

# HOSPITAL PHYSICIAN®

## GERIATRIC MEDICINE BOARD REVIEW MANUAL

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## Understanding the Pharmacology of Aging

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# Understanding the Pharmacology of Aging

## INTRODUCTION

Adults age 65 years and older currently comprise approximately 13% of the US population but consume 30% of all prescription drugs and 40% of all nonprescription drugs.<sup>1,2</sup> In the last decade, the geriatric age group accounted for one third of the overall health expenditure in the United States; by 2004, the health care cost for this group is projected to be 50% of the national health care bill. A substantial portion of this amount will be spent on medications.<sup>3</sup>

Medication use steadily increases with age in older adults because of increasing comorbidity. On average, an older adult uses 3 or more medications at any given time;<sup>2</sup> 2 of every 5 drugs taken are bought over-the-counter.<sup>4</sup> Residents of long-term care facilities take an average of 5 to 8 prescriptions, not including medications taken on an as-needed basis.<sup>2</sup> Polypharmacy (the administration of several drugs concurrently) is associated with an increase in the incidence of adverse drug events (ADEs); adverse reactions are implicated in 10% to 17% of hospital admissions of older patients in the United States.<sup>2</sup> In nursing homes, for each dollar spent on medication, \$1.33 is spent in the treatment of drug-related consequences.<sup>5</sup> Hence, it is imperative for physicians to understand the age-related changes in pharmacokinetics and pharmacodynamics in order to prescribe appropriately in this age group.

The Nursing Home Reform Amendments of the Omnibus Budget Reconciliation Act of 1987 mandated that the Health Care Financing Administration establish regulations that include the use of medications in nursing homes.<sup>6</sup> Explicit criteria that have been published regarding medication use relate to dosing and frequency, and include information on medications to be avoided in ambulatory geriatric patients.<sup>7</sup>

## AGE-RELATED CHANGES IN PHARMACOKINETICS

*Pharmacokinetics* is the study of the absorption, distribution, metabolism, and excretion of drugs. *Pharmacodynamics* is the study of the biochemical and physiologic effects of drugs. Simply stated, pharmacokinetics is “what the body does to the drug,” whereas pharmacodynamics is “what the drug does to the body.” **Figure 1**

provides a schematic representation of the drug pathway. Age-related physiologic changes that affect pharmacokinetics are summarized in **Table 1**.

### ABSORPTION

*Absorption* refers to the movement of a drug from the site of administration to the intravascular space. *Bioavailability* is the fraction of an administered drug that reaches the circulation. The bioavailability of an intravascular medication is 100%, whereas that of an oral drug is lower, depending on the amount absorbed from the gastrointestinal tract during first-pass metabolism (ie, extraction by the liver, or pre-systemic clearance).<sup>8</sup>

Age-related changes in the gastrointestinal system include decreased splanchnic perfusion and mucosal atrophy of the intestines. Changes in acid secretion are minimal to nonexistent.<sup>9</sup> These age-related changes may theoretically lessen drug absorption. In reality, however, the absorption of most oral drugs—although marginally slower—is, in fact, complete. Absorption of drugs occurs generally through passive diffusion, a process that is not altered with aging.<sup>1,8</sup>

### DISTRIBUTION

The volume of distribution of a drug is determined by comparing the amount of drug in the body to the concentration measured in the plasma or serum. It depends on the plasma protein-binding and tissue-binding properties of the drug, as well as its lipid-to-water coefficient. The volume of distribution is useful in determining the loading dose of a drug:<sup>8</sup>

$$\text{Volume of distribution} = \frac{\text{amount of drug in body}}{\text{concentration}}$$

$$\text{Loading dose} = (\text{desired concentration}) \times (\text{volume of distribution})$$

There are 2 major plasma proteins with drug-binding qualities: albumin and  $\alpha$ 1-acid glycoprotein (AAG). Levels of AAG are not affected by age. Levels of albumin are not affected by age per se, but they may decline in association with disease. Albumin binds acidic drugs (eg, warfarin, phenytoin) whereas AAG preferably binds basic drugs (eg, lidocaine, propranolol).<sup>1</sup> The albumin level should be considered when interpreting plasma drug concentration, which measures total drug levels (ie, protein-bound [inactive] as