MRSA and Non-MRSA Otorrhea in Children

A Comparative Study of Clinical Course

Nathan S. Alexander, MD; Brian D. Kulbersh, MD; C. Hope Heath, MD; Renee A. Desmond, DVM, PhD; Eric Caron, CRNP; Audie L. Woolley, MD; Jimmy Scott Hill, MD; W. Peyton Shirley, MD; Brian J. Wiatrak, MD

**Objective:** To test the perception that post–tympanostomy tube otorrhea caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is a more virulent disease than otorrhea caused by other pathogens by analyzing the clinical differences and disease courses in children diagnosed with otorrhea caused by MRSA bacteria vs non-MRSA bacteria.

**Design:** Retrospective review.

**Setting:** Tertiary children's hospital.

**Patients:** We retrospectively examined the medical records of children who presented to a tertiary children's hospital from January 1, 2003, to December 31, 2008, with otorrhea that occurred after tympanostomy tube insertion.

**Main Outcome Measures:** Otorrhea culture records were used to group the 1079 patients into those whose otitis media was due to MRSA (n=170) and those with non-MRSA otitis media (n=909). From the non-MRSA group, we randomly selected an age-matched group of 170 and examined the differences between the MRSA and age-matched non-MRSA groups in organisms isolated by culture, demographic factors (including type of medical insurance), medical history, treatments, surgical procedures performed, audiometric data, and other admissions for infection-related illnesses.

**Results:** The overall incidence of MRSA in this series was about 16% (170 of 1079 patients). Of the 170 eligible children in each age-matched group, 135 with MRSA otorrhea and 141 with non-MRSA otorrhea had data in every category selected for statistical analysis. The groups did not differ significantly in type of insurance; history of tympanostomy tube placement, cholesteatoma, or prematurity; number or type (minor/major) of surgical procedures performed; or risk of subsequent infection-related diagnoses. More patients in the MRSA group received intravenous antibiotic therapy (11% vs 3.6%; \( P < .001 \)).

**Conclusion:** In this study, a diagnosis of otorrhea due to MRSA did not carry an increased risk for surgical procedures or infection-associated sequelae compared with a diagnosis of non-MRSA otorrhea.


**More than half a million procedures are performed annually to place tympanostomy tubes in children, making this the most common surgical procedure performed in childhood.**

**Otorrhea is the most common complication associated with tympanostomy tube insertion**, with early-onset rates ranging between 10% and 20% and late-onset rates ranging between 30% and 80%. Reported rates for current and chronic post–tympanostomy tube otorrhea are 7.4% and 3.8%, respectively. Pathogens most frequently reported include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Corynebacterium diphtheriae*. In children older than 3 years, infections are more often due to *S aureus* and *P aeruginosa*. Typically, episodes of isolated otorrhea are treated effectively with topical antimicrobial agents and/or oral antibiotics, although over the last decade, there has been increasing concern about antibiotic-resistant bacteria, ie, methicillin-resistant *S aureus* (MRSA) and penicillin-resistant *S pneumoniae*.

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Post–tympanostomy tube MRSA otorrhea was first described as an emerging concern more than 10 years ago. In 2000, Hartnick et al identified 8 cases of MRSA-associated otitis media in a 14-month period, representing a MRSA-caused otitis media incidence in their population of only 0.2%. In 1998, Suh et al reported a MRSA-related otorrhea incidence of 8% after middle ear surgery. In 2000, Santos et al
or she was seen during the study period. Patients whose culture results showed the presence of MRSA at any time during the study period were assigned to the MRSA group (n=170), and those whose culture results never showed evidence of MRSA were assigned to the non-MRSA group (n=910). Within the non-MRSA group, if a patient had multiple culture results from different dates, subsequent analyses were based only on data from the first incident. An independent statistician randomly selected an age-matched subset of 170 patients from the non-MRSA group who subsequently underwent a full chart review.

