MEDICATION USE BY OLDER ADULTS

Elders use prescribed medications to a much greater extent than their younger counterparts, including over-the-counter medications and herbal preparations. A survey of 2590 non-institutionalized older adults in the United States showed increased use of all medications with advancing age [1]. Women aged 65 years and older were the most frequent users: 12% took 10 or more medications and 23% took at least five prescription drugs. Associated with this increased use of medication is a higher rate of adverse reactions due to changes in drug metabolism that occurs with aging.

Inappropriate drug use among the elderly is quite common, with a prevalence ranging from 9.8% to 41%. Patient’s poor economic situation, use of anxiolytic drugs, and polypharmacy were associated with higher potential for being prescribed inappropriate medications [2]. The rate of adverse drug event (ADE) is estimated at 50% patient-years, of which 38% were considered serious or life threatening and 42% were preventable [3]. Adverse events are up to seven times more common in persons 70-79 years of age than in those 20-29 years [4]. Nearly 5% of all hospital admissions in the United States are believed to be related to adverse drug reactions [5], and some studies report a rate as high as 28% for elderly persons [4].

Nursing home residents are particularly at higher risk for hospitalization or death following inappropriate medication use. The frequency of adverse events and their prevention rate varies by drug class (Table I). One month usage of such inappropriate medication was associated with being hospitalized for a drug related illness (Odds ratio [OR] 1.27, Confidence interval [CI] 1.09-1.47) and even death (OR 1.28; CI 1.05-1.55) [6]. Independent risk factors for ADEs among nursing home residents were newly admitted patients (OR 2.8; CI 1.5-5.2); use of antibiotics (OR 4.0; CI 2.5-6.2), antipsychotics (OR 3.2; CI 2.1-4.9), or antidepressants (OR 1.5; CI 1.1-2.3); and polypharmacy (OR 2.8; CI 1.7-4.7) [7]. In addition, the use of opioids and antidepressants were among the strong risk factors for preventable ADEs.

Symptoms of an adverse drug reaction can be subtle in an elderly patient and can mimic the progression of underlying chronic illnesses. Symptoms may be manifested by increased frequency of falls, urinary incontinence or retention, worsening confusion, excessive sedation, constipation, decreased oral intake, and failure to thrive. Physicians may respond to such symptoms by prescribing more medications and the cascade of polypharmacy and ADEs continues.

AGE-RELATED PHARMACOKINETIC CHANGES

Drug absorption

Drug absorption is the pharmacokinetic parameter least affected by age. Elderly persons may have altered esophageal emptying time, prolonged gastrointestinal motility and decreased gastrointestinal blood flow in the presence of a higher gastric pH. Although these age-related changes are expected to decrease gastrointestinal drug absorption, they are countered by decreased intestinal motility and thus prolonged absorption time. Little information exists on the absorption of extended release formulations by elderly patients or on the absorption of transdermal, buccal, or transbronchial drug preparations [8].

Drug distribution

Volume of distribution (Vd) is defined as the amount of drug in the body divided by the plasma concentration of the drug. In practical terms, it is the volume in which the-
drug appears to be distributed based on blood levels. $V^D$ is important in drug therapies that require loading doses (e.g., digoxin and amiodarone).

With aging, lean body mass and total body water decrease, resulting in decreased $V^D$. Therefore, drugs that distribute into muscle (e.g. digoxin) or into body water (e.g. aminoglycosides) will reach higher initial plasma concentration after administration as a result of the decrease in their $V^D$. Consequently, watersoluble drugs such as procainamide, quinidine, propranolol, atenolol, sotalol, theophylline, hydrochlorothiazide, various antibiotics, and several sedative-hypnotics are distributed less effectively in elders. This is further pronounced if blood flow to organs is hindered due to cardiovascular diseases such as congestive heart failure (CHF). On the other hand, the large adipose tissue noted among elders increases the $V^O$ of lipophilic drugs such as amiodarone, desipramine, diazepam, haloperidol, and digitoxin [9-11].

