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Treatment of Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infections

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Most of infections caused by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) isolates are skin and soft tissue infections, but serious, life-threatening infections also occur.¹ To select antibiotics for initial empiric treatment of community-acquired infections for which *S. aureus* is a suspected etiology, physicians should be familiar with the antibiotic susceptibility patterns of *S. aureus* isolates in their own community. However, this information will not be readily available unless local health officials, hospital or commercial laboratories or local investigators specifically determine susceptibility rates. Most experts suggest modifying empiric therapy if

more than 10–15% of community *S. aureus* isolates are MRSA.

with the inducible MLS_B phenotype (D test-positive).

LABORATORY TESTING

Microbiology laboratories should routinely test *S. aureus* isolates for susceptibility to macrolides, clindamycin, trimethoprim-sulfamethoxazole (TMP-SMX) and doxycycline or minocycline in addition to β -lactam antibiotics and gentamicin. Many CA-MRSA isolates are resistant to macrolides but remain susceptible to clindamycin. Clindamycin and TMP-SMX have become important in the management of staphylococcal infections. To avoid delays in selecting the most appropriate agent, isolates should be tested routinely for the inducible macrolide-lincosamide-streptogramin phenotype (MLS_B) using the Clinical and Laboratory Standards Institute (formerly NCCLS)-approved method.² This requires an additional step and expense for those laboratories using automated antibiotic susceptibility methods. However, treatment failures with clindamycin have been reported for infections caused by MRSA isolates

THERAPY

β -Lactam antibiotics such as dicloxacillin or cephalexin for outpatients or nafcillin, oxacillin or cefazolin for inpatients are no longer appropriate antibiotics for empiric treatment or for completing treatment when CA-MRSA is a consideration or is isolated. Vancomycin is recommended for inclusion in empiric antibiotic regimens for seriously ill patients with infections that may be due to CA-MRSA. Such cases include children with septic shock, acute infective endocarditis, pneumonia with empyema or bone and joint infections complicated by septic thrombophlebitis, among others. Gentamicin is generally added to vancomycin for suspected life-threatening MRSA infections. Nafcillin/oxacillin is more rapidly bactericidal than vancomycin for methicillin-susceptible *S. aureus* (MSSA) isolates, and clinical data in adults suggest that nafcillin/oxacillin is superior to vancomycin for the treatment of serious MSSA infections.³ Thus for these patients, naf-

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cillin/oxacillin is also recommended to optimally treat MSSA isolates.

CA-MRSA isolates typically are susceptible to clindamycin and TMP-SMX. Clindamycin is effective in treating serious infections caused by clindamycin-susceptible CA-MRSA isolates, including osteomyelitis, septic arthritis and pleural empyema.^{4,5} Clindamycin is initially administered intravenously at a dose of 30–40 mg/kg/d in 3 divided doses. Clindamycin is well-absorbed by the oral route; thus treatment can be completed with oral clindamycin at the same dose. The most concerning adverse effect of clindamycin is *Clostridium difficile* enteritis which is a relatively rare complication

In some regions of the United States, a high proportion of CA-MRSA strains are clindamycin-resistant. If the proportion of CA-MRSA isolates resistant to clindamycin exceeds 10–15%, clindamycin should not be used for empiric treatment of suspected staphylococcal infections.

Simple skin and soft tissue infections account for >90% of the infections caused by CA-MRSA isolates. Optimal management of these infections is not completely clear. In several reports, β -lactam antibiotics generally were associated with a successful outcome of skin and soft tissue infections in otherwise normal children, particularly for abscesses <5 cm in diameter that underwent incision and drainage.⁶ Incision and drainage of abscesses without antimicrobial therapy are effective in many patients. It may be that normal host defenses along with tissue levels of an antistaphylococcal β -lactam antibiotic exceeding the minimal inhibitory concentration for a short period of time is sufficient to eradicate the organism. Nevertheless in regions where CA-MRSA isolates account for 10–15% or

more of community isolates, empiric antistaphylococcal β -lactam antibiotic treatment of skin and soft tissue infections is not recommended. In this setting, TMP-SMX or clindamycin can be used. Some authorities suggest adding rifampin to TMP-SMX. However, information regarding TMP-SMX treatment of MRSA infections is limited, although in initial clinical studies TMP-SMX was effective in treating MSSA infections.^{7,8} TMP-SMX may result in hypersensitivity reactions or bone marrow suppression. TMP-SMX is not active against group A *Streptococcus*, another common cause of skin and soft tissue infections. Some experts do not recommend TMP-SMX for treatment of invasive CA-MRSA infections. Doxycycline or minocycline has been efficacious in treating adults with skin and soft tissue infections caused by MRSA and is a consideration for children older than 8 years of age.⁹

Linezolid is another option for treating CA-MRSA infections in children.¹⁰ This new oxazolidinone is equivalent to vancomycin for the treatment of serious MRSA infections, including bacteremia and pneumonia in children.¹¹ Side effects of linezolid include thrombocytopenia, optic neuritis and neuropathy. Linezolid has not been well-studied in the treatment of osteomyelitis. Linezolid is well-absorbed after oral administration, and therapy can be completed with an oral formulation. Daptomycin is approved for the treatment of serious staphylococcal infections in adults but may not be efficacious in treating pulmonary infection.¹² The dose and safety profile of daptomycin are not established for children. The AAP has outlined an approach to managing suspected CA-MRSA skin and soft tissue infections.¹³

PREVENTION

Recurrent CA-MRSA infections and spread of CA-MRSA infections among family members are common. Preventive measures include keeping fingernails clean and cut short and changing towels, washcloths, underwear and sleepwear daily. Applying mupirocin to the anterior nares may be useful to diminish nasal colonization by CA-MRSA, although a Cochrane review did not find topical antibiotics to be useful for eradicating nasal MRSA.^{14,15} Finally taking a bath twice a week for 15 minutes in water to which regular strength Clorox (1 teaspoon per gallon of water) has been added appears to be helpful in preventing recurrent infections.

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