PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

The Diagnosis and Management of Acute Otitis Media

Allan S. Lieberthal, Aaron E. Carroll, Tasnee Chonmaitree, Theodore G. Ganiats, Alejandro Hoberman, Mary Anne Jackson, Mark D. Joffe, Donald T. Miller, Richard M. Rosenfeld, Xavier D. Sevilla, Richard H. Schwartz, Pauline A. Thomas and David E. Tunkel

Pediatrics; originally published online February 25, 2013;
DOI: 10.1542/peds.2012-3488

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/early/2013/02/20/peds.2012-3488

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2013 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

CLINICAL PRACTICE GUIDELINE

The Diagnosis and Management of Acute Otitis Media

abstract

FREE

This evidence-based clinical practice guideline is a revision of the 2004 acute otitis media (AOM) guideline from the American Academy of Pediatrics (AAP) and American Academy of Family Physicians. It provides recommendations to primary care clinicians for the management of children from 6 months through 12 years of age with uncomplicated AOM.

In 2009, the AAP convened a committee composed of primary care physicians and experts in the fields of pediatrics, family practice, otolaryngology, epidemiology, infectious disease, emergency medicine, and guideline methodology. The subcommittee partnered with the Agency for Healthcare Research and Quality and the Southern California Evidence-Based Practice Center to develop a comprehensive review of the new literature related to AOM since the initial evidence report of 2000. The resulting evidence report and other sources of data were used to formulate the practice guideline recommendations.

The focus of this practice guideline is the appropriate diagnosis and initial treatment of a child presenting with AOM. The guideline provides a specific, stringent definition of AOM. It addresses pain management, initial observation versus antibiotic treatment, appropriate choices of antibiotic agents, and preventive measures. It also addresses recurrent AOM, which was not included in the 2004 guideline. Decisions were made on the basis of a systematic grading of the quality of evidence and benefit-harm relationships.

The practice guideline underwent comprehensive peer review before formal approval by the AAP.

This clinical practice guideline is not intended as a sole source of guidance in the management of children with AOM. Rather, it is intended to assist primary care clinicians by providing a framework for clinical decision-making. It is not intended to replace clinical judgment or establish a protocol for all children with this condition. These recommendations may not provide the only appropriate approach to the management of this problem. *Pediatrics* 2013;131:e964–e999

Allan S. Lieberthal, MD, FAAP, Aaron E. Carroll, MD, MS, FAAP, Tasnee Chonmaitree, MD, FAAP, Theodore G. Ganiats, MD, Alejandro Hoberman, MD, FAAP, Mary Anne Jackson, MD, FAAP, Mark D. Joffe, MD, FAAP, Donald T. Miller, MD, MPH, FAAP, Richard M. Rosenfeld, MD, MPH, FAAP, Xavier D. Sevilla, MD, FAAP, Richard H. Schwartz, MD, FAAP, Pauline A. Thomas, MD, FAAP, and David E. Tunkel, MD, FAAP, FACS

KEY WORDS

acute otitis media, otitis media, otoscopy, otitis media with effusion, watchful waiting, antibiotics, antibiotic prophylaxis, tympanostomy tube insertion, immunization, breastfeeding

ABBREVIATIONS

AAFP—American Academy of Family Physicians
AAP—American Academy of Pediatrics
AHRQ—Agency for Healthcare Research and Quality
AOM—acute otitis media
CI—confidence interval
FDA—US Food and Drug Administration
LAIV—live-attenuated intranasal influenza vaccine
MEE—middle ear effusion
MIC—minimum inhibitory concentration
NNT—number needed to treat
OM—otitis media
OME—otitis media with effusion
OR—odds ratio
PCV7—heptavalent pneumococcal conjugate vaccine
PCV13—13-valent pneumococcal conjugate vaccine
RD—rate difference
SNAP—safety-net antibiotic prescription
TIV—trivalent inactivated influenza vaccine
TM—tympanic membrane
WASP—wait-and-see prescription

This document is copyrighted and is property of the American Academy of Pediatrics and its Board of Directors. All authors have filed conflict of interest statements with the American Academy of Pediatrics. Any conflicts have been resolved through a process approved by the Board of Directors. The American Academy of Pediatrics has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

(Continued on last page)

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Key Action Statement 1A: Clinicians should diagnose acute otitis media (AOM) in children who present with moderate to severe bulging of the tympanic membrane (TM) *or* new onset of otorrhea not due to acute otitis externa. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 1B: Clinicians may diagnose AOM in children who present with mild bulging of the TM *and* recent (less than 48 hours) onset of ear pain (holding, tugging, rubbing of the ear in a nonverbal child) or intense erythema of the TM. Evidence Quality: Grade C. Strength: Recommendation.

Key Action Statement 1C: Clinicians should not diagnose AOM in children who do not have middle ear effusion (MEE) (based on pneumatic otoscopy and/or tympanometry). Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 2: The management of AOM should include an assessment of pain. If pain is present, the clinician should recommend treatment to reduce pain. Evidence Quality: Grade B. Strength: Strong Recommendation.

Key Action Statement 3A: Severe AOM: The clinician should prescribe antibiotic therapy for AOM (bilateral or unilateral) in children 6 months and older with severe signs or symptoms (ie, moderate or severe otalgia or otalgia for at least 48 hours or temperature 39°C [102.2°F] or higher). Evidence Quality: Grade B. Strength: Strong Recommendation.

Key Action Statement 3B: Nonsevere bilateral AOM in young children: The clinician should prescribe antibiotic therapy for bilateral AOM in children 6 months through 23 months of age without severe signs or symptoms (ie, mild otalgia for less than 48 hours and temperature less than 39°C [102.2°F]). Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 3C: Nonsevere unilateral AOM in young children: The clinician should either prescribe antibiotic therapy *or* offer observation with close follow-up based on joint decision-making with the parent(s)/caregiver for unilateral AOM in children 6 months to 23 months of age without severe signs or symptoms (ie, mild otalgia for less than 48 hours and temperature less than 39°C [102.2°F]). When observation is used, a mechanism must be in place to ensure follow-up and begin antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 3D: Nonsevere AOM in older children: The clinician should either prescribe antibiotic therapy *or* offer observation with close follow-up based on joint decision-making with the parent(s)/caregiver for AOM (bilateral or unilateral) in children 24 months or older without severe signs or symptoms (ie, mild otalgia for less than 48 hours and temperature less than 39°C [102.2°F]). When observation is used, a mechanism must be in place to ensure follow-up and begin antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 4A: Clinicians should prescribe amoxicillin for AOM when a decision to treat with antibiotics has been made *and* the child has not received amoxicillin in the past 30 days *or* the child does not have concurrent purulent conjunctivitis *or* the child is not allergic to penicillin. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 4B: Clinicians should prescribe an antibiotic with additional β-lactamase coverage for AOM when a decision to treat with antibiotics has been made, *and* the child has received amoxicillin in the last 30 days *or* has concurrent purulent conjunctivitis, *or* has a history of recurrent AOM unresponsive to amoxicillin. Evidence Quality: Grade C. Strength: Recommendation.

Key Action Statement 4C: Clinicians should reassess the patient if the caregiver reports that the child's symptoms have worsened or failed to respond to the initial antibiotic treatment within 48 to 72 hours and determine whether a change in therapy is needed. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 5A: Clinicians should not prescribe prophylactic antibiotics to reduce the frequency of episodes of AOM in children with recurrent AOM. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 5B: Clinicians may offer tympanostomy tubes for recurrent AOM (3 episodes in 6 months or 4 episodes in 1 year with 1 episode in the preceding 6 months). Evidence Quality: Grade B. Strength: Option.

Key Action Statement 6A: Clinicians should recommend pneumococcal conjugate vaccine to all children according to the schedule of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention, American Academy of Pediatrics (AAP), and American Academy of Family Physicians (AAFP). Evidence Quality: Grade B. Strength: Strong Recommendation.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Key Action Statement 6B: Clinicians should recommend annual influenza vaccine to all children according to the schedule of the Advisory Committee on Immunization Practices, AAP, and AAFP. Evidence Quality: Grade B. Strength: Recommendation.

2Key Action Statement 6C: Clinicians should encourage exclusive breastfeeding for at least 6 months. Evidence Quality: Grade B. Strength: Recommendation.

Key Action Statement 6D: Clinicians should encourage avoidance of tobacco smoke exposure. Evidence Quality: Grade C. Strength: Recommendation.

INTRODUCTION

In May 2004, the AAP and AAFP published the "Clinical Practice Guideline: Diagnosis and Management of Acute Otitis Media".[1] The guideline offered 8 recommendations ranked according to level of evidence and benefit-harm relationship. Three of the recommendations—diagnostic criteria, observation, and choice of antibiotics—led to significant discussion, especially among experts in the field of otitis media (OM). Also, at the time the guideline was written, information regarding the heptavalent pneumococcal conjugate vaccine (PCV7) was not yet published. Since completion of the guideline in November 2003 and its publication in May 2004, there has been a significant body of additional literature on AOM.

Although OM remains the most common condition for which antibacterial agents are prescribed for children in the United States[2,3] clinician visits for OM decreased from 950 per 1000 children in 1995–1996 to 634 per 1000 children in 2005–2006. There has been a proportional decrease in antibiotic prescriptions for OM from 760 per 1000 in 1995–1996 to 484 per 1000 in 2005–2006. The percentage of OM visits resulting in antibiotic prescriptions remained relatively stable (80% in 1995–1996; 76% in 2005–2006).[2] Many factors may have contributed to the decrease in visits for OM, including financial issues relating to insurance, such as copayments, that may limit doctor visits, public education campaigns regarding the viral nature of most infectious diseases, use of the PCV7 pneumococcal vaccine, and increased use of the influenza vaccine. Clinicians may also be more attentive to differentiating AOM from OM with effusion (OME), resulting in fewer visits coded for AOM and fewer antibiotic prescriptions written.

Despite significant publicity and awareness of the 2004 AOM guideline, evidence shows that clinicians are hesitant to follow the guideline recommendations. Vernacchio et al[4] surveyed 489 primary care physicians as to their management of 4 AOM scenarios addressed in the 2004 guideline. No significant changes in practice were noted on this survey, compared with a survey administered before the 2004 AOM guideline. Coco[5] used the National Ambulatory Medical Care Survey from 2002 through 2006 to determine the frequency of AOM visits without antibiotics before and after publication of the 2004 guideline. There was no difference in prescribing rates. A similar response to otitis guidelines was found in Italy as in the United States.[6,7] These findings parallel results of other investigations regarding clinician awareness and adherence to guideline recommendations in all specialties, including pediatrics.[8] Clearly, for clinical practice guidelines to be effective, more must be done to improve their dissemination and implementation.

This revision and update of the AAP/AAFP 2004 AOM guideline[1] will evaluate published evidence on the diagnosis and management of uncomplicated AOM and make recommendations based on that evidence. The guideline is intended for primary care clinicians including pediatricians and family physicians, emergency department physicians, otolaryngologists, physician assistants, and nurse practitioners. The scope of the guideline is the diagnosis and management of AOM, including recurrent AOM, in children 6 months through 12 years of age. It applies only to an otherwise healthy child without underlying conditions that may alter the natural course of AOM, including but not limited to the presence of tympanostomy tubes; anatomic abnormalities, including cleft palate; genetic conditions with craniofacial abnormalities, such as Down syndrome; immune deficiencies; and the presence of cochlear implants. Children with OME without AOM are also excluded.

Glossary of Terms

AOM—the rapid onset of signs and symptoms of inflammation in the middle ear[9,10]

Uncomplicated AOM—AOM without otorrhea[1]

Severe AOM—AOM with the presence of moderate to severe otalgia *or* fever equal to or higher than 39°C[9,10]

Nonsevere AOM—AOM with the presence of mild otalgia and a temperature below 39°C[9,10]

Recurrent AOM—3 or more well-documented and separate AOM episodes in the preceding 6 months *or* 4 or more episodes in the preceding 12 months with at least 1 episode in the past 6 months[11,12]

OME—inflammation of the middle ear with liquid collected in the middle ear; the signs and symptoms of acute infection are absent[9]

MEE—liquid in the middle ear without reference to etiology, pathogenesis, pathology, or duration[9]

Otorrhea—discharge from the ear, originating at 1 or more of the following sites: the external auditory canal,

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

middle ear, mastoid, inner ear, or intracranial cavity

Otitis externa—an infection of the external auditory canal

Tympanometry—measuring acoustic immittance (transfer of acoustic energy) of the ear as a function of ear canal air pressure[13,14]

Number needed to treat (NNT)—the number of patients who need to be treated to prevent 1 additional bad outcome[15]

Initial antibiotic therapy—treatment of AOM with antibiotics that are prescribed at the time of diagnosis with the intent of starting antibiotic therapy as soon as possible after the encounter

Initial observation—initial management of AOM limited to symptomatic relief, with commencement of antibiotic therapy only if the child's condition worsens at any time or does not show clinical improvement within 48 to 72 hours of diagnosis; a mechanism must be in place to ensure follow-up and initiation of antibiotics if the child fails observation

METHODS

Guideline development using an evidence-based approach requires that all evidence related to the guideline is gathered in a systematic fashion, objectively assessed, and then described so readers can easily see the links between the evidence and recommendations made. An evidence-based approach leads to recommendations that are guided by both the quality of the available evidence and the benefit-to-harm ratio that results from following the recommendation. Figure 1 shows the relationship of evidence quality and benefit-harm balance in determining the level of recommendation. Table 1 presents the AAP definitions and implications of different levels of evidence-based recommendations.[16]

In preparing for the 2004 AAP guidelines, the Agency for Healthcare Research and Quality (AHRQ) funded and conducted an exhaustive review of the literature on diagnosis and management of AOM.[17–19] In 2008, the AHRQ and the Southern California Evidence-Based Practice Center began a similar process of reviewing the literature published since the 2001 AHRQ report. The AAP again partnered with AHRQ and the Southern California Evidence-Based Practice Center to develop the evidence report, which served as a major source of data for these practice guideline recommendations.[20,21] New key questions were determined by a technical expert panel. The scope of the new report went beyond the 2001 AHRQ report to include recurrent AOM.

The key questions addressed by AHRQ in the 2010 report were as follows:

1. Diagnosis of AOM: What are the operating characteristics (sensitivity, specificity, and likelihood ratios) of clinical symptoms and otoscopic findings (such as bulging TM) to diagnose uncomplicated AOM and to distinguish it from OME?
2. What has been the effect of the use of heptavalent PCV7 on AOM microbial epidemiology, what organisms (bacterial and viral) are associated with AOM since the introduction of PCV7, and what are the patterns of antimicrobial resistance in AOM since the introduction of PCV7?
3. What is the comparative effectiveness of various treatment options for treating uncomplicated AOM in average risk children?
4. What is the comparative effectiveness of different management options for recurrent OM (uncomplicated) and persistent OM or relapse of AOM?
5. Do treatment outcomes in Questions 3 and 4 differ by characteristics of the condition (AOM), patient, environment, and/or health care delivery system?
6. What adverse effects have been observed for treatments for which outcomes are addressed in Questions 3 and 4?

For the 2010 review, searches of PubMed and the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, and Education Resources Information Center were conducted by using the same search strategies used for the 2001 report for publications from 1998 through June 2010. Additional terms or conditions not considered in the 2001 review (recurrent OM, new drugs, and heptavalent pneumococcal vaccine) were also included. The Web of Science was also used to search for citations of the 2001 report and its peer-reviewed publications. Titles were screened independently by 2

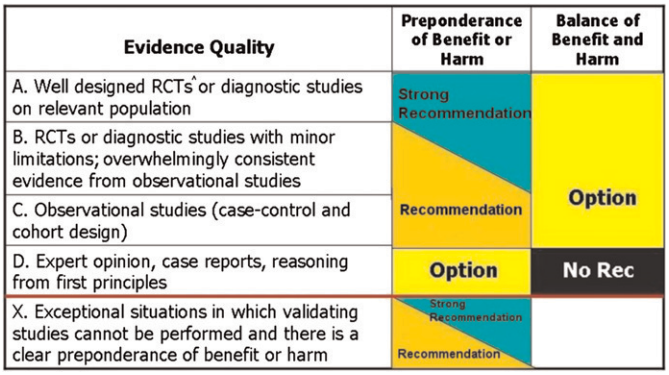

FIGURE 1
Relationship of evidence quality and benefit-harm balance in determining the level of recommendation. RCT, randomized controlled trial.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

TABLE 1 Guideline Definitions for Evidence-Based Statements

Statement	Definition	Implication
Strong Recommendation	A strong recommendation in favor of a particular action is made when the anticipated benefits of the recommended intervention clearly exceed the harms (as a strong recommendation against an action is made when the anticipated harms clearly exceed the benefits) and the quality of the supporting evidence is excellent. In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	A recommendation in favor of a particular action is made when the anticipated benefits exceed the harms, but the quality of evidence is not as strong. Again, in some clearly identified circumstances, recommendations may be made when high-quality evidence is impossible to obtain but the anticipated benefits outweigh the harms.	Clinicians would be prudent to follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Option	Options define courses that may be taken when either the quality of evidence is suspect or carefully performed studies have shown little clear advantage to 1 approach over another.	Clinicians should consider the option in their decision-making, and patient preference may have a substantial role.
No Recommendation	No recommendation indicates that there is a lack of pertinent published evidence and that the anticipated balance of benefits and harms is presently unclear.	Clinicians should be alert to new published evidence that clarifies the balance of benefit versus harm.

pediatricians with experience in conducting systematic reviews.

For the question pertaining to diagnosis, efficacy, and safety, the search was primarily for clinical trials. For the question pertaining to the effect of PCV7 on epidemiology and microbiology, the group searched for trials that compared microbiology in the same populations before and after introduction of the vaccine or observational studies that compared microbiology across vaccinated and unvaccinated populations.

In total, the reviewers examined 7646 titles, of which 686 titles were identified for further review. Of those, 72 articles that met the predetermined inclusion and exclusion criteria were reviewed in detail. Investigators abstracted data into standard evidence tables, with accuracy checked by a second investigator. Studies were quality-rated by 2 investigators by using established criteria. For randomized controlled trials, the Jadad criteria were used.[22] QUADAS criteria[23] were used to evaluate the studies that pertained to diagnosis. GRADE criteria were applied to pooled analyses.[24] Data abstracted included parameters necessary to define study groups, inclusion/exclusion criteria, influencing factors, and outcome measures. Some of the data for analysis were abstracted by a biostatistician and checked by a physician reviewer. A sequential resolution strategy was used to match and resolve the screening and review results of the 2 pediatrician reviewers.

For the assessment of treatment efficacy, pooled analyses were performed for comparisons for which 3 or more trials could be identified. Studies eligible for analyses of questions pertaining to treatment efficacy were grouped for comparisons by treatment options. Each comparison consisted of studies that were considered homogeneous across clinical practice. Because some of the key questions were addressed in the 2001 evidence report,[17] studies identified in that report were included with newly identified articles in the 2010 evidence report.[20]

Decisions were made on the basis of a systematic grading of the quality of evidence and strength of recommendations as well as expert consensus when definitive data were not available. Results of the literature review were presented in evidence tables and published in the final evidence report.[20]

In June 2009, the AAP convened a new subcommittee to review and revise the May 2004 AOM guideline.[1] The subcommittee comprised primary care physicians and experts in the fields of pediatrics, family practice, otolaryngology, epidemiology, infectious disease, emergency medicine, and guideline methodology. All panel members reviewed the AAP policy on conflict of interest and voluntary disclosure and were given an opportunity to present any potential conflicts with the subcommittee's work. All potential conflicts of interest are listed at the end of this document. The project was funded by the AAP. New literature on OM is continually being published. Although the systematic review performed by AHRQ could not be replicated with new literature, members of the Subcommittee on Diagnosis and Management of Acute Otitis Media reviewed additional articles. PubMed was searched by using the single search term "acute otitis media,"

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

approximately every 6 months from June 2009 through October 2011 to obtain new articles. Subcommittee members evaluated pertinent articles for quality of methodology and importance of results. Selected articles used in the AHRQ review were also reevaluated for their quality. Conclusions were based on the consensus of the subcommittee after the review of newer literature and reevaluation of the AHRQ evidence. Key action statements were generated using BRIDGE-Wiz (Building Recommendations in a Developers Guideline Editor), an interactive software tool that leads guideline development through a series of questions that are intended to create a more actionable set of key action statements.[25] BRIDGE-Wiz also incorporates the quality of available evidence into the final determination of the strength of each recommendation.

After thorough review by the subcommittee for this guideline, a draft was reviewed by other AAP committees and sections, selected outside organizations, and individuals identified by the subcommittee as experts in the field. Additionally, members of the subcommittee were encouraged to distribute the draft to interested parties in their respective specialties. All comments were reviewed by the writing group and incorporated into the final guideline when appropriate.

This clinical practice guideline is not intended as a sole source of guidance in the management of children with AOM. Rather, it is intended to assist clinicians in decision-making. It is not intended to replace clinical judgment or establish a protocol for the care of all children with this condition. These recommendations may not provide the only appropriate approach to the management of children with AOM.

It is AAP policy to review and update evidence-based guidelines every 5 years.

KEY ACTION STATEMENTS

Key Action Statement 1A

Clinicians should diagnose AOM in children who present with moderate to severe bulging of the TM *or* new onset of otorrhea not due to acute otitis externa. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 1A

Aggregate evidence quality	Grade B
Benefits	• Identify a population of children most likely to benefit from intervention. • Avoid unnecessary treatment of those without highly certain AOM. • Promote consistency in diagnosis.
Risks, harms, cost	May miss AOM that presents with a combination of mild bulging, intense erythema, or otalgia that may not necessarily represent less severe disease and may also benefit from intervention.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Identification of a population of children with highly certain AOM is beneficial. Accurate, specific diagnosis is helpful to the individual patient. Modification of current behavior of overdiagnosis is a goal. Increased specificity is preferred even as sensitivity is lowered.
Intentional vagueness	By using stringent diagnostic criteria, the TM appearance of less severe illness that might be early AOM has not been addressed.
Role of patient preferences	None
Exclusions	None
Strength	**Recommendation**
Notes	Tympanocentesis studies confirm that using these diagnostic findings leads to high levels of isolation of pathogenic bacteria. Evidence is extrapolated from treatment studies that included tympanocentesis.

