INTRODUCTION

Except for drugs eliminated predominantly by renal excretion, it is not possible to generalize on the type, magnitude, or importance of age-related differences in pharmacokinetics. Conflicting data in the literature for various drugs may be attributed to small numbers of subjects studied, differences in selection criteria for subjects, and variation in protocol design. Apparent age-related differences in drug disposition are multifactorial and influenced by environmental, genetic, physiological, and pathological factors.

This chapter addresses relevant pharmacokinetic and, if available, pharmacodynamic considerations in the elderly, with an emphasis on the interplay of cardiovascular medications in these processes. In this chapter,
the term cardiovascular medications encompasses all antihypertensives. Cardiovascular compounds other than antihypertensives are described in an agent- or class-specific manner.

Aging, characterized by periods of growth, development, and senescence, is a source of interindividual variability in drug response and is one of several factors that influence the optimization of therapy. This is more so in the very aged, a patient group often in most critical need of safe and effective medication administration. However, any agewise stratification into elderly or very elderly categories is quite arbitrary. Life is a continuous process, with the distinction between one time period and the next often quite arbitrary.

It is also clear that chronological age does not necessarily dictate functional age; thus, population-based pharmacokinetic suppositions do not always reflect how an individual patient will change with age. In this regard, the process of aging may begin as early as the fourth decade and can proceed at different rates from person to person. In addition, with age many individuals can develop any of several systemic illnesses that can compound age-related changes in physiology and lead to serious therapeutic challenges.

EPIDEMIOLOGY

Demographic trends at least partly dictate the relevance of age-related pharmacological changes. In this regard, the world’s population is aging at an unprecedented rate. Since 1900, there has been an 11-fold increase in the number of Americans above the age of 65 years (12.6% of the population), whereas the number of those younger than 65 years has only tripled. By 2030, one in five of all Americans will be older than 65 years (1).

The elderly are more susceptible to drug effects; adverse drug reactions are at least two to three times more frequent in geriatric patients than in adults younger than 30 years (2). Unwanted adverse drug effects are responsible for many hospital admissions in elderly patients. In one series, one in six elderly patients admitted to a general ward experienced adverse drug reactions; severe reactions occurred in 24%, with orthostatic hypotension a common cause of admission (3).

PHARMACOKINETICS IN THE ELDERLY

Drug Absorption

Drug absorption is not dramatically altered with age despite the age-related change in several variables that influence drug absorption. With