**Drug binding**

Generally, pharmacological effects of medications are determined by the free (bioavailable) drug concentration because bound drugs cannot bind to target tissues but rather serve as drug reservoirs. Most drugs are acidic and thus bind to serum albumin. Many diseases afflicting the elderly such as CHF, chronic renal disease, rheumatoid arthritis, liver cirrhosis, and some malignancies are associated with hypoalbuminemia, and therefore drug-binding capacity decreases. Significant changes in the free drug fraction can occur if a drug is displaced from plasma albumin by a competing drug. A classic example of such interaction is that between warfarin and acetylsalicylic acid. Displacement of as little as 1-2% of bound warfarin doubles or triples the concentration of active plasma anticoagulant, resulting in a potential bleed. Other highly protein-bound drugs include meperidine, phenytoin, diazepam, chloramphenicol, indomethacin, and furosemide.

Drug-binding alterations affect interpretations of serum levels for medications that are highly protein bound. A perfect example is phenytoin. Correction formulas are available to help physicians interpret serum levels based on serum albumin level.

**Drug elimination**

- **Drug clearance**

The two major organs involved in drug clearing are the liver and kidneys; other sites such as the lung and gastrointestinal tract play less important roles. The half-life of a drug is the time required for the plasma concentration to decrease by 50%. It affects dosing interval, and the time necessary to reach steady state or the removal of the drug from the body [8]. Four half-lives are needed to eliminate 90% or more of the drug from the body. The elimination half-life of drugs increases with age. This may be due to a decrease in drug clearance or an increase in distribution. The half-lives of the following commonly used drugs are increased in elderly persons: digoxin, quinidine, propranolol, nifedipine, lisinopril, enalapril, prazosin, erythro-

mycin, ampicillin, ranitidine, chlorpropamide, aspirin, diazepam, and lithium.

- **Hepatic drug metabolism**

Phase I reactions transform functional groups of the parent molecule via oxidations, reductions, and hydrolytic reactions. Several studies have demonstrated an age-related decline in phase I drug metabolism. Such decreased metabolism was reported among elderly patients taking imipramine, amitriptyline, and thioridazine.

Phase II reactions are conjugation reactions, and involve coupling the drug with acetate, glycine, glucuronide acid, or sulfate groups. Conjugation pathways are generally unchanged in the elderly. Some drugs are efficiently removed from circulation through first-pass metabolism by the liver. Examples of such drugs are tricyclic antidepressants, numerous antipsychotic agents, narcotic analgesics, propranolol, verapamil, and theophylline. Clearance of such drugs is dependent on hepatic blood flow, which is decreased by 12% to 40% in the elderly population [8]. It is important to note, however, that some medications, such as opioids, have metabolites which remain bioactive despite effective metabolism of the parent drug by the liver.

The cytochrome P450 (CYP) enzymes, a superfamily of heme proteins, are involved in metabolism of a wide variety of drugs. Approximately 1000 CYP enzymes are known, but only 50 are functionally active in humans, and about 8 to 10 isoforms in the CYP1, CYP2, and CYP3 families are involved in most metabolic pathways [8]. Several drugs induce or inhibit CYP enzymes which affect the metabolism of other drugs. For example, glucocorticoids and anticonvulsants induce CYP3A4, whereas isoniazid and chronic alcohol intake induce CYP2E1 [8]. Such changes will affect the levels of parent compounds and may in turn cause drug toxicity. Dietary items may affect the CYP system as well – the most commonly encountered interaction being between grapefruit juice and drugs metabolized by CYP3A4. Numerous drugs have been reported to have increased bioavailability due to grapefruit juice intake. These include felodipine, nifedipine, nisoldipine, nitrendipine, triazolam, midazolam, lovastatin, and simvastatin [8].

