

Non-surgical rodent models of HF are also available. The Dahl salt-sensitive rat, for example, develops heart failure when placed on a high-salt diet, but HF induction requires an extended time period. Initial hypertrophy of the left ventricle develops after 4–6 weeks, while significant HF-associated remodeling is observable after 15–20 weeks. Similarly, a modified version of the spontaneously hypertensive that is prone to heart failure develops left ventricular hypertrophy that progresses into a useful model of HF by the age of 12 months. The gradual development of symptoms and onset of remodeling is more closely related to the progression of cardiovascular disease into HF than the surgical models, but the significant costs associated with maintaining animal colonies for extended periods of time (6–12 months) is a serious drawback.<sup>43</sup>

## ANIMAL MODELS OF INFECTIOUS DISEASE

There is no question that infectious disease is a significant health challenge. Despite the development of a wide range of anti-infective agents, preventing, controlling, and treating infectious disease remains an important issue. The appearance of resistant strains of various infectious organisms (e.g., methicillin-resistant *Staphylococcus aureus* (MRSA)) has highlighted the importance of continuing research efforts in this area. The concept of curing a systemic infection with drug therapy was first introduced in 1935 when Domagk demonstrated that sulphonamido-crysoidine (Prontosil) could be used to successfully treat mice suffering from a pneumococcal infection.<sup>44</sup> Since this discovery, hundreds of animal models of infection have been described in the literature. This should come as no surprise, given the wide range of infectious agents that exist in nature. An examination of a few exemplary animal models of infectious disease is useful, but a comprehensive review is well beyond the scope of this text. Those interested in a thorough review of this area are encouraged to consult specialized texts such as *The Handbook of Animal Models of Infection*.<sup>45</sup>

### Murine Thigh Infection Model

The murine thigh infection model (Figure 7.16) is one of many animal models of infectious diseases that have been employed to identify therapeutically useful compounds. In this model, mice are first treated with cyclophosphamide over a 4-day period to render them neutropenic ( $<100$  neutrophils/ $\text{mm}^3$ ) to decrease their ability to mount an immune response. Once neutropenia is established, mice are injected in the thigh