Otitis Media

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Author Disclosure
Drs Gould and Matz have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Objectives

After completing this article, readers should be able to:

1. Differentiate acute otitis media (AOM) from otitis media with effusion (OME).
2. Plan the management of OME, including knowing the indications for tympanostomy tube placement.
3. List the common pathogenic bacteria that cause AOM.
4. Discuss a treatment course for AOM, accounting for epidemiology and resistance patterns.
5. Describe treatments for refractory AOM.

"In uncomplicated cases the patient should be kept quiet in the house, while in severe cases he should be put to bed and given a light diet.... The author formerly used the artificial leech with satisfactory results in many cases, especially those of a mild type, and still feels that in certain instances it can be used to advantage. The artificial leech is much to be preferred to the natural one, for the following reasons: 1. The scarificator and cupping-glass are always at hand, while natural leeches are frequently very difficult to obtain, especially at night. 2. Leeches are very repulsive and disagreeable to most patients, and especially to children. 3. After the artificial leech has been removed, the bleeding ceases at once, while with the natural leech it is often difficult to control the hemorrhage.... In the case of children, hot water instilled into the ear often affords great relief."

From Bacon G, Saunders TL. *A Manual of Otology.* 7th ed. New York, NY: Lea and Febiger; 1918

Introduction

In 1918, Bacon and Saunders described state-of-the-art therapy options for acute otitis media (AOM). In the preantibiotic era, supportive care and "hot water instilled into the ear" were the therapies most available to families, and as far as children were concerned, likely preferable to the leech, either natural or artificial. Treatment for otitis media obviously has progressed substantially since the advent of antibiotic use. The past decade has seen increasing antibiotic resistance and a growing controversy over whether all children who have AOM require antibiotic therapy. This article reviews the presentation, diagnosis, and treatment of AOM and otitis media with effusion (OME).

Abbreviations

AAP: American Academy of Pediatrics
AOM: acute otitis media
CSOM: chronic suppurative otitis media
hMPV: human metapneumovirus
MEE: middle ear effusion
MIC: minimum inhibitory concentration
MRSA: methicillin-resistant *Staphylococcus aureus*
OME: otitis media with effusion
PCR: polymerase chain reaction
PCV7: heptavalent pneumococcal conjugate vaccine
RSV: respiratory syncytial virus
TM: tympanic membrane
URI: upper respiratory tract infection

Definition

The term "otitis media" generally is subdivided into two major subclassifications: OME and AOM. OME describes the presence of a middle ear effusion (MEE) without signs or symptoms of infection. (1) Previously, OME has been termed serous (or secretory) otitis media as well as "glue ear." The American Academy of Pediatrics (AAP) has defined AOM as an infection of the middle ear with acute onset

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of signs and symptoms, MEE, and signs and acute symptoms of middle ear inflammation. (2)

Difficult-to-treat AOM includes both recurrent AOM and treatment-failure AOM and affects up to 20% of children who develop AOM in their first postnatal years. Treatment-failure AOM is defined as a lack of improvement in signs and symptoms within 48 to 72 hours after initiation of antibiotic therapy. Recurrent AOM is defined as three or more AOM episodes occurring in the previous 6 months or four or more AOM episodes in the preceding 12 months. OME that persists beyond 3 months often is called chronic otitis media or chronic otitis media with effusion. Chronic suppurative otitis media (CSOM) is defined as purulent otorrhea associated with a chronic tympanic membrane (TM) perforation that persists for more than 6 weeks despite appropriate treatment for AOM.

Epidemiology

AOM is responsible for more than 20 million antibiotic prescriptions and more than 24 million office visits annually in the United States and costs approximately 2 to 5.3 billion dollars annually. Because otitis media is the most common reason for antibiotic prescriptions among United States children, it is an important contributor to the problem of antibiotic-resistant bacteria. Worldwide, otitis media leads to an estimated 50,000 deaths per year in children younger than 5 years of age because of the complications of CSOM, which today is a rare entity in developed countries. CSOM is estimated to affect 65 to 330 million people worldwide, 60% of whom suffer significant hearing loss. Most otitis media in developed countries is AOM and the more common OME.

A seasonal peak in the diagnosis of AOM occurs during the winter months, paralleling the incidence of viral upper respiratory tract infection (URI). Ninety percent of children have at least one symptomatic or asymptomatic episode by 2 years of age. In the United States, the incidence peaks between 6 and 18 months of age. Onset of AOM in the first few postnatal months is a sentinel event for the development of recurrent middle ear disease. Early-onset AOM and the proportion of children who experience multiple episodes before their first birthdays have been increasing in the United States since 1989.

Risk factors for developing acute or chronic OME and AOM and recurrent AOM are listed in Table 1. Race, bottle feeding, use of a pacifier, and exposure to cigarette smoke have not been identified consistently as risk factors for AOM. Chronic OME is associated with underlying conditions such as craniofacial abnormalities, history of allergies, and chronic sinusitis.

Table 1. Risk Factors for Developing Acute or Chronic OME or AOM

- Age <2 years
- Atopy
- Bottle propping
- Chronic sinusitis
- Ciliary dysfunction
- Cleft palate and craniofacial anomalies
- Child care attendance
- Down syndrome and other genetic conditions
- First episode of AOM when younger than 6 months of age
- Immunocompromising conditions

AOM=acute otitis media, OME=otitis media with effusion

Pathogenesis

Normally, the middle ear space experiences a slight negative air pressure relative to the outside environment. This negative pressure is relieved periodically by opening of the eustachian tube during actions such as yawning and chewing. Impaired eustachian tube function is accepted as the initial mechanism that triggers otitis media. (1) Impairment may be transient, as occurs during an acute URI, gastroesophageal reflux, or allergic rhinitis, or can be more permanent, as occurs with craniofacial anomalies such as cleft palate. In addition, the relatively shorter eustachian tubes of younger children make reflux of nasopharyngeal contents more likely. Eustachian tube dysfunction during URI has been shown to be more severe in children younger than 2 years of age compared with older children, and young age has been shown to be the most important predictor of AOM complicating a URI.

Once impaired, the eustachian tube is less able to relieve the pressure difference in the middle ear, and the negative pressure deepens. Initially, this effect may be noted on physical examination by retraction of the TM. The accentuated negative pressure in the middle ear space may make it possible for nasopharyngeal contents to be aspirated or refluxed into the middle ear during transient opening of the eustachian tube. The accentuated negative pressure also can cause increased vascular permeability and can lead to development of an effusion. In addition, oro- or nasopharyngeal contents may reflux through a patent or patulous eustachian tube, leading to

inflammation in the middle ear and subsequent development of an effusion.

Eustachian tube dysfunction leading to negative middle ear pressure occurs in 75% of children who have viral URIs. Coinfection with a viral URI enhances the ability of bacterial pathogens to adhere and ascend from the nasopharynx to the middle ear via the eustachian tube. In addition, viruses can affect the local host immune response by impairing leukocyte function, exposing receptors for bacteria, and decreasing the effectiveness of the mucociliary escalator.