DEFINITION OF RISK FACTORS AND OUTCOMES

In addition to culture results, the following information was recorded, when present, from the 170 patients with MRSA ototrrhea and the 170 patients with ototrrhea due to non-MRSA pathogens: age at diagnosis of the study incident of ototrrhea; race; insurance status; medical history (any associated syndrome, cleft lip/palate, prematurity); prior tympanostomy tube placement (1 set, 2 sets, or >2 sets); treatments received (topical antibiotics, oral antibiotics, intravenous antibiotics); surgical procedures performed (minor vs major); most recent audiometric data (normal hearing or mild, moderate, or severe/profound hearing loss); and other admissions for infection-related illnesses (skin and soft-tissue infections) or complications of otitis media (eg, meningitis, sigmoid sinus thrombosis). Minor surgery was defined as myringotomy, myringotomy with tube placement, middle ear irrigation/packing with an antibiotic-soaked absorbable gelatin sponge (Gelfoam), and myringoplasty. Major surgery was defined as tympanoplasty with or without mastoidectomy. All patients were treated by the same 4 pediatric otolaryngologists (A.L.W., J.S.H., W.P.S., and B.J.W.).

STATISTICAL ANALYSES

Continuous variables were summarized as mean (SD), and values for the 2 study groups were compared by t test. Categorical variables were summarized by frequencies and compared for the MRSA and non-MRSA groups using χ² tests. All analyses were performed with SAS version 9.2 (SAS Institute).

RESULTS

CULTURE RESULTS

Of 1079 total ototrrhea cultures obtained over the 6-year study period (2003 to 2008; duplicates removed), S aureus was identified in 321 cases (18.9%) and was identified as resistant to oxacillin sodium (MRSA) in 170 of the 321 cases (53%). Of these 170 cases, 135 (79%) had sufficient data for analysis and formed the MRSA study group. Of the 170 age-matched children with non-MRSA ototrrhea, 141 (83%) had sufficient data for analysis and formed the non-MRSA study group. The predominant organisms cultured in this group were *P aeruginosa* (n=35 [24%]), (methicillin-sensitive) *S aureus* (n=23 [16%]), *S pneumoniae* (n=14 [9.9%]), and *H influenzae* (n=12 [8.5%]) (Table 1).

GROUP DIFFERENCES

As Table 2 shows, the 141 patients with non-MRSA ototrrhea and the 133 patients with MRSA ototrrhea were similar as to age (mean, 4.0 years vs 4.1 years), length of fol-

| Table 1. Non–Methicillin-Resistant *Staphylococcus aureus* Otorrhea Organisms Cultured in 141 Patients |
|---------------------------------|-----------------|
| **Organism**                     | **No. (%)**     |
| Pseudomonas aeruginosa           | 35 (24.8)       |
| Staphylococcus aureus            | 23 (16.3)       |
| Streptococcus pneumoniae         | 14 (9.9)        |
| Haemophilus influenzae           | 12 (8.5)        |
| Candida albicans                 | 9 (6.4)         |
| Candida parapsilosis             | 5 (3.5)         |
| Escherichia coli                 | 5 (3.5)         |
| Streptococcus pyogenes (group A) | 5 (3.5)         |
| Staphylococcus epidermidis (coagulase negative) | 4 (2.8) |
| Moraxella (Branhamella) catarhalis | 3 (2.1) |
| Streptococcus sanguis (viridans group) | 3 (2.1) |
| Other (n=16)                     | 23 (16.3)       |