- **Genetic polymorphism**

Large differences in drug biotransformation are noted among humans due to phenotypic differences in metabolic enzyme activity, i.e. rapid and slow metabolizer. The major deficiencies in drug metabolizing activities are inherited as an autosomal recessive trait. N-acetylation of isoniazid was the first genetic polymorphism noted. A growing number of cardiovascular agents, psychoactive agents, and morphine derivatives are now recognized as CYP2D6 substrates, creating a new interest in the role of pharmacogenetics in clinical pharmacology.

- **Renal drug excretion**

With advancing age, there is a decrease in renal mass, creatinine clearance, and renal blood flow by approximately 1% per year after the age of 50 [8]. The effect of age on kidney function can be shown by
examining the commonly used formula for estimating creatinine clearance:

\[
\text{Creatinine Clearance} = \frac{(140 - \text{Age [y]}) \times \text{Lean Body Weight (kg)}}{72 \times \text{Serum Creatinine (mg/dL)}}
\]

Renal functional decline is reported to be the most important pharmacokinetic change that occurs with aging – more so than that observed in the liver [15]. Drugs that are more than 60% excreted by the kidneys are affected by reduction in renal function. This may result in accumulation of drugs leading to higher serum levels. Examples of drugs excreted primarily by the kidneys include atenolol, sotalol, digoxin, lithium, amphotericin, procainamide, allopurinol, and many antibiotics. Such medications require dosage adjustments in elderly patients with renal impairment.

AGE-RELATED PHARMACODYNAMIC CHANGES

An example of altered pharmacodynamics is the change in autonomic function seen with aging. Homeostasis of blood pressure upon standing is impaired due to alteration in baroreceptor reflex attributed partly to an age-related decline in \(\alpha-1\) adrenergic receptor function [16]. This may explain the higher incidence of postural hypotension and the subsequent increased risk of falls among elders prescribed nitrates, diuretics, and calcium channel blockers [17]. The \(\beta\)-adrenergic receptor density in the heart is unchanged with age, but there is a diminished ability of \(\beta\)-receptor agonists to stimulate cyclic adenosine monophosphate production [18]. In addition, the number of muscarinic M2 receptors decreases with age [19], leading to decreased acetylcholine release from atrial tissue following electrical stimulation [20].

Drug-drug interactions

A drug-drug interaction is defined as the effect one drug has on another, and can be pharmacokinetic or pharmacodynamic in nature. Several conditions favor drug-drug interactions. These include:

1. High binding to albumin (> 85%)
2. Narrow therapeutic/toxic window
3. Small volume of distribution (\(V^d\)).

Drug interactions have been reported in outpatient settings (46% of patients had at least one significant interaction) [21], psychiatric wards, in-hospital settings (15-40%) [22] as well as emergency rooms [23]. Hanlon and colleagues showed that 6% of elderly inpatients had a drug-drug interaction with an adverse outcome, and 20% of these patients had an actual drug-disease interaction [24]. For example, patients admitted with digitals toxicity were 12 times more likely to have been given clarithromycin in the week prior to admission. Similarly, patients on angiotensin converting enzyme (ACE) inhibitors admitted with hyperkalemia were 20 times more likely to have been given a potassium-sparing diuretic one week prior to admission.

Many admissions of elderly patients for drug toxic effects occur after administration of another drug with known drug-drug interactions; and many of these interactions could be avoided [25].

Types of drug-drug interactions

Detecting drug interactions can be straightforward if proper prescription techniques are used, but sometimes is challenging due to the myriad of ways in which these interactions can occur. Frequently encountered interactions involve drugs with a narrow therapeutic index such as digoxin, phenytoin, or warfarin. Clues to such interactions include altered drug levels after having previously reached steady state. Another common drug-drug interaction involves medications that are substrates, inhibitors, or inducers of CYP450 isoenzymes (e.g., CYP3A4, CYP2D6).

Another category involves patients suffering from five or more comorbid conditions. Polypharmacy, defined as intake of nine or more medications, is a strong risk factor for adverse drug effects. Combining drugs needed to manage all comorbid illnesses may lead to untoward effects, not seen with individual drug usage. The incidence of ADEs increases rapidly when the number of medications administered to older adults exceeds seven.

