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Daptomycin
A Viewpoint by David A. Pegues

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Daptomycin is a novel parenteral lipopeptide antibacterial that has focused activity against aerobic Gram-positive cocci, including staphylococci, streptococci and enterococci. Daptomycin exhibits rapid, concentration-dependent bactericidal activity *in vitro*, killing cells by binding to the cell wall and forming membrane channels that result in membrane depolarisation. Daptomycin resistance emerges very infrequently *in vivo* or *in vitro*.

Daptomycin is highly protein bound (≈92%) but penetrates well into pus (≈68%). However, it penetrates poorly into lung tissue and was associated with higher rates of death and cardiovascular events than comparator-treated patients in phase III clinical trials of community-acquired pneumonia. Daptomycin has no significant drug-drug interactions and is excreted primarily in the kidneys. Patients with creatinine clearance <1.8 L/h (<30 mL/min) should have the dosing interval increased from 4 mg/kg every 24 hours to 4 mg/kg every 48 hours.

In two large, randomised trials of patients with complicated skin and skin structure infections (cSSSIs), daptomycin was as effective as anti-staphylococcal penicillin or vancomycin, and was associated with a more rapid clinical response and a 1-day shorter duration of therapy in one of the studies. The clinical success rate was lower for patients with meticillin-resistant *Staphylococcus aureus* (MRSA) cSSSI treated with daptomycin or comparator, a finding consistent with the slower *in vitro* bactericidal activity of daptomycin against MRSA than against meticillin-susceptible strains.

Although the incidence of adverse events, including elevated CPK and muscle weakness, was similar for daptomycin and comparators it appears prudent to monitor the serum CPK at least once weekly when administering daptomycin. The most common adverse events associated with daptomycin were gastrointestinal, headache and infusion site reactions. While these data support its use for cSSSI, defining the role of daptomycin for treatment of other complicated infections associated with resistant Gram-positive pathogens awaits further clinical trials. ▲