STUDY METHODS

This study was approved by the institutional review board of the University of Alabama at Birmingham. In coordination with the Infection Prevention Office at the Children’s Hospital of Alabama, Birmingham, candidates for the study were selected by searching an internal database for all “otorrhea” cultures obtained in the otolaryngology clinic between January 1, 2003, and December 31, 2008. We identified the bacterial pathogens from the culture report for each patient at each time he described 3 patients with MRSA-associated otitis, including the first neonatal case. Since that time, there has been a 16.3% increase in MRSA-associated pediatric head and neck infections, more than one-third of which have been otologic infections.12 There has also been a significant increase in the incidence of pediatric community-acquired MRSA, which is distinguished from hospital-acquired MRSA by the absence of established risk factors, such as prolonged hospitalization, multidrug or prolonged antibiotic therapy, and use of indwelling catheters.13,14 In a study of organisms causing chronic otitis media in 2773 patients of all ages over an 8-year period, the proportion of cases of community-acquired MRSA rose from 0.7% in 1998 to 11.4% in 2006; most of these infections were susceptible to trimethoprim-sulfamethoxazole and rifampin.14

The increase in incidence of MRSA infections has been reported in the media. Initial reports described drug-resistant bacteria causing widespread skin and soft-tissue infections among sports participants. In the first documented episode, which occurred in Vermont in 1993, community-acquired abscesses developed in 6 high school wrestlers.15 The many similar outbreaks reported since have caused significant, sometimes extreme, anxiety among parents with children with MRSA ototrrhea.

Despite the increased incidence of MRSA infections and specifically MRSA ototrrhea, we found little in the literature on the morbidity of MRSA ototrrhea. We therefore conducted the study reported herein to examine the prevalence of ototrrhea after tympanostomy tube placement in our large pediatric practice and to determine risk factors and outcomes of treatment for MRSA compared with non-MRSA infections.
low-up (mean, 4.3 years vs 4.2 years), insurance status, whether they had an associated congenital syndrome, and whether there was a history of prematurity. A higher percentage of patients with non-MRSA otorrhea (21.0% vs 3.7%; \(P = .001\)) had a history of prematurity; however, the non-MRSA group had a higher proportion of patients with cleft lip/palate \((11.4\% \text{ vs } 4.4\%; \ P = .03)\). Insurance status (private vs Medicaid/other) was not significantly different between the MRSA and non-MRSA groups \(\left(\ P = .97\right)\). All cultures obtained were from children who had previously undergone placement of tympanostomy tubes. Most children in both groups had a history of only 1 tympanostomy tube placement procedure \(\left(72.9\% \text{ MRSA vs } 79.2\% \text{ non-MRSA} \right)\). However, the proportion of patients who needed minor or major surgery was significantly higher among those with non-MRSA otorrhea \(\left(44.4\% \text{ vs } 21.0\%; \ P < .001\right)\).

### MEDICAL MANAGEMENT

**Table 3** shows the treatments and outcomes for the 2 groups of children. Topical therapy alone (vinegar/water irrigation with topical antibiotics) was successful in treating otorrhea in 93 of the 141 patients \(\left(66.0\% \text{ MRSA vs } 69.5\% \text{ non-MRSA} \right)\). No patient in either group was admitted to the hospital due to MRSA; however, no complications of otitis media, such as significant hearing loss or severe/profound hearing loss, were reported. The surgical treatments that patients underwent at the time of otorrhea were shown in Table 3. Equivalent percentages of patients in both groups required major or minor surgery \(\left(5.0\% \text{ MRSA vs } 3.0\% \text{ non-MRSA} \right)\). There was no significant difference in the proportions of patients who needed minor or major surgery \(\left(\ P = .35\right)\).

**SURGICAL THERAPY**

The surgical treatments that patients underwent starting on the date when otorrhea was sent for culture are shown in Table 3. Equivalent percentages of patients in the non-MRSA \(\left(43.3\% \text{ MRSA vs } 44.4\% \text{ non-MRSA} \right)\) groups required no further surgery to manage otorrhea. There was no significant difference between the 2 groups in the proportions of patients who needed minor or major surgery \(\left(\ P = .35\right)\).

