Otitis media: concepts and controversies

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Purpose of review

Otitis media is the most common bacterial infection among children, accounting for as many as 30 million office visits annually. Proper treatment has become critical as offending pathogens become increasingly resistant to antibiotics and the cost of managing the disorder has exceeded 3 billion dollars per year. However, data suggest that many practitioners still struggle with the diagnosis of otitis media and often recommend medical and surgical intervention inappropriately. This article presents recent advances in the otitis media literature and an evidence-based approach to its management.

Recent findings

Recent investigations have resulted in the following findings: (1) bacterial biofilms may account for the persistence of middle ear disease; (2) there is increasing evidence that heredity and reflux are risk factors for otitis media; (3) primary care providers may be receiving poor otitis media training, leading to inadequate diagnostic skills; (4) medical and surgical therapy are of limited utility in the management of acute and recurrent acute otitis media; (5) antibiotics and steroids are of limited value in the treatment of chronic middle ear effusion; (6) delayed management of effusion may not adversely affect development in children; (7) vaccination for pneumococcus may alter the serotypes responsible for otitis media; and (8) vaccine candidates for other middle ear pathogens are under investigation.

Summary

Management of otitis media is constantly evolving, based on research from a variety of medical subspecialties. It is incumbent on the otolaryngologist and primary care providers treating otitis media to keep pace with and synthesize these findings into a rational approach to treatment.

Keywords

acute otitis media, otitis media with effusion, risk factors, diagnosis, microbiology, management, development, vaccination

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Abbreviations

AOM	acute otitis media
OME	otitis media with effusion
rAOM	recurrent acute otitis media

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Introduction

With the exception of the common cold, otitis media is the most common disorder for which children and their families seek pediatric care [1]. It is the most frequent bacterial infection of childhood and the most common indication for antimicrobial therapy in this age group [2]. However, despite years of clinical experience with the disorder, the pathophysiology of otitis media is not fully understood, and its management continues to evolve. This article reviews the etiology, diagnosis, and basic management of middle ear disease and presents recent concepts and controversies from the medical literature.

Pathogenesis and risk factors

Otitis media is generally defined by the presence of effusion within the middle ear without reference to its cause or pathogenesis. Acute otitis media (AOM) is usually associated with the rapid onset of symptoms and signs of acute infection in the middle ear space, including fever, otalgia, inflammation or bulging of the tympanic membrane, and purulent middle ear effusion. However, there is no constellation of signs and symptoms that has been universally accepted in establishing this diagnosis [3]. Otitis media with effusion (OME) is the presence of serous, mucoid, or mucopurulent fluid in the middle ear without acute symptoms.

The pathogenesis of otitis media is multifactorial, including infection, impaired eustachian tube function, immature immune status, and allergy. In most cases, otitis media begins with a viral infection of the upper respiratory tract that causes congestion of the eustachian tube and impairment of normal tubal function, including middle ear ventilation, ciliary clearance, and drainage. As a result, pathogens colonizing the nasopharynx may gain access to the middle ear space and multiply; in such cases, acute symptoms (AOM) may develop. Immune responses, with or without antimicrobial therapy, will normally eradicate the infection and the acute symptoms; however, effusion (OME) may persist until normal tubal function returns. Glycoproteins secreted into the

middle ear from goblet cells stimulated by the inflammatory process may impart to the fluid a mucoid texture, thereby slowing its resolution [4]. Bacterial biofilm formation has also been demonstrated in OME and implicated in its persistence [5,6]. It has been postulated that viable bacteria are organized through complex intercellular communication within biofilms, affording protection from phagocytosis through formation of an exopolysaccharide matrix. This results in reduced metabolism and relative resistance to antibiotics and to growth in tissue culture.

Effusion may also occur in the absence of infection, typically in ears in which negative pressure caused by transiently or chronically impaired eustachian tube function results in atelectasis and retraction of the tympanic membrane and transudation of serous fluid into the middle ear. Such cases often begin as a result of allergy or upper respiratory illness but may also be influenced by other local conditions, such as a diseased adenoid pad, trauma from nasally placed tubes, nasopharyngeal malignancy, and anatomic abnormalities associated with clefts of the palate or trisomy 21.

Acute otitis media is primarily a disease of infancy and early childhood, with the peak age-specific attack rate occurring between 6 and 18 months of age. Nineteen to sixty-two percent of children experience their first episode of AOM by age 1 year, and 50% have experienced three or more episodes by age 3 years [7]. Children who have had little or no AOM by 3 years of age are unlikely to have subsequent severe recurrent disease. The point prevalence of OME is difficult to establish because of the milder nature of the disorder. However, screening studies using tympanometry at 3-month or 4-month intervals over a 1-year period have identified middle ear fluid on at least one occasion in 26 to 41% of children screened [7].

Risk factors for otitis media have been established by numerous investigators [8,9], with the most significant including attendance at group daycare (larger daycare size associated with higher relative risk), sibling history of recurrent otitis media, early occurrence of initial otitis media, and lack of breastfeeding. However, although children in large daycare facilities tend to manifest more episodes of upper respiratory illness, this apparent morbidity may be protective against common cold viruses during the early school years [10]. Otitis media is also more common among Native Americans and Eskimos, and in these groups, it is frequently complicated by perforation of the tympanic membrane and persistent suppurative drainage. Otitis media is nearly universal among children with unrepaired clefts of the palate.

