Is Acute Otitis Media a Treatable Disease?

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In this issue of the Journal, investigators in Pittsburgh and in Turku, Finland, respond to the question of whether infants and young children with acute otitis media benefit from amoxicillin–clavulanate therapy initiated at the time of diagnosis.1,2 Physicians who cared for children 50 years ago would be surprised — more likely shocked — that the question is being asked. Before antimicrobial agents were introduced, acute otitis media was a severe event in infants. In 1932, acute otitis media and its suppurative complications accounted for 27% of all pediatric admissions to Bellevue Hospital.3 Mastoiditis and suppurative intracranial complications were common. The introduction of effective antimicrobial agents reduced the severity of acute otitis media, and the use of an appropriate antimicrobial agent soon became the standard of care. Today, severe acute otitis media and its complications still occur, but mostly in children who live in regions with limited access to medical care.

Beginning in the 1980s, investigators in Western Europe suggested that children with acute otitis media could initially be observed rather than treated immediately with an antimicrobial agent. Van Buchem and colleagues in the Netherlands found that infants could initially be given an analgesic agent and nose drops; antimicrobial agents were administered only if the illness persisted for 3 days or longer.4 Other studies from centers in Western Europe, Britain, and the United States appeared to corroborate the Dutch observations. However, each of the studies had substantial flaws in study design, including the lack of precise criteria for the diagnosis of acute otitis media, participation of physicians who were not validated otoscopists, inadequate sample size, inclusion of older children, inclusion of children who had minimal or uncertain signs of disease, and ambiguous end points for cure or failure. Wald pointed out that the evidence from these studies was insufficient to conclude that acute otitis media in children could be safely managed without antimicrobial agents.5 Nevertheless, in 2004, the American Academy of Pediatrics and the American Academy of Family Physicians endorsed a guideline that recommended initial observation rather than immediate antimicrobial therapy for the management of acute otitis media in selected children.6

How did the perception of acute otitis media change from a severe disease with suppurative complications in the pre-antibiotic era to a modest illness that could be considered for management by observation alone in the 1980s? Four factors probably contributed to this change: First, access to medical care has changed. In the pre-antibiotic era it is probable that only children with severe acute otitis media were brought to a doctor for medical attention. Since there was no effective therapy, and medical care was expensive, most children with earaches were given hot compresses at home instead of being brought to the doctor. Today there are more appointments with physicians for sick and well visits and more opportunities for the diagnosis of mild acute otitis media. Second, the method of diagnosis has changed. In the pre-antibiotic era, the diagnosis of acute otitis media was often made when the tympanic membrane was perforated or when myringotomy was performed for incision and drainage of the middle-ear abscess. Today, myringotomy is almost never performed in the office setting. The diagnosis of acute otitis media is based on otoscopic
examination, which in the irritable, squirming infant is not easy, and overdiagnosis is a likely occurrence in many infants with uncertain otoscopic findings. Third, there has been a change in the virulence of bacterial pathogens. In the pre-antibiotic era, group A streptococcus caused a necrotizing form of acute otitis media and was the most frequent cause of mastoiditis; group A streptococcus is now a rare cause of acute otitis media; nontypable Haemophilus influenzae and Moraxella catarrhalis cause almost half the cases of bacterial acute otitis media and produce a relatively mild disease. Fourth, a number of new antibiotics have been introduced to treat acute otitis media, with aggressive marketing accompanying their introduction. Beginning with amoxicillin in the 1970s, a total of 19 antimicrobial agents have been approved by the Food and Drug Administration for the indication of acute otitis media. The increased number of diagnoses of acute otitis media and the increased number of prescriptions for antimicrobial agents to treat acute otitis media have raised concerns that multidrug-resistant bacteria will develop in the patient and in the community. In recent years, educational programs for physicians and parents have been directed toward limiting the use of antimicrobial agents for trivial (usually viral) upper respiratory tract infections, including mild acute otitis media. The key to the optimal management of acute otitis media remains the accuracy of the diagnosis.

A study with an appropriate design was needed to resolve the controversy regarding antimicrobial therapy versus observation in children with certain diagnoses of acute otitis media. The investigators in both Pittsburgh and Turku have provided such a study. They performed randomized, blinded trials of the use of amoxicillin–clavulanate as compared with placebo in the age group at greatest risk. The acute otitis media in the children who were enrolled in the studies was defined by the acute onset of the condition and the presence of middle-ear effusion, a bulging tympanic membrane, and otalgia or erythema of the tympanic membrane. In these two studies, acute otitis media was meticulously assessed by experienced otoscopists, and only children with a clear, certain diagnosis of acute otitis media were enrolled. The results of each study showed a significant benefit among children who received the drug with respect to the duration of acute signs of illness. Among children with moderate disease and children with severe disease, the rates of clinical failure were higher in the placebo group than in the amoxicillin–clavulanate group. As expected, the condition of many children in the placebo group improved without antibiotics, and more children in the antibiotic groups had associated side effects. Since the physician cannot determine at the onset of the illness which child is likely to benefit from antimicrobial therapy, we need to consider these data as applicable to all young children in whom a certain diagnosis of acute otitis media has been made. Is acute otitis media a treatable disease? The investigators in Pittsburgh and Turku have provided the best data yet to answer the question, and the answer is yes; more young children with a certain diagnosis of acute otitis media recover more quickly when they are treated with an appropriate antimicrobial agent.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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