DELIVERY METHODS

As a candidate compound progresses from the discovery stage to the development stage and clinical study, an appropriate method of delivery must be identified. The most common method of dosing is oral delivery (PO). Nearly 70% of marketed medications are delivered to patients in this manner[16] as it is the most convenient, economic, and safe method of administration. This non-invasive method, however, requires a high degree of patient compliance, as efficacy is dependent upon the patient following the proper dosing strategy. In most cases, an oral medication is given without the direct supervision of medical personnel (unless the patient is in a hospital or other medical facility), and there is no guarantee that the patient will take the medicine as directed. The emergence of bacteria that are resistant to modern antibiotics (e.g., Methicillin-resistant *Staphylococcus aureus* (MRSA)[17]) is at least in part due to non-compliance with drug regimens. Patients that feel better part way through the dosing regimen may stop taking the antibiotic, providing an opportunity for bacterial resistance to develop (Interestingly, Alexander Fleming, warned of this possibility in his lecture upon receiving the Nobel prize in 1945[18]). In order to simplify dosing regimens and maximize the likelihood of patient compliance, the majority of pharmaceutical companies target once daily dosing protocols.

It is, of course, possible to move forward with a drug that must be delivered more than once a day, but increasing the number of times a pill must be ingested through the course of a 24 h period generally decrease the patient compliance. Twice daily pills are taken every 12 h, but a pill that is administered four times a day must be taken every 6 h in order to obtain an even drug exposure across a 24 h period. If the first pill is taken at 9:00 AM, then the fourth pill must be taken at 3:00 AM to maintain the schedule (Figure 9.6). Very few people want to get up at 3:00 AM to take a pill.

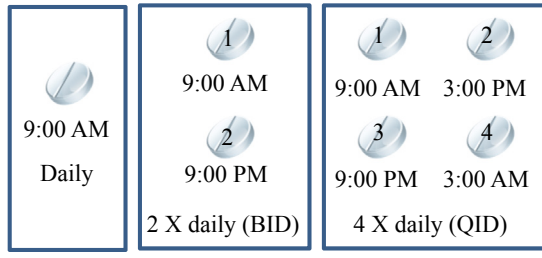

FIGURE 9.6 Dosing regimen scheduled if spaced evenly across a 24-h period.

There are many instances, however, in which oral delivery is simply not an option, as there are physicochemical issues that preclude this route of administration. If the medical need is high enough or the benefit conferred is significant enough that the targeted patient population will accept