Key Action Statement 1B

Clinicians should diagnose AOM in children who present with mild bulging of the TM *and* recent (less than 48 hours) onset of ear pain (holding, tugging, rubbing of the ear in a nonverbal child) or intense erythema of the TM. (Evidence Quality: Grade C, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 1B

Aggregate evidence quality	Grade C
Benefits	Identify AOM in children when the diagnosis is not highly certain.
Risks, harms, cost	Overdiagnosis of AOM. Reduced precision in diagnosis.
Benefits-harms assessment	Benefits greater than harms.
Value judgments	None.
Intentional vagueness	Criteria may be more subjective.
Role of patient preferences	None
Exclusions	None
Strength	**Recommendation**
Notes	Recent onset of ear pain means within the past 48 hours.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Key Action Statement 1C

Clinicians should not diagnose AOM in children who do not have MEE (based on pneumatic otoscopy and/or tympanometry). (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 1C

Aggregate evidence quality	Grade B
Benefits	Reduces overdiagnosis and unnecessary treatment. Increases correct diagnosis of other conditions with symptoms that otherwise might be attributed to AOM. Promotes the use of pneumatic otoscopy and tympanometry to improve diagnostic accuracy.
Risks, harms, cost	Cost of tympanometry. Need to acquire or reacquire skills in pneumatic otoscopy and tympanometry for some clinicians.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	AOM is overdiagnosed, often without adequate visualization of the TM. Early AOM without effusion occurs, but the risk of overdiagnosis supersedes that concern.
Intentional vagueness	None
Role of patient preferences	None
Exclusions	Early AOM evidenced by intense erythema of the TM.
Strength	**Recommendation**

Purpose of This Section

There is no gold standard for the diagnosis of AOM. In fact, AOM has a spectrum of signs as the disease develops.[26] Therefore, the purpose of this section is to provide clinicians and researchers with a working clinical definition of AOM and to differentiate AOM from OME. The criteria were chosen to achieve high specificity recognizing that the resulting decreased sensitivity may exclude less severe presentations of AOM.

Changes From AAP/AAFP 2004 AOM Guideline

Accurate diagnosis of AOM is critical to sound clinical decision-making and high-quality research. The 2004 "Clinical Practice Guideline: Diagnosis and Management of AOM"[1] used a 3-part definition for AOM: (1) acute onset of symptoms, (2) presence of MEE, and (3) signs of acute middle ear inflammation. This definition generated extensive discussion and reanalysis of the AOM diagnostic evidence. The 2004 definition lacked precision to exclude cases of OME, and diagnoses of AOM could be made in children with acute onset of symptoms, including severe otalgia and MEE, without other otoscopic findings of inflammation.[27] Furthermore, the use of "uncertain diagnosis" in the 2004 AOM guideline may have permitted diagnoses of AOM without clear visualization of the TM. Earlier studies may have enrolled children who had OME rather than AOM, resulting in the possible classification of such children as improved because their nonspecific symptoms would have abated regardless of therapy.[28–30] Two studies, published in 2011, used stringent diagnostic criteria for diagnosing AOM with much less risk of conclusions based on data from mixed patients.[31,32]

Since publication of the 2004 AOM guideline, a number of studies have been conducted evaluating scales for the presence of symptoms. These studies did not show a consistent correlation of symptoms with the initial diagnosis of AOM, especially in preverbal children.[33–35]

Recent research has used precisely stated stringent criteria of AOM for purposes of the studies.[31,32] The current guideline endorses stringent otoscopic diagnostic criteria as a basis for management decisions (described later). As clinicians use the proposed stringent criteria to diagnose AOM, they should be aware that children with AOM may also present with recent onset of ear pain and intense erythema of the TM as the only otoscopic finding.

Symptoms

Older children with AOM usually present with a history of rapid onset of ear pain. However, in young preverbal children, otalgia as suggested by tugging/rubbing/holding of the ear, excessive crying, fever, or changes in the child's sleep or behavior pattern as noted by the parent are often relatively nonspecific symptoms. A number of studies have attempted to correlate symptom scores with diagnoses of AOM.

A systematic review[36] identified 4 articles that evaluated the accuracy of symptoms.[37–40] Ear pain appeared useful in diagnosing AOM (combined positive likelihood ratio 3.0–7.3, negative likelihood ratio 0.4–0.6); however, it was only present in 50% to 60% of children with AOM. Conclusions from these studies may be limited, because they (1) enrolled children seen by specialists, not likely to represent the whole spectrum of severity of illness; (2) used a clinical diagnosis of AOM based more on symptomatology rather than on tympanocentesis; and (3) included relatively older children.[37,40]

Laine et al[34] used a questionnaire administered to 469 parents who suspected their children, aged 6 to 35 months, had AOM. Of the children, 237 had AOM using strict otoscopic criteria, and 232 had upper respiratory tract infection without AOM. Restless sleep, ear rubbing, fever, and nonspecific respiratory or gastrointestinal

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

tract symptoms did not differentiate children with or without AOM.

McCormick et al[30] used 2 symptom scores—a 3-item score (OM-3), consisting of symptoms of physical suffering such as ear pain or fever, emotional distress (irritability, poor appetite), and limitation in activity; and a 5-item score (Ear Treatment Group Symptom Questionnaire, 5 Items [ETG-5]), including fever, earache, irritability, decreased appetite, and sleep disturbance—to assess AOM symptoms at the time of diagnosis and daily during the 10-day treatment or observation period. They found both to be a responsive measure of changes in clinical symptoms. The same group[35] also tested a visual scale, Acute Otitis Media-Faces Scale (AOM-FS), with faces similar to the Wong-Baker pain scale.[41] None of the scales were adequately sensitive for making the diagnosis of AOM based on symptoms. The AOM-FS combined with an otoscopy score, OS-8,[30] were presented as a double-sided pocket card. The combination of AOM-FS and OS-8 was more responsive to change than either instrument alone.

Shaikh et al[33,42] validated a 7-item parent-reported symptom score (Acute Otitis Media Severity of Symptom Scale [AOM-SOS]) for children with AOM, following stringent guidance of the US Food and Drug Administration (FDA) on the development of patient-reported outcome scales. Symptoms included ear tugging/rubbing/holding, excessive crying, irritability, difficulty sleeping, decreased activity or appetite, and fever. AOM-SOS was correlated with otoscopic diagnoses (AOM, OME, and normal middle ear status). AOM-SOS changed appropriately in response to clinical change. Its day-to-day responsiveness supports its usefulness in following AOM symptoms over time.

Signs of AOM

Few studies have evaluated the relationship of otoscopic findings in AOM and tympanocentesis. A study by Karma et al[43] is often cited as the best single study of otoscopic findings in AOM. However, the study uses only a symptom-based diagnosis of AOM plus the presence of MEE. Thus, children with acute upper respiratory tract infection symptoms and OME would have been considered to have AOM. There also were significant differences in findings at the 2 centers that participated in the study.

The investigators correlated TM color, mobility, and position with the presence of middle ear fluid obtained by tympanocentesis. At 2 sites in Finland (Tampere and Oulu), 2911 children were followed from 6 months to 2.5 years of age. A single otolaryngologist at Tampere and a single pediatrician at Oulu examined subjects. Color, position, and mobility were recorded. Myringotomy and aspiration were performed if MEE was suspected. AOM was diagnosed if MEE was found and the child had fever, earache, irritability, ear rubbing or tugging, simultaneous other acute respiratory tract symptoms, vomiting, or diarrhea. The presence or absence of MEE was noted, but no analyses of the fluid, including culture, were performed. Pneumatic otoscopic findings were classified as follows: color—hemorrhagic, strongly red, moderately red, cloudy or dull, slightly red, or normal; position—bulging, retracted, or normal; and mobility—distinctly impaired, slightly impaired, or normal.

For this analysis, 11 804 visits were available. For visits with acute symptoms, MEE was found in 84.9% and 81.8% at the 2 sites at which the study was performed. There were significant differences among the results at the 2 centers involved in the study. Table 2 shows specific data for each finding.

The combination of a "cloudy," bulging TM with impaired mobility was the best predictor of AOM using the symptom-based diagnosis in this study. Impaired mobility had the highest sensitivity and specificity (approximately 95% and 85%, respectively). Cloudiness had the next best combination of high sensitivity (~74%) and high specificity (~93%) in this study. Bulging had high specificity (~97%) but lower sensitivity (~51%). A TM that was hemorrhagic, strongly red, or moderately red also correlated with the presence of AOM, and a TM that was only "slightly red" was not helpful diagnostically.

TABLE 2 Otoscopic Findings in Children With Acute Symptoms and MEE[a]

TM Finding in Acute Visits With MEE	Group I (Tampere, Finland), %	Group II (Oulo, Finland), %
Color		
Distinctly red	69.8	65.6
Hemorrhagic	81.3	62.9
Strongly red	87.7	68.1
Moderately red	59.8	66.0
Slightly red	39.4	16.7
Cloudy	95.7	80.0
Normal	1.7	4.9
Position		
Bulging	96.0	89
Retracted	46.8	48.6
Normal	32.1	22.2
Mobility		
Distinctly impaired	94.0	78.5
Slightly impaired	59.7	32.8
Normal	2.7	4.8

[a] Totals are greater than 100%, because each ear may have had different findings.[43]

McCormick et al reported that a bulging TM was highly associated with the presence of a bacterial pathogen, with or without a concomitant viral pathogen.[44] In a small study, 31 children (40 ears) underwent myringotomy.[45] Bulging TMs had positive bacterial cultures 75% of the time. The percentage of positive cultures for a pathogen increased to 80% if the color of the TM was yellow. The conclusion is that moderate to severe bulging of the TM represents the most important characteristic in the diagnosis of AOM—a finding that has

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

implications for clinical care, research, and education.

The committee recognized that there is a progression from the presence of MEE to the bulging of the TM, and it is often difficult to differentiate this equivocal appearance from the highly certain AOM criteria advocated in this guideline.[26] As such, there is a role for individualized diagnosis and management decisions. Examples of normal, mild bulging, moderate bulging, and severe bulging can be seen in Fig 2.

Distinguishing AOM From OME

OME may occur either as the aftermath of an episode of AOM or as a consequence of eustachian tube dysfunction attributable to an upper respiratory tract infection.[46] However, OME may also precede and predispose to the development of AOM. These 2 forms of OM may be considered segments of a disease continuum.[47] However, because OME does not represent an acute infectious process that benefits from antibiotics, it is of utmost importance for clinicians to become proficient in distinguishing normal middle ear status from OME or AOM. Doing so will avoid unnecessary use of antibiotics, which leads to increased adverse effects of medication and facilitates the development of antimicrobial resistance.

Examination of the TM

Accurate diagnosis of AOM in infants and young children may be difficult. Symptoms may be mild or overlap with those of an upper respiratory tract illness. The TM may be obscured by cerumen, and subtle changes in the TM may be difficult to discern. Additional factors complicating diagnosis may include lack of cooperation from the child; less than optimal diagnostic equipment, including lack of a pneumatic bulb; inadequate instruments for clearing cerumen from the external auditory canal; inadequate assistance for restraining the child; and lack of experience in removing cerumen and performing pneumatic otoscopy.

The pneumatic otoscope is the standard tool used in diagnosing OM. Valuable also is a surgical head, which greatly facilitates cleaning cerumen from an infant's external auditory canal. Cerumen may be removed by using a curette, gentle suction, or irrigation.[48] The pneumatic otoscope should have a light source of sufficient brightness and an air-tight seal that permits application of positive and negative pressure. In general, nondisposable specula achieve a better seal with less pain because of a thicker, smoother edge and better light transmission properties. The speculum size should be chosen to gently seal at the outer portion of the external auditory canal.

Pneumatic otoscopy permits assessment of the contour of the TM (normal, retracted, full, bulging), its color (gray, yellow, pink, amber, white, red, blue), its translucency (translucent, semiopaque, opaque), and its mobility (normal, increased, decreased, absent). The normal TM is translucent, pearly gray, and has a ground-glass appearance (Fig 2A). Specific landmarks can be visualized. They include the short process and the manubrium of the malleus and the pars flaccida, located superiorly. These are easily observed and help to identify the position of the TM. Inward movement of the TM on positive pressure in the external canal and outward movement on negative pressure should occur, especially in the superior posterior quadrant. When the TM is retracted, the short process of the malleus becomes more prominent, and the manubrium appears shortened because of its change in position within the middle ear. Inward motion occurring with positive pressure is restricted or absent, because the TM is frequently as far inward as its range of motion allows. However, outward mobility can be visualized when negative pressure is applied. If the TM does not move perceptibly with applications of gentle positive or negative pressure, MEE is likely. Sometimes, the application of pressure will make an air-fluid interface behind the TM (which is diagnostic of MEE) more evident.[49]

Instruction in the proper evaluation of the child's middle ear status should begin with the first pediatric rotation in medical school and continue throughout postgraduate training.[50]

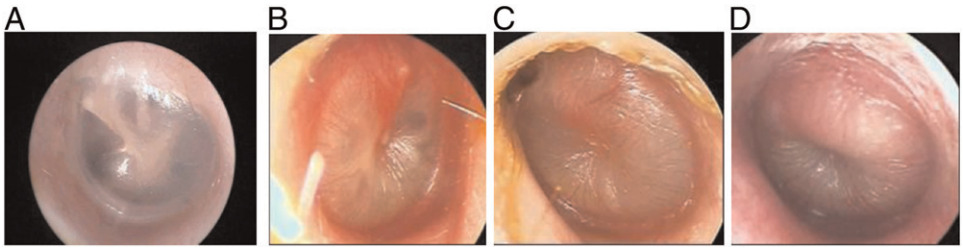

FIGURE 2
A, Normal TM. B, TM with mild bulging. C, TM with moderate bulging. D, TM with severe bulging. Courtesy of Alejandro Hoberman, MD.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Continuing medical education should reinforce the importance of, and retrain the clinician in, the use of pneumatic otoscopy.[51] Training tools include the use of a video-otoscope in residency programs, the use of Web-based educational resources,[49,52] as well as simultaneous or sequential examination of TMs with an expert otoscopist to validate findings by using a double headed or video otoscope. Tools for learning the ear examination can be found in a CD distributed by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing,[53] also available at http://www2.aap.org/sections/infectdis/video.cfm,[54] and through a Web-based program, ePROM: Enhancing Proficiency in Otitis Media.[52]

Key Action Statement 2

The management of AOM should include an assessment of pain. If pain is present, the clinician should recommend treatment to reduce pain. (Evidence Quality: Grade B, Rec. Strength: Strong Recommendation)

Key Action Statement Profile: KAS 2

Aggregate evidence quality	Grade B
Benefits	Relieves the major symptom of AOM.
Risks, harms, cost	Potential medication adverse effects. Variable efficacy of some modes of treatment.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Treating pain is essential whether or not antibiotics are prescribed.
Intentional vagueness	Choice of analgesic is not specified.
Role of patient preferences	Parents may assist in the decision as to what means of pain relief they prefer.
Exclusions	Topical analgesics in the presence of a perforated TM.
Strength	**Strong Recommendation**

Purpose of This Section

Pain is the major symptom of AOM. This section addresses and updates the literature on treating otalgia.

Changes From AAP/AAFP 2004 AOM Guideline

Only 2 new articles directly address the treatment of otalgia. Both address topical treatment. The 2 new articles are consistent with the 2004 guideline statement. The text of the 2004 guideline is, therefore, reproduced here, with the addition of discussion of the 2 new articles. Table 3 has been updated to include the new references.

Treatment of Otalgia

Many episodes of AOM are associated with pain.[55] Some children with OME also have ear pain. Although pain is a common symptom in these illnesses, clinicians often see otalgia as a peripheral concern not requiring direct attention.[56] Pain associated with AOM can be substantial in the first few days of illness and often persists longer in young children.[57] Antibiotic therapy of AOM does not provide symptomatic relief in the first 24 hours[58–61] and even after 3 to 7 days, there may be persistent pain, fever, or both in 30% of children younger than 2 years.[62] In contrast, analgesics do relieve pain associated with AOM within 24 hours[63] and should be used whether antibiotic therapy is or is not prescribed; they should be continued as long as needed. The AAP published the policy statement "The Assessment and Management of Acute Pain in Infants, Children, and Adolescents"[64] to assist the clinician in addressing pain in the context of illness. The management of pain, especially during the first 24 hours of an episode of AOM, should be addressed regardless of the use of antibiotics.

Various treatments of otalgia have been used, but none has been well studied. The clinician should select a treatment on the basis of a consideration of benefits and risks and, wherever possible, incorporate parent/caregiver and patient preference (Table 3).

TABLE 3 Treatments for Otalgia in AOM

Treatment Modality	Comments
Acetaminophen, ibuprofen[63]	Effective analgesia for mild to moderate pain. Readily available. Mainstay of pain management for AOM.
Home remedies (no controlled studies that directly address effectiveness)	May have limited effectiveness.
Distraction	
External application of heat or cold	
Oil drops in external auditory canal	
Topical agents	
Benzocaine, procaine, lidocaine[65,67,70]	Additional, but brief, benefit over acetaminophen in patients older than 5 y.
Naturopathic agents[68]	Comparable to amethocaine/phenazone drops in patients older than 6 y.
Homeopathic agents[71,72]	No controlled studies that directly address pain.
Narcotic analgesia with codeine or analogs	Effective for moderate or severe pain. Requires prescription; risk of respiratory depression, altered mental status, gastrointestinal tract upset, and constipation.
Tympanostomy/myringotomy[73]	Requires skill and entails potential risk.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Since the 2004 guideline was published, there have been only 2 significant new articles.

Bolt et al reported in 2008 on a double-blind placebo-controlled trial at the Australia Children's Hospital emergency department conducted in 2003–2004.[65] They used a convenience sample of children 3 to 17 years of age diagnosed with AOM in the ED. They excluded children with perforation of the TM, pressure-equalizing tube, allergy to local anesthetic or paracetamol, epilepsy, or liver, renal, or cardiac disease. Sixty-three eligible children were randomized to receive aqueous lidocaine or normal saline ear drops up to 3 times in 24 hours. They demonstrated a statistically significant 50% reduction in reported pain at 10 and 30 minutes but not at 20 minutes after application of topical lidocaine, compared with normal saline. Complications were minimal: 3 children reported some dizziness the next day, and none reported tinnitus. A limitation was that some children had received oral acetaminophen before administration of ear drops.

