7.7 and 2.6 mg/l, respectively, for the right and left EVD after 7.5 hours (Mueller *et al*., 2012). Data on concentrations reached in patients treated for meningitis or ventriculitis are summarized in Table 45.7.

7e. Daptomycin treatment for community-acquired MRSA infections

A retrospective chart review of data from patients enrolled in a postlabeling registry who received daptomycin for MRSA infections from January to December 2005 has been reported. Community-acquired MRSA was defined as MRSA susceptible to clindamycin and trimethoprim–sulfamethoxazole; all other phenotypes were considered as other-phenotype MRSA. Success rates were calculated by dividing success (defined as cure + improvement) by the total (including nonevaluable patients). A database search identified 352 patients (100 patients with community-acquired MRSA; 252 patients with other-phenotype MRSA) who met study criteria. Most patients (79.2%) received other antibiotics with activity against Gram-positive pathogens before daptomycin. Compared with other-phenotype MRSA, a greater proportion of patients with community-acquired MRSA were < 50 years of age (50.0% vs. 35.7%; $p = 0.014$) and had fewer underlying diseases (mean [± standard deviation]: 1.7 [1.3] vs. 2.5 [1.5]; $p < 0.001$). Success rate, time to clinical response, and duration of therapy were similar in both groups (Katz and Martone, 2007).

The use of daptomycin in an outpatient parenteral therapy program (12 months, 29 patients) has been reported. In the context of a restrictive prescribing policy, daptomycin was used successfully in a difficult-to-treat population with complicated Gram-positive infections failing or intolerant of glycopeptides, including those with bone and joint infections and left-sided endocarditis. Prolonged therapy (> 28 days) was used in 31%, and myotoxicity was observed twice (Seaton and Macconnachie, 2008).

A retrospective review of medical records of hospitalized children who received daptomycin for treatment of invasive Gram-positive bacterial infections at the Children's Medical Center, Dallas, from December 2003 to March 2007 was performed. Bacterial isolates were tested for susceptibility to daptomycin and were evaluated by pulsed-field gel electrophoresis and polymerase chain reaction for staphylococcal cassette chromosome mecA. Sixteen children (10 male; median age, 6.5 years) received daptomycin. Fifteen (94%) children had invasive staphylococcal disease (14 MRSA, of which 13 were community associated and one was MSSA), and one had urinary tract infection caused by VRE. Twelve children with disseminated staphylococcal disease had bacteremia for 2–10 days despite therapy with two or more of the following: vancomycin, clindamycin, rifampicin, aminoglycoside, or linezolid. The addition of daptomycin resulted in bacteriologic cure in 6 of 7 evaluable patients with persistent bacteremia. No adverse events were attributed to daptomycin. Overall, 14 patients improved and were discharged home, and 2 died of complications of their underlying medical conditions. The majority of patients demonstrated clinical improvement after addition of daptomycin to conventional antimicrobial therapy. Further studies are needed to assess the pharmacokinetics, pharmacodynamics, safety, and effectiveness of daptomycin in infants and children (Ardura *et al*., 2007).

7f. Respiratory tract infections

Daptomycin is not effective for the treatment of community-acquired pneumonia, including infections caused by *S. pneumoniae* and *S. aureus*, most probably because of inactivation by surfactant (see section 5b, Drug distribution). Two phase III randomized double-blind trials that enrolled adult patients hospitalized with community-acquired pneumonia were conducted. Patients received i.v. daptomycin (4 mg/kg) or ceftriaxone (2 g) once daily for 5–14 days. Aztreonam could be added for patients with Gram-negative infections. The primary efficacy endpoints were the clinical responses at the TOC visit among patients in the ITT and clinically evaluable populations. After combining data from the trials, the ITT population included 413 daptomycin-treated patients and 421 ceftriaxone-treated patients, and the clinically evaluable population included 369 daptomycin-treated patients and 371 ceftriaxone-treated patients. In the ITT population, the clinical cure rate among daptomycin-treated patients with community-acquired pneumonia was 70.9%, compared with 77.4% among ceftriaxone-treated patients (95% CI for the difference between cure rates, –12.4% to –0.6%). In the clinically evaluable population, the clinical cure rate was lower among daptomycin-treated patients (79.4%) than among ceftriaxone-treated patients (87.9%; 95% CI for the difference between cure rates, –13.8% to –3.2%). Thus, data from both studies suggested that daptomycin was potentially less efficacious than ceftriaxone for community-acquired pneumonia. However, for patients who received the equivalent of 1 day of prior effective antibacterial therapy, the cure rates were similar in both treatment groups. It appeared that 1 day of effective therapy may affect clinical outcome (Pertel *et al*., 2008).

7g. Other infections

Hyper-IgE Job syndrome (hyperimmunoglobulin E syndrome) is a congenitally acquired primary immune deficiency (impaired phagocytosis). Accordingly, these patients have difficulty in eradicating staphylococcal infections. A case of Job syndrome with MRSA mitral valve endocarditis complicated by extensive metastatic septic complications manifested as brain abscess, multiple epidural abscesses, and multifocal vertebral osteomyelitis has been described. The patient did not respond to 5 days of appropriately dosed linezolid and daptomycin and remained bacteremic despite appropriate therapy because abscess drainage was not an option. High-dose daptomycin (12 mg/kg i.v. every 24 hours) cleared the MRSA bacteremia rapidly. Because daptomycin does not cross the blood–brain barrier in therapeutic concentrations, linezolid was used to treat the brain abscess. The