The viruses isolated most frequently, alone or in combination with bacterial pathogens from the middle ears of patients who have AOM, include respiratory syncytial virus (RSV), parainfluenza (types 1, 2, 3), and influenza (A and B). The overall incidence of URI complicated by otitis media has been reported to be 61% in children between 6 months and 3 years of age, with a 37% incidence of AOM and 24% incidence of OME. (3)

Adenovirus, RSV, and coronavirus are associated with a higher rate of AOM, with 50% of children who have URIs caused by these viruses developing AOM compared with only 33% of patients who have URIs caused by parainfluenza, influenza, enterovirus, or rhinovirus developing AOM.

Recently, using reverse transcriptase polymerase chain reaction (PCR) testing, human Parechovirus was identified in the middle ear fluid of children experiencing recurrent otitis media (in 15% of episodes). Human metapneumovirus (hMPV) has been shown to cause approximately 7% of all respiratory infections in children younger than 2 years of age, and AOM develops in approximately 60% of hMPV-infected children younger than 3 years of age.

It generally is accepted that bacteria are recovered from middle ear cultures in approximately 50% to 90% of cases of AOM, with or without otorrhea, and viruses in 20% to 50%. In bacteriologic studies of AOM, no growth or growth of an organism considered a contaminant (such as diphtheroids or *Staphylococcus epidermidis*) occurs in approximately 20% to 30% of samples. Sterile bacterial cultures may be a result of infection with a nonbacterial organism such as a virus, *Chlamydia,* or *Mycoplasma*, a fastidious organism that is not isolated by routine laboratory techniques; prior antibiotic treatment; or a local host immune response that might suppress the growth of bacteria. However, the percentage of tympanocentesis specimens that are positive for a bacterial or viral agent in AOM varies, depending on the study methodology, the sensitivity of the microbiologic techniques used, the definition of AOM used in the study, whether unilateral or bilateral disease was present, whether patients had been treated with antibiotics prior to tympanocentesis, and the geographic location of the study.

In 1997, a study conducted in France showed that middle ear aspirates from children ages 6 months to 6 years of age were sterile in 35% of the children who had not received antibiotics and in 64% of those who had received antibiotics for 48 hours prior to tympanocentesis. (4) A 2003 study conducted in Israel demonstrated a 24% rate of positive bacteriologic cultures in pediatric patients who had AOM. (5)

In 2006, Finnish researchers examined the microbiology of the middle ear in patients who had AOM with new onset of otorrhea by sampling through a tympanostomy tube. (6) Using culture and PCR, they were able to identify a bacterial agent in 92% of cases and were able to identify a virus in 70% using viral culture, antigen detection, and PCR. They identified both a bacterial and viral pathogen in most of their patients (66%). More recently, a study conducted in Israel examined tympanocentesis cultures in children 3 years of age or younger who had unilateral or bilateral AOM. (7) Overall, 77% of patients had positive middle ear fluid bacterial cultures, including 83% in those having bilateral and 67% in those having unilateral AOM.

The bacterial pathogens recovered in middle ear cultures identified most commonly include *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, *Moraxella catarrhalis,* and *S pyogenes* (group A *Streptococcus*). *Staphylococcus aureus* causes AOM less commonly. Several investigators have demonstrated both in an animal model and in humans that nontypeable *H influenzae*, *S pneumoniae*, and *M catarrhalis* form biofilms in vitro and in vivo. The phenotypic characteristics of bacteria in a biofilm are such that reduced growth rate and a distinct gene expression increase their resistance to antimicrobial agents and the host defense system. Hong and associates (8) demonstrated that nontypeable *H influenzae* within a biofilm can alter its expression of a surface epitope, phosphorylcholine, thereby subverting the host inflammatory response.

The bacterial pathogens causing AOM in the first 6 weeks after birth are essentially the same as those in older children. However, in a recent study conducted in Israel, gram-negative bacilli were identified in middle ear fluid in 10.5% of infants who had AOM diagnosed in the first 2 postnatal months. (9) The most common pathogens identified in this study were *S pneumoniae* and nontypeable *H influenzae*.

Presentation

History

OME generally is preceded by one of the precipitants mentioned previously (URI, allergic rhinitis, gastroesophageal reflux). By itself, OME generally causes minimal symptoms, with mild hearing loss being the most common. Other symptoms generally are due to the precipitating disorders.

AOM can be differentiated from OME by symptoms indicative of the inflammation, specifically, the presence of otalgia and fever.

Physical Examination

Physical examination of the ear is facilitated by the use of proper equipment. Halogen bulbs provide the best light for otoscopy, along with a fully charged battery. Reusable specula are preferred over disposable specula for their length, size options, and glossy finish, which improve light transmission into the auditory canal. Newer otoscopes are available that claim increased magnification and field-of-view compared with older models.

Figure 1 demonstrates the normal landmarks visible with otoscopy. A normal TM should be translucent and show the landmarks (Fig. 2). It also should be freely mobile on insufflation. The diagnosis of OME or AOM is established by first documenting the presence of fluid in the middle ear space. Second, the presence of inflammation is used to differentiate AOM from OME. With OME, the TM may appear opaque or cloudy (Fig. 3). There also may be a visible air-fluid level or air bubbles in the middle ear. Pneumatic otoscopy remains the best method for diagnosing the presence of middle ear fluid. (10) Although a retracted TM also may demonstrate impaired mobility, immobility of the TM on pneumatic otoscopy is highly sensitive and specific for the presence of MEE. Its low cost and high availability make pneumatic otoscopy the preferred method of diagnosing MEE.

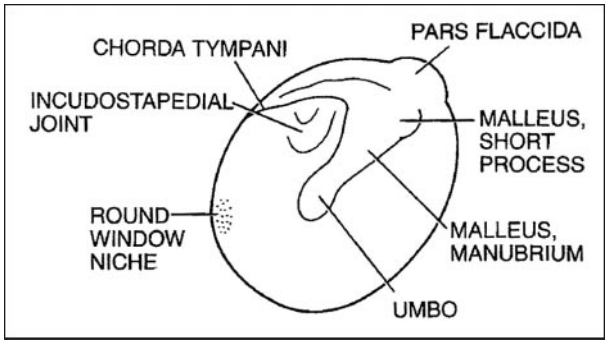

Figure 1. Important landmarks of the tympanic membrane that usually can be seen with the otoscope. Reprinted with permission from Bluestone CD, Klein JO. *Otitis Media in Infants and Children.* 4th ed. Hamilton, Ontario, Canada: BC Decker, Inc; 2007.

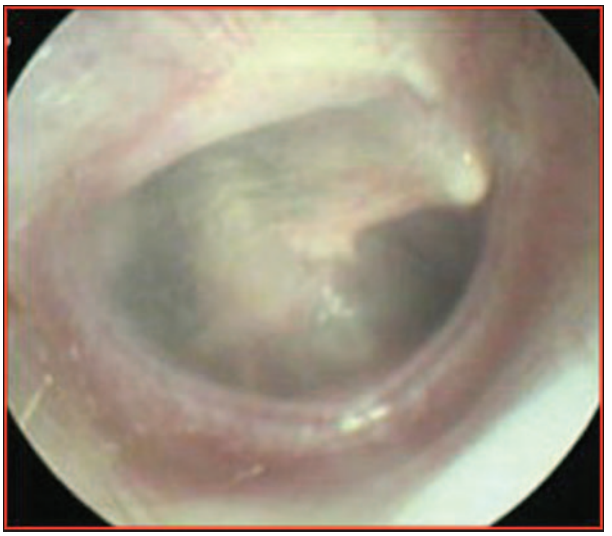

Figure 2. Normal tympanic membrane. Reprinted with permission from McConnochie KM. Potential of telemedicine in pediatric primary care. *Pediatr Rev.* 2006;27:e58–e65.

