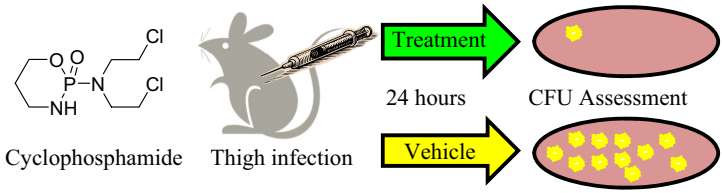

FIGURE 7.16 In the murine thigh infection model, mice are pretreated with cyclophosphamide to render them neutropenic. Introduction of a bacterial infection in the thigh is followed by a candidate compound or vehicle. After 24 h, the mice are sacrificed, and the number of colony-forming unit in treated versus untreated mice can be used to assess antibacterial efficacy of candidate compounds. CFU, colony-forming unit.

with a bacterial suspension (typically in a 10:1 dilution of the growth media) in order to establish infection. After a defined time interval, often 2–4 h, treatment with potential antibacterial agents is initiated. Both single- and multiple-dose protocols have been described in the literature. In both cases, upon completion of the dosing protocol and experimental time frame, the mice are sacrificed, and the number of colony-forming unit (CFUs) in the thigh is assessed. Efficacious compounds will decrease the number of CFUs in the thigh of treated mice relative to the untreated, control mice. Although this model is not a model of "natural" infections (pyomyositis is a very rare condition), this model is simple, versatile, and inexpensive. In addition, infection can be established with a high degree of accuracy, decreasing the number of animals required for each study, lowering the overall cost of this model.[46]

Murine Model of Systemic Infection

The murine model of systemic infection is another important infectious disease model that can be used to identify potential antibacterial agents. There are numerous variations of this procedure, but as with the thigh infection model, neutropenic mice are a typical starting point for this model. Once neutropenia is established, a lethal systemic infection is generated by intraperitoneal injection of 0.5 mL of an inoculum of an infectious bacteria (e.g., *Staphylococcus aureus*, *Listeria monocytogenes*) containing 10^7–10^8 CFU/mL. A single dose of a candidate compound is administered 1 h after inoculation and the mice are then monitored for 48 h. In the absence of effective treatment, the lethal dose of bacteria will kill the mice. Test compounds with the desired antibacterial activity will "rescue" the mice. Repeating the study with multiple doses across different groups of mice can be used to determine the ED_{50} (the dose required to rescue 50% of the mice) of candidate compounds. This