Male gender, allergy, pacifier use, exposure to cigarette smoke, heredity, and lower socioeconomic status have also been implicated, but their relative risk is lower or less consistently established. For example, whereas a recent analysis of national health survey data failed to demonstrate an increased risk of otitis with passive tobacco exposure [11], ear infection was more common among children with both passive exposure and gestational tobacco exposure [12]. Recent data also suggest that chronic exposure of the eustachian tube to products found in gastric secretions results in significant eustachian tube dysfunction (ETD) and middle ear disease [13]. In a longitudinal study of more than 1300 twins, heredity was confirmed as a risk factor for both otitis media and for eustachian tube dysfunction [14].

Microbiology and antibiotic resistance

The bacterial species involved in AOM have not changed significantly over the last 2 decades [15,16]. *Streptococcus pneumoniae* continues to be the most prominent pathogen, accounting for approximately 40% of cases. It is also the organism most likely to produce otalgia and fever and least likely to resolve without medical management. The other two most common organisms are *Haemophilus influenzae* and *Moraxella catarrhalis*. The microbiology of OME differs from that of AOM in that a much higher proportion of aspirates fail to grow an organism in culture, and β-lactamase–producing *H. influenzae* and *M. catarrhalis* and resistant strains of *S. pneumoniae* are more frequently isolated [17].

The risk factors postulated for development of antimicrobial resistance are low dose and prolonged treatment with β-lactam antibiotics, recent exposure to antibiotics, attendance in a large child daycare environment, young otitis-prone infants, and winter season [9,17]. Unfortunately, these bacterial strains are also highly resistant to other β-lactam antibiotics, trimethoprim/sulfa, and macrolides. Poole [18] have reported rates of drug-resistant *S. pneumoniae* as high as 90% in some communities and macrolide resistances exceeding those of β-lactams in some populations. Sutton *et al.* [17] found penicillin resistance in 38% of *S. pneumoniae* cultures and β-lactamase production in 65% of *H. influenzae* and 100% of *M. catarrhalis* cultures in effusions from children undergoing tympanostomy tube surgery.

Over the past decade, penicillin resistance to *S. pneumoniae* has become a worldwide problem, complicating medical management of otitis media. Studies also suggest that resistant bacteria may be associated with a higher incidence of infectious complications of otitis media [19]. Recent studies indicate that in the United States, more than 50% of strains of *S. pneumoniae* are penicillin nonsusceptible because of alterations in penicillin binding proteins [20]. This pattern of resistance can often be overcome effectively by increasing the dosage of the antibiotic (*eg*, high-dose amoxicillin).

Drug-resistant *H. influenzae* and *M. catarrhalis* produce β-lactamase, an enzyme that inactivates β-lactam antibiotics. Approximately 40% of *Haemophilus* strains [19] and nearly all *Moraxella* strains produce this enzyme. This mode of resistance cannot be overcome by high-dose amoxicillin treatment but may be treated effectively with antibiotics containing β-lactamase inhibitors such as clavulanic acid. Alternatively, cephalosporins, which are also β-lactamase–stable, can be used to eradicate these organisms [19].

Viral illness is well established as a cause of eustachian tube dysfunction leading to otitis media; however, it remains unclear whether a virus can be the sole pathogen causing otitis media [21•].

Diagnosis

Diagnosis of AOM cannot be made on the basis of symptoms alone. Although earache has a specificity of 82 to 92%, its sensitivity is only 54 to 60% [22]. Rubbing the ears, restlessness, and fever are even less reliable, and no particular constellation of symptoms is predictive. In children with OME, parents' subjective ratings of their children's hearing loss caused by effusion do not correlate with audiometric findings [23]. Furthermore, aural fullness caused by OME may cause rubbing of the ears that may be construed as acute symptomatology.

Diagnosis of middle ear effusion is more reliably made on the basis of pneumatic otoscopy and tympanometry. Examination by a trained otoscopist achieves a sensitivity of 81 to 94% and a specificity of 74 to 93% when compared with findings at myringotomy [22]. However, one recent study indicates that 41% of pediatric residency programs have no formal training in otitis media [24], and in another, only 66% of residents in family practice used pneumatic otoscopy [25]. Other studies suggest that OME is overdiagnosed as AOM by primary care practitioners and residents, resulting in potentially unnecessary antibiotics in as many as 26% of cases [26,27•].

When the diagnosis of otitis media is in doubt, tympanometry may be a useful adjunct. A flat tympanogram may be considered more than 90% sensitive and more than 75% specific in predicting middle ear effusion [22]. Acoustic reflectometry, which analyzes the spectral gradient of sound reflected off the tympanic membrane, does not appear to aid the diagnosis in these equivocal cases [28].

Management of acute otitis media

Natural history of acute otitis media

The natural history of an individual episode of AOM is quite favorable. In observational studies and randomized clinical trials, 70 to 90% of children with AOM treated with placebo or no drug demonstrated spontaneous clinical resolution in 7 to 14 days [29]. Meta-analysis data suggest that seven to eight children with AOM need to be treated with antimicrobials to improve a single child beyond what would be expected from the natural course of infection [30]. Moreover, pooled data suggest an incidence of acute mastoiditis of less than 0.1%, reflecting no increased risk of sequelae or complications among patients closely observed compared with their antibiotic-treated counterparts [29]. Persistence of middle ear effusion is 40% at 1 month and 26% at 3 months, compared with 40% and 10%, respectively, in antibiotic-treated patients [29]. Based on the high likelihood of spontaneous resolution, it is common practice in many countries to medicate patients with AOM for pain only, observing the patient closely and reserving use of antibiotics for refractory cases [31]. Most advocates of watchful waiting in the United States still recommend antimicrobial therapy for children younger than 2 years.