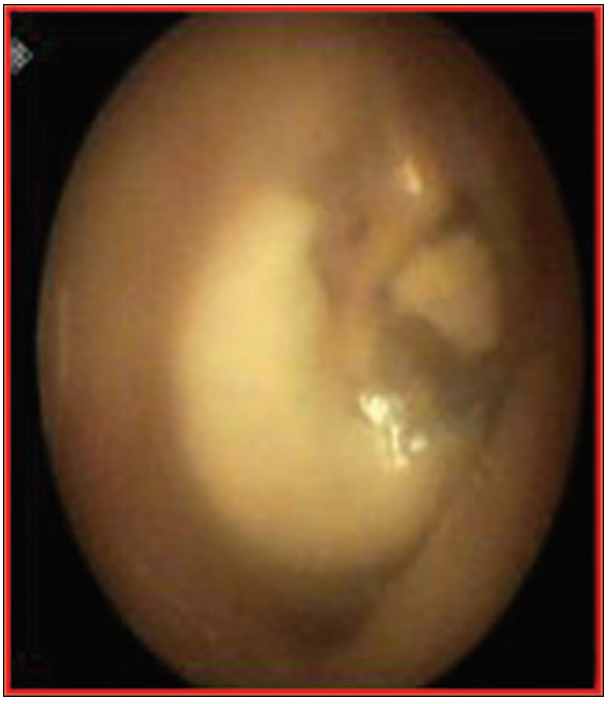

Figure 3. Otitis media with effusion. Reprinted with permission from McConnochie KM. Potential of telemedicine in pediatric primary care. *Pediatr Rev.* 2006;27:e58–e65.

Because clinician competence in pneumatic otoscopy may vary, diagnostic adjuncts may be used. The most prevalent of these techniques is tympanometry, which measures the compliance of the TM. The tympanometer is placed into the ear canal, creating a pressure-tight seal. Sound waves are transmitted from the device and reflected off the TM. The energy of these reflected sound waves, measured by the tympanometer, is an indicator of the compliance of the TM.

The tympanometer also includes a pressure transducer, which alters the pressure in the ear canal across a range from negative to positive pressures (as compared with atmospheric pressure). As the ear canal pressure is changed, the device transmits sound waves and measures the energy of the reflected waves. Measurements of TM compliance across the pressure range are placed in a graph. The resulting graphs generally are subdivided into three categories, although multiple subcategories exist (Fig. 4). An "A" curve represents a normal TM, which exhibits maximum compliance, with an auditory canal pressure equal to atmospheric pressure. A "B" curve appears flat due to poor or no mobility of the TM across the pressure range. This curve generally is associated with an MEE, either OME or AOM. A "C" curve represents near-normal compliance, but with the peak shifted toward negative pressures. This effect is due to increasing negative pressure in the middle ear, generally a precursor to an effusion. "A" and "B" type curves are reasonably specific and sensitive at diagnosing MEE, although tympanometry is less useful in younger infants.

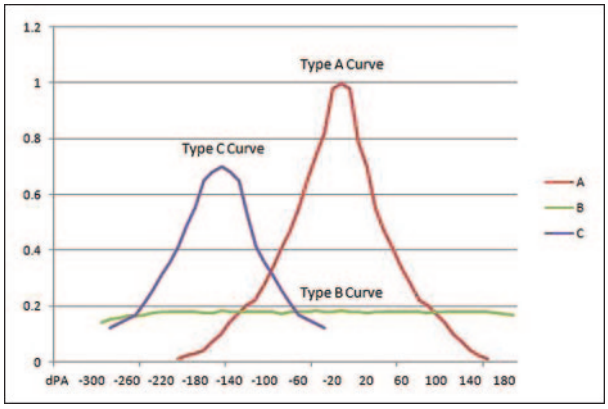

Figure 4. Examples of common tympanometry curves. Type A curves represent normal tympanic membrane compliance. Type B curves reflect poor compliance of the tympanic membrane (likely due to a middle ear effusion). Type C curves are shifted to the left, or negative, side of the graph, indicating progressive negative pressure in the middle ear space.

An alternative method for documenting the presence of an MEE is acoustic reflectometry. The instrument plays a sound that is reflected off the TM. Normal TMs absorb more sound; MEEs cause more sound to be reflected. Acoustic reflectometry has similar sensitivity and specificity to that of tympanometry.

Once the presence of an MEE has been established, signs of inflammation can differentiate an AOM from an OME. Middle ear fluid in AOM is more likely to be opaque. Generally, red or dark-yellow discoloration of the TM or bulging of the TM is an accepted physical finding indicative of an AOM (Fig. 5). (2)

Microbiology of AOM

S pneumoniae

S pneumoniae is carried in the nasopharynx in approximately 50% of children attending child care and approximately 5% to 10% of adults. Colonization is the first step leading to local disease such as AOM or systemic invasion such as bacteremia and meningitis. Dramatic reductions in invasive *S pneumoniae* disease have occurred in the United States as a result of widespread adoption of the heptavalent pneumococcal conjugate vaccine (PCV7), which initially was employed in 2000. A Finnish study was the first to report that PCV7 reduced the number of episodes of AOM due to any cause by 6%, reduced culture-confirmed pneumococcal AOM episodes by 34%, and reduced the number of AOM episodes due to serotypes contained in PCV7 by 57%. (11) The number of episodes caused by cross-reactive serotypes decreased

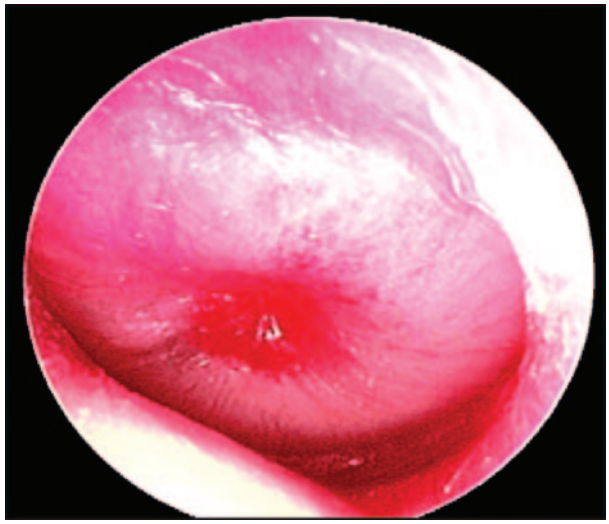

Figure 5. Acute otitis media. Reprinted with permission from Siegel RM, Bien JP. Acute otitis media in children: a continuing story. *Pediatr Rev.* 2004;25:187–193.

by 51%; the number of episodes due to all other serotypes actually increased by 33%.

A Kaiser Permanente double-blind study involving 37,868 children who were randomized to receive PCV7 or placebo demonstrated that children who received the primary series of PCV7 had otitis media visits reduced by 7.8%, antibiotic prescriptions by 5.7%, and tympanostomy tube placements by 24%. (12) For children who had recurrent AOM, PCV7 reduced the risk of three visits by 10% and the risk of 10 visits by 20% within a 6-month period.

