

Clinical Insights® in

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Issue No. 5, January 2006, is part of a 12-part CME activity (September 2005 – August 2006).

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Applicants will receive a certificate of participation from PPS by return mail within 6 to 8 weeks of the date of receipt of the completed evaluation/registration form.

Learning Objectives

After studying the literature presented in this Pediatric Respiratory Care series, participants will be able to:

- Identify respiratory disorders in pediatric patients
- Summarize risk factors for respiratory disorders in pediatric patients
- Select an appropriate therapeutic regimen for patients with pediatric respiratory disorders

Target Audience

This educational activity is designed for pediatricians, primary care physicians, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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Community-acquired MRSA: An emerging problem needs a therapeutic solution

Methicillin-resistant *Staphylococcus aureus* (MRSA) are known worldwide as nosocomial pathogens. In recent years, however, infections referred to as community-acquired (CA)-MRSA have been documented worldwide in healthy community-dwelling persons, including children. Exposure to areas of high population density, such as day care centers or schools, or participation in sports activities may raise a child's risk of contracting CA-MRSA. Individuals of Native American, Native Alaskan, or Pacific Island descent also appear to be at higher risk of CA-MRSA infection. The increased frequency of CA-MRSA infection means it has overtaken *streptococcus pneumoniae* as a major cause of bacterial and metastatic pulmonary disease and primary pneumonia with complicated effusions in children. (See accompanying article.)

A recent study by Kuehnert and colleagues at the Centers for Disease Control and Prevention (CDC), estimates that 32.4% (89.4 million persons) and 0.8% (2.3 million persons) of the US population ≥1 year old were colonized with *S aureus* and MRSA, respectively. Prevalence was highest among males and children 6 to 11 years of age. When the analysis was limited to MRSA, age ≥60 years and being female increased the risk for colonization.

CA-MRSA strains have distinct genetic fingerprints with characteristic antimicrobial

resistant patterns that can vary from region to region. Strain USA300 has become a dominant CA-MRSA strain in the community setting and is also occurring within the healthcare setting. The increasing threat of CA-MRSA has spurred interest in identifying potential treatments, as

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recently reviewed by Ellis and Lewis. Clinical trials involving numerous, recently approved (linezolid, daptomycin) or emerging (tigecycline, dalbavancin,* and telavancin*) anti-staphylococcal agents demonstrate that all agents show promise, but caveats exist for their usefulness.

- Linezolid's use in MRSA pneumonia may be best for patients with renal insufficiency for whom appropriate vancomycin dosing might be problematic.
- Daptomycin may provide an advantage over some newer agents based on its bactericidal activity, although this has not been conclusively proven. Daptomycin is not recommended for pneumonia because of binding to surfactant. Further, its complicated susceptibility testing makes it a challenge for clinicians.

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Disclosures:

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Community-acquired MRSA: An emerging problem needs a therapeutic solution

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- Tigecycline is able to overcome many of the resistance mechanisms that have limited the usefulness of older tetracyclines, but concerns regarding its tolerability and a paucity of data for this drug may affect enthusiasm.
- Remaining pipeline antimicrobials (dalbavancin* and telavancin*) are also plagued by a dearth of data.

Based on potential cost issues associated with the newer drugs and the favorable broad susceptibility pattern of CA-MRSA, several studies are re-examining the usefulness of older antimicrobials in treating this infection.

- Tetracyclines may still be useful in the fight against CA-MRSA, but prospective studies are needed to determine whether these agents should be used as monotherapy or combined with other antimicrobials.
- For the fluoroquinolones, CA-MRSA susceptibility is quite varied; however, the newer agents (moxifloxacin and gatifloxacin) may be useful, especially in combination with other agents.
- Rifampin has been routinely added to various agents in the treatment of CA-MRSA, even though there are sparse

data to support this practice. Conflicting reports have left the question of rifampin use clouded and in need of further prospective investigation.

- Trimethoprim-sulfamethoxazole appears to be an excellent agent for treating CA-MRSA, but clinicians appear to routinely underdose this drug based on their experience treating urinary tract infections.
- Finally, clindamycin, although effective, is less predictably active against CA-MRSA.