Medical therapy for acute otitis media

The advent of antibiotic therapy in the mid-20th century brought a tremendous downturn in the incidence of complications of AOM. Treatment with antibiotics rapidly became the standard of care in the United States and other developed countries. However, the development of bacterial resistance, expense, and the potential for side effects have led clinicians to reconsider the need for medical intervention. Furthermore, antimicrobial therapy has demonstrated only a modest effect on AOM. In clinical trials, antibiotics did not affect symptomatic relief at 24 hours but did improve symptom resolution at 2 to 3 days by 4% and at 7 to 14 days by 12 to 14% [32]. Neither choice of antibiotic nor duration of therapy influenced the overall success rate, and no antibiotic was found to be superior to amoxicillin. Amoxicillin and erythromycin, however, resulted in fewer severe gastrointestinal side effects than amoxicillin/clavulanate and second-generation and third-generation cephalosporins. Because most studies excluded children younger than 2 years and those with severe symptoms, it is important to not extrapolate these results to younger children and those with more severe symptoms, because these may be the children most likely to benefit from antibiotic therapy.

Once a decision for medical management has been made, selection of a particular antimicrobial agent is based on clinical and microbiologic efficacy, acceptability of the preparation, absence of side effects and toxicity, convenience of dosing schedule, and cost. In 1999, the report issued by the Drug-resistant *Streptococcus pneumoniae* Therapeutic Work Group concluded that amoxicillin is the most appropriate first-line therapy [33]. Recommended doses were 45 mg/kg/d for children at average risk, and 80 to 90 mg/kg/d to achieve maximum middle ear concentrations for children considered at high risk for resistant pneumococcus. Although β-lactamase–

producing organisms (*M. catarrhalis* and *H. influenzae*) are less likely to be eradicated by amoxicillin, infections caused by these organisms are less severe and tend to resolve uneventfully. In cases of treatment failure, second-line therapy should be guided by the likelihood of untreated drug-resistant organisms. The second-line agents recommended for these resistant infections include high-dose amoxicillin/clavulanate, cefuroxime, and ceftriaxone. Thus far, primary care providers appear to be poorly compliant with these recommendations [27•]. Duration of antibiotic therapy is typically as long as 10 days, depending on the oral antimicrobial agent used, although a shorter duration of therapy may be appropriate in children older than 2 years or in less severe cases [34]. Optimum duration of therapy is not universal and should reflect both the severity of illness and the antibiotic selected. Single-dose therapy is reasonable when using ceftriaxone or azithromycin.

The typical clinical course of a child who receives an appropriate antimicrobial agent includes significant resolution of acute signs within 48 to 72 hours; a change of antibiotic coverage should be considered if acute signs persist beyond this time. Children with severe otalgia, sepsis, immune compromise, or suppurative complications of otitis media may benefit from tympanocentesis to identify the causative organism or tympanostomy tube placement to facilitate drainage and improve ventilation. Homeopathic remedies to date have demonstrated no efficacy in AOM when compared with placebo [35].

Surgical therapy for acute otitis media

Most studies of myringotomy with or without antibiotic therapy for AOM suggest no significant advantage over antibiotic therapy alone [36]. As a result, the primary value of myringotomy or tympanocentesis is for culture to guide antibiotic therapy. In some cases, laser-assisted tympanic membrane fenestration (OtoLAM; Lumenis, Santa Clara, CA) may provide more efficient drainage for relief of otalgia and prolonged ventilation; however, the device has not been studied expressly for this indication.

Management of recurrent acute otitis media

Goals of therapy

The goals of therapy for recurrent AOM (rAOM) should be (1) reduction in symptoms and (2) reduction in frequency of AOM.

Natural history of recurrent acute otitis media

The natural history of rAOM is revealed in randomized trials comparing antimicrobial prophylaxis to placebo. In an analysis of 13 such trials, patients meeting entrance criteria had an average of five or more episodes per year; during the trials, an average of 1.6 episodes of AOM occurred per child [29]. During a median observation period of 6 months, 51% had no further episodes of AOM. These findings suggest a trend toward improvement with watchful waiting. Similarly, in a 1997 study, among 375 children with a history of at least three episodes of otitis media in a 6-month period, only 12% continued to have otitis media with this frequency [37]. As a result, for children with rAOM whose episodes are nonsevere or have occurred only for a limited period, watchful waiting is often indicated.

Medical therapy for recurrent acute otitis media

Despite clinical trial data showing very limited efficacy in prevention of acute episodes and the increased risk of bacterial resistance, antibiotic chemoprophylaxis is still used by many primary care providers for treatment of rAOM. This treatment usually consists of administering half the usual daily dose of amoxicillin or a sulfa derivative on a daily or twice-daily basis, typically during winter months. Among the 13 clinical trials mentioned, the absolute decrease in AOM recurrence attributable to therapy was approximately 1.5 episodes per patient per year [32]. This result suggests that 8 months of prophylaxis are required to prevent a single episode of AOM. One recent study evaluating outcome measures with more restricted use of antibiotic chemoprophylaxis demonstrated that there was no significant decreased rate of development of AOM or decreased rate of tympanostomy tube insertion [38], and another revealed similar otitis-free rates of 60 to 65% among patients treated with twice-daily amoxicillin, once-daily amoxicillin, or placebo [39]. In light of its marginal benefit and potential contribution to antimicrobial resistance, antibiotic chemoprophylaxis is a practice to be discouraged.

Surgical therapy for recurrent acute otitis media

Only three clinical trials have been performed that support the use of tympanostomy tubes in the management of rAOM. Two of these studies included children with effusions at enrollment and had follow-up periods of only 6 months, and only one of these two demonstrated a reduction in the AOM attack rate (otorrhea) [40,41]. The third study, which had fewer design flaws and a follow-up period of 2 years, failed to demonstrate a reduced AOM attack rate, but did note fewer days with otorrhea and a reduction in symptoms in the tympanostomy tube group [42]. As a result, surgery for rAOM should be recommended only for patients with severe symptoms and a history of at least three or four episodes in a 6-month period, anticipating at best a modest reduction in the frequency of infection. Both objective and subjective quality of life measurements have demonstrated significant benefit in children appropriately treated with insertion of tympanostomy tubes [43,44•].

