph 2008</a>  |
| Antispasmodics:<br>Atropine (excludes ophthalmic)<br>Belladonna alkaloids<br>Clidinium-   | Highly anticholinergic, uncertain effectiveness   | Avoid          | Moderate            | Strong                     | <a href="#">Lechevallier-Michel 2005</a><br><a href="#">Rudolph 2008</a>  |

**Some Potentially Inappropriate  
Medication Use in Older Adults  
According to American Geriatric Society  
Beers Criteria**

# **Potentially Inappropriate Medication Use in Older Adults**

- 1. Anticholinergics + other drugs with anticholinergic activity such as antihistamines:**
  - Rationale: elimination reduced in older adults.**
  - Risk: confusion, dry mouth, constipation, urine retention.**
- 2. Nitrofurantoin:**
  - Rationale: potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy.**

# **Potentially Inappropriate Medication Use in Older Adults**

## **3. Peripheral and central $\alpha$ -blockers:**

- Rationale: High risk of adverse effects, orthostatic hypotension, and CNS adverse effects.**

## **4. Immediate-release nifedipine:**

- Rationale: potential for hypotension and myocardial ischemia (coronary steal syndrome).**



# Potentially Inappropriate Medication Use in Older Adults

## 5. Amiodaraone:

- **Rationale:** High risk of many adverse effects (Blurry vision, seeing halos around lights, vision loss; Heart failure, cardiac arrhythmias; Hypothyroidism or hyperthyroidism; Liver injury, jaundice; Pulmonary fibrosis; Bluish-gray skin discoloration).

## 6. Tricyclic antidepressants (+):

- **Rationale:** highly anticholinergic, sedating, orthostatic hypotension and myocardial ischemia.

# Potentially Inappropriate Medication Use in Older Adults

## 7. Antipsychotics:

- **Rationale: cognitive decline, dementia, metabolic abnormalities, increased risk of CVA (promoting blood clots, orthostatic hypotension, arrhythmias, causing excessive sedation which can lead to dehydration, and inducing weight gain).**

# **Potentially Inappropriate Medication Use in Older Adults**

## **8. Barbiturates & benzodiazepines:**

- **Rationale: highly rate of dependence, tolerance, sedation, cognitive impairment, delirium, falls, fractures.**

## **9. Long-acting sulfonylureas:**

- **Rationale: increased risk of hypoglycemia.**

# **Potentially Inappropriate Medication Use in Older Adults**

- 10. Insulin sliding scale (refers to the progressive increase in the pre-meal or night-time insulin dose, based on pre-defined blood glucose ranges).**
- Rationale: increased risk of hypoglycemia.**

# Potentially Inappropriate Medication Use in Older Adults

## 11. Metoclopramide:

- Rationale: increased risk of extrapyramidal adverse effects, dyskinesia.

## 12. Proton pump inhibitors:

- Rationale: risk of *Clostridium difficile* infection.

# Potentially Inappropriate Medication Use in Older Adults

## 13. Meperidine (pethidine):

- Rationale: high risk of neurotoxicity, including delirium.

## 14. NSAIDs:

- Rationale: Increased risk of peptic ulcer disease, cardiovascular disease, **renal failure**.

# **Potentially Inappropriate Medication Use in Older Adults**

## **15. Central muscle relaxants (chlorzoxazone, cyclobenzaprine, orphenadrine):**

- Rationale: poorly tolerated because of anticholinergic effects, sedation, increased risk of falls and fractures.**