In addition, Poehling and associates (13) described a 17% to 28% reduction in the frequency of AOM and a 16% to 23% reduction in the frequency of tympanostomy tube placements from 2000 to 2001 (pre-PCV7) to 2001 to 2002 (post-PCV7). Grijalva and colleagues (14) also studied rates of ambulatory visits for otitis media from 1994 to 1999 and 2002 to 2003 (post-PCV7) and demonstrated a 20% decrease in visits for otitis media in children younger than 2 years of age, representing an annual decrease of 246 fewer visits per 1,000 children younger than 2 years of age. Two studies conducted in the post-PCV7 period revealed that the proportion of AOM caused by *S pneumoniae* serotypes contained in PCV7 declined by 50% and by 24% in patients who had recurrent AOM and treatment-failure AOM. (15)(16)

However, several studies have demonstrated that serotype replacement by serotypes not included in the vaccine is occurring and causing local and invasive pneumococcal disease. The Centers for Disease Control and Prevention have reported that the annual incidence of pneumococcal disease due to nonvaccine serotypes in children younger than 5 years of age has increased from an average of 16.3 cases per 100,000 population during prevaccine years (1998 to 1999) to 19.9 cases per 100,000 population in 2004. Significant increases in the incidence of disease due to serotypes 3, 15, 19A, 22F, and 33F occurred during this period, with serotype 19A, which is closely related to vaccine type 19F, becoming the predominant cause of invasive disease in United States children.

Among the primary serotypes causing replacement disease, nonsusceptibility to penicillin or other antimicrobials was most common for serotype 19A. A dramatic increase in the percentage of serotype 19A isolates that were resistant to penicillin was observed in children, with 10% during the prevaccine era and 31% in 2004. In addition, the percentage of serotype 19A isolates that were not susceptible to erythromycin increased significantly from 23% to 46%. Among children younger than 5 years of age, nonsusceptibility to both penicillin and erythromycin was seen only with serotype 15A (0% prevaccine to 6% in 2004).

In 2001, a United States study revealed that 42% of 500 middle-ear *S pneumoniae* isolates were penicillin-resistant, having minimum inhibitory concentrations (MICs) of 2 mcg/mL or greater, and 17% were amoxicillin-resistant. Resistance to macrolides and azalides also has become more common. A study performed by Pichichero and colleagues (17) demonstrated that *S pneumoniae* that are not susceptible to penicillin are re-emerging as important pathogens in patients who have treatment-failure and recurrent AOM in the post-PCV7 era. In addition, they reported a multidrug-resistant strain of *S pneumoniae* expressing a 19A capsular serotype. This strain was resistant to all antimicrobials approved by the United States Food and Drug Administration for treating AOM.

Most patients infected with this strain were diagnosed as having recurrent AOM and treatment-failure AOM, although two of the nine total patients acquired this strain with their first episode of AOM. These two patients had received three PCV7 doses. All of the patients required either tympanostomy tube placement or tympanocentesis followed by levofloxacin (an unapproved antibiotic for AOM in children) for cure. (18) In 2006, the AAP advocated the limited use of fluoroquinolones in situations in which the risk-benefit ratio indicates that use of these agents is necessary. Risk factors for acquiring AOM caused by *S pneumoniae* that has reduced susceptibility to antibiotics include age younger than 2 years, recent treatment with antibiotics, season of the year (late winter to early spring), and group child care.

A recent pediatric study from Texas Children's Hospital has revealed that the number of cases of pneumococcal mastoiditis (a common suppurative complication of AOM) caused by the 19A serotype is increasing and that all patients who had 19A disease had subperiosteal abscesses on computed tomography scans of the mastoid bones, with 89% requiring surgery. (19) These patients had more aggressive disease compared with those having non19A disease and were more complicated to treat because the circulating 19A clones were multidrug-resistant.

Nontypeable *H influenzae*

Nontypeable *H influenzae* remains the pathogen isolated most frequently in patients who have recurrent AOM or AOM with treatment failure. The clinical entity "otitis-conjunctivitis syndrome" is associated with isolation of this pathogen from both the middle ear and the conjunctiva in older children and has been described recently in

infants in their first 2 postnatal months. Pichichero and associates (17) studied the microbiology of recurrent and treatment-failure AOM across three respiratory seasons from 2003 to 2006 and demonstrated that nontypeable *H influenzae* was the predominant organism (51%) isolated by tympanocentesis, followed by *S pneumoniae* (38%). However, in 2005 to 2006, the proportion of *S pneumoniae* infections increased and the proportion of nontypeable *H influenzae* isolates decreased. Fifty-three percent of nontypeable *H influenzae* isolates recovered from patients who had recurrent and treatment-failure AOM in the post-PCV7 era were beta-lactamase-resistant. Neither the proportion of nontypeable *H influenzae* that produce beta-lactamase nor the proportion of *S pneumoniae* that were penicillin-susceptible changed during the 3-year period.

M catarrhalis

M catarrhalis has been isolated from middle ear cultures of children who have AOM. *M catarrhalis* causes approximately 4 to 5 million of the total 25 million episodes of AOM annually in the United States. The organism is more prevalent in the first year after birth. It is estimated to cause approximately 12% to 20% of bacterial AOM, with 100% of isolates producing beta-lactamase. Studies of middle ear fluid from children who had AOM have shown an increased proportion of *M catarrhalis* in PCV7-immunized children.

S pyogenes (Group A *Streptococcus*)

S pyogenes infection occurs most commonly in children older than 5 years of age. It is isolated from approximately 3% of middle ear fluid samples in patients who have AOM and are younger than 18 years of age. AOM caused by *S pyogenes* is characterized by older age and more aggressive disease as well as by higher rates of TM perforation and mastoiditis.

S agalactiae (Group B *Streptococcus*)

S agalactiae is isolated primarily from the middle ears of neonates and young infants.

S aureus

S aureus is carried in the anterior nares by approximately 10% of children younger than 2 years of age and by approximately 35% of the general population. *S aureus* is isolated from approximately 3% of middle-ear cultures taken from children who have AOM and intact TMs. Recent studies have shown an increased incidence of *S aureus* in recurrent AOM after PCV7 vaccination. It is a more important pathogen in children who have acute otorrhea associated with tympanostomy tubes. In addition, community-acquired methicillin-resistant *S aureus* (MRSA) has emerged as a pathogen in acute otorrhea among children who have tympanostomy tubes.

Gram-negative Bacilli

In a recent study conducted in Israel, gram-negative bacilli isolated in middle-ear fluid cultures from infants who had AOM in the first 2 months after birth included *Klebsiella pneumoniae* (3.9%), *Escherichia coli* (2.7%), *Pseudomonas aeruginosa* (2.3%), *Enterobacter* (1.1%), and *Proteus* (0.4%). (9)

Bullous Myringitis

Bullous myringitis is defined as blisters on the TM, usually in association with AOM. The microbial pathology of bullous myringitis is similar to that of AOM. In one study, a respiratory virus was detected in 70% of nasopharyngeal aspirate samples and in 27% of middle-ear fluid samples. The distribution of bacterial pathogens was similar to that of AOM.