A chronically infected adenoid pad, independent of its size, can seed the middle ear (ME) with pathogenic bacteria and lead to otitis media [45,46]. However, studies suggest that adenoidectomy is of marginal benefit as a

primary adjunctive procedure for rAOM and in children having a second set of tympanostomy tubes [47•,48].

Management of otitis media with effusion

Goals of therapy

By definition, OME is a relatively asymptomatic process. As a result, management is initiated with two goals in mind: restoration of normal hearing and avoidance of middle ear sequelae.

Otitis media with effusion is associated with conductive hearing loss causing an average threshold elevation of 25 to 30 dB [49]. Children often present with complaints of difficulty hearing the telephone or television, or with teacher concerns of inattentiveness in class, and data suggest that OME is associated with reduced speech recognition in competing noise [49]. However, long-term effects of hearing loss in OME are still hotly debated in the literature. Studies of speech, language, cognition, and behavior in children plagued by OME have been fraught with methodologic flaws and confounding variables. However, the evidence through 1999 seems to suggest the following [50]:

(1) Speech reception and production have been inadequately studied, particularly in preschool-age children. Some results imply that prolonged early OME may be associated with more speech errors in children of school age.
(2) Persistent, early OME seems to have some adverse effect on language development during the early preschool period; however, the effect decreases with age. Expressive language is more likely to be affected than receptive skills. Effects on children of school age are not well studied.
(3) Available trials regarding effects of OME on cognition are sparse and yield conflicting results.
(4) Behavioral studies consistently suggest that children with prolonged OME are more easily distracted and less attentive, with effects potentially extending to early school age and teenage years [51,52].

In a recent longitudinal study of 429 children meeting "specified criteria" for tympanostomy tube placement, those randomized to undergo tube insertion demonstrated no difference in speech, language, cognitive, or psychosocial development at 3 or 4 years of age from those in whom intervention was delayed 6 to 9 months [53••]. Although the study has been criticized for inclusion of minimally affected children (unilateral effusion, minimal hearing loss, discontinuous disease), stratification still revealed no significant differences in more severely affected subgroups [54••]. These results may not be generalizable to children with bilateral disease of long duration associated with significant hearing loss.

Middle ear sequelae of chronic otitis result from chronic or intermittent negative pressure causing tympanic membrane retraction. This process may result in flaccidity and atelectasis in the posterosuperior tympanic membrane and the pars flaccida, culminating in ossicular discontinuity or cholesteatoma [55].

Natural history of otitis media with effusion

Otitis media with effusion may result from resolving AOM or may arise *de novo* because of eustachian tube dysfunction. After an episode of untreated AOM, spontaneous clearance of OME may be expected in approximately 75% of children within 3 months; with treatment of the acute episode, clearance at 3 months may be as high as 90% [29]. However, many middle ear effusions have been present for uncertain periods at the time of diagnosis. In such cases, clearance rates are approximately 50% at 1 month, 60% at 2 to 3 months, and 75% at 4 to 6 months [29]. Patients with effusions with duration of at least 3 months at the time of diagnosis have the poorest prognosis, with only 27% clearance at 6 months and 32% at 1 year [29]. Given the dependence of these highly variable outcomes on duration of OME at presentation, it is incumbent on the otolaryngologist to obtain an accurate history from the referring primary care provider before determining appropriate therapy.

Medical therapy for otitis media with effusion

Antibiotic therapy for OME has been justified in the past on the basis of cultures demonstrating viable bacteria [15,56] and more recently on the presence of bacterial nuclear material and biofilms [5,6,57]. Meta-analysis of blinded clinical trials suggests a mild improvement in clearance rates of approximately 15% with antibiotic therapy, or a need to treat seven children to effect a cure in one [32]. As a result, it seems reasonable to treat an episode of OME with one course of antibiotics before consideration of tympanostomy tubes, but the risk and expense of additional courses may not be justified.

Treatment of OME with corticosteroids has been studied with and without antibiotic therapy. In theory, steroids may speed resolution of the effusion by diminishing eustachian tube inflammation and by reducing the concentration of inflammatory mediators in the effusion, resulting in decreased glycoprotein production by goblet cells [58]. Levels of inflammatory mediators have been found even higher in the middle ear fluid of children with allergy compared with those in nonallergic people [59,60]. Data pooled for meta-analysis suggested clinical importance but did not yield statistical significance because of small sample sizes [32]. A recent study by Mandel *et al.* [61••] demonstrated improved resolution of effusion with steroids plus amoxicillin at 14 days compared with placebo plus amoxicillin. However, by the 4-month visit, nearly 70% of those who had cleared in each group had recurred. Additional amoxicillin after 2

weeks did not improve the clearance rate. It may be concluded that steroids have potential short-term benefit but do not guarantee long-term middle ear patency. Dangers associated with oral steroids in a child with systemic viral infection should be kept in mind when using this mode of therapy, and the parents should be questioned regarding the child's chicken pox history and varicella vaccination status. Studies suggest that intranasal steroids may be useful as adjunctive therapy for short-term treatment of OME but offer no long-term protection against AOM or OME [62,63].

