Neonatal Legionellosis

The Tip of the Iceberg for Pediatric Hospital-Acquired Pneumonia?

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In a provocative case report in this issue of *Pediatric Infectious Disease Journal*, Shachor-Meyouhas et al describe an 11-day-old neonate who contracted Legionnaires' disease in a hospital.[1] The pneumonia was severe as judged by tachypnea and the presence of diffuse infiltrates on chest radiograph. *Legionella pneumophila* was diagnosed both by culture and PCR from tracheal aspirate and autopsy lung specimens. The source of the infection was likely the tap water of the hospital where the delivery occurred.

The clinical presentation of legionellosis is that of pneumonia. In pediatric patients, fever and cough are the most common symptoms while tachypnea and abnormal lung examination are the most common findings.[2] In an extensive review of pediatric legionellosis, 17% (13/76) required mechanical ventilation.[2] In adults, a number of clinical features are said to be distinctive for Legionnaires' disease including diarrhea, confusion, high fever (>39°C), hyponatremia, hepatic dysfunction, and hematuria.[3] However, none of these features are pathognomonic and more likely are a result of severe, inadequately-treated pneumonia in patients described from early outbreaks. In subsequent observational studies in which legionellosis was specifically sought, only the presence of hyponatremia proved to be a consistent feature. Gastrointestinal symptoms especially diarrhea can be prominent in adults with Legionnaires' disease but are uncommon in pediatric patients.

In most children with legionellosis, underlying disease is common. In the review by Greenberg et al, 78% had an overt underlying disease or immunosuppressive condition.[2] We suspect ascertainment bias in which opportunistic infections are more likely sought in patients with compromised immune systems than in patients without underlying disease; specialized laboratory tests for *Legionella* are more likely to be ordered in these patients as compared with patients without underlying disease.

The first inkling that immunocompetent children might contract legionellosis occurred in a report of neonates with legionellosis confirmed by culture at a Phoenix hospital.[4] Specialized *Legionella* culture media was available in the clinical microbiology laboratory of this Phoenix hospital, because a community-acquired pneumonia protocol in adults had been introduced to assess a new anti-*Legionella* antibiotic. Respiratory tract secretions of 2 neonates with pneumonia unresponsive to beta-lactam antimicrobial therapy were fortuitously placed on this media. *Legionella* was isolated from both patients with the one surviving patient also experiencing a 4-fold antibody seroconversion to *Legionella*.

The survival for neonatal legionellosis was 54% (7/13) in the report by Shachor-Meyouhas.[1] However, it should be noted that for those neonates who received macrolide antibiotic therapy, 7 of 8 (88%) survived. The one patient that succumbed received initial antibiotic therapy that did not cover *Legionella*; macrolide antibiotic therapy was initiated only after transfer to the pediatric intensive care unit (PICU).

The question for the readers of this journal is "How many undiagnosed cases of legionellosis occur in children?" This is a relevant question particularly since the incidence of legionellosis appears to be increasing worldwide[5–7]; and the spectrum of empiric antibiotic therapy for pneumonia in pediatrics—be it community or hospital-acquired—usually does not cover for *Legionella*.

HOSPITAL-ACQUIRED LEGIONELLOSIS AND TAP WATER

In a CDC survey, 72% of reported pediatric cases of legionellosis were hospital-acquired.[8] For hospital-acquired legionellosis, the source of the pathogen is the hospital tap water and the mode of transmission is usually aspiration in pediatric cases.[2,9] Although *Legionella* was isolated from the hospital tap water in this case report, the percentage *Legionella* positivity of faucets was not reported. Quantitative counts (cfu/mL) have proven not to be predictive of occurrence of Legionnaires' disease within a hospital; however, greater than 30% positivity of tap water sites has proven to be a robust predictor of occurrence of cases of Legionnaire disease in adult hospitals.[10–12]

With this new report by Schachor-Meyouhas, at least 3 cases of a neonatal legionellosis[13,14] and one dramatic outbreak involving 11 neonates[15] have occurred as a result of being exposed to contaminated water. Two of the cases were linked to "water birth" delivery.[13,14] The present case was a neonate who was rinsed in a hospital sink[1] while the outbreak of 11 neonates was linked to hospital tap water.[15] Water birth delivery is a process where the mother labors in a warm water bath and delivery of the infant occurs into the water bath. This approach has enjoyed widespread popularity especially in Europe. Perinatal mortality has not been found to be higher in water birth deliveries as compared with conventional deliveries,[16] although the theoretical risk of aspiration of water has been raised.[17] Tap water at 37°C is used—an ideal temperature for *Legionella* replication.

Thirteen of the 14 neonates were healthy full term infants and one was a late preterm (36–37 weeks). The ages for the 14 neonates at the time of onset of legionellosis ranged from 4 to 11 days. The most common presenting symptoms were fever and dyspnea or grunting. The pneumonia was severe in almost all cases as judged by the presence of tachypnea and cyanosis. The appearance of pulmonary infiltrates confirmed the presence of pneumonia. Multilobar or bilateral pulmonary infiltrates at the time of diagnosis was seen in the 3 reported neonates.[1,13,14] Legionellosis was established in the 14 neonates by cultures of respiratory secretions or lung, direct fluorescent staining, PCR, serum antibody tests, or urinary antigen tests.

Almost none of the neonates received a macrolide as initial empiric therapy. Macrolide therapy was ultimately administered to 12 neonates because of unresponsiveness of empiric beta-lactam therapy and/or results of *Legionella* testing and 8 of these 12

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neonates recovered with no overt sequelae.[1,14,15] Two never received anti-*Legionella* therapy and both died.

