

August 10, 2002

To: Medical Staff of Le Bonheur Children's Medical Center

From: The Division of Pediatric Infectious Disease

Re: Macrolide resistance in Group A Streptococcus and in *Streptococcus pneumoniae*

In April 2002, an article appeared in the *New England Journal of Medicine* describing an outbreak of pharyngitis caused by a single strain of erythromycin-resistant *Streptococcus pyogenes* (Group A Streptococcus [GAS]) among children in a school in Pittsburgh, PA from October 2000 to May 2001 (*New Engl J Med* 2002;346:1200-6). The article garnered considerable attention from the national media, and locally was the subject of an article in *The Commercial Appeal* (April 18, 2002). Although macrolide resistance among GAS isolates was previously observed in the United States and high levels of resistance had been reported in several other countries, never before had such high rates of GAS macrolide resistance been noted in a community in the United States. The dramatic increase in resistance rates observed in Pittsburgh raised the question of whether erythromycin could continue to serve as the alternative drug of choice for treatment of streptococcal pharyngitis in patients with serious allergies to penicillin.

The Infectious Disease Laboratory at Le Bonheur routinely performs susceptibility testing for erythromycin (and other antibiotics) on GAS isolates only if they are recovered from normally sterile body sites (e.g., blood, pleural fluid, etc.); pharyngeal isolates are not tested routinely. In order to assess macrolide resistance among pharyngeal GAS isolates at Le Bonheur, our laboratory performed erythromycin susceptibility testing on 124 consecutive GAS pharyngeal isolates from May 16 to June 2, 2002. Of these, 93% were fully susceptible, 4% intermediately susceptible and 3% resistant to erythromycin. It should be noted that erythromycin-resistant GAS isolates are also resistant to the newer macrolides used in children, clarithromycin and azithromycin. These data suggest that while there is some resistance to macrolides among GAS isolates in Memphis, we have not experienced anything resembling the very high resistance rates seen in Pittsburgh. Therefore, in our community erythromycin may continue to be used as an alternative agent for the treatment of streptococcal pharyngitis for children who are allergic to or otherwise unable to take penicillin or other beta-lactams. Surveillance for macrolide-resistant GAS in our laboratory will continue to be performed on a periodic basis.

Unfortunately, not all news regarding macrolide resistance in Memphis is good. Erythromycin resistance among isolates of *Streptococcus pneumoniae* has been increasingly common in our laboratory, reflecting a trend that has been seen in nationwide surveillance studies (*JAMA*: 2001; 286:1857-62). As is true of GAS, *S. pneumoniae* isolates that are resistant to erythromycin are also resistant to azithromycin and clarithromycin. Macrolide resistance is particularly prevalent among *S. pneumoniae* isolates that are nonsusceptible to penicillin; among such isolates from children in the greater Memphis area, the rate of erythromycin

resistance was 83% in 2000 and 73% in 2001 (data submitted for publication). Data from multiple published studies suggest that the increasing macrolide resistance rates observed nationwide are directly related to increasing consumption of the newer macrolide antibiotics. Azithromycin appears particularly likely to induce resistance in pneumococci (*Pediatr Infect Dis J* 2000; 19:41-6), probably because the antibiotic remains present in subtherapeutic concentrations in the respiratory epithelium for extended periods of time.

The Le Bonheur Division of Infectious Disease endorses published guidelines for the management of acute otitis media (sponsored by the Centers for Disease Control and Prevention; *Pediatr Infect Dis J* 1999;18:1-9) and sinusitis (sponsored by the American Academy of Pediatrics; *Pediatrics* 2001;108:798-808). These guidelines recommend that amoxicillin be used as first-line therapy for otitis media and sinusitis and that amoxicillin/clavulanate be used in children who have recently been treated with antibiotics or who fail to improve while receiving amoxicillin. Increasing the dose of amoxicillin to 80-90 mg/kg/day is recommended in children likely to be infected with penicillin-nonsusceptible pneumococci (including children aged less than 2 years, attending day care or treated recently with antibiotics). Recommended second-line agents in both guidelines include cefuroxime axetil and ceftriaxone; the sinusitis guideline also lists cefdinir and cefpodoxime as acceptable second-line agents. Neither guideline endorses the use of azithromycin for these infections. If a macrolide agent must be used for treatment of otitis media or sinusitis, we recommend clarithromycin over azithromycin because the former is more likely to eradicate *S. pneumoniae* and less likely to select for the development of resistant strains.

Please contact the Le Bonheur infectious disease physician on call (572-3292 or 579-4707) for questions about these recommendations.

Sincerely,

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