A Cochrane review of topical analgesia for AOM[66] searched the Cochrane register of controlled trials, randomized controlled trials, or quasi-randomized controlled trials that compared otic preparations to placebo or that compared 2 otic preparations. It included studies of adults and children, without TM perforation. It identified 5 trials in children 3 to 18 years of age. Two (including Bolt et al,[65] discussed above) compared anesthetic drops and placebo at diagnosis of AOM. In both studies, some children also received oral analgesics. Three studies compared anesthetic ear drops with naturopathic herbal drops. Naturopathic drops were favored 15 to 30 minutes after installation, and 1 to 3 days after diagnosis, but the difference was not statistically significant. The Cochrane group concluded that there is limited evidence that ear drops are effective at 30 minutes and unclear if results from these studies are a result of the natural course of illness, placebo effect of receiving treatment, soothing effect of any liquid in the ear, or the drops themselves. Three of the studies included in this review were cited in the 2004 AAP guideline[67–69] and the 1 new paper by Bolt et al.[65]

Key Action Statement 3A

Severe AOM

The clinician should prescribe antibiotic therapy for AOM (bilateral or unilateral) in children 6 months and older with severe signs or symptoms (ie, moderate or severe otalgia or otalgia for at least 48 hours, or temperature 39°C [102.2°F] or higher). (Evidence Quality: Grade B, Rec. Strength: Strong Recommendation)

Key Action Statement Profile: KAS 3A

Aggregate evidence quality	Grade B
Benefits	Increased likelihood of more rapid resolution of symptoms. Increased likelihood of resolution of AOM.
Risks, harms, cost	Adverse events attributable to antibiotics, such as diarrhea, diaper dermatitis, and allergic reactions. Overuse of antibiotics leads to increased bacterial resistance. Cost of antibiotics.
Benefits-harms assessment	Preponderance of benefit over harm.
Value judgments	None
Role of patient preference	None
Intentional vagueness	None
Exclusions	None
Strength	**Strong Recommendation**

Key Action Statement 3B

Nonsevere Bilateral AOM in Young Children

The clinician should prescribe antibiotic therapy for bilateral AOM in children younger than 24 months without severe signs or symptoms (ie, mild otalgia for less than 48 hours, temperature less than 39°C [102.2°F]). (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 3B

Aggregate evidence quality	Grade B
Benefits	Increased likelihood of more rapid resolution of symptoms. Increased likelihood of resolution of AOM.
Risks, harms, cost	Adverse events attributable to antibiotics, such as diarrhea, diaper dermatitis, and allergic reactions. Overuse of antibiotics leads to increased bacterial resistance. Cost of antibiotics.
Benefits-harms assessment	Preponderance of benefit over harm.
Value judgments	None
Role of patient preference	None
Intentional vagueness	None
Exclusions	None
Strength	**Recommendation**

Key Action Statement 3C

Nonsevere Unilateral AOM in Young Children

The clinician should either prescribe antibiotic therapy *or* offer observation with close follow-up based on joint decision-making with the parent(s)/caregiver for unilateral AOM in children 6 months to 23 months of age without severe signs or symptoms (ie, mild otalgia for less than 48 hours, temperature less than 39°C [102.2°F]). When observation is used, a mechanism must be in place to ensure

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

follow-up and begin antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 3C

Aggregate evidence quality	Grade B
Benefits	Moderately increased likelihood of more rapid resolution of symptoms with initial antibiotics. Moderately increased likelihood of resolution of AOM with initial antibiotics.
Risks, harms, cost	Adverse events attributable to antibiotics, such as diarrhea, diaper dermatitis, and allergic reactions. Overuse of antibiotics leads to increased bacterial resistance. Cost of antibiotics.
Benefits-harms assessment	Moderate degree of benefit over harm.
Value judgments	Observation becomes an alternative as the benefits and harms approach balance.
Role of patient preference	Joint decision-making with the family is essential before choosing observation.
Intentional vagueness	Joint decision-making is highly variable from family to family
Exclusions	None
Strength	**Recommendation**
Note	In the judgment of 1 Subcommittee member (AH), antimicrobial treatment of these children is preferred because of a preponderance of benefit over harm. AH did not endorse Key Action Statement 3C

Key Action Statement 3D

Nonsevere AOM in Older Children

The clinician should either prescribe antibiotic therapy *or* offer observation with close follow-up based on joint decision-making with the parent(s)/caregiver for AOM (bilateral or unilateral) in children 24 months or older without severe signs or symptoms (ie, mild otalgia for less than 48 hours, temperature less than 39°C [102.2°F]). When observation is used, a mechanism must be in place to ensure follow-up and begin antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms. (Evidence Quality: Grade B, Rec Strength: Recommendation)

Key Action Statement Profile: KAS 3D

Aggregate evidence quality	Grade B
Benefits	*Initial antibiotic treatment*: Slightly increased likelihood of more rapid resolution of symptoms; slightly increased likelihood of resolution of AOM. *Initial observation*: Decreased use of antibiotics; decreased adverse effects of antibiotics; decreased potential for development of bacterial resistance.
Risks, harms, cost	*Initial antibiotic treatment*: Adverse events attributable to antibiotics such as diarrhea, rashes, and allergic reactions. Overuse of antibiotics leads to increased bacterial resistance. *Initial observation*: Possibility of needing to start antibiotics in 48 to 72 h if the patient continues to have symptoms. Minimal risk of adverse consequences of delayed antibiotic treatment. Potential increased phone calls and doctor visits.
Benefits-harms assessment	Slight degree of benefit of initial antibiotics over harm.
Value judgments	Observation is an option as the benefits and harms approach balance.
Role of patient preference	Joint decision-making with the family is essential before choosing observation.
Intentional vagueness	Joint decision-making is highly variable from family to family.
Exclusions	None
Strength	**Recommendation.**

Purpose of This Section

The purpose of this section is to offer guidance on the initial management of AOM by helping clinicians choose between the following 2 strategies:

1. *Initial antibiotic therapy*, defined as treatment of AOM with antibiotics that are prescribed at the time of diagnosis with the intent of starting antibiotic therapy as soon as possible after the encounter.
2. *Initial observation*, defined as initial management of AOM limited to symptomatic relief, with commencement of antibiotic therapy only if the child's condition worsens at any time or does not show clinical improvement within 48 to 72 hours of diagnosis. A mechanism must be in place to ensure follow-up and initiation of antibiotics if the child fails observation.

This section assumes that the clinician has made an accurate diagnosis of AOM by using the criteria and strategies outlined earlier in this guideline. Another assumption is that a clear distinction is made between the role of analgesics and antibiotics in providing symptomatic relief for children with AOM.

Changes From Previous AOM Guideline

The AOM guideline published by the AAP and AAFP in 2004 proposed, for the first time in North America, an "observation option" for selected children with AOM, building on successful implementation of a similar policy in the state of New York[74] and the use of a similar paradigm in many countries in Europe. A common feature of both approaches was to prioritize initial antibiotic therapy according to diagnostic certainty, with greater reliance on observation when the diagnosis was uncertain. In response to criticism that allowing an "uncertain

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

diagnosis" might condone incomplete visualization of the TM or allow inappropriate antibiotic use, this category has been eliminated with greater emphasis now placed on maximizing diagnostic accuracy for AOM.

Since the earlier AOM guideline was published, there has been substantial new research on initial management of AOM, including randomized controlled trials of antibiotic therapy versus placebo or no therapy,[31,32,75] immediate versus delayed antibiotic therapy,[30,76,77] or delayed antibiotic with or without a concurrent prescription.[78] The Hoberman and Tähtinen articles are especially important as they used stringent criteria for diagnosing AOM.[31,32] Systematic reviews have been published on delayed antibiotic therapy,[79] the natural history of AOM in untreated children,[57] predictive factors for antibiotic benefits,[62] and the effect of antibiotics on asymptomatic MEE after therapy.[80] Observational studies provide additional data on outcomes of initial observation with delayed antibiotic therapy, if needed,[81] and on the relationship of previous antibiotic therapy for AOM to subsequent acute mastoiditis.[82,83]

In contrast to the earlier AOM guideline,[1] which recommended antibiotic therapy for all children 6 months to 2 years of age with a certain diagnosis, the current guideline indicates a choice between initial antibiotic therapy or initial observation in this age group for children with unilateral AOM and mild symptoms but only after joint decision-making with the parent(s)/caregiver (Table 4). This change is supported by evidence on the safety of observation or delayed prescribing in young children.[30,31,32,75,76,81] A mechanism must be in place to ensure follow-up and begin antibiotics if the child fails observation.

Importance of Accurate Diagnosis

The recommendations for management of AOM assume an accurate diagnosis on the basis of criteria outlined in the diagnosis section of this guideline. Many of the studies since the 2004 AAP/AAFP AOM guideline[1] used more stringent and well-defined AOM diagnostic definitions than were previously used. Bulging of the TM was required for diagnosis of AOM for most of the children enrolled in the most recent studies.[31,32] By using the criteria in this guideline, clinicians will more accurately distinguish AOM from OME. The management of OME can be found in guidelines written by the AAP, AAFP, and American Academy of Otolaryngology-Head and Neck Surgery.[84,85]

TABLE 4 Recommendations for Initial Management for Uncomplicated AOM[a]

Age	Otorrhea With AOM[a]	Unilateral or Bilateral AOM[a] With Severe Symptoms[b]	Bilateral AOM[a] Without Otorrhea	Unilateral AOM[a] Without Otorrhea
6 mo to 2 y	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy or additional observation
≥2 y	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy or additional observation	Antibiotic therapy or additional observation[c]

[a] Applies only to children with well-documented AOM with high certainty of diagnosis (see Diagnosis section).
[b] A toxic-appearing child, persistent otalgia more than 48 h, temperature ≥39°C (102.2°F) in the past 48 h, or if there is uncertain access to follow-up after the visit.
[c] This plan of initial management provides an opportunity for shared decision-making with the child's family for those categories appropriate for additional observation. If observation is offered, a mechanism must be in place to ensure follow-up and begin antibiotics if the child worsens or fails to improve within 48 to 72 h of AOM onset.

Age, Severity of Symptoms, Otorrhea, and Laterality

Rovers et al[62] performed a systematic search for AOM trials that (1) used random allocation of children, (2) included children 0 to 12 years of age with AOM, (3) compared antibiotics with placebo or no treatment, and (4) had pain or fever as an outcome. The original investigators were asked for their original data.

Primary outcome was pain and/or fever (>38°C) at 3 to 7 days. The adverse effects of antibiotics were also analyzed. Baseline predictors were age <2 years versus ≥2 years, bilateral AOM versus unilateral AOM, and the presence versus absence of otorrhea. Statistical methods were used to assess heterogeneity and to analyze the data.

Of the 10 eligible studies, the investigators of 6 studies[30,75,86–89] provided the original data requested, and 4 did not. A total of 1642 patients were included in the 6 studies from which data were obtained. Of the cases submitted, the average age was 3 to 4 years, with 35% of children younger than 2 years. Bilateral AOM was present in 34% of children, and 42% of children had a bulging TM. Otorrhea was present in 21% of children. The antibiotic and control groups were comparable for all characteristics.

The rate difference (RD) for pain, fever, or both between antibiotic and control groups was 13% (NNT = 8). For children younger than 2 years, the RD was 15% (NNT = 7); for those ≥2 years, RD was 11% (NNT = 10). For unilateral AOM, the RD was 6% (NNT = 17); for bilateral AOM, the RD was 20% (NNT = 5). When unilateral AOM was broken into age groups, among those younger than 2 years, the RD was 5% (NNT = 20), and among those ≥2 years, the RD was 7% (NNT = 15). For bilateral AOM in children younger than 2 years, the RD was 25% (NNT = 4); for

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

bilateral AOM in children ≥2 years, the RD was 12% (NNT = 9). For otorrhea, the RD was 36% (NNT = 3). One child in the control group who developed meningitis had received antibiotics beginning on day 2 because of worsening status. There were no cases of mastoiditis.

In a Cochrane Review, Sanders et al[59] identified 10 studies that met the following criteria: (1) randomized controlled trial, (2) compared antibiotic versus placebo or antibiotic versus observation, (3) age 1 month to 15 years, (4) reported severity and duration of pain, (5) reported adverse events, and (6) reported serious complications of AOM, recurrent attacks, and hearing problems. Studies were analyzed for risk of bias and assessment of heterogeneity. The studies were the same as analyzed by Rovers et al[62] but included the 4 studies for which primary data were not available to Rovers.[60,61,90,91]

The authors' conclusions were that antibiotics produced a small reduction in the number of children with pain 2 to 7 days after diagnosis. They also concluded that most cases spontaneously remitted with no complications (NNT = 16). Antibiotics were most beneficial in children younger than 2 years with bilateral AOM and in children with otorrhea.

Two recent studies only included children younger than 3 years[32] or younger than 2 years.[31] Both included only subjects in whom the diagnosis of AOM was certain. Both studies used improvement of symptoms and improvement in the appearance of the TM in their definitions of clinical success or failure.

Hoberman et al[31] conducted a randomized, double-blind, placebo-controlled study of the efficacy of antimicrobial treatment on AOM. The criteria for AOM were acute symptoms with a score of at least 3 on the AOM-SOS, a validated symptom scale[33,92]; MEE; and moderate or marked bulging of the TM or slight bulging accompanied by either otalgia or marked erythema of the TM. They chose to use high-dose amoxicillin-clavulanate (90 mg/kg/day) as active treatment, because it has the best oral antibiotic coverage for organisms causing AOM. Included in the study were 291 patients 6 to 23 months of age: 144 in the antibiotic group and 147 in the placebo group. The primary outcome measures were the time to resolution of symptoms and the symptom burden over time. The initial resolution of symptoms (ie, the first recording of an AOM-SOS score of 0 or 1) was recorded among the children who received amoxicillin-clavulanate in 35% by day 2, 61% by day 4, and 80% by day 7. Among children who received placebo, an AOM-SOS score of 0 or 1 was recorded in 28% by day 2, 54% by day 4, and 74% by day 7 (P = .14 for the overall comparison). For sustained resolution of symptoms (ie, the time to the second of 2 successive recordings of an AOM-SOS score of 0 or 1), the corresponding values were 20% at day 2, 41% at day 4, and 67% at day 7 with amoxicillin-clavulanate, compared with 14%, 36%, and 53% with placebo (P = .04 for the overall comparison). The symptom burden (ie, mean AOM-SOS scores) over the first 7 days were lower for the children treated with amoxicillin-clavulanate than for those who received placebo (P = .02). Clinical failure at or before the 4- to 5-day visit was defined as "either a lack of substantial improvement in symptoms, a worsening of signs on otoscopic examination, or both," and clinical failure at the 10- to 12-day visit was defined as "the failure to achieve complete or nearly complete resolution of symptoms and of otoscopic signs, without regard to the persistence or resolution of middle ear effusion." Treatment failure occurred by day 4 to 5 in 4% of the antimicrobial treatment group versus 23% in the placebo group ($P < .001$) and at day 10 to 12 in 16% of the antimicrobial treatment group versus 51% in the placebo group (NNT = 2.9, $P < .001$). In a comparison of outcome in unilateral versus bilateral AOM, clinical failure rates by day 10 to 12 in children with unilateral AOM were 9% in those treated with amoxicillin-clavulanate versus 41% in those treated with placebo (RD, 32%; NNT = 3) and 23% vs 60% (RD, 37%; NNT = 3) in those with bilateral AOM. Most common adverse events were diarrhea (25% vs 15% in the treatment versus placebo groups, respectively; P = .05) and diaper dermatitis (51% vs 35% in the treatment versus placebo groups, respectively; P = .008). One placebo recipient developed mastoiditis. According to these results, antimicrobial treatment of AOM was more beneficial than in previous studies that used less stringent diagnostic criteria.

Tähtinen et al[32] conducted a randomized, double-blind, placebo-controlled, intention-to-treat study of amoxicillin-clavulanate (40 mg/kg/day) versus placebo. Three hundred nineteen patients from 6 to 35 months of age were studied: 161 in the antibiotic group and 158 in the placebo group. AOM definition was the presence of MEE, distinct erythema over a bulging or yellow TM, and acute symptoms such as ear pain, fever, or respiratory symptoms. Compliance was measured by using daily patient diaries and number of capsules remaining at the end of the study. Primary outcome was time to treatment failure defined as a composite of 6 independent components: no improvement in overall condition by day 3, worsening of the child's condition at any time, no improvement in otoscopic signs by day 8, perforation of the TM,

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

development of severe infection (eg, pneumonia, mastoiditis), and any other reason for stopping the study drug/placebo.

Groups were comparable on multiple parameters. In the treatment group, 135 of 161 patients (84%) were younger than 24 months, and in the placebo group, 124 of 158 patients (78%) were younger than 24 months. Treatment failure occurred in 18.6% of the treatment group and 44.9% in the placebo group (NNT = 3.8, $P < .001$). Rescue treatment was needed in 6.8% of the treatment group and 33.5% of placebo patients ($P < .001$). Contralateral AOM developed in 8.2% and 18.6% of treatment and placebo groups, respectively ($P = .007$). There was no significant difference in use of analgesic or antipyretic medicine, which was used in 84.2% of the amoxicillin-clavulanate group and 85.9% of the placebo group.

Parents of child care attendees on placebo missed more days of work ($P = .005$). Clinical failure rates in children with unilateral AOM were 17.2% in those treated with amoxicillin-clavulanate versus 42.7% in those treated with placebo; for bilateral AOM, clinical failure rates were 21.7% for those treated with amoxicillin-clavulanate versus 46.3% in the placebo group. Reported rates of treatment failure by day 8 were 17.2% in the amoxicillin-clavulanate group versus 42.7% in the placebo group in children with unilateral AOM and 21.7% vs 46.3% among those with bilateral disease.

Adverse events, primarily diarrhea and/or rash, occurred in 52.8% of the treatment group and 36.1% of the placebo group ($P = .003$). Overall condition as evaluated by the parents and otoscopic appearance of the TM showed a benefit of antibiotics over placebo at the end of treatment visit ($P < .001$). Two placebo recipients developed a severe infection; 1 developed pneumococcal bacteremia, and 1 developed radiographically confirmed pneumonia.

Most studies have excluded children with severe illness and all exclude those with bacterial disease other than AOM (pneumonia, mastoiditis, meningitis, streptococcal pharyngitis). Kaleida et al[91] compared myringotomy alone with myringotomy plus antibiotics. Severe AOM was defined as temperature >39°C (102.2°F) or the presence of severe otalgia. Patients with severe AOM in the group that received only myringotomy (without initial antibiotics) had much worse outcomes.

Initial Antibiotic Therapy

The rationale for antibiotic therapy in children with AOM is based on a high prevalence of bacteria in the accompanying MEE.[93] Bacterial and viral cultures of middle ear fluid collected by tympanocentesis from children with AOM showed 55% with bacteria only and 15% with bacteria and viruses. A beneficial effect of antibiotics on AOM was first demonstrated in 1968,[94] followed by additional randomized trials and a meta-analysis[95] showing a 14% increase in absolute rates of clinical improvement. Systematic reviews of the literature published before 2011[21,59,62] revealed increases of clinical improvement with initial antibiotics of 6% to 12%.

Randomized clinical trials using stringent diagnostic criteria for AOM in young children[31,32] show differences in clinical improvement of 26% to 35% favoring initial antibiotic treatment as compared with placebo. Greater benefit of immediate antibiotic therapy was observed for bilateral AOM[62,96] or AOM associated with otorrhea.[62] In most randomized trials,[30,75,77,88,89] antibiotic therapy also decreased the duration of pain, analgesic use, or school absence and parent days missed from work.

Children younger than 2 years with AOM may take longer to improve clinically than older children,[57] and although they are more likely to benefit from antibiotics,[31,32] AOM in many children will resolve without antibiotics.[62] A clinically significant benefit of immediate antibiotic therapy is observed for bilateral AOM,[62,96] *Streptococcus pneumoniae* infection, or AOM associated with otorrhea.[62]

Initial Observation for AOM

In systematic reviews of studies that compare antibiotic therapy for AOM with placebo, a consistent finding has been the overall favorable natural history in control groups (NNT = 8–16).[12,59,62,95] However, randomized trials in these reviews had varying diagnostic criteria that would have permitted inclusion of some children with OME, viral upper respiratory infections, or myringitis, thereby limiting the ability to apply these findings to children with a highly certain AOM diagnosis. In more recent AOM studies[31,32] using stringent diagnostic criteria, approximately half of young children (younger than 2–3 years) experienced clinical success when given placebo, but the effect of antibiotic therapy was substantially greater than suggested by studies without precise diagnosis (NNT = 3–4).

Observation as initial management for AOM in properly selected children does not increase suppurative complications, provided that follow-up is ensured and a rescue antibiotic is given for persistent or worsening symptoms.[17] In contrast, withholding of antibiotics in all children with AOM, regardless of clinical course, would risk a return to the suppurative complications observed in the

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

preantibiotic era. At the population level, antibiotics halve the risk of mastoiditis after AOM, but the high NNT of approximately 4800 patients to prevent 1 case of mastoiditis precludes a strategy of universal antibiotic therapy as a means to prevent mastoiditis.[83]

The favorable natural history of AOM makes it difficult to demonstrate significant differences in efficacy between antibiotic and placebo when a successful outcome is defined by relief or improvement of presenting signs and symptoms. In contrast, when otoscopic improvement (resolution of TM bulging, intense erythema, or both) is also required for a positive outcome,[31,32] the NNT is 3 to 4, compared with 8 to 16 for symptom improvement alone in older studies that used less precise diagnostic criteria. MEE, however, may persist for weeks or months after an AOM episode and is not a criterion for otoscopic failure.

National guidelines for initial observation of AOM in select children were first implemented in the Netherlands[97] and subsequently in Sweden,[98] Scotland,[99] the United States,[1] the United Kingdom,[100] and Italy.[101] All included observation as an initial treatment option under specified circumstances.

In numerous studies, only approximately one-third of children initially observed received a rescue antibiotic for persistent or worsening AOM,[30,32,76,81,89,102] suggesting that antibiotic use could potentially be reduced by 65% in eligible children. Given the high incidence of AOM, this reduction could help substantially in curtailing antibiotic-related adverse events.

McCormick et al[30] reported on 233 patients randomly assigned to receive immediate antibiotics (amoxicillin, 90 mg/kg/day) or to undergo watchful waiting. Criteria for inclusion were symptoms of ear infection, otoscopic evidence of AOM, and nonsevere AOM based on a 3-item symptom score (OM-3) and TM appearance based on an 8-item scale (OS-8). Primary outcomes were parent satisfaction with AOM care, resolution of AOM symptoms after initial treatment, AOM failure and recurrence, and nasopharyngeal carriage of *S pneumoniae* strains resistant to antibiotics after treatment. The study was confounded by including patients who had received antibiotics in the previous 30 days.

In the watchful waiting group, 66% of children completed the study without antibiotics. There was no difference in parent satisfaction scores at day 12. A 5-item symptom score (ETG-5) was assessed at days 0 to 10 by using patient diaries. Subjects receiving immediate antibiotics resolved their symptoms faster than did subjects who underwent watchful waiting (P = .004). For children younger than 2 years, the difference was greater (P = .008). Otoscopic and tympanogram scores were also lower in the antibiotic group as opposed to the watchful waiting group (P = .02 for otoscopic score, P = .004 for tympanogram). Combining all ages, failure and recurrence rates were lower for the antibiotic group (5%) than for the watchful waiting group (21%) at 12 days. By day 30, there was no difference in failure or recurrence for the antibiotic and watchful waiting groups (23% and 24%, respectively). The association between clinical outcome and intervention group was not significantly different between age groups. Immediate antibiotics resulted in eradication of *S pneumoniae* carriage in the majority of children, but *S pneumoniae* strains cultured from children in the antibiotic group at day 12 were more likely to be multidrug resistant than were strains cultured from children in the watchful waiting group.

The decision not to give initial antibiotic treatment and observe should be a joint decision of the clinician and the parents. In such cases, a system for close follow-up and a means of beginning antibiotics must be in place if symptoms worsen or no improvement is seen in 48 to 72 hours.

Initial observation of AOM should be part of a larger management strategy that includes analgesics, parent information, and provisions for a rescue antibiotic. Education of parents should include an explanation about the self-limited nature of most episodes of AOM, especially in children 2 years and older; the importance of pain management early in the course; and the potential adverse effects of antibiotics. Such an approach can substantially reduce prescription fill rates for rescue antibiotics.[103]

A critical component of any strategy involving initial observation for AOM is the ability to provide a rescue antibiotic if needed. This is often done by using a "safety net" or a "wait-and-see prescription,"[76,102] in which the parent/caregiver is given an antibiotic prescription during the clinical encounter but is instructed to fill the prescription only if the child fails to improve within 2 to 3 days or if symptoms worsen at any time. An alternative approach is not to provide a written prescription but to instruct the parent/caregiver to call or return if the child fails to improve within 2 to 3 days or if symptoms worsen.