Chronic Suppurative Otitis Media

CSOM is defined as discharge through a perforated TM for more than 6 weeks despite appropriate treatment for AOM. CSOM primarily affects people from Southeast Asia, the Western Pacific, and Africa, as well as ethnic minorities. The most common pathogens isolated from chronically draining ears of older children who have CSOM are *P aeruginosa,* other enteric gram-negative bacilli, and *S aureus,* including MRSA. *P aeruginosa* and S *aureus* often are found together. Occasionally, anaerobes are causative, and *S pneumoniae* and nontypeable *H influenzae* are found rarely.

Management of AOM

By 24 hours after diagnosis, 61% of children who have AOM have decreased symptoms, whether they receive placebo or antibiotics, and by 1 week, approximately 75% have resolution of their symptoms. (20) It also has been estimated that between 7 and 20 children must be treated with antibiotics for 1 child to derive benefit. (21)(22)(23)

Concerns regarding the United States problem with antibiotic resistance, the potential adverse effects of antibiotics, and the marginal effects of antibiotics in treating uncomplicated AOM or OME have persuaded some to recommend clinical observation for 48 hours while providing pain control medication. If the patient is not better after 48 to 72 hours, a first-line antibiotic is prescribed. The AAP guidelines (Table 2) provide

recommendations for "watchful waiting" for 48 to 72 hours, which includes pain control with ibuprofen or acetaminophen and topical agents such as benzocaine. (2) The use of adjunctive therapies, such as antihistamines and decongestants, never has been proven effective and has no role in the treatment of AOM.

The AAP guidelines state that the decision to observe or treat is based on the child's age, the certainty of the diagnosis, and the illness severity. For this therapeutic approach to be successful, there must be a "ready means" of communication between the caregiver and the clinician, a system in place that permits re-examination of the patient, and a convenient method for the caregiver to obtain antibiotics. The AAP recommends that this option be limited to "otherwise healthy children 6 months to 2 years of age with nonsevere illness at presentation *and* an uncertain diagnosis *and* to children 2 years of age and older without severe symptoms at presentation *or* with an uncertain diagnosis." Nonsevere illness is defined as mild otalgia and a temperature less than 39.0°C in the past 24 hours. A certain diagnosis of AOM meets all three of these criteria: rapid onset of symptoms, signs of MEE, and signs and symptoms of middle-ear inflammation.

It is not clear whether early initiation of antibiotics helps to prevent the development of mastoiditis, although the incidence of this complication is about half as common in the United States as in countries in which "watchful waiting" is practiced. The Agency for Healthcare Research and Quality report on AOM examined six randomized trials and two cohort studies whose pooled data revealed comparable rates of mastoiditis in children who received initial antibiotics versus those who received placebo or observation. (24) They concluded that mastoiditis is not increased with initial observation if children are followed closely and antibiotic therapy is initiated in those who do not improve. In addition, several studies have shown that routine antibiotic therapy for AOM is not an absolute defense against the development of mastoiditis and other complications because most affected children have received prior antibiotic therapy. The AAP guidelines recommend that clinicians be aware that antibiotic treatment may mask signs and symptoms of mastoiditis and delay the diagnosis. (2)

The AAP recommends the use of amoxicillin 90 mg/kg per day twice daily (Table 3) for initial AOM therapy. Several studies have demonstrated that courses of antibiotics shorter than the traditional 10 days are effective in low-risk children who have mild disease. Those who may be able to be treated with a short course (5 to 7 days) are children 6 years of age and older who have intact TMs and have not had AOM within 1 month of diagnosis. For younger children and for children who have severe disease, a standard 10-day course is recommended. All oral antibiotics, with the exception of azithromycin, should be dosed according to the age of the patient and the severity of the illness.

Studies also have shown that a single dose of parenteral ceftriaxone (50 mg/kg per day) is as effective as a full course of oral antibiotic therapy in cases of uncomplicated AOM. For patients suffering severe pain and temperature greater than 39.0°C, high-dose amoxicillin-clavulanate (90 mg/kg per day amoxicillin; 6.4 mg/kg per day clavulanate) is recommended as initial therapy. For treatment of clinical failure 3 days into antibiotic therapy, the AAP recommends high-dose amoxicillin-clavulanate (90 mg/kg per day amoxicillin; 6.4 mg/kg per day clavulanate) or intramuscular ceftriaxone for 1 to 3 days. Daily doses of ceftriaxone for 3 days are more effective than a single dose in obtaining a bacteriologic

Table 2. Criteria for Initial Antibacterial Agents or Observation in Children Who Have Acute Otitis Media

Age	Certain Diagnosis	Uncertain Diagnosis
<6 months	Antibacterial therapy	Antibacterial therapy
6 months to 2 years	Antibacterial therapy	Antibacterial therapy if severe illness; observation option* if nonsevere illness
≥2 years	Antibacterial therapy if severe illness; observation option* if nonsevere illness	Observation option*

This table was modified with permission from the New York State Department of Health and the New York Region Otitis Project Committee.
*Observation is an appropriate option only when follow-up can be ensured and antibacterial agents started if symptoms persist or worsen. Nonsevere illness is mild otalgia and temperature <39.0°C in the past 24 hours. Severe illness is moderate-to-severe otalgia or temperature ≥39.0°C. A certain diagnosis of acute otitis media meets all three criteria: 1) rapid onset, 2) signs of middle ear effusion, and 3) signs and symptoms of middle ear inflammation.
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Table 3. Recommended Antibacterial Agents for Acute Otitis Media

Temperature ≥39.0°C and/or Severe Otalgia	At Diagnosis for Patients Being Treated Initially With Antibacterial Agents		Clinically Defined Treatment Failure at 48 to 72 Hours After Initial Management With Observation Option		Clinically Defined Treatment Failure at 48 to 72 Hours After Initial Management With Antibacterial Agents	
	Recommended	Alternative for Penicillin Allergy	Recommended	Alternative for Penicillin Allergy	Recommended	Alternative for Penicillin Allergy
No	Amoxicillin, 80 to 90 mg/kg per day	Non-type I: Cefdinir, cefuroxime, cefpodoxime Type I: Azithromycin, clarithromycin	Amoxicillin, 80 to 90 mg/kg per day	Non-type I: Cefdinir, cefuroxime, cefpodoxime Type I: Azithromycin, clarithromycin	Amoxicillin-clavulanate, 90 mg/kg per day of amoxicillin component, with 6.4 mg/kg per day of clavulanate	Non-type I: Ceftriaxone, 3 days Type I: Clindamycin
Yes	Amoxicillin-clavulanate, 90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate	Ceftriaxone, 1 or 3 days	Amoxicillin-clavulanate, 90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate	Ceftriaxone, 1 or 3 days	Ceftriaxone, 3 days	Tympanocentesis, clindamycin

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cure. Second-line agents also are recommended if beta-lactamase-producing organisms (such as nontypeable *H influenzae* or *M catarrhalis*) are suspected. For AOM due to highly penicillin-resistant *S pneumoniae* (MIC ≥2 mcg/mL), a 10-day course of high-dose (90 mg/kg per day) amoxicillin administered twice daily or a three-dose regimen of ceftriaxone (50 mg/kg per day) has proven efficacious. (2)

For the patient who has a type I penicillin allergy (urticaria, laryngeal spasm, wheezing, anaphylaxis), the AAP recommends the use of azalides or macrolides such as azithromycin (10 mg/kg per day on day 1 followed by 5 mg/kg per day for 4 days as a single daily dose) and clarithromycin (15 mg/kg per day in two divided doses for 10 days or for 5 to 7 days if ≥6 years of age and has mild-to-moderate disease). However, a substantial proportion of *S pneumoniae* organisms are resistant to these agents.