For the 2 water births, *Legionella* was isolated from the water bath where the delivery was performed[13,14]; molecular subtyping confirmed a match between the infecting *Legionella* in the neonate to the *Legionella* in the water in one report.[13] Aspiration was the presumed mode of transmission for most of the neonatal cases.

Sterility of water has not been generally emphasized, although disposable filters have been recommended by some advocacy groups involved in water birthing. In a bacteriologic study of water taken from the delivery tub used in 300 water birth deliveries, coliform bacteria (*Pseudomonas aeruginosa*, enterococci, *Escherichia coli*) and *L. pneumophila* were isolated pre- and postdelivery.[18] Coliforms, especially *E. coli*, were isolated in notably greater quantities following delivery showing that these bacteria were expelled from the mother during the bearing-down phase of delivery. *L. pneumophila* and *P. aeruginosa* were present in 29% and 22%, respectively, of the water specimens taken before the water delivery. It seems prudent that water used for water birth delivery in hospitals be sterilized before immersion of the mother. The simple installation of a filter within the supply hose to the birthing tub was shown to remove both *Legionella* and *P. aeruginosa* effectively from the water.[18]

RECOMMENDATIONS

In the 2 reviews on pediatric and neonatal legionellosis, respectively by Greenberg et al and Levy et al,[2,19] the authors came to the same conclusion: maintain a high index of suspicion for Legionnaires' disease in any child with pneumonia. The CDC has recommended that *Legionella* be sought as a causative agent for pediatric pneumonia.[8] Since most pediatric hospitals do not follow this recommendation, we propose a strategy to remedy this shortfall.

Focusing on those circumstances in which legionellosis would be most likely present and could do the most harm would be a logical starting point. Most cases of pediatric legionellosis are hospital-acquired.[2,19] It is noteworthy that outbreaks of hospital-acquired legionellosis in pediatrics were first seen in hospitals which had already experienced outbreaks of adult hospital-acquired legionellosis (Ohio State,[20] University of Pittsburgh,[21] Stanford University).

The first step would be to culture the tap water of pediatric hospitals.[22] We would especially recommend sampling in higher risk areas of the PICUs and oncology and stem cell transplant units. If the percentage positivity is greater than 30% (the cut-point used in adult hospitals), selective culture media for *Legionella* should be introduced into the clinical microbiology laboratory of that hospital. Culture is important since species of *Legionella* other than *L. pneumophila* have been observed in infected children.[4,23,24] If the *Legionella* in the tap water proves to be *L. pneumophila*, serogroup 1, then the urinary antigen for *Legionella* should also be made available. (The urinary antigen test is useful only for *L. pneumophila,* serogroup 1). In the above reports of neonatal legionellosis, urinary antigen was applied in 9 neonates.[13,15] This is clinically relevant because the urinary antigen is a rapid point-of-care test. Children with hospital-acquired pneumonia should routinely undergo *Legionella* testing in hospitals in which the tap water is colonized with *L. pneumophila*. If such an approach uncovers pediatric legionellosis, then studies could be expanded to include children with community-acquired pneumonia. Such an approach has uncovered undiagnosed legionellosis in adult hospitals[11,12,22] and community-acquired pneumonia.[25,26] In community-acquired legionellosis in children, 63% had no underlying disease or risk factors.[2]

In Pittsburgh, county health department guidelines for prevention of legionellosis mandate culturing of hospital tap water even in the absence of known Legionnaires' disease; this proactive approach has been documented to be inexpensive and effective in prevention; and, most importantly, the issues of litigation and negative media publicity has been eliminated.[27] For hospitals that are proactive in culturing their tap water, decisions can be made on evidence rather than based on pressures resulting from adverse media publicity and litigation. On the other hand, to culture the tap water if only 1 or 2 children with legionellosis are detected seems short-sighted and undesirable. Yet, this is the current approach recommended by the US Centers for Disease Control and Prevention.[28]

Evidence-based measures should be applied to prevention. For example, in Europe, maintenance of high temperatures for hot water in the water distribution system is widely used, despite the fact it is not a proven method for suppressing or eradicating *Legionella*. Cases have occurred in hospitals utilizing such an approach.[29] While prevention of hospital-acquired legionellosis is possible with disinfection of the hospital tap water, we are not recommending installation of expensive disinfection systems for pediatric hospitals until epidemiologic studies document the risk. It is possible that intermittent (rather than continuous) disinfection could be as effective and much less expensive in pediatric hospitals.

CONCLUSION

The clinical implications of this proposed approach are relevant for patient care in pediatric hospitals. An increased index of suspicion would lead to greater use of *Legionella* tests for diagnosis with the anticipated uncovering of more cases of legionellosis. The tip of the iceberg is neonatal legionellosis. If *Legionella* were discovered to be a more common pathogen of pediatric pneumonia in the hospital setting, targeted use of macrolides as empiric therapy for selected cases of pneumonia combined with preventive measures directed at hospital tap water should lead to the saving of lives of many children. In our opinion, such deaths are unnecessary today.

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ERRATUM

Outbreak of *Salmonella* Wandsworth and Typhimurium Infections in Infants and Toddlers Traced to a Commercial Vegetable-Coated Snack Food: ERRATUM

In the article that appeared on page 1041 of volume 28, number 12, the first subheading in the Results section was incorrect. The subheading should have appeared as *Salmonella* Wandsworth.

Reference

Sotir MJ, Ewald G, Kimura AC, et al. Outbreak of *Salmonella* Wandsworth and Typhimurium Infections in Infants and Toddlers Traced to a Commercial Vegetable-Coated Snack Food. *Pediatr Infect Dis J*. 2009;28:1041–1046.