dosage form. The third factor focuses upon the patient to whom the drug will be given and encompasses the clinical state of the patient and how the patient will be managed. Finally, atypical factors may influence the dosage regimen. Collectively, all of these factors influence the dosage regimen.

The regimen of a drug may simply involve a single dose, as with pinworm medication, or may call for multiple doses. In the latter instance, the objective of pharmacokinetic dosing is to design a regimen that will continually maintain a drug's therapeutic serum or plasma concentration within the therapeutic index, that is, above the MEC but below the MTC.

Frequently, drugs are administered one to four times per day, most often in a fixed dose, for example, 75 mg three times daily after meals. As mentioned earlier, after a drug is administered, its level within the body varies because of the influence of all of the processes, ADME. A drug will accumulate in the body when the dosing interval is less than the time needed for the body to eliminate a single dose. Figure 5.17 illustrates the plasma concentration for a drug given by intravenous administration and oral administration. The 50-mg dose of this drug was given at a dosing interval of 8 hours. The drug has an elimination half-life of 12 hours. As one can see, with continued dosing, the drug concentration reaches a *steady-state* or *plateau* concentration. At this limit, the amount of drug lost per interval is replenished when the drug is dosed again. Consequently, the concentration of drug in the plasma or serum fluctuates. Thus, for certain patient types, it is optimal to target dosing so that the plateau concentration resides within the therapeutic index of a drug to maintain a MEC. For example, the asthmatic patient maintained on theophylline must have a serum concentration between 10 and 20 mg/mL. Otherwise, the patient may be susceptible to an asthma attack. Thus, when dosing the asthmatic patient, it is preferable to give theophylline around the clock four times daily to sustain levels at least above the MEC. If this medicine is administered only every 4 hours during the waking hours, it is possible that the minimum concentration will fall below effective levels between the bedtime dose and the morning dose. Consequently, the patient may awaken in the middle of the night and have an asthma attack.

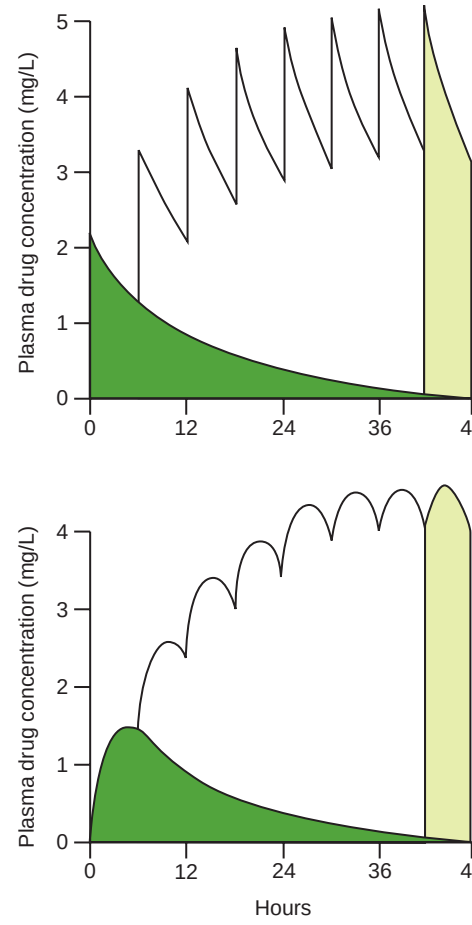

FIGURE 5.17 Plasma concentration of a drug given intravenously (*top*) and orally (*bottom*) on a fixed dose of 50 mg and fixed dosing interval of 8 hours. The half-life is 12 hours. The area under the plasma concentration–time curve during a dosing interval at steady state is equal to the total AUC for a single dose. The fluctuation of the concentration is diminished for oral administration (half-life of absorption is 1.4 hours), but the average steady-state concentration is the same as after intravenous administration, since f = 1. (Adapted with permission from Rowland M, Tozer TN. Clinical Pharmacokinetics. 3rd Ed. Baltimore, MD: Lippincott Williams & Wilkins, 1995.)

Patients can be monitored pharmacokinetically through appropriate plasma, serum, or blood samples, and some hospital