The authors stress that selection of specific antimicrobials for treatment of CA-MRSA should be governed by the severity of the disease, susceptibility patterns of the infecting strain, clinical response to therapy, and cost.

NOTE: the FDA has not approved the discussed use of the drug in this study.

Ellis MW, Lewis JS II. Treatment approaches for community-acquired methicillin-resistant *Staphylococcus aureus* infections. *Curr Opin Infect Dis.* 2005; 18:496-501.

Additional article of interest: Kuehnert M et al. Prevalence of *Staphylococcus aureus* nasal colonization in the United States, 2001–2002. *J Infect Dis.* 2006;193:172-179.

Pulmonary involvement and correlation of virulence factor genes with pediatric CA *S aureus* infections

In some communities, community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has largely supplanted *Streptococcus pneumoniae* as the most common pathogen isolated from patients with complicated pneumonia. One additional consequence of invasive *S aureus* infection is an increase in metastatic pulmonary infection. Several *S aureus* virulence determinants, including the genes encoding the Pantan-Valentine leukocidin (PVL), and collagen adhesion (CNA), have been postulated as important for certain disease processes. In a recent publication, Gonzalez and colleagues report their efforts to describe the

pulmonary involvement in children with CA *S aureus* invasive infection at Texas Children's Hospital (TCH), and to determine whether the presence of the genes encoding PVL or CNA is correlated with pulmonary manifestations. The study group was composed of patients with invasive staphylococcal infections admitted to TCH between August 2001 and June 2004.

Patients with CA-MRSA (67%) demonstrated a significantly ($P < 0.001$) higher rate of abnormal findings upon pulmonary imaging when compared to patients infected with methicillin-susceptible strains (CA-MSSA; 28%). Furthermore 45% of the CA-MRSA-infected individuals with abnormal pulmonary

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Pulmonary involvement and correlation of virulence factor genes with pediatric CA *S aureus* infections

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findings received a primary diagnosis of pneumonia and 43% of this group received a primary diagnosis of osteomyelitis. For individuals with CA-MSSA infections and abnormal pulmonary findings (N=10), only two received a primary diagnosis of pneumonia and six received a diagnosis of bone and/or joint infections. Regardless of methicillin-sensitivity, individuals with invasive *S aureus* infections leading to a primary diagnosis of pneumonia were younger than patients with other invasive diseases (CA-MRSA, mean age 3.5 yrs vs 9.9 yrs, $P=0.001$; CA-MSSA, mean age 0.7 yrs vs 12.1 yrs). Metastatic pulmonary disease was seen mainly in patients with bone and joint infections.

In a survey of isolates, the genes encoding PVL were highly associated with pulmonary manifestations in children with invasive staphylococcal infections. Although these findings suggest that PVL may play a role in pulmonary tissue damage, its exact role needs further clarification. The gene encoding CNA did not exhibit a similar association.

Taken together, these findings suggest that pulmonary abnormalities in children with invasive staphylococcal infections are common. The authors suggest that once CA-MRSA isolates account for a large proportion of the CA *S aureus* isolates in a community, *S aureus* is likely to be a common cause of primary pneumonia, especially in cases complicated by emphysema or abscesses. However, this is somewhat dependent on the specific clones in circulation within a particular community. Nonetheless, initial antimicrobial treatment for children with suspected pleural empyema (or other serious invasive infections for which *S aureus* may be a possibility) should include an agent effective against the CA-MRSA strains in the community.

Gonzalez BE, Hulten KG, Dishop MK, et al. Pulmonary manifestations in children with invasive community-acquired *Staphylococcus aureus* infection. *Clin Infect Dis*. 2005; 41:583-590.

PRCI™ MISSION STATEMENT

The PRCI™ is a multicomponent educational program on pediatric respiratory disorders designed for pediatricians, primary care physicians, infectious disease specialists, allergists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients. PRCI™ programs address issues concerning asthma, respiratory syncytial virus and other respiratory tract infections and disorders. Methods to prevent, control, and treat respiratory illnesses in children are also evaluated.

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Clinical Insights® in Pediatric Respiratory Care is edited by PRCI™ faculty member Pedro A. Piedra, MD.

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