In one of the first major studies of observation with a safety-net antibiotic prescription (SNAP), Siegel et al[102] enrolled 194 patients with protocol defined AOM, of whom 175 completed the study. Eligible patients were given a SNAP with instructions to fill the prescription only if symptoms worsened or did not improve in 48 hours. The SNAP was valid for 5 days. Pain medicine was recommended to be taken as needed. A phone interview was conducted 5 to 10 days after diagnosis.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

One hundred twenty of 175 families did not fill the prescription. Reasons for filling the prescription (more than 1 reason per patient was acceptable) were as follows: continued pain, 23%; continued fever, 11%; sleep disruption, 6%; missed days of work, 3%; missed days of child care, 3%; and no reason given, 5%. One 16-month-old boy completed observation successfully but 6 weeks later developed AOM in the opposite ear, was treated with antibiotics, and developed postauricular cellulitis.

In a similar study of a "wait-and-see prescription" (WASP) in the emergency department, Spiro et al[76] randomly assigned 283 patients to either a WASP or standard prescription. Clinicians were educated on the 2004 AAP diagnostic criteria and initial treatment options for AOM; however, diagnosis was made at the discretion of the clinician. Patients were excluded if they did not qualify for observation per the 2004 guidelines. The primary outcome was whether the prescription was filled within 3 days of diagnosis. Prescriptions were not filled for 62% and 13% of the WASP and standard prescription patients, respectively ($P < .001$). Reasons for filling the prescription in the WASP group were fever (60%), ear pain (34%), or fussy behavior (6%). No serious adverse events were reported.

Strategies to observe children with AOM who are likely to improve on their own without initial antibiotic therapy reduces common adverse effects of antibiotics, such as diarrhea and diaper dermatitis. In 2 trials, antibiotic therapy significantly increased the absolute rates of diarrhea by 10% to 20% and of diaper rash or dermatitis by 6% to 16%.[31,32] Reduced antibiotic use may also reduce the prevalence of resistant bacterial pathogens. Multidrug-resistant *S pneumoniae* continues to be a significant concern for AOM, despite universal immunization of children in the United States with heptavalent pneumococcal conjugate vaccine.[104,105] In contrast, countries with low antibiotic use for AOM have a low prevalence of resistant nasopharyngeal pathogens in children.[106]

Key Action Statement 4A

Clinicians should prescribe amoxicillin for AOM when a decision to treat with antibiotics has been made *and* the child has not received amoxicillin in the past 30 days *or* the child does not have concurrent purulent conjunctivitis *or* the child is not allergic to penicillin. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 4A

Aggregate evidence quality	Grade B
Benefits	Effective antibiotic for most children with AOM. Inexpensive, safe, acceptable taste, narrow antimicrobial spectrum.
Risks, harms, cost	Ineffective against β-lactamase–producing organisms. Adverse effects of amoxicillin.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Better to use a drug that has reasonable cost, has an acceptable taste, and has a narrow antibacterial spectrum.
Intentional vagueness	The clinician must determine whether the patient is truly penicillin allergic.
Role of patient preferences	Should be considered if previous bad experience with amoxicillin.
Exclusions	Patients with known penicillin allergy.
Strength	**Recommendation.**

Key Action Statement 4B

Clinicians should prescribe an antibiotic with additional β-lactamase coverage for AOM when a decision to treat with antibiotics has been made *and* the child has received amoxicillin in the past 30 days *or* has concurrent purulent conjunctivitis *or* has a history of recurrent AOM unresponsive to amoxicillin. (Evidence Quality: Grade C, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 4B

Aggregate evidence quality	Grade C
Benefits	Successful treatment of β-lactamase–producing organisms.
Risks, harms, cost	Cost of antibiotic. Increased adverse effects.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Efficacy is more important than taste.
Intentional vagueness	None.
Role of patient preferences	Concern regarding side effects and taste.
Exclusions	Patients with known penicillin allergy.
Strength	**Recommendation**

Key Action Statement 4C

Clinicians should reassess the patient if the caregiver reports that the child's symptoms have worsened or failed to respond to the initial antibiotic treatment within 48 to 72 hours and determine whether a change in therapy is needed. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Key Action Statement Profile: KAS 4C

Aggregate evidence quality	Grade B
Benefits	Identify children who may have AOM caused by pathogens resistant to previous antibiotics.
Risks, harms, cost	Cost. Time for patient and clinician to make change. Potential need for parenteral medication.
Benefit-harm assessment	Preponderance of benefit.
Value judgments	None.
Intentional vagueness	"Reassess" is not defined. The clinician may determine the method of assessment.
Role of patient preferences	Limited.
Exclusions	Appearance of TM improved.
Strength	**Recommendation**

Purpose of This Section

If an antibiotic will be used for treatment of a child with AOM, whether as initial management or after a period of observation, the clinician must choose an antibiotic that will have a high likelihood of being effective against the most likely etiologic bacterial pathogens with considerations of cost, taste, convenience, and adverse effects. This section proposes first- and second-line antibiotics that best meet these criteria while balancing potential benefits and harms.

Changes From AAP/AAFP 2004 AOM Guideline

Despite new data on the effect of PCV7 and updated data on the in vitro susceptibility of bacterial pathogens most likely to cause AOM, the recommendations for the first-line antibiotic remains unchanged from 2004. The current guideline contains revised recommendations regarding penicillin allergy based on new data. The increase of multidrug-resistant strains of pneumococci is noted.

Microbiology

Microorganisms detected in the middle ear during AOM include pathogenic bacteria, as well as respiratory viruses.[107–110] AOM occurs most frequently as a consequence of viral upper respiratory tract infection,[111–113] which leads to eustachian tube inflammation/dysfunction, negative middle ear pressure, and movement of secretions containing the upper respiratory tract infection causative virus and pathogenic bacteria in the nasopharynx into the middle ear cleft. By using comprehensive and sensitive microbiologic testing, bacteria and/or viruses can be detected in the middle ear fluid in up to 96% of AOM cases (eg, 66% bacteria and viruses together, 27% bacteria alone, and 4% virus alone).[114] Studies using less sensitive or less comprehensive microbiologic assays have yielded less positive results for bacteria and much less positive results for viruses.[115–117] The 3 most common bacterial pathogens in AOM are *S pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis*.[111] *Streptococcus pyogenes* (group A β-hemolytic streptococci) accounts for less than 5% of AOM cases. The proportion of AOM cases with pathogenic bacteria isolated from the middle ear fluids varies depending on bacteriologic techniques, transport issues, and stringency of AOM definition. In series of reports from the United States and Europe from 1952–1981 and 1985–1992, the mean percentage of cases with bacterial pathogens isolated from the middle ear fluids was 69% and 72%, respectively.[118] A large series from the University of Pittsburgh Otitis Media Study Group reported bacterial pathogens in 84% of the middle ear fluids from 2807 cases of AOM.[118] Studies that applied more stringent otoscopic criteria and/or use of bedside specimen plating on solid agar in addition to liquid transport media have a reported rate of recovery of pathogenic bacteria from middle ear exudates ranging from 85% to 90%.[119–121] When using appropriate stringent diagnostic criteria, careful specimen handling, and sensitive microbiologic techniques, the vast majority of cases of AOM will involve pathogenic bacteria either alone or in concert with viral pathogens.

Among AOM bacterial pathogens, *S pneumoniae* was the most frequently cultured in earlier reports. Since the debut and routine use of PCV7 in 2000, the ordinal frequency of these 3 major middle ear pathogens has evolved.[105] In the first few years after PCV7 introduction, *H influenzae* became the most frequently isolated middle ear pathogen, replacing *S pneumoniae*.[122,123] Shortly thereafter, a shift to non-PCV7 serotypes of *S pneumoniae* was described.[124] Pichichero et al[104] later reported that 44% of 212 AOM cases seen in 2003–2006 were caused by *H influenzae*, and 28% were caused by *S pneumoniae*, with a high proportion of highly resistant *S pneumoniae*. In that study, a majority (77%) of cases involved recurrent disease or initial treatment failure. A later report[125] with data from 2007 to 2009, 6 to 8 years after the introduction of PCV7 in the United States, showed that PCV7 strains of *S pneumoniae* virtually disappeared from the middle ear fluid of children with AOM who had been vaccinated. However, the frequency of isolation of non-PCV7 serotypes of *S pneumoniae* from the middle ear fluid overall was increased; this has made isolation of *S pneumoniae* and *H influenzae* of children with AOM nearly equal.

In a study of tympanocentesis over 4 respiratory tract illness seasons in a private practice, the percentage of

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

S pneumoniae initially decreased relative to *H influenzae.* In 2005–2006 (*N* = 33), 48% of bacteria were *S pneumoniae*, and 42% were *H influenzae.* For 2006–2007 (*N* = 37), the percentages were equal at 41%. In 2007–2008 (*N* = 34), 35% were *S pneumoniae*, and 59% were *H influenzae.* In 2008–2009 (*N* = 24), the percentages were 54% and 38%, respectively, with an increase in intermediate and nonsusceptible *S pneumoniae.*[126] Data on nasopharyngeal colonization from PCV7-immunized children with AOM have shown continued presence of *S pneumoniae* colonization. Revai et al[127] showed no difference in *S pneumoniae* colonization rate among children with AOM who have been unimmunized, underimmunized, or fully immunized with PCV7. In a study during a viral upper respiratory tract infection, including mostly PCV7-immunized children (6 months to 3 years of age), *S pneumoniae* was detected in 45.5% of 968 nasopharyngeal swabs, *H influenzae* was detected in 32.4%, and *M catarrhalis* was detected in 63.1%.[128] Data show that nasopharyngeal colonization of children vaccinated with PCV7 increasingly is caused by *S pneumoniae* serotypes not contained in the vaccine.[129–132] With the use of the recently licensed 13-valent pneumococcal conjugate vaccine (PCV13),[133] the patterns of nasopharyngeal colonization and infection with these common AOM bacterial pathogens will continue to evolve.

Investigators have attempted to predict the type of AOM pathogenic bacteria on the basis of clinical severity, but results have not been promising. *S pyogenes* has been shown to occur more commonly in older children[134] and to cause a greater degree of inflammation of the middle ear and TM, a greater frequency of spontaneous rupture of the TM, and more frequent progression to acute mastoiditis compared with other bacterial pathogens.[134–136] As for clinical findings in cases with *S pneumoniae* and nontypeable *H influenzae*, some studies suggest that signs and symptoms of AOM caused by *S pneumoniae* may be more severe (fever, severe earache, bulging TM) than those caused by other pathogens.[44,121,137] These findings were refuted by results of the studies that found AOM caused by nontypeable *H influenzae* to be associated with bilateral AOM and more severe inflammation of the TM.[96,138] Leibovitz et al[139] concluded, in a study of 372 children with AOM caused by *H influenzae* (*N* = 138), *S pneumoniae* (*N* = 64), and mixed *H influenzae* and *S pneumoniae* (*N* = 64), that clinical/otologic scores could not discriminate among various bacterial etiologies of AOM. However, there were significantly different clinical/otologic scores between bacterial culture negative and culture positive cases. A study of middle ear exudates of 82 cases of bullous myringitis has shown a 97% bacteria positive rate, primarily *S pneumoniae*. In contrast to the previous belief, mycoplasma is rarely the causative agent in this condition.[140] Accurate prediction of the bacterial cause of AOM on the basis of clinical presentation, without bacterial culture of the middle ear exudates, is not possible, but specific etiologies may be predicted in some situations. Published evidence has suggested that AOM associated with conjunctivitis (otitis-conjunctivitis syndrome) is more likely caused by nontypeable *H influenzae* than by other bacteria.[141–143]

Bacterial Susceptibility to Antibiotics

Selection of antibiotic to treat AOM is based on the suspected type of bacteria and antibiotic susceptibility pattern, although clinical pharmacology and clinical and microbiologic results and predicted compliance with the drug are also taken into account. Early studies of AOM patients show that 19% of children with *S pneumoniae* and 48% with *H influenzae* cultured on initial tympanocentesis who were not treated with antibiotic cleared the bacteria at the time of a second tympanocentesis 2 to 7 days later.[144] Approximately 75% of children infected with *M catarrhalis* experienced bacteriologic cure even after treatment with amoxicillin, an antibiotic to which it is not susceptible.[145,146]

Antibiotic susceptibility of major AOM bacterial pathogens continues to change, but data on middle ear pathogens have become scanty because tympanocentesis is not generally performed in studies of children with uncomplicated AOM. Most available data come from cases of persistent or recurrent AOM. Current US data from a number of centers indicates that approximately 83% and 87% of isolates of *S pneumoniae* from all age groups are susceptible to regular (40 mg/kg/day) and high-dose amoxicillin (80–90 mg/kg/day divided twice daily), respectively.[130,147–150] Pediatric isolates are smaller in number and include mostly ear isolates collected from recurrent and persistent AOM cases with a high percentage of multidrug-resistant *S pneumoniae*, most frequently nonvaccine serotypes that have recently increased in frequency and importance.[104]

High-dose amoxicillin will yield middle ear fluid levels that exceed the minimum inhibitory concentration (MIC) of all *S pneumoniae* serotypes that are intermediately resistant to penicillin (penicillin MICs, 0.12–1.0 μg/mL), and many but not all highly resistant serotypes (penicillin MICs, ≥2 μg/mL) for a longer period of the dosing interval and has been shown to improve bacteriologic and clinical efficacy

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

compared with the regular dose.[151–153] Hoberman et al[154] reported superior efficacy of high-dose amoxicillin-clavulanate in eradication of *S pneumoniae* (96%) from the middle ear at days 4 to 6 of therapy compared with azithromycin.

The antibiotic susceptibility pattern for *S pneumoniae* is expected to continue to evolve with the use of PCV13, a conjugate vaccine containing 13 serotypes of *S pneumoniae*.[133,155,156] Widespread use of PCV13 could potentially reduce diseases caused by multidrug-resistant pneumococcal serotypes and diminish the need for the use of higher dose of amoxicillin or amoxicillin-clavulanate for AOM.

Some *H influenzae* isolates produce β-lactamase enzyme, causing the isolate to become resistant to penicillins. Current data from different studies with non-AOM sources and geographic locations that may not be comparable show that 58% to 82% of *H influenzae* isolates are susceptible to regular- and high-dose amoxicillin.[130,147,148,157,158] These data represented a significant decrease in β-lactamase–producing *H influenzae*, compared with data reported in the 2004 AOM guideline.

Nationwide data suggest that 100% of *M catarrhalis* derived from the upper respiratory tract are β-lactamase–positive but remain susceptible to amoxicillin-clavulanate.[159] However, the high rate of spontaneous clinical resolution occurring in children with AOM attributable to *M catarrhalis* treated with amoxicillin reduces the concern for the first-line coverage for this microorganism.[145,146] AOM attributable to *M catarrhalis* rarely progresses to acute mastoiditis or intracranial infections.[102,160,161]

Antibiotic Therapy

High-dose amoxicillin is recommended as the first-line treatment in most patients, although there are a number of medications that are clinically effective (Table 5). The justification for the use of amoxicillin relates to its effectiveness against common AOM bacterial pathogens as well as its safety, low cost, acceptable taste, and narrow microbiologic spectrum.[145,151] In children who have taken amoxicillin in the previous 30 days, those with concurrent conjunctivitis, or those for whom coverage for β-lactamase–positive *H influenzae* and *M catarrhalis* is desired, therapy should be initiated with high-dose amoxicillin-clavulanate (90 mg/kg/day of amoxicillin, with 6.4 mg/kg/day of clavulanate, a ratio of amoxicillin to clavulanate of 14:1, given in 2 divided doses, which is less likely to cause diarrhea than other amoxicillin-clavulanate preparations).[162]

Alternative initial antibiotics include cefdinir (14 mg/kg per day in 1 or 2 doses), cefuroxime (30 mg/kg per day in 2 divided doses), cefpodoxime (10 mg/kg per day in 2 divided doses), or ceftriaxone (50 mg/kg, administered intramuscularly). It is important to note that alternative antibiotics vary in their efficacy against AOM pathogens. For example, recent US data on in vitro susceptibility of *S pneumoniae* to cefdinir and cefuroxime are 70% to 80%, compared with 84% to 92% amoxicillin efficacy.[130,147–149] In vitro efficacy of cefdinir and cefuroxime against *H influenzae* is approximately 98%, compared with 58% efficacy of amoxicillin and nearly 100% efficacy of amoxicillin-clavulanate.[158] A multicenter double tympanocentesis open-label study of

TABLE 5 Recommended Antibiotics for (Initial or Delayed) Treatment and for Patients Who Have Failed Initial Antibiotic Treatment

Initial Immediate or Delayed Antibiotic Treatment		Antibiotic Treatment After 48–72 h of Failure of Initial Antibiotic Treatment	
Recommended First-line Treatment	Alternative Treatment (if Penicillin Allergy)	Recommended First-line Treatment	Alternative Treatment
Amoxicillin (80–90 mg/ kg per day in 2 divided doses)	Cefdinir (14 mg/kg per day in 1 or 2 doses)	Amoxicillin-clavulanate[a] (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate in 2 divided doses)	Ceftriaxone, 3 d Clindamycin (30–40 mg/kg per day in 3 divided doses), with or without third-generation cephalosporin
or	Cefuroxime (30 mg/kg per day in 2 divided doses)	or	Failure of second antibiotic
Amoxicillin-clavulanate[a] (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate [amoxicillin to clavulanate ratio, 14:1] in 2 divided doses)	Cefpodoxime (10 mg/kg per day in 2 divided doses)	Ceftriaxone (50 mg IM or IV for 3 d)	Clindamycin (30–40 mg/kg per day in 3 divided doses) plus third-generation cephalosporin
	Ceftriaxone (50 mg IM or IV per day for 1 or 3 d)		Tympanocentesis[b]
			Consult specialist[b]

IM, intramuscular; IV, intravenous.

[a] May be considered in patients who have received amoxicillin in the previous 30 d or who have the otitis-conjunctivitis syndrome.

[b] Perform tympanocentesis/drainage if skilled in the procedure, or seek a consultation from an otolaryngologist for tympanocentesis/drainage. If the tympanocentesis reveals multidrug-resistant bacteria, seek an infectious disease specialist consultation.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

cefdinir in recurrent AOM attributable to *H influenzae* showed eradication of the organism in 72% of patients.[163]

For penicillin-allergic children, recent data suggest that cross-reactivity among penicillins and cephalosporins is lower than historically reported.[164–167] The previously cited rate of cross-sensitivity to cephalosporins among penicillin-allergic patients (approximately 10%) is likely an overestimate. The rate was based on data collected and reviewed during the 1960s and 1970s. A study analyzing pooled data of 23 studies, including 2400 patients with reported history of penicillin allergy and 39 000 with no penicillin allergic history concluded that many patients who present with a history of penicillin allergy do not have an immunologic reaction to penicillin.[166] The chemical structure of the cephalosporin determines the risk of cross-reactivity between specific agents.[165,168] The degree of cross-reactivity is higher between penicillins and first-generation cephalosporins but is negligible with the second- and third-generation cephalosporins. Because of the differences in the chemical structures, cefdinir, cefuroxime, cefpodoxime, and ceftriaxone are highly unlikely to be associated with cross-reactivity with penicillin.[165] Despite this, the Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; and Joint Council of Allergy, Asthma and Immunology[169] stated that "cephalosporin treatment of patients with a history of penicillin allergy, selecting out those with severe reaction histories, show a reaction rate of 0.1%." They recommend a cephalosporin in cases without severe and/or recent penicillin allergy reaction history when skin test is not available.

Macrolides, such as erythromycin and azithromycin, have limited efficacy against both *H influenzae* and *S pneumoniae*.[130,147–149] Clindamycin lacks efficacy against *H influenzae*. Clindamycin alone (30–40 mg/kg per day in 3 divided doses) may be used for suspected penicillin-resistant *S pneumoniae*; however, the drug will likely not be effective for the multidrug-resistant serotypes.[130,158,166]

Several of these choices of antibiotic suspensions are barely palatable or frankly offensive and may lead to avoidance behaviors or active rejection by spitting out the suspension. Palatability of antibiotic suspensions has been compared in many studies.[170–172] Specific antibiotic suspensions such as cefuroxime, cefpodoxime, and clindamycin may benefit from adding taste-masking products, such as chocolate or strawberry flavoring agents, to obscure the initial bitter taste and the unpleasant aftertaste.[172,173] In the patient who is persistently vomiting or cannot otherwise tolerate oral medication, even when the taste is masked, ceftriaxone (50 mg/kg, administered intramuscularly in 1 or 2 sites in the anterior thigh, or intravenously) has been demonstrated to be effective for the initial or repeat antibiotic treatment of AOM.[174,175] Although a single injection of ceftriaxone is approved by the US FDA for the treatment of AOM, results of a double tympanocentesis study (before and 3 days after single dose ceftriaxone) by Leibovitz et al[175] suggest that more than 1 ceftriaxone dose may be required to prevent recurrence of the middle ear infection within 5 to 7 days after the initial dose.

Initial Antibiotic Treatment Failure

When antibiotics are prescribed for AOM, clinical improvement should be noted within 48 to 72 hours. During the 24 hours after the diagnosis of AOM, the child's symptoms may worsen slightly. In the next 24 hours, the patient's symptoms should begin to improve. If initially febrile, the temperature should decline within 48 to 72 hours. Irritability and fussiness should lessen or disappear, and sleeping and drinking patterns should normalize.[176,177] If the patient is not improved by 48 to 72 hours, another disease or concomitant viral infection may be present, or the causative bacteria may be resistant to the chosen therapy.