A third category is cascade interactions (Table II). For example, a patient develops an ADE which is misinterpreted as a new illness, and another drug is then prescribed. The patient becomes at risk of developing additional ADEs related to this unnecessary treatment. Symptom management in geriatric medicine sometimes involves withdrawing a medication – and thus arresting the cascade trap. The role of the pharmacist, as part of the interdisciplinary team, is invaluable in identifying such cascades [26].

<table>
<thead>
<tr>
<th>Initial drug therapy</th>
<th>Adverse drug event</th>
<th>Subsequent drug therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics</td>
<td>Extrapyramidal signs &amp; symptoms</td>
<td>Antiparkinsonian therapy</td>
</tr>
<tr>
<td>Cholinesterase</td>
<td>Urinary incontinence</td>
<td>Incontinence treatment</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>Hyperuricemia</td>
<td>Gout treatment</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Increased blood pressure</td>
<td>Antihypertensive therapy</td>
</tr>
</tbody>
</table>

QUALITY OF DRUG PRESCRIBING

Various criteria have been developed by expert panels in Canada [27] and in the United States [28] to assess the quality of prescribing practices and medication use in elderly individuals.

Beers criteria

The Beers criteria are the most widely used criteria to assess inappropriate drug prescribing [28]. Developed
originally by an expert consensus panel in 1991, and subsequently revised in 2003, the Beers criteria produced a list of medications that are considered inappropriate for use in older patients, either because of ineffectiveness or high risk for adverse events [29]. Inappropriate medications were subdivided into three groups: those that should always be avoided (e.g., barbiturates, chlorpropamide); those that are rarely appropriate (e.g., diazepam); and those with specific indications but are often misused (e.g., oxybutynin) (Table III) [30].

In a 1994 survey conducted in the United States, 19 to 23.5% of community-dwelling elderly were found to be using one or more inappropriate medication(s) [31]. Three percent used at least one medication that should always be avoided by older adults [30-31]. The same applies for older patients living outside the United States (3-20%). Risk factors for inappropriate medication use include poor economic situations, age 85 years and older, and living alone [32]. Drugs with the highest potential for problematic use were NSAIDs and benzodiazepines [24].

<table>
<thead>
<tr>
<th>Drug therapy</th>
<th>Therapy description</th>
<th>Reason for concern</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALWAYS AVOID</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Hypnotic</td>
<td>Highly addictive</td>
</tr>
<tr>
<td>Belladonna alkaloids</td>
<td>Antispasmodic</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Chlorpropamide</td>
<td>Oral antihyperglycemic</td>
<td>Long half-life, inappropriate ADH secretion</td>
</tr>
<tr>
<td>Dicycloverine</td>
<td>Antispasmodic</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Benzodiazepine</td>
<td>Long half-life</td>
</tr>
<tr>
<td>Hyoscyamine</td>
<td>Antispasmodic</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>Hypnotic</td>
<td>Highly addictive</td>
</tr>
<tr>
<td>Pentazocine</td>
<td>Opioid</td>
<td>Poor adverse effect profile</td>
</tr>
<tr>
<td>Pethidine (Meperidine)</td>
<td>Opioid</td>
<td>Ineffective orally</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Antispasmodic</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Trimethobenzamide</td>
<td>Antimetic</td>
<td>Extrapyramidal adverse effects</td>
</tr>
<tr>
<td><strong>RARELY APPROPRIATE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carisoprodol</td>
<td>Skeletal muscle relaxant</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Benzodiazepine</td>
<td>Long half-life</td>
</tr>
<tr>
<td>Chlorzoxazone</td>
<td>Skeletal muscle relaxant</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>Skeletal muscle relaxant</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Benzodiazepine</td>
<td>Long half-life</td>
</tr>
<tr>
<td>Metaxalone</td>
<td>Skeletal muscle relaxant</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Methocarbamol</td>
<td>Skeletal muscle relaxant</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Opioid</td>
<td>Poor adverse effect profile</td>
</tr>
<tr>
<td><strong>SOME INDICATIONS (BUT OFTEN MISUSED)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Antidepressant</td>
<td>Strong anticholinergic properties and sedation</td>
</tr>
<tr>
<td>Chlorphenamine</td>
<td>Antihistamine</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>Antihistamine</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Metaxalone</td>
<td>Skeletal muscle relaxant</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Antihistamine</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Platelet inhibitor</td>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Antiarrhythmic</td>
<td>Can induce heart failure, strong anticholinergic properties</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Antidepressant</td>
<td>Strong anticholinergic properties and sedation</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>Antihistamine</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>NSAID</td>
<td>More CNS adverse effects than other NSAIDs</td>
</tr>
<tr>
<td>Methylidopa</td>
<td>Antihypertensive</td>
<td>Can cause bradycardia and exacerbate depression</td>
</tr>
<tr>
<td>Oxybutynin</td>
<td>Antimuscarinic</td>
<td>Strong anticholinergic properties, sedation and weakness</td>
</tr>
<tr>
<td>Promethazine</td>
<td>Antihistamine</td>
<td>Strong anticholinergic properties</td>
</tr>
<tr>
<td>Reserpine</td>
<td>Antihypertensive</td>
<td>Can induce depression and sedation</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>Platelet inhibitor</td>
<td>Poor adverse effect profile</td>
</tr>
</tbody>
</table>