Patients who have severe disease should receive a combination of clindamycin (30 to 40 mg/kg per day in three divided doses) to cover *S pneumoniae* and sulfisoxazole for nontypeable *H influenzae*. Those patients who have nontype I penicillin allergies should receive oral cephalosporins such as cefdinir (14 mg/kg per day divided twice a day or daily, with twice-daily therapy approved for 5 to 10 days), cefuroxime (30 mg/kg per day in two divided doses), cefpodoxime (10 mg/kg per day once daily), or intramuscular ceftriaxone (50 mg/kg for 1 to 3 days). (2)

To help guide antibiotic selection, tympanocentesis for both diagnostic and therapeutic purposes is recommended for patients who have severe illness and have failed second-line antibiotic management or for those who have failed first-line agents and who also have a penicillin allergy. Tympanocentesis also should be considered strongly for seriously ill patients, immunocompromised patients, neonates younger than 2 weeks of age, and patients who have AOM that has been refractory to treatment. In addition, some experts recommend tympanocentesis if AOM is present in infants within the first 2 months of birth to identify the causative organisms and target antibiotic therapy more accurately.

The opening in the TM resulting from tympanocentesis can be extended to facilitate better drainage (myringotomy). Myringotomy has been recommended in the past to facilitate drainage of fluid in AOM, although studies have found equivalent improvement when compared with antibiotic therapy alone. Because

myringotomy and tympanocentesis have become a "lost art" among general pediatricians, their utility in everyday practice has waned. Practitioners should receive sufficient training before attempting these procedures.

Generally, the opening in the TM heals quickly after tympanocentesis (few days) or myringotomy (few weeks). Serious complications are rare. Direct injury to the ear canal or middle ear can occur but usually is mild. Although most of the incisions heal spontaneously, some persist, leading to chronic otorrhea. Persistently draining incisions eventually require tympanoplasty.

Relapse and recurrence are defined as development of AOM after an initial symptomatic response to antibiotic treatment or within some defined period after completion of therapy. Differentiating relapse from recurrence requires identifying the microbiology of both episodes, and this information usually is not available in clinical practice. Pichichero and associates (17) defined recurrent AOM as a history of three episodes of AOM in the past 6 months or four in the past 12 months. Two studies have demonstrated that most such events are due to new pathogens or to different serotypes of the same pathogen. (25) In addition, studies have shown that after treatment with appropriate antibiotics, susceptible isolates of *S pneumoniae* are eliminated from the nasopharynx with little effect on resistant strains. Therefore, patients who are receiving 3 to 4 days of antibiotics at the time they acquire new *S pneumoniae* colonization usually become colonized with antibiotic-resistant strains. The risk of nasopharyngeal colonization with a resistant strain increases during and after antibiotic treatment if resistant strains are present in the community. Pichichero's study on recurrent AOM and AOM with treatment failure revealed that *S pneumoniae* cause about 50% of these cases, and 50% of these strains are not susceptible to penicillin. (17) The other 50% of these infections are caused by nontypeable *H influenzae*, and 50% of these strains produce beta-lactamase. Therefore, recurrent episodes of AOM are more likely due to resistant pathogens. The AAP recommends that treatment of recurrent episodes within 30 days of a prior AOM may require the use of broader-spectrum antibiotics such as ceftriaxone or high-dose amoxicillin-clavulanate to cover potentially drug-resistant pathogens. The AAP recommends high-dose amoxicillin-clavulanate or cefuroxime, cefpodoxime, cefdinir, or ceftriaxone for patients who have failed therapy or who have recently been treated with high-dose amoxicillin. These antibiotics have improved efficacy against beta-lactamase-producing nontypeable *H influenzae* and nonsusceptible *S pneumoniae*. (2)

Indications for Changing Antibiotics

The common indications for changing antibiotic therapy during treatment of AOM include persistent or recurrent ear pain or fever or both after 2 to 3 days of therapy or the development of a suppurative complication. When a patient fails to respond to amoxicillin, neither trimethoprim-sulfamethoxazole nor erythromycin-sulfisoxazole is optimal. A patient who fails amoxicillin-clavulanate therapy should be treated with a 3-day course of parenteral ceftriaxone because of its superior efficacy against *S pneumoniae* compared with alternative oral agents. The AAP recommends that if AOM continues to persist, tympanocentesis should be performed to make a bacteriologic diagnosis. If tympanocentesis cannot be performed, a course of clindamycin may be considered for the rare case of penicillin-resistant pneumococcal infection not responding to previous regimens. If the patient fails to respond to clindamycin, tympanocentesis is necessary. (2)

Antimicrobial Prophylaxis for Recurrent Otitis Media

Multiple studies have demonstrated that antibiotic prophylaxis lowers the frequency of nasopharyngeal colonization with otopathogens and decreases the number of cases of AOM and OME. It also has been shown that children younger than 2 years of age who have had multiple episodes per year benefit the most from antibiotic prophylaxis. However, the benefits are short-lived because most otitis-prone children continue to have recurrent episodes once the antibiotic prophylaxis is discontinued. In addition, a significant problem resulting from the use of prophylactic antibiotics is the potential selection of drug-resistant otopathogens that could complicate further the management of a new episode of AOM.

Therefore, the management of a new episode of AOM for a child receiving antimicrobial prophylaxis should include treatment with an oral antimicrobial different from the one used for prophylaxis. (2) If a child has had at least three well-documented separate episodes of AOM in 6 months or four episodes in 12 months, he or she may be considered a potential candidate for chemoprophylaxis. Most of the published studies that demonstrated benefit used either amoxicillin or sulfonamides at half the dose recommended to treat AOM given once a day. If chemoprophylaxis is attempted, usually it is provided for 6 months, ideally throughout the winter and spring, when circulating respiratory viruses are most prevalent.

Suppurative Complications

The most common suppurative complication of AOM is mastoiditis. *S pneumoniae*, *S pyogenes,* and nontypeable *H influenzae* are the most common pathogens that cause acute mastoiditis. *P aeruginosa* and staphylococcal species also are common. Acute labyrinthitis is another common suppurative complication of AOM. Rare complications of AOM include petrositis (extension of the infection into the petrous portion of the temporal bone, resulting in osteomyelitis); meningitis; brain abscess; epidural abscess; and otitic hydrocephalus due to thrombosis of the transverse, lateral, or sigmoid sinus.

It is important to note the existence of an otogenic variant of Lemierre syndrome that is characterized by acute mastoiditis, suppurative thrombophlebitis of the lateral or cavernous sinuses, meningitis, and evidence of distant septic metastasis. The most common organism implicated in this infection is *Fusobacterium necrophorum*, an obligate, anaerobic, pleomorphic gram-negative rod. However, the entity is not uniquely anaerobic; methicillin-sensitive and -resistant *S aureus* and viridans streptococci also have been implicated.