Some children with AOM and persistent symptoms after 48 to 72 hours of initial antibacterial treatment may have combined bacterial and viral infection, which would explain the persistence of ongoing symptoms despite appropriate antibiotic therapy.[109,178,179] Literature is conflicting on the correlation between clinical and bacteriologic outcomes. Some studies report good correlation ranging from 86% to 91%,[180,181] suggesting continued presence of bacteria in the middle ear in a high proportion of cases with persistent symptoms. Others report that middle ear fluid from children with AOM in whom symptoms are persistent is sterile in 42% to 49% of cases.[123,182] A change in antibiotic may not be required in some children with mild persistent symptoms.

In children with persistent, severe symptoms of AOM and unimproved otologic findings after initial treatment, the clinician may consider changing the antibiotic (Table 5). If the child was initially treated with amoxicillin and failed to improve, amoxicillin-clavulanate should be used. Patients who were given amoxicillin-clavulanate or oral third-generation cephalosporins may receive intramuscular ceftriaxone (50 mg/kg). In the treatment of AOM unresponsive to initial antibiotics, a 3-day course of ceftriaxone has been shown to be better than a 1-day regimen.[175]

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Although trimethoprim-sulfamethoxazole and erythromycin-sulfisoxazole had been useful as therapy for patients with AOM, pneumococcal surveillance studies have indicated that resistance to these 2 combination agents is substantial.[130,149,183] Therefore, when patients fail to improve while receiving amoxicillin, neither trimethoprim-sulfamethoxazole[184] nor erythromycin-sulfisoxazole is appropriate therapy.

Tympanocentesis should be considered, and culture of middle ear fluid should be performed for bacteriologic diagnosis and susceptibility testing when a series of antibiotic drugs have failed to improve the clinical condition. If tympanocentesis is not available, a course of clindamycin may be used, with or without an antibiotic that covers nontypeable *H influenzae* and *M catarrhalis*, such as cefdinir, cefixime, or cefuroxime.

Because *S pneumoniae* serotype 19A is usually multidrug-resistant and may not be responsive to clindamycin,[104,149] newer antibiotics that are not approved by the FDA for treatment of AOM, such as levofloxacin or linezolid, may be indicated.[185–187] Levofloxacin is a quinolone antibiotic that is not approved by the FDA for use in children. Linezolid is effective against resistant Gram-positive bacteria. It is not approved by the FDA for AOM treatment and is expensive. In children with repeated treatment failures, every effort should be made for bacteriologic diagnosis by tympanocentesis with Gram stain, culture, and antibiotic susceptibility testing of the organism (s) present. The clinician may consider consulting with pediatric medical subspecialists, such as an otolaryngologist for possible tympanocentesis, drainage, and culture and an infectious disease expert, before use of unconventional drugs such as levofloxacin or linezolid.

When tympanocentesis is not available, 1 possible way to obtain information on the middle ear pathogens and their antimicrobial susceptibility is to obtain a nasopharyngeal specimen for bacterial culture. Almost all middle ear pathogens derive from the pathogens colonizing the nasopharynx, but not all nasopharyngeal pathogens enter the middle ear to cause AOM. The positive predictive value of nasopharyngeal culture during AOM (likelihood that bacteria cultured from the nasopharynx is the middle ear pathogen) ranges from 22% to 44% for *S pneumoniae*, 50% to 71% for nontypeable *H influenzae*, and 17% to 19% for *M catarrhalis*. The negative predictive value (likelihood that bacteria not found in the nasopharynx are not AOM pathogens) ranges from 95% to 99% for all 3 bacteria.[188,189] Therefore, if nasopharyngeal culture is negative for specific bacteria, that organism is likely not the AOM pathogen. A negative culture for *S pneumoniae*, for example, will help eliminate the concern for multidrug-resistant bacteria and the need for unconventional therapies, such as levofloxacin or linezolid. On the other hand, if *S pneumoniae* is cultured from the nasopharynx, the antimicrobial susceptibility pattern can help guide treatment.

Duration of Therapy

The optimal duration of therapy for patients with AOM is uncertain; the usual 10-day course of therapy was derived from the duration of treatment of streptococcal pharyngotonsillitis. Several studies favor standard 10-day therapy over shorter courses for children younger than 2 years.[162,190–194] Thus, for children younger than 2 years and children with severe symptoms, a standard 10-day course is recommended. A 7-day course of oral antibiotic appears to be equally effective in children 2 to 5 years of age with mild or moderate AOM. For children 6 years and older with mild to moderate symptoms, a 5- to 7-day course is adequate treatment.

Follow-up of the Patient With AOM

Once the child has shown clinical improvement, follow-up is based on the usual clinical course of AOM. There is little scientific evidence for a routine 10- to 14-day reevaluation visit for all children with an episode of AOM. The physician may choose to reassess some children, such as young children with severe symptoms or recurrent AOM or when specifically requested by the child's parent.

Persistent MEE is common and can be detected by pneumatic otoscopy (with or without verification by tympanometry) after resolution of acute symptoms. Two weeks after successful antibiotic treatment of AOM, 60% to 70% of children have MEE, decreasing to 40% at 1 month and 10% to 25% at 3 months after successful antibiotic treatment.[177,195] The presence of MEE without clinical symptoms is defined as OME. OME must be differentiated clinically from AOM and requires infrequent additional monitoring but not antibiotic therapy. Assurance that OME resolves is particularly important for parents of children with cognitive or developmental delays that may be affected adversely by transient hearing loss associated with MEE. Detailed recommendations for the management of the child with OME can be found in the evidence-based guideline from the AAP/AAFP/American Academy of Otolaryngology-Head and Neck Surgery published in 2004.[84,85]

Key Action Statement 5A

Clinicians should *NOT* prescribe prophylactic antibiotics to reduce the frequency of episodes of AOM in children with recurrent AOM. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Key Action Statement Profile: KAS 5A

Aggregate evidence quality	Grade B
Benefits	No adverse effects from antibiotic. Reduces potential for development of bacterial resistance. Reduced costs.
Risks, harms, cost	Small increase in episodes of AOM.
Benefit-harm assessment	Preponderance of benefit.
Value judgments	Potential harm outweighs the potential benefit.
Intentional vagueness	None.
Role of patient preferences	Limited.
Exclusions	Young children whose only alternative would be tympanostomy tubes.
Strength	**Recommendation**

Key Action Statement 5B

Clinicians may offer tympanostomy tubes for recurrent AOM (3 episodes in 6 months or 4 episodes in 1 year, with 1 episode in the preceding 6 months). (Evidence Quality: Grade B, Rec. Strength: Option)

Key Action Statement Profile: KAS 5B

Aggregate evidence quality	**Grade B**
Benefits	Decreased frequency of AOM. Ability to treat AOM with topical antibiotic therapy.
Risks, harms, cost	Risks of anesthesia or surgery. Cost. Scarring of TM, chronic perforation, cholesteatoma. Otorrhea.
Benefits-harms assessment	Equilibrium of benefit and harm.
Value judgments	None.
Intentional vagueness	Option based on limited evidence.
Role of patient preferences	Joint decision of parent and clinician.
Exclusions	Any contraindication to anesthesia and surgery.
Strength	**Option**

Purpose of This Section

Recurrent AOM has been defined as the occurrence of 3 or more episodes of AOM in a 6-month period or the occurrence of 4 or more episodes of AOM in a 12-month period that includes at least 1 episode in the preceding 6 months.[20] These episodes should be well documented and separate acute infections.[11]

Winter season, male gender, and passive exposure to smoking have been associated with an increased likelihood of recurrence. Half of children younger than 2 years treated for AOM will experience a recurrence within 6 months. Symptoms that last more than 10 days may also predict recurrence.[196]

Changes From AAP/AAFP 2004 AOM Guideline

Recurrent AOM was not addressed in the 2004 AOM guideline. This section addresses the literature on recurrent AOM.

Antibiotic Prophylaxis

Long-term, low-dose antibiotic use, referred to as antibiotic prophylaxis or chemoprophylaxis, has been used to treat children with recurrent AOM to prevent subsequent episodes.[85] A 2006 Cochrane review analyzed 16 studies of long-term antibiotic use for AOM and found such use prevented 1.5 episodes of AOM per year, reducing in half the number of AOM episodes during the period of treatment.[197] Randomized placebo-controlled trials of prophylaxis reported a decrease of 0.09 episodes per month in the frequency of AOM attributable to therapy (approximately 0.5 to 1.5 AOM episodes per year for 95% of children). An estimated 5 children would need to be treated for 1 year to prevent 1 episode of OM. The effect may be more substantial for children with 6 or more AOM episodes in the preceding year.[12]

This decrease in episodes of AOM occurred only while the prophylactic antibiotic was being given. The modest benefit afforded by a 6-month course of antibiotic prophylaxis does not have longer-lasting benefit after cessation of therapy. Teele showed no differences between children who received prophylactic antibiotics compared with those who received placebo in AOM recurrences or persistence of OME.[198]

Antibiotic prophylaxis is not appropriate for children with long-term MEE or for children with infrequent episodes of AOM. The small reduction in frequency of AOM with long-term antibiotic prophylaxis must be weighed against the cost of such therapy; the potential adverse effects of antibiotics, principally allergic reaction and gastrointestinal tract consequences, such as diarrhea; and their contribution to the emergence of bacterial resistance.

Surgery for Recurrent AOM

The use of tympanostomy tubes for treatment of ear disease in general, and for AOM in particular, has been controversial.[199] Most published studies of surgical intervention for OM focus on children with persistent MEE with or without AOM. The literature on surgery for recurrent AOM as defined here is scant. A lack of consensus among otolaryngologists regarding the role of surgery for recurrent AOM was reported in a survey of Canadian otolaryngologists in which 40% reported they would "never," 30% reported they would "sometimes," and 30% reported they would "often or always" place tympanostomy tubes for a hypothetical 2-year-old child with frequent OM without persistent MEE or hearing loss.[200]

Tympanostomy tubes, however, remain widely used in clinical practice for both OME and recurrent OM.[201] Recurrent

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

AOM remains a common indication for referral to an otolaryngologist.

Three randomized controlled trials have compared the number of episodes of AOM after tympanostomy tube placement or no surgery.[202] Two found significant improvement in mean number of AOM episodes after tympanostomy tubes during a 6-month follow-up period.[203,204] One study randomly assigned children with recurrent AOM to groups receiving placebo, amoxicillin prophylaxis, or tympanostomy tubes and followed them for 2 years.[205] Although prophylactic antibiotics reduced the rate of AOM, no difference in number of episodes of AOM was noted between the tympanostomy tube group and the placebo group over 2 years. A Cochrane review of studies of tympanostomy tubes for recurrent AOM analyzed 2 studies[204,206] that met inclusion criteria and found that tympanostomy tubes reduced the number of episodes of AOM by 1.5 episodes in the 6 months after surgery.[207] Tympanostomy tube insertion has been shown to improve disease-specific quality-of-life measures in children with OM.[208] One multicenter, nonrandomized observational study showed large improvements in a disease-specific quality-of-life instrument that measured psychosocial domains of physical suffering, hearing loss, speech impairment, emotional distress, activity limitations, and caregiver concerns that are associated with ear infections.[209] These benefits of tympanostomy tubes have been demonstrated in mixed populations of children that include children with OME as well as recurrent AOM.

Beyond the cost, insertion of tympanostomy tubes is associated with a small but finite surgical and anesthetic risk. A recent review looking at protocols to minimize operative risk reported no major complications, such as sensorineural hearing loss, vascular injury, or ossicular chain disruption, in 10 000 tube insertions performed primarily by residents, although minor complications such as TM tears or displaced tubes in the middle ear were seen in 0.016% of ears.[210] Long-term sequelae of tympanostomy tubes include TM structural changes including focal atrophy, tympanosclerosis, retraction pockets, and chronic perforation. One meta-analysis found tympanosclerosis in 32% of patients after placement of tympanostomy tubes and chronic perforations in 2.2% of patients who had short-term tubes and 16.6% of patients with long-term tubes.[211]

Adenoidectomy, without myringotomy and/or tympanostomy tubes, did not reduce the number of episodes of AOM when compared with chemoprophylaxis or placebo.[212] Adenoidectomy alone should not be used for prevention of AOM but may have benefit when performed with placement of tympanostomy tubes or in children with previous tympanostomy tube placement in OME.[213]

Prevention of AOM: Key Action Statement 6A

Pneumococcal Vaccine

Clinicians should recommend pneumococcal conjugate vaccine to all children according to the schedule of the Advisory Committee on Immunization Practices, AAP, and AAFP. (Evidence Quality: Grade B, Rec. Strength: Strong Recommendation)

Key Action Statement Profile: KAS 6A

Aggregate evidence quality	Grade B
Benefits	Reduced frequency of AOM attributable to vaccine serotypes. Reduced risk of serious pneumococcal systemic disease.
Risks, harms, cost	Potential vaccine side effects. Cost of vaccine.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Potential vaccine adverse effects are minimal.
Intentional vagueness	None.
Role of patient preferences	Some parents may choose to refuse the vaccine.
Exclusions	Severe allergic reaction (eg, anaphylaxis) to any component of pneumococcal vaccine or any diphtheria toxoid-containing vaccine.
Strength	**Strong Recommendation**

Key Action Statement 6B

Influenza Vaccine: Clinicians should recommend annual influenza vaccine to all children according to the schedule of the Advisory Committee on Immunization Practices, AAP, and AAFP. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 6B

Aggregate evidence quality	Grade B
Benefits	Reduced risk of influenza infection. Reduction in frequency of AOM associated with influenza.
Risks, harms, cost	Potential vaccine adverse effects. Cost of vaccine. Requires annual immunization.
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Potential vaccine adverse effects are minimal.
Intentional vagueness	None
Role of patient preferences	Some parents may choose to refuse the vaccine.
Exclusions	See CDC guideline on contraindications (http://www.cdc.gov/flu/professionals/acip/shouldnot.htm).
Strength	**Recommendation**

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Key Action Statement 6C

Breastfeeding: Clinicians should encourage exclusive breastfeeding for at least 6 months. (Evidence Quality: Grade B, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 6C

Aggregate evidence quality	Grade B
Benefits	May reduce the risk of early AOM. Multiple benefits of breastfeeding unrelated to AOM.
Risk, harm, cost	None
Benefit-harm assessment	Preponderance of benefit.
Value judgments	The intervention has value unrelated to AOM prevention.
Intentional vagueness	None
Role of patient preferences	Some parents choose to feed formula.
Exclusions	None
Strength	**Recommendation**

Key Action Statement 6D

Clinicians should encourage avoidance of tobacco smoke exposure. (Evidence Quality: Grade C, Rec. Strength: Recommendation)

Key Action Statement Profile: KAS 6D

Aggregate evidence quality	Grade C
Benefits	May reduce the risk of AOM.
Risks, harms, cost	None
Benefits-harms assessment	Preponderance of benefit.
Value judgments	Avoidance of tobacco exposure has inherent value unrelated to AOM.
Intentional vagueness	None
Role of patient preferences	Many parents/caregivers choose not to stop smoking. Some also remain addicted, and are unable to quit smoking.
Exclusions	None
Strength	**Recommendation**

Purpose of This Section

The 2004 AOM guideline noted data on immunizations, breastfeeding, and lifestyle changes that would reduce the risk of acquiring AOM. This section addresses new data published since 2004.

Changes From AAP/AAFP 2004 AOM Guideline

PCV7 has been in use in the United States since 2000. PCV13 was introduced in the United States in 2010. The 10-valent pneumococcal nontypeable *H influenzae* protein D-conjugate vaccine was recently licensed in Europe for prevention of diseases attributable to *S pneumoniae* and nontypeable *H influenzae*. Annual influenza immunization is now recommended for all children 6 months of age and older in the United States.[214,215] Updated information regarding these vaccines and their effect on the incidence of AOM is reviewed.

The AAP issued a new breastfeeding policy statement in February 2012.[216] This guideline also includes a recommendation regarding tobacco smoke exposure. Bottle propping, pacifier use, and child care are discussed, but no recommendations are made because of limited evidence. The use of xylitol, a possible adjunct to AOM prevention, is discussed; however, no recommendations are made.

Pneumococcal Vaccine

Pneumococcal conjugate vaccines have proven effective in preventing OM caused by pneumococcal serotypes contained in the vaccines. A meta-analysis of 5 studies with AOM as an outcome determined that there is a 29% reduction in AOM caused by all pneumococcal serotypes among children who received PCV7 before 24 months of age.[217] Although the overall benefit seen in clinical trials for all causes of AOM is small (6%–7%),[218–221] observational studies have shown that medical office visits for otitis were reduced by up to 40% comparing years before and after introduction of PCV7.[222–224] Grijvala[223] reported no effect, however, among children first vaccinated at older ages. Poehling et al[225] reported reductions of frequent AOM and PE tube use after introduction of PCV7. The observations by some of greater benefit observed in the community than in clinical trials is not fully understood but may be related to effects of herd immunity or may be attributed to secular trends or changes in AOM diagnosis patterns over time.[223,226–229] In a 2009 Cochrane review,[221] Jansen et al found that the overall reduction in AOM incidence may only be 6% to 7% but noted that even that small rate may have public health relevance. O'Brien et al concurred and noted in addition the potential for cost savings.[230] There is evidence that serotype replacement may reduce the long-term efficacy of pneumococcal conjugate vaccines against AOM,[231] but it is possible that new pneumococcal conjugate vaccines may demonstrate an increased effect on reduction in AOM.[232–234] Data on AOM reduction secondary to the PCV13 licensed in the United States in 2010 are not yet available.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

The *H influenzae* protein D-conjugate vaccine recently licensed in Europe has potential benefit of protection against 10 serotypes of *S pneumoniae* and nontypeable *H influenzae*.[221,234]

Influenza Vaccine

Most cases of AOM follow upper respiratory tract infections caused by viruses, including influenza viruses. As many as two-thirds of young children with influenza may have AOM.[235] Investigators have studied the efficacy of trivalent inactivated influenza vaccine (TIV) and live-attenuated intranasal influenza vaccine (LAIV) in preventing AOM. Many studies have demonstrated 30% to 55% efficacy of influenza vaccine in prevention of AOM during the respiratory illness season.[6,235–239] One study reported no benefit of TIV in reducing AOM burden; however, 1 of the 2 respiratory illness seasons during which this study was conducted had a relatively low influenza activity. A pooled analysis[240] of 8 studies comparing LAIV versus TIV or placebo[241–248] showed a higher efficacy of LAIV compared with both placebo and with TIV. Influenza vaccination is now recommended for all children 6 months of age and older in the United States.[214,215]

Breastfeeding

Multiple studies provide evidence that breastfeeding for at least 4 to 6 months reduces episodes of AOM and recurrent AOM.[249–253] Two cohort studies, 1 retrospective study[250] and 1 prospective study,[253] suggest a dose response, with some protection from partial breastfeeding and the greatest protection from exclusive breastfeeding through 6 months of age. In multivariate analysis controlling for exposure to child care settings, the risk of nonrecurrent otitis is 0.61 (95% confidence interval [CI]: 0.4–0.92) comparing exclusive breastfeeding through 6 months of age with no breastfeeding or breastfeeding less than 4 months. In a prospective cohort, Scariatti[253] found a significant dose-response effect. In this study, OM was self-reported by parents. In a systematic review, McNiel et al[254] found that when exclusive breastfeeding was set as the normative standard, the recalculated odds ratios (ORs) revealed the risks of any formula use. For example, any formula use in the first 6 months of age was significantly associated with increased incidence of OM (OR: 1.78; 95% CI: 1.19–2.70; OR: 4.55; 95% CI: 1.64–12.50 in the available studies; pooled OR for any formula in the first 3 months of age, 2.00; 95% CI: 1.40–2.78). A number of studies[255–259] addressed the association of AOM and other infectious illness in infants with duration and exclusivity of breastfeeding, but all had limitations and none had a randomized controlled design. However, taken together, they continue to show a protective effect of exclusive breastfeeding. In all studies, there has been a predominance of white subjects, and child care attendance and smoking exposure may not have been completely controlled. Also, feeding methods were self-reported.

The consistent finding of a lower incidence of AOM and recurrent AOM with increased breastfeeding supports the AAP recommendation to encourage exclusive breastfeeding for the first 6 months of life and to continue for at least the first year and beyond for as long as mutually desired by mother and child.[216]

Lifestyle Changes

In addition to its many other benefits,[260] eliminating exposure to passive tobacco smoke has been postulated to reduce the incidence of AOM in infancy.[252,261–264] Bottles and pacifiers have been associated with AOM. Avoiding supine bottle feeding ("bottle propping") and reducing or eliminating pacifier use in the second 6 months of life may reduce AOM incidence.[265–267] In a recent cohort study, pacifier use was associated with AOM recurrence.[268]

During infancy and early childhood, reducing the incidence of upper respiratory tract infections by altering child care-center attendance patterns can reduce the incidence of recurrent AOM significantly.[249,269]

Xylitol

Xylitol, or birch sugar, is chemically a pentitol or 5-carbon polyol sugar alcohol. It is available as chewing gum, syrup, or lozenges. A 2011 Cochrane review[270] examined the evidence for the use of xylitol in preventing recurrent AOM. A statistically significant 25% reduction in the risk of occurrence of AOM among healthy children at child care centers in the xylitol group compared with the control group (relative risk: 0.75; 95% CI: 0.65 to 0.88; RD: –0.07; 95% CI: –0.12 to –0.03) in the 4 studies met criteria for analysis.[271–274] Chewing gum and lozenges containing xylitol appeared to be more effective than syrup. Children younger than 2 years, those at the greatest risk of having AOM, cannot safely use lozenges or chewing gum. Also, xylitol needs to be given 3 to 5 times a day to be effective. It is not effective for treating AOM and it must be taken daily throughout the respiratory illness season to have an effect. Sporadic or as-needed use is not effective.