There have been a few trials of other medical interventions for OME. Efficacy studies of antihistamines and decongestants have found these medications of no clinical benefit for treatment of OME [32]. Oxidants and reactive chemicals have been found in high concentration in the middle ear effusions (MEEs) of children with persistent OME and thus likely play an important role in its pathogenesis. Glutathione, an antioxidant, can scavenge these reactive species, and when aerosolized transnasally has been found to be very effective in resolving OME [64]. Exogenous surfactant may assist with mucociliary clearance and eustachian tube (ET) opening and is currently being investigated for a potential role in treatment of otitis media [65,66].

Surgical management of otitis media with effusion

Surgical management of OME consists of tympanostomy tube placement, because neither myringotomy nor laser fenestration accomplishes long-term freedom from effusion and improved ventilation in most patients [36,67]. However, many trials now demonstrate that adenoidectomy is efficacious when performed as an adjunctive procedure to tubes [36], and at least one study suggests that adenoidectomy with myringotomy may yield results equivalent to those of adenoidectomy with tube placement [68]. Children with adenoidectomy tend to have fewer episodes of OME and seem to require fewer repeat tube insertions [69,70•].

Tympanostomy tubes are a reasonable consideration in patients with at least 3 months of bilateral or 6 months of unilateral effusion, or in patients in whom a majority of the previous year was spent with middle ear disease. Patients with effusions for less time but who also have severe symptoms, severe hearing loss, or development of atelectasis or retraction packets should also be considered. Adenoidectomy may be reserved for the second set of tubes, but should be considered primarily in patients with a history of chronic nasal obstruction or adenoiditis.

Follow-up of tympanostomy tubes

Once ventilation tubes have been placed, it is important to offer children appropriate follow-up treatment. The American Academy of Pediatrics Section on Otolaryngology has published guidelines for follow-up that include an initial visit by the surgeon with subsequent physician visits at intervals of no longer than 6 months [71]. These visits can be performed by the either the surgeon or the primary care provider as long as there is documented communication between the two physicians. Guidelines for earlier referral back to the surgeon are also established.

Prevention and vaccination

When present, modifiable risk factors should be addressed with the patient's family. Tobacco exposure should be minimized and the use of pacifiers discouraged. Daycare exposure should be limited to small group settings, and patients with suspected allergy should be evaluated and appropriately treated.

The heptavalent pneumococcal vaccine (Prevnar; Wyeth Pharmaceuticals, Philadelphia, PA) was approved by the Food and Drug Administration in 2000 for prevention of invasive infections caused by *S. pneumoniae*. However, it has resulted in only a modest reduction in incidence of otitis media. In the Finnish trial, the vaccine reduced the number of episodes of AOM from any cause by 6%, culture-confirmed pneumococcal episodes by 34%, and the number of episodes caused by the serotypes contained in the vaccine by 57% [16]. The number of episodes attributed to serotypes cross-reactive with those in the vaccine was reduced by 51%, whereas the number of episodes caused by all other serotypes increased by 33%, and recent studies confirm that nonvaccine serotypes may be playing an increasing role in otitis media in vaccinated children [72]. Current recommendations call for universal immunization of children younger than 2 years and selective vaccination of older children with significant risk factors for rAOM [73].

Vaccination against influenza with heat-killed and live attenuated virus has demonstrated a significant reduction in influenza-related otitis media. Vaccines for nontypeable *H. influenzae* and *M. catarrhalis* have been difficult to develop because of highly variable surface determinants [74]. Current candidates include outer membrane proteins, pili and fimbriae (attachment organs), high molecular weight adhesion proteins, and detoxified lipooligosaccharide-protein conjugates [75,76].

Conclusion

Management of otitis media has become quite costly and increasingly difficult because of the emergence of resistant pathogens. Reduced medical and surgical therapy is indicated, particularly in light of the favorable natural history of the disorder and the low likelihood of significant effects on development in children. Recent surveys suggest, however, that such approaches to middle ear disease will require improvement in the diagnostic accuracy of primary care providers and their willingness to consider treatment recommendations in published guidelines. Preventive measures such as reduced daycare

attendance and size, limitation of tobacco exposure and pacifier use, and control of reflux and allergy are imperative, and patients should be urged to follow through with current immunization recommendations.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • Of special interest
- •• Of outstanding interest

1 Fried VM, Makuc DM, Rooks RN: Ambulatory health care visits by children: principal diagnosis and place of visit. Vital Health Stat 10 1998, 13:1–23.

2 Nash DR, Harman J, Wald ER, et al.: Antibiotic prescribing by primary care physicians for children with upper respiratory tract infections. Arch Pediatr Adolesc Med 2002, 156:1114–1119.

3 Chan LS, Takata GS, Shekelle P, et al.: Evidence assessment of management of acute otitis media, II: research gaps and priorities for future research. Pediatrics 2001, 108:248–254.

4 Lim DJ, Chun YM, Lee HY, et al.: Cell biology of tubotympanum in relation to pathogenesis of otitis media–a review. Vaccine 2000, 19(suppl 1): S17–S25.

5 Ehrlich GD, Veeh R, Wang X, et al.: Mucosal biofilm formation on middle-ear mucosal in the chinchilla model of otitis media. JAMA 2002, 287:1710–1715.

6 Post JC: Direct evidence of bacterial biofilms in otitis media. Laryngoscope 2001, 111:2083–2094.

7 Casselbrant ML, Mandel EM: Epidemiology. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:117–136.

8 Paradise JL, Rockette HE, Colborn DK, et al.: Otitis media in 2253 Pittsburgh area infants: prevalence and risk factors during the first two years of life. Pediatrics 1997, 99:318–332.

9 Uhari M, Mantysaari K, Niemela M: A meta-analytic review of the risk factors for acute otitis media. Clin Infect Dis 1996, 22:1079–1083.

