

be effective in the treatment of human disease. The drug development process is briefly described at the end of this chapter.

The first steps in the discipline of clinical pharmacology were empirical descriptions of the influence of disease on drug actions and of individuals or families with unusual sensitivities to adverse drug reactions (ADRs). These important descriptive findings are now being replaced by an understanding of the molecular mechanisms underlying variability in drug actions. Importantly, it is often the personal interaction of the patient with the physician or other health care provider that first identifies unusual variability in drug actions; maintained alertness to unusual drug responses continues to be a key component of improving drug safety.

One useful unifying framework is to consider that the effects of disease, drug coadministration, or familial factors in modulating drug action reflect variability in expression or function of specific genes whose products determine pharmacokinetics and pharmacodynamics. This idea forms the basis for pharmacogenomic science; a few examples are cited in this chapter, and further details are addressed in [Chap. 68](#).

■ GLOBAL CONSIDERATIONS

It is true across all cultures and diseases that factors such as compliance, genetic variants affecting pharmacokinetics or pharmacodynamics (which themselves vary by ancestry), and drug interactions contribute to drug responses. Cost issues or cultural factors may determine the likelihood that specific drugs, drug combinations, or over-the-counter (OTC) remedies are prescribed. The broad principles of clinical pharmacology enunciated here can be used to analyze the mechanisms underlying successful or unsuccessful therapy with any drug.

■ INDICATIONS FOR DRUG THERAPY: RISK VERSUS BENEFIT

It is self-evident that the benefits of drug therapy should outweigh the risks. Benefits fall into broad categories: alleviation of symptoms, prevention of disease progression or complications, and prolonged life. However, establishing the balance between risk and benefit for