Future Research

Despite advances in research partially stimulated by the 2004 AOM guideline, there are still many unanswered clinical questions in the field. Following are possible clinical research questions that still need to be resolved.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Diagnosis

There will probably never be a gold standard for diagnosis of AOM because of the continuum from OME to AOM. Conceivably, new techniques that could be used on the small amount of fluid obtained during tympanocentesis could identify inflammatory markers in addition to the presence of bacteria or viruses. However, performing tympanocentesis studies on children with uncomplicated otitis is likely not feasible because of ethical and other considerations.

Devices that more accurately identify the presence of MEE and bulging that are easier to use than tympanometry during office visits would be welcome, especially in the difficult-to-examine infant. Additional development of inexpensive, easy-to-use video pneumatic otoscopes is still a goal.

Initial Treatment

The recent studies of Hoberman[31] and Tähtinen[32] have addressed clinical and TM appearance by using stringent diagnostic criteria of AOM. However, the outcomes for less stringent diagnostic criteria, a combination of symptoms, MEE, and TM appearance not completely consistent with OME can only be inferred from earlier studies that used less stringent criteria but did not specify outcomes for various grades of findings. Randomized controlled trials on these less certain TM appearances using scales similar to the OS-8 scale[35] could clarify the benefit of initial antibiotics and initial observation for these less certain diagnoses. Such studies must also specify severity of illness, laterality, and otorrhea.

Appropriate end points must be established. Specifically is the appearance of the TM in patients without clinical symptoms at the end of a study significant for relapse, recurrence, or persistent MEE. Such a study would require randomization of patients with unimproved TM appearance to continued observation and antibiotic groups.

The most efficient and acceptable methods of initial observation should continue to be studied balancing the convenience and benefits with the potential risks to the patient.

Antibiotics

Amoxicillin-clavulanate has a broader spectrum than amoxicillin and may be a better initial antibiotic. However, because of cost and adverse effects, the subcommittee has chosen amoxicillin as first-line AOM treatment. Randomized controlled trials comparing the 2 with adequate power to differentiate clinical efficacy would clarify this choice. Stringent diagnostic criteria should be the standard for these studies. Antibiotic comparisons for AOM should now include an observation arm for patients with nonsevere illness to ensure a clinical benefit over placebo. Studies should also have enough patients to show small but meaningful differences.

Although there have been studies on the likelihood of resistant *S pneumoniae* or *H influenzae* in children in child care settings and with siblings younger than 5 years, studies are still needed to determine whether these and other risk factors would indicate a need for different initial treatment than noted in the guideline.

New antibiotics that are safe and effective are needed for use in AOM because of the development of multidrug-resistant organisms. Such new antibiotics must be tested against the currently available medications.

Randomized controlled trials using different durations of antibiotic therapy in different age groups are needed to optimize therapy with the possibility of decreasing duration of antibiotic use. These would need to be performed initially with amoxicillin and amoxicillin-clavulanate but should also be performed for any antibiotic used in AOM. Again, an observation arm should be included in nonsevere illness.

Recurrent AOM

There have been adequate studies regarding prophylactic antibiotic use in recurrent AOM. More and better controlled studies of tympanostomy tube placement would help determine its benefit versus harm.

Prevention

There should be additional development of vaccines targeted at common organisms associated with AOM.[275] Focused epidemiologic studies on the benefit of breastfeeding, specifically addressing AOM prevention, including duration of breastfeeding and partial versus exclusive breastfeeding, would clarify what is now a more general database. Likewise, more focused studies of the effects of lifestyle changes would help clarify their effect on AOM.

Complementary and Alternative Medicine

There are no well-designed randomized controlled trials of the usefulness of complementary and alternative medicine in AOM, yet a large number of families turn to these methods. Although most alternative therapies are relatively inexpensive, some may be costly. Such studies should compare the alternative therapy to observation rather than antibiotics and only use an antibiotic arm if the alternative therapy is shown to be better than observation. Such studies should focus on children with less stringent criteria of AOM but using the same descriptive criteria for the patients as noted above.

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

DISSEMINATION OF GUIDELINES

An Institute of Medicine Report notes that "Effective multifaceted implementation strategies targeting both individuals and healthcare systems should be employed by implementers to promote adherence to trustworthy [clinical practice guidelines]."[230]

Many studies of the effect of clinical practice guidelines have been performed. In general, the studies show little overt change in practice after a guideline is published. However, as was seen after the 2004 AOM guideline, the number of visits for AOM and the number of prescriptions for antibiotics for AOM had decreased publication. Studies of educational and dissemination methods both at the practicing physician level and especially at the resident level need to be examined.

SUBCOMMITTEE ON DIAGNOSIS AND MANAGEMENT OF ACUTE OTITIS MEDIA

Allan S. Lieberthal, MD, FAAP (Chair, general pediatrician, no conflicts)

Aaron E. Carroll, MD, MS, FAAP (Partnership for Policy Implementation [PPI] Informatician, general academic pediatrician, no conflicts)

Tasnee Chonmaitree, MD, FAAP (pediatric infectious disease physician, no financial conflicts; published research related to AOM)

Theodore G. Ganiats, MD (family physician, American Academy of Family Physicians, no conflicts)

Alejandro Hoberman, MD, FAAP (general academic pediatrician, no financial conflicts; published research related to AOM)

Mary Anne Jackson, MD, FAAP (pediatric infectious disease physician, AAP Committee on Infectious Disease, no conflicts)

Mark D. Joffe, MD, FAAP (pediatric emergency medicine physician, AAP Committee/Section on Pediatric Emergency Medicine, no conflicts)

Donald T. Miller, MD, MPH, FAAP (general pediatrician, no conflicts)

Richard M. Rosenfeld, MD, MPH, FAAP (otolaryngologist, AAP Section on Otolaryngology, Head and Neck Surgery, American Academy of Otolaryngology-Head and Neck Surgery, no financial conflicts; published research related to AOM)

Xavier D. Sevilla, MD, FAAP (general pediatrics, Quality Improvement Innovation Network, no conflicts)

Richard H. Schwartz, MD, FAAP (general pediatrician, no financial conflicts; published research related to AOM)

Pauline A. Thomas, MD, FAAP (epidemiologist, general pediatrician, no conflicts)

David E. Tunkel, MD, FAAP, FACS (otolaryngologist, AAP Section on Otolaryngology, Head and Neck Surgery, periodic consultant to Medtronic ENT)

CONSULTANT

Richard N. Shiffman, MD, FAAP, FACMI (informatician, guideline methodologist, general academic pediatrician, no conflicts)

STAFF

Caryn Davidson, MA

Oversight by the Steering Committee on Quality Improvement and Management, 2009–2012

REFERENCES

1. American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics*. 2004;113(5):1451–1465
2. Grijalva CG, Nuorti JP, Griffin MR. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA*. 2009;302(7):758–766
3. McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA*. 2002;287(23):3096–3102
4. Vernacchio L, Vezina RM, Mitchell AA. Management of acute otitis media by primary care physicians: trends since the release of the 2004 American Academy of Pediatrics/American Academy of Family Physicians clinical practice guideline. *Pediatrics*. 2007;120(2):281–287
5. Coco A, Vernacchio L, Horst M, Anderson A. Management of acute otitis media after publication of the 2004 AAP and AAFP clinical practice guideline. *Pediatrics*. 2010;125(2):214–220
6. Marchisio P, Mira E, Klersy C, et al. Medical education and attitudes about acute otitis media guidelines: a survey of Italian pediatricians and otolaryngologists. *Pediatr Infect Dis J*. 2009;28(1):1–4
7. Arkins ER, Koehler JM. Use of the observation option and compliance with guidelines in treatment of acute otitis media. *Ann Pharmacother*. 2008;42(5):726–727
8. Flores G, Lee M, Bauchner H, Kastner B. Pediatricians' attitudes, beliefs, and practices regarding clinical practice guidelines: a national survey. *Pediatrics*. 2000;105(3 pt 1):496–501
9. Bluestone CD. Definitions, terminology, and classification. In: Rosenfeld RM, Bluestone CD, eds. *Evidence-Based Otitis Media*. Hamilton, Canada: BC Decker; 2003:120–135
10. Bluestone CD, Klein JO. Definitions, terminology, and classification. In: Bluestone CD, Klein JO, eds. *Otitis Media in Infants and Children*. 4th ed. Hamilton, Canada: BC Decker; 2007:1–19
11. Dowell SF, Marcy MS, Phillips WR, et al. Otitis media: principles of judicious use of antimicrobial agents. *Pediatrics*. 1998;101(suppl):165–171
12. Rosenfeld RM. Clinical pathway for acute otitis media. In: Rosenfeld RM, Bluestone CD, eds. *Evidence-Based Otitis Media*. 2nd ed. Hamilton, Canada: BC Decker; 2003:280–302
13. Carlson LH, Carlson RD. Diagnosis. In: Rosenfeld RM, Bluestone CD, eds. *Evidence-Based Otitis Media*. Hamilton, Canada: BC Decker; 2003: 136–146
14. Bluestone CD, Klein JO. Diagnosis. In: *Otitis Media in Infants and Children*. 4th ed. Hamilton, Canada: BC Decker; 2007:147–212
15. University of Oxford, Centre for Evidence Based Medicine. Available at: www.cebm.net/index.aspx?o=1044. Accessed July 17, 2012
16. American Academy of Pediatrics Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. *Pediatrics*. 2004;114(3):874–877
17. Marcy M, Takata G, Shekelle P, et al. *Management of Acute Otitis Media*. Evidence Report/Technology Assessment No. 15. Rockville, MD: Agency for Healthcare Research and Quality; 2000

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

18. Chan LS, Takata GS, Shekelle P, Morton SC, Mason W, Marcy SM. Evidence assessment of management of acute otitis media: II. Research gaps and priorities for future research. *Pediatrics*. 2001;108(2):248–254
19. Takata GS, Chan LS, Shekelle P, Morton SC, Mason W, Marcy SM. Evidence assessment of management of acute otitis media: I. The role of antibiotics in treatment of uncomplicated acute otitis media. *Pediatrics*. 2001;108(2):239–247
20. Shekelle PG, Takata G, Newberry SJ, et al. *Management of Acute Otitis Media: Update*. Evidence Report/Technology Assessment No. 198. Rockville, MD: Agency for Healthcare Research and Quality; 2010
21. Coker TR, Chan LS, Newberry SJ, et al. Diagnosis, microbial epidemiology, and antibiotic treatment of acute otitis media in children: a systematic review. *JAMA*. 2010;304(19):2161–2169
22. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials*. 1996;17(1):1–12
23. Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol*. 2003;3:25
24. Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924–926
25. Hoffman RN, Michel G, Rosenfeld RM, Davidson C. Building better guidelines with BRIDGE-Wiz: development and evaluation of a software assistant to promote clarity, transparency, and implementability. *J Am Med Inform Assoc*. 2012;19(1):94–101
26. Kalu SU, Ataya RS, McCormick DP, Patel JA, Revai K, Chonmaitree T. Clinical spectrum of acute otitis media complicating upper respiratory tract viral infection. *Pediatr Infect Dis J*. 2011;30(2):95–99
27. Block SL, Harrison CJ. *Diagnosis and Management of Acute Otitis Media*. 3rd ed. Caddo, OK: Professional Communications; 2005:48–50
28. Wald ER. Acute otitis media: more trouble with the evidence. *Pediatr Infect Dis J*. 2003;22(2):103–104
29. 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(3):318–333
30. McCormick DP, Chonmaitree T, Pittman C, et al. Nonsevere acute otitis media: a clinical trial comparing outcomes of watchful waiting versus immediate antibiotic treatment. *Pediatrics*. 2005;115(6):1455–1465
31. Hoberman A, Paradise JL, Rockette HE, et al. Treatment of acute otitis media in children under 2 years of age. *N Engl J Med*. 2011;364(2):105–115
32. Tähtinen PA, Laine MK, Huovinen P, Jalava J, Ruuskanen O, Ruohola A. A placebo-controlled trial of antimicrobial treatment for acute otitis media. *N Engl J Med*. 2011;364(2):116–126
33. Shaikh N, Hoberman A, Paradise JL, et al. Development and preliminary evaluation of a parent-reported outcome instrument for clinical trials in acute otitis media. *Pediatr Infect Dis J*. 2009;28(1):5–8
34. Laine MK, Tähtinen PA, Ruuskanen O, Huovinen P, Ruohola A. Symptoms or symptom-based scores cannot predict acute otitis media at otitis-prone age. *Pediatrics*. 2010;125(5). Available at: www.pediatrics.org/cgi/content/full/125/5/e1154
35. Friedman NR, McCormick DP, Pittman C, et al. Development of a practical tool for assessing the severity of acute otitis media. *Pediatr Infect Dis J*. 2006;25(2):101–107
36. Rothman R, Owens T, Simel DL. Does this child have acute otitis media? *JAMA*. 2003;290(12):1633–1640
37. Niemela M, Uhari M, Jounio-Ervasti K, Luotonen J, Alho OP, Vierimaa E. Lack of specific symptomatology in children with acute otitis media. *Pediatr Infect Dis J*. 1994;13(9):765–768
38. Heikkinen T, Ruuskanen O. Signs and symptoms predicting acute otitis media. *Arch Pediatr Adolesc Med*. 1995;149(1):26–29
39. Ingvarsson L. Acute otalgia in children—findings and diagnosis. *Acta Paediatr Scand*. 1982;71(5):705–710
40. Kontiokari T, Koivunen P, Niemelä M, Pokka T, Uhari M. Symptoms of acute otitis media. *Pediatr Infect Dis J*. 1998;17(8):676–679
41. Wong DL, Baker CM. Pain in children: comparison of assessment scales. *Pediatr Nurs*. 1988;14(1):9–17
42. Shaikh N, Hoberman A, Paradise JL, et al. Responsiveness and construct validity of a symptom scale for acute otitis media. *Pediatr Infect Dis J*. 2009;28(1):9–12
43. Karma PH, Penttilä MA, Sipilä MM, Kataja MJ. Otoscopic diagnosis of middle ear effusion in acute and non-acute otitis media. I. The value of different otoscopic findings. *Int J Pediatr Otorhinolaryngol*. 1989;17(1):37–49
44. McCormick DP, Lim-Melia E, Saeed K, Baldwin CD, Chonmaitree T. Otitis media: can clinical findings predict bacterial or viral etiology? *Pediatr Infect Dis J*. 2000;19(3):256–258
45. Schwartz RH, Stool SE, Rodriguez WJ, Grundfast KM. Acute otitis media: toward a more precise definition. *Clin Pediatr (Phila)*. 1981;20(9):549–554
46. Rosenfeld RM. Antibiotic prophylaxis for recurrent acute otitis media. In: Alper CM, Bluestone CD, eds. *Advanced Therapy of Otitis Media*. Hamilton, Canada: BC Decker; 2004
47. Paradise J, Bernard B, Colborn D, Smith C, Rockette H; Pittsburgh-area Child Development/Otitis Media Study Group. Otitis media with effusion: highly prevalent and often the forerunner of acute otitis media during the first year of life [abstract]. *Pediatr Res*. 1993;33:121A
48. Roland PS, Smith TL, Schwartz SR, et al. Clinical practice guideline: cerumen impaction. *Otolaryngol Head Neck Surg*. 2008;139(3 suppl 2):S1–S21
49. Shaikh N, Hoberman A, Kaleida PH, Ploof DL, Paradise JL. Videos in clinical medicine. Diagnosing otitis media—otoscopy and cerumen removal. *N Engl J Med*. 2010;362(20):e62
50. Pichichero ME. Diagnostic accuracy, tympanocentesis training performance, and antibiotic selection by pediatric residents in management of otitis media. *Pediatrics*. 2002;110(6):1064–1070
51. Kaleida PH, Ploof DL, Kurs-Lasky M, et al. Mastering diagnostic skills: Enhancing Proficiency in Otitis Media, a model for diagnostic skills training. *Pediatrics*. 2009;124(4). Available at: www.pediatrics.org/cgi/content/full/124/4/e714
52. Kaleida PH, Ploof D. ePROM: Enhancing Proficiency in Otitis Media. Pittsburgh, PA: University of Pittsburgh School of Medicine. Available at: http://pedsed.pitt.edu. Accessed December 31, 2011
53. Innovative Medical Education. *A View Through the Otoscope: Distinguishing Acute Otitis Media from Otitis Media with Effusion*. Paramus, NJ: Innovative Medical Education; 2000
54. American Academy of Pediatrics. Section on Infectious Diseases. A view through the otoscope: distinguishing acute otitis media from otitis media with effusion [video]. Available at: http://www2.aap.org/sections/infectdis/video.cfm. Accessed January 20, 2012
55. Hayden GF, Schwartz RH. Characteristics of earache among children with acute

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

otitis media. *Am J Dis Child*. 1985;139(7): 721–723

56. Schechter NL. Management of pain associated with acute medical illness. In: Schechter NL, Berde CB, Yaster M, eds. *Pain in Infants, Children, and Adolescents*. Baltimore, MD: Williams & Wilkins; 1993: 537–538
57. Rovers MM, Glasziou P, Appelman CL, et al. Predictors of pain and/or fever at 3 to 7 days for children with acute otitis media not treated initially with antibiotics: a meta-analysis of individual patient data. *Pediatrics*. 2007;119(3):579–585
58. Burke P, Bain J, Robinson D, Dunleavey J. Acute red ear in children: controlled trial of nonantibiotic treatment in children: controlled trial of nonantibiotic treatment in general practice. *BMJ*. 1991;303(6802): 558–562
59. Sanders S, Glasziou PP, DelMar C, Rovers M. Antibiotics for acute otitis media in children [review]. *Cochrane Database Syst Rev*. 2009;(2):1–43
60. van Buchem FL, Dunk JH, van't Hof MA. Therapy of acute otitis media: myringotomy, antibiotics, or neither? A double-blind study in children. *Lancet*. 1981;2(8252): 883–887
61. Thalin A, Densert O, Larsson A, et al. Is penicillin necessary in the treatment of acute otitis media? In: *Proceedings of the International Conference on Acute and Secretory Otitis Media. Part 1*. Amsterdam, Netherlands: Kugler Publications; 1986:441–446
62. Rovers MM, Glasziou P, Appelman CL, et al. Antibiotics for acute otitis media: an individual patient data meta-analysis. *Lancet*. 2006;368(9545):1429–1435
63. Bertin L, Pons G, d'Athis P, et al. A randomized, double-blind, multicentre controlled trial of ibuprofen versus acetaminophen and placebo for symptoms of acute otitis media in children. *Fundam Clin Pharmacol*. 1996;10(4):387–392
64. American Academy of Pediatrics. Committee on Psychosocial Aspects of Child and Family Health; Task Force on Pain in Infants, Children, and Adolescents. The assessment and management of acute pain in infants, children, and adolescents. *Pediatrics*. 2001;108(3): 793–797
65. Bolt P, Barnett P, Babl FE, Sharwood LN. Topical lignocaine for pain relief in acute otitis media: results of a double-blind placebo-controlled randomised trial. *Arch Dis Child*. 2008;93(1):40–44
66. Foxlee R, Johansson AC, Wejfalk J, Dawkins J, Dooley L, Del Mar C. Topical analgesia for acute otitis media. *Cochrane Database Syst Rev*. 2006;(3):CD005657
67. Hoberman A, Paradise JL, Reynolds EA, Urkin J. Efficacy of Auralgan for treating ear pain in children with acute otitis media. *Arch Pediatr Adolesc Med*. 1997; 151(7):675–678
68. Sarrell EM, Mandelberg A, Cohen HA. Efficacy of naturopathic extracts in the management of ear pain associated with acute otitis media. *Arch Pediatr Adolesc Med*. 2001;155(7):796–799
69. Sarrell EM, Cohen HA, Kahan E. Naturopathic treatment for ear pain in children. *Pediatrics*. 2003;111(5 pt 1):e574–e579
70. Adam D, Federspil P, Lukes M, Petrowicz O. Therapeutic properties and tolerance of procaine and phenazone containing ear drops in infants and very young children. *Arzneimittelforschung*. 2009;59(10):504–512
71. Barnett ED, Levatin JL, Chapman EH, et al. Challenges of evaluating homeopathic treatment of acute otitis media. *Pediatr Infect Dis J*. 2000;19(4):273–275
72. 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(2):177–183
73. Rosenfeld RM, Bluestone CD. Clinical efficacy of surgical therapy. In: Rosenfeld RM, Bluestone CD, eds. *Evidence-Based Otitis Media. 2003*. Hamilton, Canada: BC Decker; 2003:227–240
74. Rosenfeld RM. Observation option toolkit for acute otitis media. *Int J Pediatr Otorhinolaryngol*. 2001;58(1):1–8
75. Le Saux N, Gaboury I, Baird M, et al. A randomized, double-blind, placebo-controlled noninferiority trial of amoxicillin for clinically diagnosed acute otitis media in children 6 months to 5 years of age. *CMAJ*. 2005;172(3):335–341
76. Spiro DM, Tay KY, Arnold DH, Dziura JD, Baker MD, Shapiro ED. Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial. *JAMA*. 2006;296(10):1235–1241
77. Neumark T, Mölstad S, Rosén C, et al. Evaluation of phenoxymethylpenicillin treatment of acute otitis media in children aged 2–16. *Scand J Prim Health Care*. 2007;25(3):166–171
78. Chao JH, Kunkov S, Reyes LB, Lichten S, Crain EF. Comparison of two approaches to observation therapy for acute otitis media in the emergency department. *Pediatrics*. 2008;121(5). Available at: www.pediatrics.org/cgi/content/full/121/5/e1352
79. Spurling GK, Del Mar CB, Dooley L, Foxlee R. Delayed antibiotics for respiratory infections. *Cochrane Database Syst Rev*. 2007;(3):CD004417
80. Koopman L, Hoes AW, Glasziou PP, et al. Antibiotic therapy to prevent the development of asymptomatic middle ear effusion in children with acute otitis media: a meta-analysis of individual patient data. *Arch Otolaryngol Head Neck Surg*. 2008;134(2):128–132
81. Marchetti F, Ronfani L, Nibali SC, Tamburlini G; Italian Study Group on Acute Otitis Media. Delayed prescription may reduce the use of antibiotics for acute otitis media: a prospective observational study in primary care. *Arch Pediatr Adolesc Med*. 2005; 159(7):679–684
82. Ho D, Rotenberg BW, Berkowitz RG. The relationship between acute mastoiditis and antibiotic use for acute otitis media in children. *Arch Otolaryngol Head Neck Surg*. 2008;34(1):45–48
83. Thompson PL, Gilbert RE, Long PF, Saxena S, Sharland M, Wong IC. Effect of antibiotics for otitis media on mastoiditis in children: a retrospective cohort study using the United Kingdom general practice research database. *Pediatrics*. 2009; 123(2):424–430
84. American Academy of Family Physicians; American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. Otitis media with effusion. *Pediatrics*. 2004;113(5):1412–1429
85. Rosenfeld RM, Culpepper L, Doyle KJ, et al; American Academy of Pediatrics Subcommittee on Otitis Media with Effusion; American Academy of Family Physicians; American Academy of Otolaryngology—Head and Neck Surgery. Clinical practice guideline: otitis media with effusion. *Otolaryngol Head Neck Surg*. 2004;130(suppl 5): S95–S118
86. Appelman CL, Claessen JQ, Touw-Otten FW, Hordijk GJ, de Melker RA. Co-amoxiclav in recurrent acute otitis media: placebo controlled study. *BMJ*. 1991;303(6815): 1450–1452
87. Burke P, Bain J, Robinson D, Dunleavey J. Acute red ear in children: controlled trial of nonantibiotic treatment in children: controlled trial of nonantibiotic treatment in general practice. *BMJ*. 1991;303(6802): 558–562
88. van Balen FA, Hoes AW, Verheij TJ, de Melker RA. Primary care based randomized, double blind trial of amoxicillin versus placebo in children aged under 2 years. *BMJ*. 2000;320(7231):350–354

