A dynamic equilibrium exists between the concentration of the drug in the blood plasma and the drug at its site(s) of action. This is what is termed *distribution*, the degree of which will depend largely on the physicochemical properties of the drug, in particular its lipophilicity. As it is frequently difficult to access the drug at its site(s) of action, its concentration in the plasma is often taken as a surrogate for the concentration at its site(s) of action. Even though the unbound drug in the plasma would give a better estimate of the concentration of the drug at its site(s) of action, this requires much more complex and sensitive assays than a measurement of the total concentration of the drug (i.e. the sum of the bound and unbound drug) within the blood plasma. Thus it is this total drug concentration within the plasma that is usually measured for clinical purposes. Therefore, plasma protein binding is a critical parameter to consider when investigating the therapeutic effect of a drug molecule.

The concentration of the drug in blood plasma depends on numerous factors. These include the amount of an administered dose that is *absorbed* and reaches the systemic circulation; the extent of *distribution* of the drug between the systemic circulation and other tissues and fluids (which is usually a rapid and reversible process) and the rate of *elimination* of the drug from the body. The drug can either be eliminated unchanged, or be enzymatically cleaved or biochemically transformed, in which case it is said to have been *metabolized*. The study and characterization of the time course of drug **a**bsorption, **d**istribution, **m**etabolism and **e**limination (ADME) is termed *pharmacokinetics*. In contrast, *pharmacodynamics* is the study of the biochemical and physiological effects of the drug on the body. The majority of drugs either mimic normal physiological or biochemical processes or inhibit pathological processes. More simply; pharmacokinetics has also been defined as what the body does to the drug; whilst in contrast pharmacodynamics may be defined as what the drug does to the body. Pharmacokinetics can be used in the clinical setting to enhance the safe and effective therapeutic management of individual patients and increasingly pharmacodynamic markers are used to assess the success of therapy.

Figure 18.1 illustrates some of the factors that can influence the concentration of the drug in the blood plasma and also at its site(s) of action. Biopharmaceutics is concerned with the first stage – getting the drug from its route of administration into the blood stream or systemic circulation.

Concept of bioavailability

If a drug is given intravenously, it is administered directly into the blood and therefore we can be sure

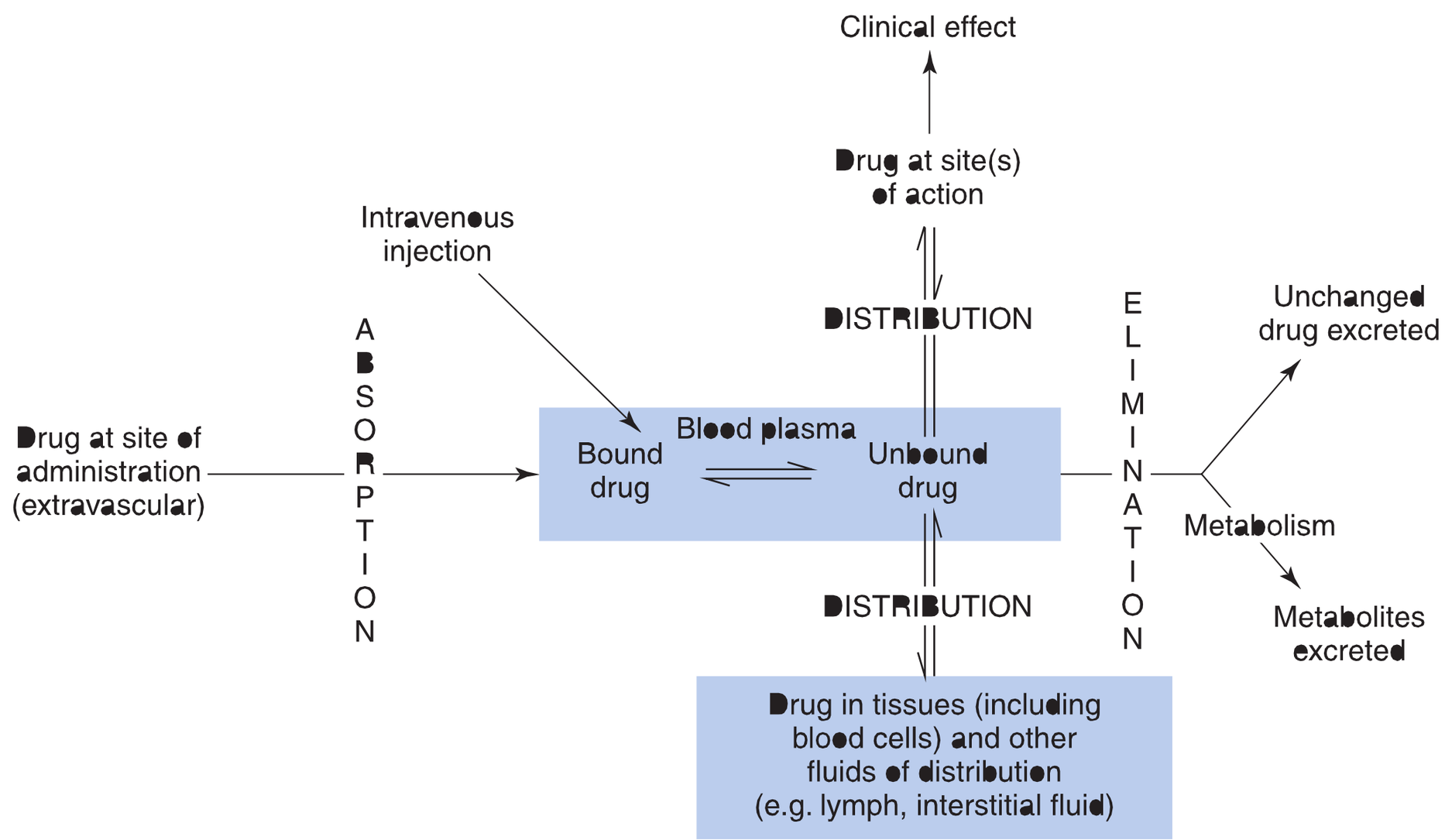

Fig. 18.1 • Schematic representation of drug absorption, distribution and elimination.