ADH: antidiuretic hormone  NSAIDs: non-steroidal anti-inflammatory drugs  CNS: central nervous system
Avoiding drug interactions and ADEs

Practical suggestions on how to improve drug prescriptions were outlined in the Assessing Care of Vulnerable Elders (ACOVE) project [33]. These include:

1. Documenting the indication for new drug therapy.
2. Educating patients on the benefits and risks associated with each medication.
3. Maintaining a current medication list.
4. Documenting response to therapy.
5. Periodically reviewing the ongoing need for a drug therapy.

The ACOVE indicators additionally specify medications that should be avoided in older adults or that warrant careful monitoring once initiated, and provide safety guidelines.

Computerized physician order entry (CPOE), computerized drug interaction software, and computerized decision support systems (CDSS) that detect and alert the physician and pharmacist to potentially serious outcomes may decrease the risk of drug errors and have become widely used in Western medicine. Another approach to avoid and detect ADEs is through a multidisciplinary geriatric team, the hallmark of geriatric care, consisting of a geriatrician, nurse, pharmacist, dietitian, and other healthcare professionals. Communication between team members and combining their knowledge and skills to form a comprehensive plan of care can reduce the risk of drug interactions [26].

Underutilization of medication

Inappropriate medications use is not limited to overprescribing but extends to under-prescribing necessary medications. While attempting to avoid polypharmacy, some physicians may omit prescribing recommended medications such as statins for dyslipidemia in a patient with coronary artery disease or β-blockers following a myocardial infarction. Overconcerned physicians may do a better job in avoiding inappropriate medications than prescribing indicated drug therapies. In several studies, this pattern ranged from 50-64% [34]. Factors leading to underutilization include clinicians not recognizing medication benefit in the older population, affordability, and dose availability.

POLYPHARMACY AND THE LEBANESE HEALTHCARE SYSTEM

Several factors relevant to the practice of medicine in Lebanon potentially promote polypharmacy and the subsequent risk of ADE. Primarily among them is the tendency for patients to seek care directly from specialists (often multiple) without the oversight of a primary-care provider. As the number of ailments increase with age, care is delivered piecemeal by multiple specialists independent of each other. Such fragmented care can result in polypharmacy and drug cascades. A possible solution is to relinquish care to qualified general practitioners such as internists, family medicine specialists, and geriatricians. These providers can address most of the acute and chronic problems facing the older Lebanese, and can supervise and coordinate care when specialists are needed. This shift towards coordinated care requires a change in the culture of medicine in Lebanon and a rethinking of the attitude towards the general practitioner, neither of which are welcome or appealing to the public. Furthermore, the severe shortage of well-trained general practitioners (let alone geriatricians) further propagates the status quo. Including geriatric education in the curriculum of medical schools and residency programs is an early step that can be taken today to produce a next generation of physicians who are sensitive to the needs of the elderly.