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

89. Little P, Gould C, Williamson I, Moore M, Warner G, Dunleavey J. Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. *BMJ*. 2001;322(7282):336–342
90. Mygind N, Meistrup-Larsen K-I, Thomsen J, Thomsen VF, Josefsson K, Sørensen H. Penicillin in acute otitis media: a double-blind placebo-controlled trial. *Clin Otolaryngol Allied Sci*. 1981;6(1):5–13
91. Kaleida PH, Casselbrant ML, Rockette HE, et al. Amoxicillin or myringotomy or both for acute otitis media: results of a randomized clinical trial. *Pediatrics*. 1991;87(4):466–474
92. Shaikh N, Hoberman A, Paradise JL, et al. Responsiveness and construct validity of a symptom scale for acute otitis media. *Pediatr Infect Dis J*. 2009;28(1):9–12
93. Heikkinen T, Chonmaitree T. Importance of respiratory viruses in acute otitis media. *Clin Microbiol Rev*. 2003;16(2):230–241
94. Halsted C, Lepow ML, Balassanian N, Emmerich J, Wolinsky E. Otitis media. Clinical observations, microbiology, and evaluation of therapy. *Am J Dis Child*. 1968;115(5):542–551
95. Rosenfeld RM, Vertrees J, Carr J, et al. Clinical efficacy of antimicrobials for acute otitis media: meta-analysis of 5,400 children from 33 randomized trials. *J Pediatr*. 1994;124(3):355–367
96. McCormick DP, Chandler SM, Chonmaitree T. Laterality of acute otitis media: different clinical and microbiologic characteristics. *Pediatr Infect Dis J*. 2007;26(7):583–588
97. Appelman CLM, Bossen PC, Dunk JHM, Lisdonk EH, de Melker RA, van Weert HCPM. NHG Standard Otitis Media Acuta (Guideline on acute otitis media of the Dutch College of General Practitioners). *Huisarts Wet*. 1990;33:242–245
98. Swedish Medical Research Council. Treatment for acute inflammation of the middle ear: consensus statement. Stockholm, Sweden: Swedish Medical Research Council; 2000. Available at: http://soapimg.icecube.snowfall.se/strama/Konsensut_ora_eng.pdf. Accessed July 18, 2012
99. Scottish Intercollegiate Guideline Network. Diagnosis and management of childhood otitis media in primary care. Edinburgh, Scotland: Scottish Intercollegiate Guideline Network; 2000. Available at: www.sign.ac.uk/guidelines/fulltext/66/index.html. Accessed July 18, 2012
100. National Institute for Health and Clinical Excellence, Centre for Clinical Practice. Respiratory tract infections—antibiotic prescribing: prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. NICE Clinical Guideline 69. London, United Kingdom: National Institute for Health and Clinical Excellence; July 2008. Available at: www.nice.org.uk/CG069. Accessed July 18, 2012
101. Marchisio P, Bellussi L, Di Mauro G, et al. Acute otitis media: from diagnosis to prevention. Summary of the Italian guideline. *Int J Pediatr Otorhinolaryngol*. 2010;74(11):1209–1216
102. Siegel RM, Kiely M, Bien JP, et al. Treatment of otitis media with observation and a safety-net antibiotic prescription. *Pediatrics*. 2003;112(3 pt 1):527–531
103. Pshetizky Y, Naimer S, Shvartzman P. Acute otitis media—a brief explanation to parents and antibiotic use. *Fam Pract*. 2003;20(4):417–419
104. Pichichero ME, Casey JR. Emergence of a multiresistant serotype 19A pneumococcal strain not included in the 7-valent conjugate vaccine as an otopathogen in children. *JAMA*. 2007;298(15):1772–1778
105. Pichichero ME, Casey JR. Evolving microbiology and molecular epidemiology of acute otitis media in the pneumococcal conjugate vaccine era. *Pediatr Infect Dis J*. 2007;26(suppl 10):S12–S16
106. Nielsen HUK, Konradsen HB, Lous J, Frimodt-Møller N. Nasopharyngeal pathogens in children with acute otitis media in a low-antibiotic use country. *Int J Pediatr Otorhinolaryngol*. 2004;68(9):1149–1155
107. Pitkäranta A, Virolainen A, Jero J, Arruda E, Hayden FG. Detection of rhinovirus, respiratory syncytial virus, and coronavirus infections in acute otitis media by reverse transcriptase polymerase chain reaction. *Pediatrics*. 1998;102(2 pt 1):291–295
108. Heikkinen T, Thint M, Chonmaitree T. Prevalence of various respiratory viruses in the middle ear during acute otitis media. *N Engl J Med*. 1999;340(4):260–264
109. Chonmaitree T. Acute otitis media is not a pure bacterial disease. *Clin Infect Dis*. 2006;43(11):1423–1425
110. Williams JV, Tollefson SJ, Nair S, Chonmaitree T. Association of human metapneumovirus with acute otitis media. *Int J Pediatr Otorhinolaryngol*. 2006;70(7):1189–1193
111. Chonmaitree T, Heikkinen T. Role of viruses in middle-ear disease. *Ann N Y Acad Sci*. 1997;830:143–157
112. Klein JO, Bluestone CD. Otitis media. In: Feigin RD, Cherry JD, Demmler-Harrison GJ, Kaplan SL, eds. *Textbook of Pediatric Infectious Diseases*. 6th ed. Philadelphia, PA: Saunders; 2009:216–237
113. Chonmaitree T, Revai K, Grady JJ, et al. Viral upper respiratory tract infection and otitis media complication in young children. *Clin Infect Dis*. 2008;46(6):815–823
114. Ruohola A, Meurman O, Nikkari S, et al. Microbiology of acute otitis media in children with tympanostomy tubes: prevalences of bacteria and viruses. *Clin Infect Dis*. 2006;43(11):1417–1422
115. Ruuskanen O, Arola M, Heikkinen T, Ziegler T. Viruses in acute otitis media: increasing evidence for clinical significance. *Pediatr Infect Dis J*. 1991;10(6):425–427
116. Chonmaitree T. Viral and bacterial interaction in acute otitis media. *Pediatr Infect Dis J*. 2000;19(suppl 5):S24–S30
117. Nokso-Koivisto J, Räty R, Blomqvist S, et al. Presence of specific viruses in the middle ear fluids and respiratory secretions of young children with acute otitis media. *J Med Virol*. 2004;72(2):241–248
118. Bluestone CD, Klein JO. Microbiology. In: Bluestone CD, Klein JO, eds. *Otitis Media in Infants and Children*. 4th ed. Hamilton, Canada: BC Decker; 2007:101–126
119. Del Beccaro MA, Mendelman PM, Inglis AF, et al. Bacteriology of acute otitis media: a new perspective. *J Pediatr*. 1992;120(1):81–84
120. Block SL, Harrison CJ, Hedrick JA, et al. Penicillin-resistant *Streptococcus pneumoniae* in acute otitis media: risk factors, susceptibility patterns and antimicrobial management. *Pediatr Infect Dis J*. 1995;14(9):751–759
121. Rodriguez WJ, Schwartz RH. *Streptococcus pneumoniae* causes otitis media with higher fever and more redness of tympanic membranes than *Haemophilus influenzae* or *Moraxella catarrhalis*. *Pediatr Infect Dis J*. 1999;18(10):942–944
122. Block SL, Hedrick J, Harrison CJ, et al. Community-wide vaccination with the heptavalent pneumococcal conjugate significantly alters the microbiology of acute otitis media. *Pediatr Infect Dis J*. 2004;23(9):829–833
123. Casey JR, Pichichero ME. Changes in frequency and pathogens causing acute otitis media in 1995–2003. *Pediatr Infect Dis J*. 2004;23(9):824–828
124. McEllistrem MC, Adams JM, Patel K, et al. Acute otitis media due to penicillin-nonsusceptible *Streptococcus pneumoniae* before and after the introduction of the pneumococcal conjugate vaccine. *Clin Infect Dis*. 2005;40(12):1738–1744
125. Casey JR, Adlowitz DG, Pichichero ME. New patterns in the otopathogens causing acute otitis media six to eight years after introduction of pneumococcal conjugate vaccine. *Pediatr Infect Dis J*. 2010;29(4):304–309

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

126. Grubb MS, Spaugh DC. Microbiology of acute otitis media, Puget Sound region, 2005–2009. *Clin Pediatr (Phila)*. 2010;49(8): 727–730
127. Revai K, McCormick DP, Patel J, Grady JJ, Saeed K, Chonmaitree T. Effect of pneumococcal conjugate vaccine on nasopharyngeal bacterial colonization during acute otitis media. *Pediatrics*. 2006;117(5): 1823–1829
128. Pettigrew MM, Gent JF, Revai K, Patel JA, Chonmaitree T. Microbial interactions during upper respiratory tract infections. *Emerg Infect Dis*. 2008;14(10):1584–1591
129. O'Brien KL, Millar EV, Zell ER, et al. Effect of pneumococcal conjugate vaccine on nasopharyngeal colonization among immunized and unimmunized children in a community-randomized trial. *J Infect Dis*. 2007;196(8):1211–1220
130. Jacobs MR, Bajaksouzian S, Windau A, Good C. Continued emergence of nonvaccine serotypes of *Streptococcus pneumoniae* in Cleveland. *Proceedings of the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy*; 2009:G1-G1556
131. Hoberman A, Paradise JL, Shaikh N, et al. Pneumococcal resistance and serotype 19A in Pittsburgh-area children with acute otitis media before and after introduction of 7-valent pneumococcal polysaccharide vaccine. *Clin Pediatr (Phila)*. 2011;50(2): 114–120
132. Huang SS, Hinrichsen VL, Stevenson AE, et al. Continued impact of pneumococcal conjugate vaccine on carriage in young children. *Pediatrics*. 2009;124(1). Available at: www.pediatrics.org/cgi/content/full/124/1/e1
133. Centers for Disease Control and Prevention (CDC). Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children—Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Morb Mortal Wkly Rep*. 2010;59(9):258–261
134. Segal N, Givon-Lavi N, Leibovitz E, Yagupsky P, Leiberman A, Dagan R. Acute otitis media caused by *Streptococcus pyogenes* in children. *Clin Infect Dis*. 2005;41(1):35–41
135. Luntz M, Brodsky A, Nusem S, et al. Acute mastoiditis—the antibiotic era: a multicenter study. *Int J Pediatr Otorhinolaryngol*. 2001;57(1):1–9
136. Nielsen JC. *Studies on the Aetiology of Acute Otitis Media*. Copenhagen, Denmark: Ejnar Mundsgaard Forlag; 1945
137. Palmu AA, Herva E, Savolainen H, Karma P, Mäkelä PH, Kilpi TM. Association of clinical signs and symptoms with bacterial findings in acute otitis media. *Clin Infect Dis*. 2004;38(2):234–242
138. Leibovitz E, Asher E, Piglansky L, et al. Is bilateral acute otitis media clinically different than unilateral acute otitis media? *Pediatr Infect Dis J*. 2007;26(7):589–592
139. Leibovitz E, Satran R, Piglansky L, et al. Can acute otitis media caused by *Haemophilus influenzae* be distinguished from that caused by *Streptococcus pneumoniae? Pediatr Infect Dis J*. 2003;22(6): 509–515
140. Palmu AA, Kotikoski MJ, Kaijalainen TH, Puhakka HJ. Bacterial etiology of acute myringitis in children less than two years of age. *Pediatr Infect Dis J*. 2001;20(6): 607–611
141. Bodor FF. Systemic antibiotics for treatment of the conjunctivitis-otitis media syndrome. *Pediatr Infect Dis J*. 1989;8(5): 287–290
142. Bingen E, Cohen R, Jourenkova N, Gehanno P. Epidemiologic study of conjunctivitis-otitis syndrome. *Pediatr Infect Dis J*. 2005;24(8):731–732
143. Barkai G, Leibovitz E, Givon-Lavi N, Dagan R. Potential contribution by nontypable *Haemophilus influenzae* in protracted and recurrent acute otitis media. *Pediatr Infect Dis J*. 2009;28(6):466–471
144. Howie VM, Ploussard JH. Efficacy of fixed combination antibiotics versus separate components in otitis media. Effectiveness of erythromycin estrolate, triple sulfonamide, ampicillin, erythromycin estolate-triple sulfonamide, and placebo in 280 patients with acute otitis media under two and one-half years of age. *Clin Pediatr (Phila)*. 1972;11(4):205–214
145. Klein JO. Microbiologic efficacy of antibacterial drugs for acute otitis media. *Pediatr Infect Dis J*. 1993;12(12): 973–975
146. Barnett ED, Klein JO. The problem of resistant bacteria for the management of acute otitis media. *Pediatr Clin North Am*. 1995;42(3):509–517
147. Tristram S, Jacobs MR, Appelbaum PC. Antimicrobial resistance in *Haemophilus influenzae*. *Clin Microbiol Rev*. 2007;20(2): 368–389
148. Critchley IA, Jacobs MR, Brown SD, Traczewski MM, Tillotson GS, Janjic N. Prevalence of serotype 19A *Streptococcus pneumoniae* among isolates from U.S. children in 2005≠2006 and activity of faropenem. *Antimicrob Agents Chemother*. 2008;52(7): 2639–2643
149. Jacobs MR, Good CE, Windau AR, et al. Activity of ceftaroline against emerging serotypes of Streptococcus pneumoniae. *Antimicrob Agents Chemother*. 2010;54(6): 2716–2719
150. Jacobs MR. Antimicrobial-resistant *Streptococcus pneumoniae:* trends and management. *Expert Rev Anti Infect Ther*. 2008;6(5):619–635
151. Piglansky L, Leibovitz E, Raiz S, et al. Bacteriologic and clinical efficacy of high dose amoxicillin for therapy of acute otitis media in children. *Pediatr Infect Dis J*. 2003;22(5):405–413
152. Dagan R, Johnson CE, McLinn S, et al. Bacteriologic and clinical efficacy of amoxicillin/clavulanate vs. azithromycin in acute otitis media. *Pediatr Infect Dis J*. 2000;19(2):95–104
153. Dagan R, Hoberman A, Johnson C, et al. Bacteriologic and clinical efficacy of high dose amoxicillin/clavulanate in children with acute otitis media. *Pediatr Infect Dis J*. 2001;20(9):829–837
154. Hoberman A, Dagan R, Leibovitz E, et al. Large dosage amoxicillin/clavulanate, compared with azithromycin, for the treatment of bacterial acute otitis media in children. *Pediatr Infect Dis J*. 2005;24 (6):525–532
155. De Wals P, Erickson L, Poirier B, Pépin J, Pichichero ME. How to compare the efficacy of conjugate vaccines to prevent acute otitis media? *Vaccine*. 2009;27(21): 2877–2883
156. Shouval DS, Greenberg D, Givon-Lavi N, Porat N, Dagan R. Serotype coverage of invasive and mucosal pneumococcal disease in Israeli children younger than 3 years by various pneumococcal conjugate vaccines. *Pediatr Infect Dis J*. 2009;28(4): 277–282
157. Jones RN, Farrell DJ, Mendes RE, Sader HS. Comparative ceftaroline activity tested against pathogens associated with community-acquired pneumonia: results from an international surveillance study. *J Antimicrob Chemother*. 2011;66(suppl 3): iii69–iii80
158. Harrison CJ, Woods C, Stout G, Martin B, Selvarangan R. Susceptibilities of Haemophilus influenzae, Streptococcus pneumoniae, including serotype 19A, and Moraxella catarrhalis paediatric isolates from 2005 to 2007 to commonly used antibiotics. *J Antimicrob Chemother*. 2009;63(3):511–519
159. Doern GV, Jones RN, Pfaller MA, Kugler K. *Haemophilus influenzae* and *Moraxella catarrhalis* from patients with community-acquired respiratory tract infections: antimicrobial susceptibility patterns from the SENTRY antimicrobial Surveillance Program (United States and Canada, 1997).