10 Ball TM, Holberg CJ, Aldous M, et al.: Influence of attendance at day care on the common cold from birth through 13 years of age. Arch Pediatr Adolesc Med 2002, 156:121–126.

11 Dubin MG, Pollock HW, Ebert CS, et al.: Eustachian tube dysfunction after tobacco smoke exposure. Otolaryngol Head Neck Surg 2002, 126:14–19.

12 Lieu JEC, Feinstein AR: Effects of gestational and passive smoke exposure on ear infections in children. Arch Pediatr Adolesc Med 2002, 156:147–154.

13 Tasker A, Dettmar PW, Panetti M, et al.: Is gastric reflux a cause of otitis media with effusion in children? Laryngoscope 2002, 112:1930–1934.

14 Rovers M, Haggard M, Gannon M, et al.: Heritability of symptom domains in otitis media: a longitudinal study of 1,373 twin pairs. Am J Epidemiol 2002, 155:958–964.

15 Bluestone CD, Stephenson JS, Martin LM: Ten-year review of otitis media pathogens. Pediatr Infect Dis J 1992, 11:S7–S11.

16 Eskola J, Kilpi T, Palmu A, et al.: Efficacy of a pneumococcal conjugate vaccine against acute otitis media. N Engl J Med 2001, 344:403–409.

17 Sutton DV, Derkay CS, Darrow DH, et al.: Resistant bacteria in middle ear fluid at the time of tympanostomy tube surgery. Ann Otol Rhinol Laryngol 2000, 109:24–29.

18 Poole MD: Declining antibiotic effectiveness in otitis media: a convergence of data. Ear Nose Throat J 1998, 77:444–447.

19 Zapalac JS, Billings KR, Schwade ND, et al.: Suppurative complications of acute otitis media in the era of antibiotic resistance. Arch Otolaryngol Head Neck Surg 2002, 128:660–663.

20 Jacobs MR, Bajaksouzian S, Zilles A, et al.: Susceptibilities of Streptococcus pneumoniae and Haemophilus influenzae to 10 oral antimicrobial agents based on pharmacodynamic parameters: 1997 U.S. surveillance study. Antimicrob Agents Chemother 1999, 43:1901–1908.

21 • Heikkinen T, Chonmaitree T: Importance of respiratory viruses in acute otitis media. Clin Microbiol Rev 2003, 16:230–241.
An excellent article reviewing the viral pathogenesis of otitis media.

22 Carlson LH, Stool SE: Diagnosis. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:105–115.

23 Brody R, Rosenfeld RM, Goldsmith AJ, et al.: Parents cannot detect mild hearing loss in children. Otolaryngol Head Neck Surg 1999, 121:681–686.

24 Steinbach WJ, Sectish TC: Pediatric resident training in the diagnosis and treatment of acute otitis media. Pediatrics 2002, 109:404–408.

25 MacClements JE, Parchman M, Passmore C: Otitis media in children: use of diagnostic tools by family practice residents. Fam Med 2002, 34:598–603.

26 Rosenfeld RM: Diagnostic certainty for acute otitis media. Int J Pediatr Otorhinolaryngol 2002, 64:89–95.

27 • Garbutt J, Jeffe DB, Shackelford P: Diagnosis and treatment of acute otitis media: an assessment. Pediatrics 2003, 112:143–149.
This study assessed the compliance of St. Louis area pediatricians with the Centers for Disease Control and Prevention evidence-based guidelines for the judicious use of antimicrobials in children with AOM. Compliance with recommended diagnostic criteria was 38% by chart audit and 41% by self-report. Antimicrobial selection assessed by chart audit was consistent with Centers for Disease Control and Prevention guidelines in 68% of visits for a new infection, 63% of visits for treatment failure, and 50% for recurrent disease. Self-reported compliance with treatment guidelines for new infection was 100%, and 83% for treatment failure. The authors recommend improving diagnostic accuracy, limiting the use of broad-spectrum antimicrobials, and ensuring that amoxicillin dosing regimens are optimal.

28 Barnett ED, Klein JO, Hawkins KA, et al.: Comparison of spectral gradient acoustic reflectometry and other diagnostic techniques for detection of middle ear effusion in children with middle ear disease. Pediatr Infect Dis J 1998, 17:556–559.

29 Rosenfeld RM: Natural history of untreated otitis media. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:157–177.

30 Rosenfeld RM, Vertrees JE, Carr J, et al.: Clinical efficacy of antimicrobial drugs for acute otitis media: metaanalysis of 5400 children from thirty-three randomized trials. J Pediatr 1994, 124:355–367.

31 Froom J, Culpepper L, Green LA, et al.: A cross-national study of acute otitis media: risk factors, severity, and treatment at initial visit: report from the International Primary Care Network (IPCN) and the Ambulatory Sentinel Practice Network (ASPN). J Am Board Fam Pract 2001, 14:406–417.

32 Rosenfeld RM: What to expect from medical therapy. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:179–205.

33 Dowell SF, Butler JC, Giebink GS, et al.: Acute otitis media: management and surveillance in an era of pneumococcal resistance–a report from the Drug-resistant Streptococcus pneumoniae Therapeutic Working Group. Pediatr Infect Dis J 1999, 18:1–9.

34 Kozyrskyj AL, Hildes-Ripstein GE, Longstaffe SE, et al.: Treatment of acute otitis media with a shortened course of antibiotics: a meta-analysis. JAMA 1998, 279:1736–1742.

35 Jacobs J, Springer DA, Crothers D: Homeopathic treatment of acute otitis media in children: a preliminary randomized placebo-controlled trial. Pediatr Infect Dis J 2001, 20:177–183.