CSOM

CSOM is a challenging condition to treat because patients often fail to respond to standard topical and systemic antibiotic therapy. Two Cochrane reviews of interventions for CSOM found that topical quinolone antibiotics (such as ciprofloxacin) were more effective than systemic quinolone antibiotics in eradicating ear discharge at 1 to 2 weeks and that topical quinolone antibiotics without corticosteroids achieved similar results to topical nonquinolone antibiotics without corticosteroids. (26)(27) A recent randomized, double-blind study comparing topical ciprofloxacin to a topical aminoglycoside in Australian aboriginal children who had otic discharge for at least 2 weeks found that after 9 days of treatment, children who received ciprofloxacin were more likely to have dry ears. (28) However, a large percentage of children in the study were lost to follow-up.

In contrast to topical aminoglycosides, which are ototoxic, topical ciprofloxacin is not and generally is well tolerated. In addition, topical antibiotics allow for the delivery of a high concentration of drug at the site of the infection without causing systemic adverse effects and are less likely to promote the selection of drug-resistant bacteria. Topical antibiotics, however, are unlikely to work if the ear canal contains copious amounts of purulent fluid and debris. Therefore, daily suctioning is recommended to clear the external canal prior to instillation of topical antibiotics.

AOM in the Neonate

AOM diagnosed in the first 6 weeks after birth requires careful evaluation and follow-up because of the risk of invasive disease and the higher rate of recurrent AOM in neonates. A toxic-appearing neonate who has AOM should undergo diagnostic tympanocentesis by an otolaryngologist and evaluation of cerebrospinal fluid and blood for culture. Initial therapy for febrile neonates who have AOM in the first 2 postnatal weeks is similar to that for neonatal sepsis. A neonate who is older than 2 weeks of age, who had a normal delivery and course in the nursery, and who has been well since hospital discharge probably has AOM caused by *S pneumoniae* or nontypeable *H influenzae*. Such patients may be treated with an appropriate oral antibiotic (amoxicillin) as outpatients as long as meticulous follow-up can be assured. Cultures of blood and cerebrospinal fluid, parenteral antibiotics, and hospitalization are warranted for term infants who have AOM and appear toxic on examination because of the possibility of systemic infection.

Management of OME

The spontaneous resolution rate for OME is high. When residual OME occurs after an episode of AOM, more than 75% of cases resolve within 3 months. OME found incidentally has a lower, but still significant, resolution rate. The presence of a persistent effusion should be documented with pneumatic otoscopy or tympanometry. The AAP policy on OME recommends watchful waiting for 3 months after diagnosis because the harm of a persistent OME is slight when compared with possible harm from treatment. (5) Parents should understand that the child might experience a temporary hearing deficit while the effusion persists, but a short-lived effusion should have minimal effect on a child's language development. Risk factors for acquiring persistent effusions include prolonged duration of OME, onset of OME in summer or fall, moderate hearing loss, history of receiving tympanostomy tubes, and having intact adenoids. (5)

Unfortunately, therapies for management of effusions that persist beyond 3 months are limited. Antihistamines, decongestants, and intranasal corticosteroids never have been proven effective. Antibiotics result in a transient improvement but have not been shown to have long-term benefit. Oral corticosteroids have no effect when used alone, but smaller trials have shown short-term improvement when oral corticosteroids were combined with antibiotics. A 10- to 14-day course of antibiotics, alone or in conjunction with oral corticosteroids, may be considered as an attempt to prevent the need for surgery,

but the risks associated with therapy must be weighed against the lack of evidence of long-term benefit. (5)

When OME persists beyond 3 months or moderate-to-severe hearing deficit, language delay, or developmental delay is a concern, the child's hearing should be evaluated. Although OME can cause hearing loss that leads to language delays, children who otherwise are not identified by developmental surveillance or screening as being at risk are not likely to experience significant language delays from persistent OME. Short-term hearing loss and language delays may result from persistent effusions, but these conditions are likely to resolve without additional management in most children.

For many children, the first step can be a hearing evaluation in the primary care office. However, any child who is younger than 4 years old, who is unable to complete screening in the primary office, or who fails primary screening should be referred for a comprehensive audiologic evaluation. A child who is identified as having any degree of hearing loss should be screened for language delays. This screening also can be performed in the primary care office, with comprehensive evaluation reserved for children failing primary screening or when caregivers express concern about a child's development.

Children who have normal hearing despite persistent effusions should be re-evaluated every 3 to 6 months. The physical examination should focus on scrutiny of the TM and middle ear, looking specifically for evidence of retraction pockets (with or without keratin debris), erosion of the ossicles, or atrophy of the TM. Pneumatic otoscopy and tympanometry should be used to document the presence of the effusion. Children who have any of these conditions require a comprehensive audiologic evaluation as well as referral to an otolaryngologist. (5)

As long as a low-risk child experiences minimal symptoms and shows no signs of hearing loss, OME can be observed without intervention. The ongoing study by Paradise and associates (29) has shown consistently no significant effect of early tympanostomy tube placement on developmental progress, which is the true outcome measure of concern in most children affected by OME. This trial, begun in 1991, enrolled a large cohort of children from birth and has monitored them for evidence of MEE. Eligible children who had persistent effusions were randomized to prompt or delayed insertion of tympanostomy tubes. The children have had periodic developmental testing, most recently at ages 9 to 11 years. The periodic assessments have shown consistently no difference in developmental outcomes between the two groups. The authors state that their findings may not be generalizable to children who have underlying medical problems, more significantly prolonged effusions, or extreme hearing loss.

The current AAP guideline on OME suggests that children at risk for (or experiencing) developmental delays, experiencing symptoms attributable to the OME (otalgia, vestibular disturbance, hearing loss), or living in a nonenriching environment may benefit from intervention for a persistent OME. In the end, the decision to intervene must be made jointly by the child's parents, pediatrician, and the consulting otolaryngologist and should be based on the duration and severity of symptoms rather than the simple existence of the effusion. If the decision is made to intervene, first-line surgical therapy is placement of tympanostomy tubes. In a minority of children, OME recurs and persists after extrusion of the tympanostomy tubes. In that case, adenoidectomy should be considered when the tubes are reinserted, especially in children older than 4 years of age.

Follow-up

After AOM is diagnosed, the need for short-term follow-up care can be determined by the child's symptoms. As mentioned, most treatment failures manifest by 48 to 72 hours after initiation of therapy. A 2-week follow-up "ear check" is not necessary in the asymptomatic child. However, longer-term follow-up is important to assess the resolution of the associated MEE. Because such effusions can persist normally up to 12 weeks after an AOM episode, follow-up should occur at that time so resolution or persistence of the effusion can be documented. Persistent effusions should be managed as discussed previously. Hearing evaluation is not mandatory after every episode of AOM that resolves rapidly with treatment. However, children experiencing refractory or recurrent AOM should have hearing evaluations to document any hearing loss resulting from these episodes.