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

Antimicrob Agents Chemother. 1999;43(2):385–389

160. Nussinovitch M, Yoeli R, Elishkevitz K, Varsano I. Acute mastoiditis in children: epidemiologic, clinical, microbiologic, and therapeutic aspects over past years. *Clin Pediatr (Phila)*. 2004;43(3):261–267
161. Roddy MG, Glazier SS, Agrawal D. Pediatric mastoiditis in the pneumococcal conjugate vaccine era: symptom duration guides empiric antimicrobial therapy. *Pediatr Emerg Care*. 2007;23(11):779–784
162. Hoberman A, Paradise JL, Burch DJ, et al. Equivalent efficacy and reduced occurrence of diarrhea from a new formulation of amoxicillin/clavulanate potassium (Augmentin) for treatment of acute otitis media in children. *Pediatr Infect Dis J*. 1997;16(5):463–470
163. Arguedas A, Dagan R, Leibovitz E, Hoberman A, Pichichero M, Paris M. A multicenter, open label, double tympanocentesis study of high dose cefdinir in children with acute otitis media at high risk of persistent or recurrent infection. *Pediatr Infect Dis J*. 2006;25(3):211–218
164. Atanasković-Marković M, Velicković TC, Gavrović-Jankulović M, Vucković O, Nestorović B. Immediate allergic reactions to cephalosporins and penicillins and their cross-reactivity in children. *Pediatr Allergy Immunol*. 2005;16(4):341–347
165. Pichichero ME. Use of selected cephalosporins in penicillin-allergic patients: a paradigm shift. *Diagn Microbiol Infect Dis*. 2007;57(suppl 3):13S–18S
166. Pichichero ME, Casey JR. Safe use of selected cephalosporins in penicillin-allergic patients: a meta-analysis. *Otolaryngol Head Neck Surg*. 2007;136(3):340–347
167. DePestel DD, Benninger MS, Danziger L, et al. Cephalosporin use in treatment of patients with penicillin allergies. *J Am Pharm Assoc (2003)*. 2008;48(4):530–540
168. Fonacier L, Hirschberg R, Gerson S. Adverse drug reactions to a cephalosporins in hospitalized patients with a history of penicillin allergy. *Allergy Asthma Proc*. 2005;26(2):135–141
169. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol*. 2010;105(4):259–273
170. Powers JL, Gooch WM, III, Oddo LP. Comparison of the palatability of the oral suspension of cefdinir vs. amoxicillin/clavulanate potassium, cefprozil and azithromycin in pediatric patients. *Pediatr Infect Dis J*. 2000;19(suppl 12):S174–S180
171. Steele RW, Thomas MP, Bégué RE. Compliance issues related to the selection of antibiotic suspensions for children. *Pediatr Infect Dis J*. 2001;20(1):1–5
172. Steele RW, Russo TM, Thomas MP. Adherence issues related to the selection of antistaphylococcal or antifungal antibiotic suspensions for children. *Clin Pediatr (Phila)*. 2006;45(3):245–250
173. Schwartz RH. Enhancing children's satisfaction with antibiotic therapy: a taste study of several antibiotic suspensions. *Curr Ther Res*. 2000;61(8):570–581
174. Green SM, Rothrock SG. Single-dose intramuscular ceftriaxone for acute otitis media in children. *Pediatrics*. 1993;91(1):23–30
175. Leibovitz E, Piglansky L, Raiz S, Press J, Leiberman A, Dagan R. Bacteriologic and clinical efficacy of one day vs. three day intramuscular ceftriaxone for treatment of nonresponsive acute otitis media in children. *Pediatr Infect Dis J*. 2000;19(11):1040–1045
176. Rosenfeld RM, Kay D. Natural history of untreated otitis media. *Laryngoscope*. 2003;113(10):1645–1657
177. Rosenfeld RM, Kay D. Natural history of untreated otitis media. In: Rosenfeld RM, Bluestone CD, eds. *Evidence-Based Otitis Media*. 2nd ed. Hamilton, Canada: BC Decker; 2003:180–198
178. Arola M, Ziegler T, Ruuskanen O. Respiratory virus infection as a cause of prolonged symptoms in acute otitis media. *J Pediatr*. 1990;116(5):697–701
179. Chonmaitree T, Owen MJ, Howie VM. Respiratory viruses interfere with bacteriologic response to antibiotic in children with acute otitis media. *J Infect Dis*. 1990;162(2):546–549
180. Dagan R, Leibovitz E, Greenberg D, Yagupsky P, Fliss DM, Leiberman A. Early eradication of pathogens from middle ear fluid during antibiotic treatment of acute otitis media is associated with improved clinical outcome. *Pediatr Infect Dis J*. 1998;17(9):776–782
181. Carlin SA, Marchant CD, Shurin PA, Johnson CE, Super DM, Rehmus JM. Host factors and early therapeutic response in acute otitis media. *J Pediatr*. 1991;118(2):178–183
182. Teele DW, Pelton SI, Klein JO. Bacteriology of acute otitis media unresponsive to initial antimicrobial therapy. *J Pediatr*. 1981;98(4):537–539
183. Doern GV, Pfaller MA, Kugler K, Freeman J, Jones RN. Prevalence of antimicrobial resistance among respiratory tract isolates of *Streptococcus pneumoniae* in North America: 1997 results from the SENTRY antimicrobial surveillance program. *Clin Infect Dis*. 1998;27(4):764–770
184. Leiberman A, Leibovitz E, Piglansky L, et al. Bacteriologic and clinical efficacy of trimethoprim-sulfamethoxazole for treatment of acute otitis media. *Pediatr Infect Dis J*. 2001;20(3):260–264
185. Humphrey WR, Shattuck MH, Zielinski RJ, et al. Pharmacokinetics and efficacy of linezolid in a gerbil model of *Streptococcus pneumoniae*-induced acute otitis media. *Antimicrob Agents Chemother*. 2003;47(4):1355–1363
186. Arguedas A, Dagan R, Pichichero M, et al. An open-label, double tympanocentesis study of levofloxacin therapy in children with, or at high risk for, recurrent or persistent acute otitis media. *Pediatr Infect Dis J*. 2006;25(12):1102–1109
187. Noel GJ, Blumer JL, Pichichero ME, et al. A randomized comparative study of levofloxacin versus amoxicillin/clavulanate for treatment of infants and young children with recurrent or persistent acute otitis media. *Pediatr Infect Dis J*. 2008;27(6):483–489
188. Howie VM, Ploussard JH. Simultaneous nasopharyngeal and middle ear exudate culture in otitis media. *Pediatr Digest*. 1971;13:31–35
189. Gehanno P, Lenoir G, Barry B, Bons J, Boucot I, Berche P. Evaluation of nasopharyngeal cultures for bacteriologic assessment of acute otitis media in children. *Pediatr Infect Dis J*. 1996;15(4):329–332
190. Cohen R, Levy C, Boucherat M, Langue J, de La Rocque F. A multicenter, randomized, double-blind trial of 5 versus 10 days of antibiotic therapy for acute otitis media in young children. *J Pediatr*. 1998;133(5):634–639
191. Pessey JJ, Gehanno P, Thoroddsen E, et al. Short course therapy with cefuroxime axetil for acute otitis media: results of a randomized multicenter comparison with amoxicillin/clavulanate. *Pediatr Infect Dis J*. 1999;18(10):854–859
192. Cohen R, Levy C, Boucherat M, et al. Five vs. ten days of antibiotic therapy for acute otitis media in young children. *Pediatr Infect Dis J*. 2000;19(5):458–463
193. Pichichero ME, Marsocci SM, Murphy ML, Hoeger W, Francis AB, Green JL. A prospective observational study of 5-, 7-, and 10-day antibiotic treatment for acute otitis media. *Otolaryngol Head Neck Surg*. 2001;124(4):381–387

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

194. Kozyrskyj AL, Klassen TP, Moffatt M, Harvey K. Short-course antibiotics for acute otitis media. *Cochrane Database Syst Rev*. 2010;(9):CD001095
195. Shurin PA, Pelton SI, Donner A, Klein JO. Persistence of middle-ear effusion after acute otitis media in children. *N Engl J Med*. 1979;300(20):1121–1123
196. Damoiseaux RA, Rovers MM, Van Balen FA, Hoes AW, de Melker RA. Long-term prognosis of acute otitis media in infancy: determinants of recurrent acute otitis media and persistent middle ear effusion. *Fam Pract*. 2006;23(1):40–45
197. Leach AJ, Morris PS. Antibiotics for the prevention of acute and chronic suppurative otitis media in children. *Cochrane Database Syst Rev*. 2006;(4):CD004401
198. Teele DW, Klein JO, Word BM, et al; Greater Boston Otitis Media Study Group. Antimicrobial prophylaxis for infants at risk for recurrent acute otitis media. *Vaccine*. 2000;19(suppl 1):S140–S143
199. Paradise JL. On tympanostomy tubes: rationale, results, reservations, and recommendations. *Pediatrics*. 1977;60(1):86–90
200. McIsaac WJ, Coyte PC, Croxford R, Asche CV, Friedberg J, Feldman W. Otolaryngologists' perceptions of the indications for tympanostomy tube insertion in children. *CMAJ*. 2000;162(9):1285–1288
201. Casselbrandt ML. Ventilation tubes for recurrent acute otitis media. In: Alper CM, Bluestone CD, eds. *Advanced Therapy of Otitis Media*. Hamilton, Canada: BC Decker; 2004:113–115
202. Shin JJ, Stinnett SS, Hartnick CJ. Pediatric recurrent acute otitis media. In: Shin JJ, Hartnick CJ, Randolph GW, eds. *Evidence-Based Otolaryngology*. New York, NY: Springer; 2008:91–95
203. Gonzalez C, Arnold JE, Woody EA, et al. Prevention of recurrent acute otitis media: chemoprophylaxis versus tympanostomy tubes. *Laryngoscope*. 1986;96(12):1330–1334
204. Gebhart DE. Tympanostomy tubes in the otitis media prone child. *Laryngoscope*. 1981;91(6):849–866
205. 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(4):278–286
206. El-Sayed Y. Treatment of recurrent acute otitis media chemoprophylaxis versus ventilation tubes. *Aust J Otolaryngol*. 1996;2(4):352–355
207. McDonald S, Langton Hewer CD, Nunez DA. Grommets (ventilation tubes) for recurrent acute otitis media in children. *Cochrane Database Syst Rev*. 2008;(4):CD004741
208. Rosenfeld RM, Bhaya MH, Bower CM, et al. Impact of tympanostomy tubes on child quality of life. *Arch Otolaryngol Head Neck Surg*. 2000;126(5):585–592
209. Witsell DL, Stewart MG, Monsell EM, et al. The Cooperative Outcomes Group for ENT: a multicenter prospective cohort study on the outcomes of tympanostomy tubes for children with otitis media. *Otolaryngol Head Neck Surg*. 2005;132(2):180–188
210. Isaacson G. Six Sigma tympanostomy tube insertion: achieving the highest safety levels during residency training. *Otolaryngol Head Neck Surg*. 2008;139(3):353–357
211. Kay DJ, Nelson M, Rosenfeld RM. Meta-analysis of tympanostomy tube sequelae. *Otolaryngol Head Neck Surg*. 2001;124(4):374–380
212. Koivunen P, Uhari M, Luotonen J, et al. Adenoidectomy versus chemoprophylaxis and placebo for recurrent acute otitis media in children aged under 2 years: randomised controlled trial. *BMJ*. 2004;328(7438):487
213. Rosenfeld RM. Surgical prevention of otitis media. *Vaccine*. 2000;19(suppl 1):S134–S139
214. Centers for Disease Control and Prevention (CDC). Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep*. 2011;60(33):1128–1132
215. American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2011–2012. *Pediatrics*. 2011;128(4):813–825
216. Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics*. 2012;129(3). Available at: www.pediatrics.org/cgi/content/full/129/3/e827
217. Pavia M, Bianco A, Nobile CG, Marinelli P, Angelillo IF. Efficacy of pneumococcal vaccination in children younger than 24 months: a meta-analysis. *Pediatrics*. 2009;123(6). Available at: www.pediatrics.org/cgi/content/full/123/6/e1103
218. Eskola J, Kilpi T, Palmu A, et al; Finnish Otitis Media Study Group. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. *N Engl J Med*. 2001;344(6):403–409
219. Black S, Shinefield H, Fireman B, et al; Northern California Kaiser Permanente Vaccine Study Center Group. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. *Pediatr Infect Dis J*. 2000;19(3):187–195
220. Jacobs MR. Prevention of otitis media: role of pneumococcal conjugate vaccines in reducing incidence and antibiotic resistance. *J Pediatr*. 2002;141(2):287–293
221. Jansen AG, Hak E, Veenhoven RH, Damoiseaux RA, Schilder AG, Sanders EA. Pneumococcal conjugate vaccines for preventing otitis media. *Cochrane Database Syst Rev*. 2009;(2):CD001480
222. Fireman B, Black SB, Shinefield HR, Lee J, Lewis E, Ray P. Impact of the pneumococcal conjugate vaccine on otitis media. *Pediatr Infect Dis J*. 2003;22(1):10–16
223. Grijalva CG, Poehling KA, Nuorti JP, et al. National impact of universal childhood immunization with pneumococcal conjugate vaccine on otitis media. *Pediatr Infect Dis J*. 2006;118(3):865–873
224. Zhou F, Shefer A, Kong Y, Nuorti JP. Trends in acute otitis media-related health care utilization by privately insured young children in the United States, 1997–2004. *Pediatrics*. 2008;121(2):253–260
225. Poehling KA, Szilagyi PG, Grijalva CG, et al. Reduction of frequent otitis media and pressure-equalizing tube insertions in children after introduction of pneumococcal conjugate vaccine. *Pediatrics*. 2007;119(4):707–715
226. Pelton SI. Prospects for prevention of otitis media. *Pediatr Infect Dis J*. 2007;26(suppl 10):S20–S22
227. Pelton SI, Leibovitz E. Recent advances in otitis media. *Pediatr Infect Dis J*. 2009;28(suppl 10):S133–S137
228. De Wals P, Erickson L, Poirier B, Pépin J, Pichichero ME. How to compare the efficacy of conjugate vaccines to prevent acute otitis media? *Vaccine*. 2009;27(21):2877–2883
229. Plasschaert AI, Rovers MM, Schilder AG, Verheij TJ, Hak E. Trends in doctor consultations, antibiotic prescription, and specialist referrals for otitis media in children: 1995–2003. *Pediatrics*. 2006;117(6):1879–1886
230. O'Brien MA, Prosser LA, Paradise JL, et al. New vaccines against otitis media: projected benefits and cost-effectiveness. *Pediatrics*. 2009;123(6):1452–1463
231. Hanage WP, Auranen K, Syrjänen R, et al. Ability of pneumococcal serotypes and clones to cause acute otitis media: implications for the prevention of otitis media by conjugate vaccines. *Infect Immun*. 2004;72(1):76–81
232. Prymula R, Peeters P, Chrobok V, et al. Pneumococcal capsular polysaccharides

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

conjugated to protein D for prevention of acute otitis media caused by both Streptococcus pneumoniae and non-typable *Haemophilus influenzae*: a randomised double-blind efficacy study. *Lancet*. 2006; 367(9512):740–748

233. Prymula R, Schuerman L. 10-valent pneumococcal nontypeable *Haemophilus influenzae* PD conjugate vaccine: Synflorix. *Expert Rev Vaccines*. 2009;8(11):1479–1500
234. Schuerman L, Borys D, Hoet B, Forsgren A, Prymula R. Prevention of otitis media: now a reality? *Vaccine*. 2009;27(42):5748–5754
235. Heikkinen T, Ruuskanen O, Waris M, Ziegler T, Arola M, Halonen P. Influenza vaccination in the prevention of acute otitis media in children. *Am J Dis Child*. 1991;145(4):445–448
236. Clements DA, Langdon L, Bland C, Walter E. Influenza A vaccine decreases the incidence of otitis media in 6- to 30-month-old children in day care. *Arch Pediatr Adolesc Med*. 1995;149(10):1113–1117
237. Belshe RB, Gruber WC. Prevention of otitis media in children with live attenuated influenza vaccine given intranasally. *Pediatr Infect Dis J*. 2000;19(suppl 5):S66–S71
238. Marchisio P, Cavagna R, Maspes B, et al. Efficacy of intranasal virosomal influenza vaccine in the prevention of recurrent acute otitis media in children. *Clin Infect Dis*. 2002;35(2):168–174
239. Ozgur SK, Beyazova U, Kemaloglu YK, et al. Effectiveness of inactivated influenza vaccine for prevention of otitis media in children. *Pediatr Infect Dis J*. 2006;25(5): 401–404
240. Block SL, Heikkinen T, Toback SL, Zheng W, Ambrose CS. The efficacy of live attenuated influenza vaccine against influenza-associated acute otitis media in children. *Pediatr Infect Dis J*. 2011;30(3):203–207
241. Ashkenazi S, Vertruyen A, Arístegui J, et al; CAIV-T Study Group. Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections. *Pediatr Infect Dis J*. 2006;25(10):870–879
242. Belshe RB, Edwards KM, Vesikari T, et al; CAIV-T Comparative Efficacy Study Group. Live attenuated versus inactivated influenza vaccine in infants and young children [published correction appears in *N Engl J Med*. 2007;356(12):1283]. *N Engl J Med*. 2007;356(7):685–696
243. Bracco Neto H, Farhat CK, Tregnaghi MW, et al; D153-P504 LAIV Study Group. Efficacy and safety of 1 and 2 doses of live attenuated influenza vaccine in vaccine-naive children. *Pediatr Infect Dis J*. 2009;28(5): 365–371
244. Tam JS, Capeding MR, Lum LC, et al; Pan-Asian CAIV-T Pediatric Efficacy Trial Network. Efficacy and safety of a live attenuated, cold-adapted influenza vaccine, trivalent against culture-confirmed influenza in young children in Asia. *Pediatr Infect Dis J*. 2007;26(7):619–628
245. Vesikari T, Fleming DM, Aristegui JF, et al; CAIV-T Pediatric Day Care Clinical Trial Network. Safety, efficacy, and effectiveness of cold-adapted influenza vaccine-trivalent against community-acquired, culture-confirmed influenza in young children attending day care. *Pediatrics*. 2006;118(6):2298–2312
246. Forrest BD, Pride MW, Dunning AJ, et al. Correlation of cellular immune responses with protection against culture-confirmed influenza virus in young children. *Clin Vaccine Immunol*. 2008;15(7): 1042–1053
247. Lum LC, Borja-Tabora CF, Breiman RF, et al. Influenza vaccine concurrently administered with a combination measles, mumps, and rubella vaccine to young children. *Vaccine*. 2010;28(6):1566–1574
248. Belshe RB, Mendelman PM, Treanor J, et al. The efficacy of live attenuated, cold-adapted, trivalent, intranasal influenzavirus vaccine in children. *N Engl J Med*. 1998;338(20): 1405–1412
249. Daly KA, Giebink GS. Clinical epidemiology of otitis media. *Pediatr Infect Dis J*. 2000; 19(suppl 5):S31–S36
250. Duncan B, Ey J, Holberg CJ, Wright AL, Martinez FD, Taussig LM. Exclusive breastfeeding for at least 4 months protects against otitis media. *Pediatrics*. 1993;91(5): 867–872
251. Duffy LC, Faden H, Wasielewski R, Wolf J, Krystofik D. Exclusive breastfeeding protects against bacterial colonization and day care exposure to otitis media. *Pediatrics*. 1997;100(4). Available at: www.pediatrics.org/cgi/content/full/100/4/e7
252. Paradise JL. Short-course antimicrobial treatment for acute otitis media: not best for infants and young children. *JAMA*. 1997;278(20):1640–1642
253. Scariati PD, Grummer-Strawn LM, Fein SB. A longitudinal analysis of infant morbidity and the extent of breastfeeding in the United States. *Pediatrics*. 1997;99(6). Available at: www.pediatrics.org/cgi/content/full/99/6/e5
254. McNiel ME, Labbok MH, Abrahams SW. What are the risks associated with formula feeding? A re-analysis and review. *Breastfeed Rev*. 2010;18(2):25–32
255. Chantry CJ, Howard CR, Auinger P. Full breastfeeding duration and associated decrease in respiratory tract infection in US children. *Pediatrics*. 2006;117(2):425–432
256. Hatakka K, Piirainen L, Pohjavuori S, Poussa T, Savilahti E, Korpela R. Factors associated with acute respiratory illness in day care children. *Scand J Infect Dis*. 2010;42(9):704–711
257. Ladomenou F, Kafatos A, Tselentis Y, Galanakis E. Predisposing factors for acute otitis media in infancy. *J Infect*. 2010;61(1):49–53
258. Ladomenou F, Moschandreas J, Kafatos A, Tselentis Y, Galanakis E. Protective effect of exclusive breastfeeding against infections during infancy: a prospective study. *Arch Dis Child*. 2010;95(12):1004–1008
259. Duijts L, Jaddoe VW, Hofman A, Moll HA. Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. *Pediatrics*. 2010;126(1). Available at: www.pediatrics.org/cgi/content/full/126/1/e18
260. Best D; Committee on Environmental Health; Committee on Native American Child Health; Committee on Adolescence. From the American Academy of Pediatrics: technical report—secondhand and prenatal tobacco smoke exposure. *Pediatrics*. 2009;124(5). Available at: www.pediatrics.org/cgi/content/full/124/5/e1017
261. Etzel RA, Pattishall EN, Haley NJ, Fletcher RH, Henderson FW. Passive smoking and middle ear effusion among children in day care. *Pediatrics*. 1992;90(2 pt 1): 228–232
262. Ilicali OC, Keleş N, Değer K, Savaş I. Relationship of passive cigarette smoking to otitis media. *Arch Otolaryngol Head Neck Surg*. 1999;125(7):758–762
263. Wellington M, Hall CB. Pacifier as a risk factor for acute otitis media [letter]. *Pediatrics*. 2002;109(2):351–352, author reply 353
264. Kerstein R. Otitis media: prevention instead of prescription. *Br J Gen Pract*. 2008;58(550):364–365
265. Brown CE, Magnuson B. On the physics of the infant feeding bottle and middle ear sequela: ear disease in infants can be associated with bottle feeding. *Int J Pediatr Otorhinolaryngol*. 2000;54(1):13–20
266. Niemelä M, Pihakari O, Pokka T, Uhari M. Pacifier as a risk factor for acute otitis media: a randomized, controlled trial of parental counseling. *Pediatrics*. 2000;106(3): 483–488

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

267. Tully SB, Bar-Haim Y, Bradley RL. Abnormal tympanography after supine bottle feeding. *J Pediatr*. 1995;126(6):S105–S111
268. Rovers MM, Numans ME, Langenbach E, Grobbee DE, Verheij TJ, Schilder AG. Is pacifier use a risk factor for acute otitis media? A dynamic cohort study. *Fam Pract*. 2008;25(4):233–236
269. Adderson EE. Preventing otitis media: medical approaches. *Pediatr Ann*. 1998;27(2):101–107
270. Azarpazhooh A, Limeback H, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. *Cochrane Database Syst Rev*. 2011;(11):CD007095
271. Hautalahti O, Renko M, Tapiainen T, Kontiokari T, Pokka T, Uhari M. Failure of xylitol given three times a day for preventing acute otitis media. *Pediatr Infect Dis J*. 2007;26(5):423–427
272. Tapiainen T, Luotonen L, Kontiokari T, Renko M, Uhari M. Xylitol administered only during respiratory infections failed to prevent acute otitis media. *Pediatrics*. 2002;109(2). Available at: www.pediatrics.org/cgi/content/full/109/2/e19
273. Uhari M, Kontiokari T, Koskela M, Niemelä M. Xylitol chewing gum in prevention of acute otitis media: double blind randomised trial. *BMJ*. 1996;313(7066):1180–1184
274. Uhari M, Kontiokari T, Niemelä M. A novel use of xylitol sugar in preventing acute otitis media. *Pediatrics*. 1998;102(4 pt 1):879–884
275. O'Brien MA, Prosser LA, Paradise JL, et al. New vaccines against otitis media: projected benefits and cost-effectiveness. *Pediatrics*. 2009;123(6):1452–1463

(Continued from first page)

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

www.pediatrics.org/cgi/doi/10.1542/peds.2012-3488

doi:10.1542/peds.2012-3488

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2013 by the American Academy of Pediatrics

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013

The Diagnosis and Management of Acute Otitis Media

Allan S. Lieberthal, Aaron E. Carroll, Tasnee Chonmaitree, Theodore G. Ganiats, Alejandro Hoberman, Mary Anne Jackson, Mark D. Joffe, Donald T. Miller, Richard M. Rosenfeld, Xavier D. Sevilla, Richard H. Schwartz, Pauline A. Thomas and David E. Tunkel

Pediatrics; originally published online February 25, 2013;
DOI: 10.1542/peds.2012-3488

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/early/2013/02/20/peds.2012-3488
Citations	This article has been cited by 1 HighWire-hosted articles: http://pediatrics.aappublications.org/content/early/2013/02/20/peds.2012-3488#related-urls
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): **Surgery** http://pediatrics.aappublications.org/cgi/collection/surgery
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://pediatrics.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2013 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from pediatrics.aappublications.org at Univ of Florida Health Science Center on April 8, 2013