**HEARING OUTCOME**

Of those patients with follow-up audiograms available for review, a slightly higher proportion in the MRSA group had mild hearing loss \(\left(11.4\% \text{ vs } 6.2\% \right)\). This difference was not statistically significant \(\left(\ P = .08\right)\); slight differences in the proportions of the patients with moderate or severe/profound hearing loss were also not significant \(\left(\ P = .08\right)\).

**COMPLICATIONS OF INFECTION**

No patient in either group was admitted to the hospital for the treatment of skin or soft-tissue infection. Furthermore, no complications of otitis media, such as sig-
mroid sinus thrombosis, facial paralysis, or meningitis, were seen.

**COMMENT**

Community-acquired MRSA typically causes skin and soft-tissue infection, but this organism has also been reported to cause necrotizing pneumonia and necrotizing fasciitis. Its increased prevalence among young sports participants and primary school populations has been noted by, and has often led to anxiety in, our patients' families. Among health care professionals, increasing rates of MRSA-associated post–tympanostomy tube otorrhea have prompted increased attention to infection control policies and treatment algorithms for this pathogen, referred to by the Canadian Department of Infectious Diseases as "the superbug at our doorstep."15

The treatment of patients with MRSA otorrhea has changed substantially over the last decade, both nationwide and in our pediatric otolaryngology practice. Many of the first patients with culture-proven MRSA otorrhea were hospitalized for a 2-week course of parenteral antibiotics and were more likely to undergo mastoidectomy if they developed chronic infection of middle ear mucosa or granulation tissue. Treatment of mild to moderate MRSA otorrhea has become much less aggressive but no less successful, as documented in a literature review by Baugher et al.12 They found that previously healthy patients with mild (no fever) to moderate (with fever) MRSA infections had good outcomes after a course of oral trimethoprim-sulfamethoxazole combined with gentamicin, polymyxin B–neomycin-hydrocortisone, or ofloxacin topical antibiotics. For patients with moderate to severe infections (toxic appearance, immunocompromised, or limb-threatening and requiring hospitalization), the first-choice antibiotic was usually vancomycin, often combined with rifampin or gentamicin.12

Choi et al16 studied the effectiveness of treating chronic MRSA supplicative otitis media by aural toilet with dilute acetic acid (comparable to the 1-part vinegar/1-part tap water solution that we used) vs intravenous vancomycin or teicoplanin and found that the results were similar for similar treatment durations. In the present study, we prescribed aural irrigations with a 1:1 vinegar-water solution and topical antibiotic drops—typically a fluoroquinolone, although this could be changed as appropriate based on each patient's culture results—with the addition of an oral or an intravenous antibiotic, if indicated by culture results. In our study, about the same proportions of patients with MRSA otorrhea (44%) vs non-MRSA otorrhea (43%) had resolution of the infection with medical treatment, and our success rate with medical treatment was similar to rates reported in other series (Table 3).8,11,12,16

Despite our success with fluoroquinolone preparations as a first line therapy for post–tympanostomy tube otorrhea, these agents must be used with caution, because studies have shown that they may actually promote the development of antibiotic resistance.8,17 In light of the increasing frequency of fluoroquinolone resistance, it was often necessary to use oral antibiotics in our MRSA patient population. The increased necessity of the use of oral antibiotics was reflected in that there was a significantly larger percentage of patients with MRSA otitis media (40.7% MRSA vs 24.8% non-MRSA) requiring oral antibiotics as a part of their treatment. Typically, the treatment consisted of a 2- to 3-week course of trimethoprim-sulfamethoxazole or clindamycin, the selection of which was based on culture results and sensitivity data. A significantly higher proportion of patients whose infections were caused by MRSA (11%) compared with non-MRSA (3%) pathogens required more aggressive medical treatment (culture-directed intravenous antibiotics). These findings confirm the importance of obtaining a culture of post–tympanostomy tube otorrhea and switching the type or mode of administration of antibiotic(s) based on culture results.

