



Medication Use in the Elderly

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Significance

- Persons ≥ 65 years of age compose only about 12% of the US population
- 1/3 (33%) of all drugs are prescribed for them
- Consume more than 50% of over-the-counter medicines as well.
- More than 80% of all older people take at least one medication daily.

- Pharmacokinetics: study of the action of a drug in the body over a period of time, changes with age
- Age-related physiologic changes:
 - Absorption
 - Distribution
 - Metabolism
 - Excretion

Age-related changes

- Effects are variable
- Difficult to predict
- Substantial individual variation
- Related solely to aging vs most likely are due to the combined effects of age, disease, and the environment

Age-related changes

Absorption:

- ↓ absorptive surface
- ↓ splanchnic blood flow
- ↑ gastric pH
- Altered gastrointestinal motility

Clinically: passive diffusion-little change in absorption with age

Age-related changes

- More important changes result from concurrent administration of several medications
 - antacids decrease the oral absorption of cimetidine
 - alcohol accelerates the absorption of chloral hydrate.

Age-related changes

Distribution

- ↓ total body water
- ↓ lean body mass
- ↑ body fat
- ↓ serum albumin
- Altered protein binding

Age-related changes

Clinical significance:

- Higher concentration of drugs that distribute in body fluids
- ↑ distribution
- prolonged elimination half-life of fat-soluble drugs
- ↑ free fraction in plasma of some highly protein-bound acidic drugs

Age-related changes

- Increased distribution of fat-soluble drugs such as hypnotics and analgesics; given in single doses and on an intermittent basis
 - Diazepam:
 - ✓ Volume of distribution of diazepam is increased almost twofold in older patients
 - ✓ the elimination half-life is prolonged from 24 hours in young patients to approximately 90 hours in older patients

Age-related changes

Water-soluble compounds:

- Volume of distribution ↓ in older patients
- dose required is ↓
- Digoxin lower dose in older patients
- loading dose of aminoglycosides is less in older patients

Volume of Distribution of Common Drugs

Increased Volume	Decreased Volume
Acetaminophen	Cimetidine
Diazepam	Gentamicin
Prazosin	Meperidine
Prazosin	Meperidine

Age-related changes

Metabolism

- Reduced hepatic mass
- Reduced hepatic blood flow
- ↓ phase I metabolism

Clinical significance:

- ↓ first-pass metabolism
- ↓ rate of biotransformation of some drugs

Phase I metabolism (cytochrome P450 system)

- Drug oxidation, reduction and hydrolysis
- Decreases substantially with age
- Drugs that are metabolized through phase I have prolonged half-lives (Amitriptyline Barbiturates Diazepam Diphenhydramine Flurazepam Ibuprofen Labetalol Lidocaine)
- ADR occur due to either inhibition or induction of cytochrome P450 enzymes
 - CYP3A, involved in the metabolism of more than half of the currently prescribed drugs

Phase II metabolism: conjugation of drugs or their metabolites to organic substrates

- glucuronidation, sulfation, acetylation, and methylation
- altered less with age
- drugs that require only phase II metabolism for excretion (e.g., triazolam) do not have a prolonged half-life in older people

Variable effect of age on drug metabolism is due to other factors

- cigarette smoking, alcohol intake, dietary modification, drugs, viral illness, caffeine intake, and other unknown factors also affect the rate of drug metabolism

Elimination

- Reduced renal plasma flow
- Reduced glomerular filtration rate
- ↓ tubular secretion function

Clinical significance:

- ↓ renal elimination of drugs and metabolites
- marked inter-individual variation

- Drugs that depend on glomerular function (e.g., gentamicin) and drugs that depend on tubular secretion (e.g., penicillin) for elimination both exhibit reduced excretion in older patients
- Average creatinine clearance declines by 50% from age 25 to age 85 despite a serum creatinine level that remains unchanged at approximately 1.0 mg/dL

Altered renal clearance leads to two clinically relevant consequences:

- the half-lives of renally excreted drugs are prolonged
- the serum levels of these drugs are increased

Drugs with large therapeutic index (e.g., penicillin); little clinical importance

Drugs with a narrower therapeutic index (e.g., digoxin, cimetidine, aminoglycosides), side effects in older patients if dose reductions are not made

. Digoxin is the drug that most often causes side effects in the elderly, especially if the dose exceeds 0.125 mg daily

Pharmacodynamics: the biochemical and physiologic effects of drugs and their mechanisms of action

- effects of aging are not clearly known

Tissue sensitivity

- Alterations in receptor number
- Alterations in receptor affinity
- Alterations in second-messenger function
- Alteration in cellular and nuclear responses

Clinical significance:

- Patients are "more sensitive" or "less sensitive" to an agent

Adherence

- The extent to which a patient's behavior concurs with the directions provided by his or her physician
- Nonadherence is more common in older patients
 - Older patients use more medications than younger ones
 - Nonadherence increases in proportion to the number of medications used

Nonadherence

- Occurs in one third to one half of older patients
- Approximately one in five prescriptions is not filled
- Between one third and two thirds of patients who do fill their prescriptions use the medication in a manner different from that intended.

Effect on Adherence

- Belief by the patient that the medication will treat or prevent the disease or condition: ↑
- Careful explanation by the doctor of the purpose of the medication: ↑
- Number of drugs used, Long duration of therapy, Complex scheduling, Safety closure bottles: ↓

ADRs

- Older patients experience adverse outcomes about twice as often as younger patients
- Older patients experience more adverse reactions than younger patients regardless of the number of drugs they use
- Proportion of people over 75 years of age is expected to continue to increase, and the prevalence of major chronic diseases such as hypertension, arthritis, stroke, cancer, and diabetes also increases with age
 - a larger proportion of older patients can be expected to be exposed to therapeutic drugs
- Clinicians must be attentive to the goals and consequences of drug therapy in the elderly and must individualize therapy as much as feasible

- Most common form of iatrogenic illness
- Incidence in hospitalized patients increases from about 10% in 40- to 50-year-old patients to 25% in patients older than 80 years of age
- Drug-related morbidity and mortality cost \$76.6 billion in ambulatory patients in the United States
 - largest component of this total cost was associated with drug-related hospitalizations

Limitations of the data

- Small number of older people included in premarketing studies
- Oldest-old (≥ 80) generally not included in clinical trials of investigational drugs
- Older subjects who do participate in trials tend to be healthy "young-old" people

Conclusion

- The individual patient, physiologic status (i.e., hydration, nutrition, and cardiac output), and how this status affects the pharmacology of a particular drug is more important in prescribing that drug than any specific age-related changes