In addition, the lack of electronic charts, the absence of an interdisciplinary approach, and poor communication between professionals further compound the problem. Due to financial hardship many patients bypass physicians altogether and obtain medications directly from pharmacies without adequate diagnosis and monitoring. When medications are out of stock, they may be substituted haphazardly with similar drugs without regards to outcome or follow-up. Such problems can be ameliorated by instituting interdisciplinary teams (a hallmark of the geriatric approach to care) and electronic records that alert about drug-drug interactions or inappropriate dosing due to renal or hepatic dysfunction.

SPECIFIC EXAMPLES OF MEDICATIONS ASSOCIATED WITH ADVERSE EVENTS

Cardiovascular drugs

Many cardiovascular drugs have narrow therapeutic windows and high incidence of adverse effects in the elderly. For example, the bioavailability of drugs such as propranolol, verapamil, and labetalol is increased because of reduced first-pass hepatic metabolism, making older subjects more susceptible to their effects. Another example is the higher sensitivity to anticoagulation. Although there is a tendency towards reduced drug clearance due to reductions in renal or hepatic blood flow and function, changes in receptor sensitivity or lower dietary vitamin K intake may be more important factors [35]. As a result there is an exponential increase in bleeding risk with a linear increase in anticoagulation. In the Sixty-Plus study, for example, the annual risk of bleeding increased from 1.6% in non-anticoagulated older subjects to 5% (relative risk 3.0) at an INR of 2.5, to 50% (relative risk 30) at an INR of 4.0 [36]. Due to the decline in cognitive function, some elderly patients fail to mention the intake of oral anticoagulants including aspirin. They may also not recognize that many medications interact with anticoagulants, such as ciprofloxacin, a commonly prescribed antibiotic. Comorbid illnesses such as diverticulitis or cerebral amyloid angiopathy may predispose patients to bleeding. In addition, elders are at increased risk of falls and serious injuries such as subdural hematomas. However, the risk of a subdural hematoma from a fall is so small that a person with an average risk of stroke from atrial fibrillation (5%/year) would have to fall approximately 300 times in a year for the risk of anticoagulation to outweigh its benefits [37-38].
Antipsychotic drugs

Dementia is often associated with psychological and behavioral problems necessitating the use of atypical antipsychotic medications. These are the most frequent drugs associated with adverse events in long-term care [39]. In particular, there is an increased risk of falls (OR 1.73, 95% CI 1.52-1.97) with the use of psychotropic medications [40]. Despite the limited evidence to support the efficacy of such medications in the management of behavioral and psychological symptoms in the elderly, the use of antipsychotic medications in long-term care facilities is quite prevalent (17% within 100 days of admission, and 24% within one year) [41]. Patients treated with atypical antipsychotic therapy were 1.6 to 1.7 times more likely to die within a year than those given placebo therapy.

CONCLUSIONS

Polypharmacy is a major and serious problem among elders. It can be associated with higher morbidity and mortality. This increased susceptibility is due to changes in drug pharmacokinetics and pharmacodynamics, as well as the number of medications used by older adults. Adverse events can be reduced if physicians are cognizant of these age-related changes and diligent in taking steps to avoid them. These include a stepwise approach to pharmacotherapy, periodic medication review and monitoring, and discontinuation of unnecessary drugs. In addition, physicians should consider ADEs as a potential cause for any new symptom and whenever possible opt for non-pharmacological approaches. They should always aim to substitute current drugs with safer alternatives and to use the minimal effective dose. Finally, they should not deprive elders from the benefit of indicated therapies out of fear of adverse events.

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