36 Rosenfeld RM: What to expect from surgical therapy. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:207–221.

37 Alho OP: How common is recurrent acute otitis media? Acta Otolaryngol Suppl 1997, 529:8–10.

38 Block SL, Harrison CJ, Hedrick J, et al.: Restricted use of antibiotic prophylaxis for recurrent acute otitis media in the era of penicillin non-susceptible Streptococcus pneumoniae. Int J Pediatr Otorhinolaryngol 2001, 61:47–60.

39 Roark R, Berman S: Continuous twice daily or once daily amoxicillin prophylaxis compared with placebo for children with recurrent acute otitis media. Pediatr Infect Dis J 1997, 16:376–381.

40 Gebhart DE: Tympanostomy tubes in the otitis media-prone child. Laryngoscope 1981, 91:849–866.

41 Gonzalez C, Arnold JE, Woody EA, et al.: Prevention of recurrent acute otitis media: chemoprophylaxis versus tympanostomy tubes. Laryngoscope 1986, 96:1330–1334.

42 Casselbrant ML, Kaleida PH, Rockette HE, et al.: Efficacy of antimicrobial prophylaxis and of tympanostomy tube insertion for prevention of recurrent acute otitis media: results of a randomized clinical trial. Pediatr Infect Dis J 1992, 11:278–286.

43 Rosenfeld RM, Bhaya MH, Bower CM, et al.: Impact of tympanostomy tubes on child quality of life. Arch Otolaryngol Head Neck Surg 2000, 126:585–592.

44 Richards M, Giannoni C: Quality-of-life outcomes after surgical intervention
• for otitis media. Arch Otolaryngol Head Neck Surg 2002, 128:776–782.
The authors used a prospective questionnaire-based study design to assess the change in disease-specific quality of life in children with rAOM, OME, or both treated with surgical intervention. They demonstrated a significant improvement in quality of life of children with rAOM, OME, or both after surgical intervention. The amount of parental worry concerning their children's ear problems also significantly improved after surgery, and most caregivers would opt again for tube placement.

45 Linder TE, Marder HP, Munzinger J: Role of adenoids in the pathogenesis of otitis media: a bacteriologic and immunohistochemical analysis. Ann Otol Rhinol Laryngol 1997, 106:619–623.

46 Brook I, Shah K, Jackson W: Microbiology of healthy and diseased adenoids. Laryngoscope 2000, 110:994–999.

47 Mattila PS, Joki-Erkkila VP, Kilpi T, et al.: Prevention of otitis media by ade-
• noidectomy in children younger than 2 years. Arch Otolaryngol Head Neck Surg 2003, 129:163–168.
This prospective study investigated the effect of adenoidectomy with tympanostomy compared with tympanostomy alone in the prevention of otitis media in children younger than 2 years. Over a mean follow-up of 7 months, the average reduction in the rate of all AOM media episodes in the adenoidectomy group was 19% in the randomized arm of the trial and 25% in the nonrandomized arm. Although the authors concluded that concurrent adenoidectomy during the insertion of tympanostomy tubes has little advantage over tubes alone in preventing otitis media, the results suggest that the procedure may be of value in severely affected people.

48 Paradise JL, Bluestone CD, Colborn DK, et al.: Adenoidectomy and adenotonsillectomy for recurrent acute otitis media: parallel randomized clinical trials in children not previously treated with tympanostomy tubes. JAMA 1999, 282:945–953.

49 Madell JR: Impact of otitis media on auditory function. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:337–351.

50 Feagens LV: Impact of otitis media on speech, language, cognition, and behavior. In Evidence-Based Otitis Media. Edited by Rosenfeld RM, Bluestone CD. Hamilton, Ontario: BC Decker; 1999:353–373.

51 Feagens LV, Sanyal M, Henderson F, et al.: Relationship of middle-ear disease in early childhood to later narrative and attention skills. J Pediatr Psychol 1994, 19:347–367.

52 Bennett KE, Haggard MP, Silva PA, et al.: Behaviour and developmental effects of otitis media with effusion into the teens. Arch Dis Child 2001, 85:91–95.

53 Paradise JL, Dollaghan CA, Campbell TF, et al.: Otitis media and tympanos-
•• tomy tube insertion during the first three years of life: developmental outcomes at the age of four years. Pediatrics 2003, 112:265–277.
The authors reported updated results from their long-term study of effects of persistent otitis media in the first 3 years of life on later impairments of cognitive, language, speech, or psychosocial development, and of the effect of prompt insertion of tympanostomy tubes on such impairments. They concluded that in otherwise healthy children who are younger than 3 years, persistent MEE meeting the criteria for duration in this study is negligibly associated with and probably does not affect developmental outcomes at 4 years of age; and furthermore, that prompt insertion of tympanostomy tubes does not measurably improve developmental outcomes at 4 years of age. It is recommended that the reader consider the distribution of hearing loss and the duration of middle ear disease in the study cohort when interpreting the results.

54 Paradise JL, Feldman HM, Campbell TF, et al.: Early versus delayed insertion
•• of tympanostomy tubes for persistent otitis media: developmental outcomes at the age of three years in relation to prerandomization illness patterns and hearing levels. Pediatr Infect Dis J 2003, 22:309–314.
The authors returned to their 2001 report of 429 children meeting criteria for tube insertion in whom delay of the procedure did not seem to affect subsequent developmental impairment assessed at 3 years of age. In the present study, they analyzed subgroups of these children who may have been the most severely affected, including those who had been randomized on the basis of bilateral, continuous MEE rather than unilateral or discontinuous MEE or both and those who had the greatest degrees of hearing loss. In none of the subgroups were scores on any outcome measure significantly more favorable in children in the early treatment group than in the late treatment group.

