Respiratory Viruses and Otitis Media in Young Children

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(See the Major Article by Chonmaitree et al on pages 1–9.)

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Otitis media (OM) remains a major health problem for children throughout the world. In addition to the short-term morbidity and costs of the illness, children with persistent middle ear effusion may be at risk for long-term detrimental effects on speech and language. The annual cost of the medical and surgical treatment of OM in the United States alone is estimated at between $3 and $4 billion dollars. The pathogenesis of the disease is multifactorial. Infection by bacteria and viruses, abnormal function of the Eustachian tube, and relative immaturity of a child’s immune system are all known to be important in the development of acute otitis media (AOM) in young children.

Upper respiratory tract infections (URTIs) with a number of viruses have long been associated with the development of OM. Early studies using relatively insensitive detection techniques such as viral culture and viral-specific antibody responses demonstrated clear associations between URTI with respiratory syncytial virus, influenza (type A or B), and adenovirus and the development of OM [1]. Weaker, but still significant associations were seen with infections caused by parainfluenza virus, enterovirus, and rhinovirus. Evidence that respiratory viruses themselves had a central pathogenic role was provided by later studies in which culture and antigen detection techniques demonstrated virus in the middle ear fluid itself of infected children [2]. Respiratory syncytial virus was the most frequently identified virus in middle ear fluid specimens, followed by parainfluenza and influenza. These early studies were hampered by the fact that even with the rigorous methods used, viral etiologies could be established for only about 40% of children with OM associated with URTIs.

The field has changed dramatically over the last 10 years with the development of polymerase chain reaction (PCR)–based methods for the detection of common respiratory viruses [3–5]. Viruses such as rhinovirus, human coronaviruses, human bocavirus, and human metapneumovirus, viruses whose presence had been difficult if not impossible to demonstrate using older methods, were now readily detected if present in respiratory secretion samples from individuals with URTIs [6, 7]. Clinical studies using the PCR-based techniques in children with URTIs routinely demonstrated the presence of 1 or more viruses in ≥75% of subjects. The same viruses documented in earlier work as being associated with AOM were confirmed as such in these later studies, but infection with additional viruses including rhinovirus and bocavirus were also found to have strong associations with the development of OM. These more recent studies also demonstrated that a significant percentage of asymptomatic children harbored viruses in their respiratory tracts when samples were examined by PCR [3, 6, 7].

It is against this backdrop that the study by Chonmaitree and coworkers in this issue of Clinical Infectious Diseases was undertaken. This is one in a series of papers from this Galveston-based group based upon their studies of young children with viral URTIs and AOM in an outpatient setting [4, 8, 9]. In the current work, the investigators defined the contribution of respiratory viruses to symptomatic disease and asymptomatic infection in infants <1 year of age, a population that has not yet been systematically investigated with respect to viral respiratory infections and OM. A large cohort of children from birth to 1 year of age were examined monthly with
collection of nasopharyngeal specimens both at well visits and with episodes of viral URTIs. Ear examinations were performed at each visit by validated otoscopyists to document the presence or absence of associated OM. The nasopharyngeal specimens were assayed using a sensitive high-throughput quantitative PCR assay for the detection of nucleic acid from a large panel of respiratory viruses.

The authors detected viruses in 76% of the URTI specimens and 27% of specimens from asymptomatic children, with rhinovirus being the most common virus in each group. The detection of several viruses including respiratory syncytial virus, influenza virus, rhinovirus, metapneumovirus, and adenovirus was strongly associated with the presence of URTI symptoms, as were higher viral loads, in the aggregate. A diagnosis of AOM was also strongly associated with infection with respiratory syncytial virus, rhinovirus, enterovirus, adenovirus, and bocavirus. Interestingly, the authors did not find an association between higher viral loads and the presence of AOM, an association that had been reported previously with respiratory syncytial virus and AOM in a study of somewhat older children [8]. Despite the frequent detection of viruses in asymptomatic children, AOM attributable to these “asymptomatic” infections was never observed. It is notable that the viral load in the specimens from asymptomatic children was significantly lower than that in the children with symptomatic disease, suggesting that a critical viral titer threshold may need to be reached before AOM will develop [3].

Although viruses alone are capable of causing AOM in some children, nasopharyngeal colonization with pathogenic bacteria is an independent risk factor for AOM development [1, 8]. Chonmaitree and coworkers did not report on the nasopharyngeal colonization status of their study subjects with nontypeable Haemophilus influenzae, Streptococcus pneumoniae, and Moraxella catarrhalis, the bacteria most commonly associated with AOM. It is conceivable that even stronger associations might have been found between viral URTIs and AOM if the presence of nasopharyngeal bacterial pathogens could have been assessed and then controlled for in their analyses. As an example, Pettigrew and coworkers reported highly significant associations between respiratory syncytial viral URTIs, S. pneumoniae nasopharyngeal colonization, and AOM as well as between human bocaviral URTIs, nontypeable H. influenzae nasopharyngeal colonization, and AOM [8, 10].

Even in the absence of these sorts of viral–bacterial interaction studies, the careful and detailed characterization of viral URTIs in very young children, as described by Chonmaitree et al, and determination of their contribution or lack thereof to AOM development are seen as important contributions to the field. The information provided significantly advances our understanding of OM disease pathogenesis and should help guide future therapeutic and vaccine development efforts. Chonmaitree and colleagues are to be commended for their excellent work.

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**References**


