Staphylococcus aureus Infections in Children: The Implications of Changing Trends

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In this issue of Pediatrics, Sutter et al.1 report the antibiotic susceptibility trends of Staphylococcus aureus isolates recovered from >39,000 children who received care at sites within the US military health system from 2005 through 2014. S. aureus is the most common pathogen causing skin and soft tissue infections (SSTIs) as well as some invasive infections such as osteomyelitis and septic arthritis in children.2 S. aureus is also 1 of the most common organisms isolated from children with healthcare-associated infections, regardless of whether these infections had their onset in the community or were acquired in the hospital. Thus, the initial empiric treatment of an SSTI or invasive infection in a child almost always includes an antibiotic effective against S. aureus. Before the 1990s, penicillinase-resistant β-lactam antibiotics with activity against methicillin-susceptible S. aureus isolates (methicillin, nafcillin, oxacillin, or cefazolin for invasive infections or oral agents such as dicloxacillin or cephalaxin for outpatient SSTIs) were typically administered for suspected staphylococcal infections with onset in the community. Up until that time, methicillin-resistant S. aureus (MRSA) isolates were almost always associated with hospital-acquired infections. In the late 1990s and early 2000s, investigators around the United States and subsequently worldwide described the emergence of different clones of S. aureus that were methicillin resistant but causing infections that were community-acquired (ie, CA-MRSA).3-6 One clone (USA300) quickly dominated in the United States, causing SSTIs, severe invasive infections, and, notably, recurrent infections. Furthermore, the USA300 CA-MRSA clone also became a common nosocomial pathogen.7

Why different clones emerged simultaneously around the world remains somewhat of a mystery. Initially, there was uncertainty regarding what percentage of community S. aureus isolates labeled CA-MRSA (10%, 25%, or 50%) would justify a change in empiric therapy, especially for invasive infections. Of course, this situation also meant that physicians caring for children needed to know what proportion of S. aureus isolates recovered from children in their community were indeed methicillin-resistant, which is not a readily available piece of information. However, in a short period of time, the majority of CA S. aureus isolates from children in many areas of the United States were the USA300 clone of CA-MRSA, which appears to have a unique virulence factor or factors, resulting in a highly successful pathogen. This information lead to changes in the recommendations for empiric treatment of suspected S. aureus infections to include an antibiotic effective against these USA300 CA-MRSA isolates, which were typically susceptible to clindamycin and trimethoprim/sulfamethoxazole.8 However, over the years, clindamycin susceptibility among S. aureus isolates has declined, likely related to the increased use of this agent for empiric as well as definitive treatment of...
CA-MRSA infections, encouraging the transmission of the genes associated with clindamycin resistance. In the United States have indicated that the percentage of CA-MRSA isolates among S. aureus—causing community infections has plateaued and that the incidence of health care–associated invasive MRSA infections has declined. \(^\text{10, 11}\) In the study by Sutter et al., \(^\text{1}\) isolates recovered from outpatients and inpatients were grouped together, and thus no distinctions were made for infections that were CA, health care associated but with community onset, or hospital acquired. The most common site of infection was skin and soft tissue, but the second most common site was "other" infections, which were not further identified. Respiratory infections were the third most common site, and it was again unclear what type of infections these represent (eg, sinus, eye, pneumonia). When all isolates were considered, the proportion of isolates labeled MRSA each year reached a peak in 2007 (46.4%) and then declined steadily to 31.6% in 2014. Similar proportions were reported just for isolates associated with SSTIs, although no significant changes were noted for isolates from sterile site infections. The authors do not speculate about the reason(s) for these findings. In contrast, resistance to clindamycin slowly increased over these same years from 9.3% in 2005 to 14% in 2014, and this rise was primarily related to increases among methicillin-susceptible S. aureus isolates. Trimethoprim/sulfamethoxazole remained highly active throughout the years (>98% of isolates were susceptible).

What are the implications of the findings from the report by Sutter et al. \(^\text{1}\) with respect to the selection of empiric antibiotics for children with suspected S. aureus infections? Currently, considering the still substantial MRSA resistance rates that exceed the 10% to 15% level suggested by many experts as the threshold above which agents effective against CA-MRSA isolates should be administered for empiric treatment (http://www.cdc.gov/mrsa/pdf/MRSA-Strategies-ExpMtgSummary2006.pdf), changes in the selection of empiric antibiotics are not warranted. If rates of MRSA among S. aureus isolates from otherwise normal children are documented to drop below the 10% to 15% threshold in different communities, a modification of current recommendations should be considered. It would also be important to understand why methicillin resistance is declining among S. aureus isolates from CA infections; this information may provide clues for preventing CA-MRSA infections with the use of vaccines or other means. The epidemiology of S. aureus infections in children has been changing over the past 2 decades, which is why it is critical to keep a very close eye on this common pathogen.

**ABBREVIATIONS**

CA: community-acquired MRSA: methicillin-resistant *Staphylococcus aureus* SSTI: skin and soft tissue infections

**REFERENCES**

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