55 Bluestone CD, Klein JO: Complications and sequelae: intratemporal. In Otitis Media in Infants and Children, edn 2. Philadelphia: WB Saunders; 1995:241–291.

56 Brook I, Yocum P, Shah K, et al.: Microbiology of serous otitis media in children: correlation with age and length of effusion. Ann Otol Rhinol Laryngol 2001, 110:87–90.

57 Rayner MG, Zhang Y, Gorry MC, et al.: Evidence of bacterial metabolic activity in culture-negative otitis media with effusion. JAMA 1998, 279:296–299.

58 Lin J, Juhn SK, Adams GL, et al.: Dexamethasone inhibits mucous glycoprotein secretion via a phospholipase A2-dependent mechanism in cultured chinchilla middle ear epithelial cells. Acta Otolaryngol 1997, 117:406–413.

59 Jang CH, Kim YH: Characterization of cytokines present in pediatric otitis media with effusion: comparison of allergy positive and negative. Int J Pediatr Otorhinolaryngol 2002, 66:37–40.

60 Hurst DS, Venge P: The impact of atopy on neutrophil activity in middle ear effusion from children and adults with chronic otitis media. Arch Otolaryngol Head Neck Surg 2002, 128:561–566.

61 Mandel EM, Casselbrant ML, Rockette HE, et al.: Systemic steroid for chronic
•• otitis media with effusion in children. Pediatrics 2002, 110:1071–1080.
This study investigates the efficacy of a short course of prednisolone given with amoxicillin compared with amoxicillin alone for the treatment of OME. The efficacy of additional treatment with amoxicillin was also assessed. The authors found a significant difference in the proportion of children who were effusion-free immediately after 14 days of treatment with steroid and amoxicillin compared with those who were treated with amoxicillin only for 14 days. However, within 2 weeks of finishing treatment, there was no longer a significant difference between the two groups regardless of whether amoxicillin was continued. The study supports judicious use of medical therapy for OME.

62 Tracy JM, Demain JG, Hoffman KM, et al.: Intranasal beclomethasone as an adjunct to treatment of chronic middle ear effusion. Ann Allergy Asthma Immunol 1998, 80:198–206.

63 Ruohola A, Heikkinen T, Waris M, et al.: Intranasal fluticasone propionate does not prevent acute otitis media during viral upper respiratory infection in children. J Allergy Clin Immunol 2000, 106:467–471.

64 Testa B, Testa D, Masolella M, et al.: Management of chronic otitis media with effusion: the role of glutathione. Laryngoscope 2001, 111:1486–1489.

65 McGuire JF: Surfactant in the middle ear and eustachian tube: a review. Int J Pediatr Otorhinolaryngol 2002, 66:1–15.

66 Venkatayan N, Troublefield YL, Connelly PE, et al.: Intranasal surfactant aerosol therapy for otitis media with effusion. Laryngoscope 2000, 110:1857–1860.

67 Siegel G, Brodsky L, Waner M, et al.: Office-based laser assisted tympanic membrane fenestration in adults and children: pilot data to support an alternative to traditional approaches to otitis media. Int J Pediatr Otorhinolaryngol 2000, 53:111–120.

68 Gates GA, Avery CA, Prihoda TJ, et al.: Effectiveness of adenoidectomy and tympanostomy tubes in the treatment of chronic otitis media with effusion. N Engl J Med 1987, 317:1444–1451.

69 Coyte PC, Croxford R, McIsaac W, et al.: The role of adjuvant adenoidectomy and tonsillectomy in the outcome of the insertion of tympanostomy tubes. New Engl J Med 2001, 344:1188–1195.

70 Boston M, McCook J, Burke B, et al.: Incidence of and risk factors for addi-
• tional tympanostomy tube insertion in children. Arch Otolaryngol Head Neck Surg 2003, 129:293–296.
In this retrospective case review, the authors investigated the incidence and risk factors that account for additional tympanostomy tube placement among children who have undergone an initial placement of ventilation tubes. Data revealed that one in five patients subsequently required a second set of ventilation tubes. Age younger than 18 months at the time of the initial procedure was associated with an increased risk for additional surgery but was not an independent risk factor. Adenoidectomy reduced the incidence of subsequent tube insertion after initial surgery.

71 Cunningham MJ, Darrow DH, Goldstein MN, et al.: Follow-up management of children with tympanostomy tubes. Pediatrics 2002, 109:328–329.

72 Dagan R, Givon-Lavi N, Zamir O, et al.: Reduction of nasopharyngeal carriage of Streptococcus pneumoniae after administration of a 9-valent pneumococcal conjugate vaccine to toddlers attending day care centers. J Infect Dis 2002, 185:927–936.

73 American Academy of Pediatrics, Committee on Infectious Diseases: Policy statement: recommendations for the prevention of pneumococcal infections, including the use of pneumococcal conjugate vaccine (Prevnar), pneumococcal polysaccharide vaccine, and antibiotic prophylaxis. Pediatrics 2000, 106:362–366.

74 Rafei K: Influenza virus vaccines in children and their impact on the incidence of otitis media. Semin Pediatr Infect Dis 2002, 13:129–133.

75 Murphy TF: Respiratory infections caused by non-typeable Haemophilus influenzae. Curr Opin Infect Dis 2003, 16:129–134.

76 Jiao X, Hirano T, Hou Y, et al.: Specific immune responses and enhancement of murine pulmonary clearance of Moraxella catarrhalis by intranasal immunization with a detoxified lipooligosaccharide conjugate vaccine. Infect Immun 2002, 70:5982–5989.