Nonsuppurative Complications

The presence of inflammatory mediators in persistent OME or CSOM can cause atrophy of the TM over time, particularly in the pars tensa portion of the TM (Fig. 6). These retraction pockets generally are asymptomatic and self-limited, but they may lead to atelectasis of the middle ear space, with adhesion formation and erosion of the ossicles as well as cholesteatoma. Because of the potential severity of such complications, otolaryngologic input should be sought. Although most lower-grade retraction pockets can be managed expectantly, higher-grade retractions and those associated with hearing loss may benefit from tympanostomy tube insertion. (30)

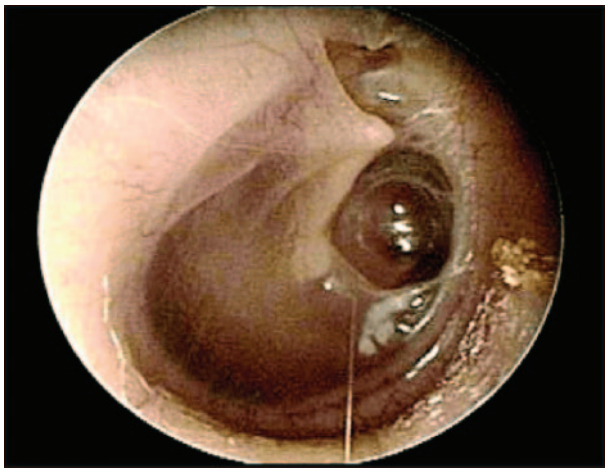

Figure 6. Tympanic membrane with retraction pocket. Reprinted with permission from Siegel RM, Bien JP. Acute otitis media in children: a continuing story. *Pediatr Rev.* 2004; 25:187–193.

Persistent inflammation or TM retraction pockets can lead to the development of a cholesteatoma. (31) Cholesteatomas develop when squamous epithelial tissue begins to grow within the middle ear space. The incidence of cholesteatoma in the United States is estimated to be 3 to 6 per 100,000 per year. As this squamous epithelial tissue grows, it can become locally invasive and destructive. Cholesteatomas generally present with complaints of hearing loss and persistent otorrhea, as is seen often with CSOM. On examination, a retraction pocket filled with squamous epithelial debris may be seen. Alternatively, a whitish mass may be noted behind the TM. If physical examination suggests the presence of a cholesteatoma, otolaryngologic consultation is mandatory because the mainstay of treatment is surgical excision. (30) The recurrence rate after repair is significant, so ongoing otolaryngologist involvement is important.

Conclusion

The state of the art for managing otitis media in the 21st century has changed dramatically since Bacon and Saunders published their 1918 manual. We now have a better understanding of the pathogenesis of otitis media and the development of new diagnostic tools, antimicrobials for treatment and prevention, and evidence-based guidelines to assist clinicians in delivering the best care for their patients. The implementation of PCV7 immunization has led to impressive reductions in the number of otitis media cases, while the indiscriminate use of antimicrobials has resulted in more resistant otopathogens. Current evidence has suggested that routine antibiotic therapy no longer is required for all cases of AOM and that shorter courses of antibiotics may be just as efficacious. It is incumbent on all clinicians to use antimicrobials wisely to continue progress in the diagnosis, treatment, and prevention of otitis media.

Summary

- Based on observational research, the diagnosis of AOM should consist of an acute onset of symptoms, evidence of a middle ear effusion, and signs or symptoms of middle ear inflammation. (2)
- Based on some research evidence, the AAP recommends a period of "watchful waiting" or observation without antibiotic therapy for select children who have AOM based on diagnostic certainty, age, illness severity, and assurance of follow-up. (2)
- Based on strong research evidence, PCV7 has had a substantial clinical impact on AOM and has changed the microbiology of AOM such that *S pneumoniae* that are nonsusceptible to penicillin are re-emerging as important pathogens in patients experiencing treatment failure or recurrent AOM. (7)(8)
- Based on strong research evidence, the AAP recommends the use of high-dose amoxicillin for treating initial episodes of nonsevere AOM and amoxicillin-clavulanate for initial therapy in patients who have severe disease. Ceftriaxone or amoxicillin-clavulanate is recommended for clinical failure after 3 days of antibiotic therapy. (2)
- Based on strong research evidence, children who have OME but do not have risk factors for developmental delay or hearing loss or evidence of injury to the TM or middle ear can be managed expectantly. In these low-risk children, early placement of tympanostomy tubes does not improve developmental outcome.
- Based on strong research evidence, placement of tympanostomy tubes is the appropriate procedure for children who have persistent OME as well as for those who have risk factors for developmental delay or evidence of damage to the middle ear. (5)

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PIR Quiz

Quiz also available online at http://pedsinreview.aappublications.org.

6. A 19-month-old girl comes to your office in March with a 2-day history of nasal discharge, cough, and subjective low-grade fever. You have documented two bouts of bilateral acute otitis media in the past 7 months, from which she apparently has recovered uneventfully with appropriate antibiotic therapy. Her first episode of acute otitis media was diagnosed at age 12 months. Her ears were normal at her 15-month health supervision examination. Her last episode of acute otitis media occurred 3 months ago. Her symptoms disappeared within 2 days, and she seemed well until the present illness. On examination, she is afebrile and smiling. You note that both tympanic membranes are poorly mobile and cloudy. There is no erythema or bulging, but you do see a few air bubbles behind the inferior quadrant of the left tympanic membrane. Your diagnosis is:

   A. Acute left otitis media.
   B. Bilateral otitis media with effusion.
   C. Chronic suppurative otitis media.
   D. Recurrent acute otitis media.
   E. Treatment-failure acute otitis media.

7. In addition to pain relief, a plan for follow-up, and reassurance of the parents, the best option for management of this 19-month-old patient at this time is:

   A. Chemoprophylaxis with an oral sulfonamide.
   B. Observation alone.
   C. 10-day course of high-dose oral amoxicillin.
   D. 10-day course of high-dose oral amoxicillin-clavulanate.
   E. Tympanocentesis.

8. A previously healthy 2-year-old boy develops the sudden onset of a *severe* earache after 2 days of runny nose and cough. He has not been vomiting. He has no known allergies to medication. On physical examination, his rectal temperature is 39.5°C. His only other abnormality, aside from obvious discomfort, is a red and bulging right tympanic membrane. The *most* appropriate initial choice of therapy is:

   A. A 5-day course of oral azithromycin.
   B. A 10-day course of high-dose oral amoxicillin.
   C. A 10-day course of high-dose oral amoxicillin-clavulanate.
   D. A 10-day course of oral trimethoprim-sulfamethoxazole.
   E. Watchful waiting.

9. Three days later, the 2-year-old boy is still febrile and uncomfortable. Examination reveals neither significant dehydration nor signs of complications. The eardrum is still red and bulging. At this time, the most appropriate therapy is to:

   A. Administer a 3-day course of parenteral ceftriaxone.
   B. Begin a 10-day course of erythromycin-sulfisoxazole.
   C. Begin a 10-day course of fluoroquinolone.
   D. Continue to adhere to your original plan.
   E. Refer the boy to otolaryngology for emergency tympanocentesis.

10. Despite appropriate therapy, an otherwise healthy 4-year-old boy has had persistent otitis media with effusion for the past 6 months. His hearing continues to be normal in the clinic. You should be especially concerned about:

   A. Chronic mastoiditis.
   B. Development of permanent hearing loss.
   C. Irreversible developmental delay.
   D. Permanent language impairment.
   E. Presence of retraction pockets on examination.