Our finding that a similar proportion of children with MRSA otorrhea and non-MRSA otorrhea required surgical procedures (minor or major) confirms the safety of the trend to match treatment aggressiveness to infection severity rather than treating more aggressively based on the specific pathogen (MRSA). We believe that our selection of specific antibiotic agent based on the culture results and scrupulous attention to infection control practices helps to decrease the risk of new drug resistances developing.

Our 2 study groups had similar hearing levels after surgery. There appeared to be a trend toward a higher percentage of mild hearing loss in the MRSA population (Table 3, P = .08). Any pathologic finding associated with recurrent acute otitis media (eg, presence of a perforation, granulation, myringosclerosis, or chronic scar tissue causing a conductive hearing loss) could alter the audiogram and mask the final hearing status of a patient. Therefore, because of the multifactorial nature of hearing loss and the fact that different proportions of patients in the 2 groups had their hearing tested after surgery (76 of 135 patients with MRSA otitis vs 97 of 141 patients with non-MRSA otitis), our study does not answer the question of whether MRSA causes any pathogen-related hearing loss morbidity.

Our study had several limitations. First, it is subject to the inherent limitations of a retrospective review; ie, the accuracy of the data depends on the accuracy of the medical records. Second, the 4 pediatric otolaryngologists who treated all of the patients in the study differ somewhat in their algorithm of medical and surgical management. However, this bias was minimized by a relatively even distribution of patients with MRSA otitis vs non-MRSA otitis among the surgeons. Third, although we engaged an independent statistician to randomly select children for the aged-matched non-MRSA group, some selection bias is always a possibility, so patients in the non-MRSA age-matched group may not have been equally matched for other categorical variables. Finally, we made the assumptions that (1) we provided all treatments for these patients throughout the period of the study, (2) none of the patients had recurrent infections of which we were unaware, and (3) no patients were unavailable for follow-up. We believe that these were valid assumptions based on the nature of our practice: most children referred to us for the treatment of chronic otitis media or surgical man-

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management of recurrent acute otitis media do remain in our practice until their otologic problems resolve. The assignment of children to the MRSA group at the first diagnosis of MRSA otorrhea and the random assignment of an equal number of age-matched children to the non-MRSA otorrhea group helped to ensure that we were studying equivalent groups.

In conclusion, MRSA otorrhea as a complication of tympanostomy tube placement has become more prevalent since the late 1990s. In our study of this complication in a large group of children with MRSA otorrhea vs non-MRSA otorrhea, most cases in both groups resolved with medical management alone (aural toilet and culture-directed topical and oral antibiotics). Children with MRSA otorrhea were more likely to receive intravenous and oral antibiotics, but they were not more likely to need additional surgical procedures to control otorrhea or to be hospitalized for infection-related diagnoses or to suffer complications of otitis media. These findings should facilitate appropriate care for MRSA otorrhea after tympanostomy tube placement and help to decrease parental anxiety regarding a diagnosis of MRSA otorrhea vs non-MRSA otorrhea.

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Correspondence: Brian J. Wiatrak, MD, Pediatric ENT Associates of Alabama, Children’s Hospital of Alabama, 1940 Elmer J. Bissell Rd, Birmingham, AL 35243 (Brian.Wiatrak@chsbs.org).

Author Contributions: Drs Alexander, Kulbersh, Desmond, Woolley, Hill, Shirley, and Wiatrak had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Alexander, Hill, and Wiatrak. Acquisition of data: Alexander, Kulbersh, Heath, Caron, Woolley, and Shirley. Analysis and interpretation of data: Alexander, Desmond, and Wiatrak. Drafting of the manuscript: Alexander, Heath, Desmond, and Caron. Critical revision of the manuscript for important intellectual content: Alexander, Kulbersh, Woolley, Hill, Shirley, and Wiatrak. Statistical analysis: Desmond. Administrative, technical, and material support: Alexander, Kulbersh, Heath, Caron, Woolley, Hill, Shirley, and Wiatrak. Study supervision: Wiatrak.

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REFERENCES