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# New guidelines on acute otitis media: An overview of their key principles for practice

**T**he proper management of acute otitis media (AOM) has received much attention in recent years.<sup>1</sup> Studies have shown this condition to be overdiagnosed and, hence, overtreated as much 50% of the time by clinicians caring for children.<sup>2</sup> The resulting unnecessary use of antimicrobials and the consequent increased prevalence of antibiotic resistance was felt by the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP) to warrant development of clear guidelines defining the current status of expert opinion on the appropriate diagnosis and optimal management of AOM. This article summarizes these new AAP/AAFP guidelines,<sup>3</sup> focusing on five key principles they set forth, with the aim of laying the groundwork for the roundtable discussion that follows.

## ■ HOW THE GUIDELINES TOOK SHAPE, AND THE QUESTIONS THEY TOOK ON

The AAP and AAFP developed the guidelines primarily by using data generated under a grant from the federal Agency for Healthcare Research and Quality (AHRQ) through the Southern California Evidence-Based Practice Center and the RAND Corporation.

At the request of these groups, experts in AOM were asked to identify the principal contemporary questions in the diagnosis and treatment of AOM. More than 40 such questions were identified and prioritized. The following seven were considered the most important:

- What is the natural history of AOM?
- What is the outcome of AOM treated with antimicrobials vs no antimicrobial therapy?
- What is the efficacy of amoxicillin compared with that of other antimicrobials?
- What is the efficacy of high-dose (80 to 90

mg/kg/day) vs standard-dose (40 mg/kg/day) amoxicillin therapy?

- What is the efficacy of twice-daily vs thrice-daily therapy?
- What is the efficacy of short-term (3-, 5-, or 7-day) vs long-term (10-day) therapy?
- What are the complications of AOM in untreated children?

To answer these questions, MEDLINE and six other databases were searched for relevant studies published between 1966 and March 1999. Approximately 3,500 citations were reviewed, of which 760 considered the identified research questions; 74 of these were randomized controlled trials that were felt to be adequate to provide a database for resolution of the key questions.

The results of this search were published as an AHRQ monograph,<sup>4</sup> which provided a basis for development of the AAP/AAFP guidelines. Because the AAP/AAFP guidelines were developed after completion of the literature review and publication of the monograph, they also include the results of studies published through September 2003.

## ■ DEFINITION AND DIAGNOSIS OF AOM

The first portion of the guidelines deals with the definition of AOM. AOM is defined as the recent, abrupt onset (< 48 hours) of middle ear effusion accompanied by signs or symptoms of inflammation of the middle ear. Each of the three criteria of this definition—(1) recent, abrupt onset; (2) presence of middle ear effusion; and (3) presence of middle ear inflammation—is necessary to establish the diagnosis. It is often disregarded that middle ear effusion is a *sine qua non*: without it there can be no diagnosis of AOM. A red tympanic membrane is not enough.

**AOM cannot be diagnosed without middle ear effusion—a red tympanic membrane is not enough**

The guidelines are limited to consideration of uncomplicated AOM—that is, AOM limited to the middle ear cleft—in otherwise healthy children from 2 months to 12 years of age. While it is recognized that the guidelines may also apply to older children and adolescents, the published studies reviewed for development of the guidelines are almost all limited to this age group.

#### Principle 1:

To reliably diagnose AOM, the clinician should confirm a history of abrupt onset (≥ 48 hours) of middle ear effusion and inflammation

This principle is based on the perceived need to improve the diagnosis of AOM. The diagnosis can be suspected clinically when the signs and symptoms of an upper respiratory tract infection, which frequently precedes AOM by 3 to 5 days, are accompanied by ear pain, irritability, or pulling at the ear. It is important to note, however, that pulling at the ear is an unreliable sign, as no more than 10% of children who pull at the ear actually have AOM. Fever is generally less than 40°C, and one third of children with AOM who present in the physician's office have no fever at all. Purulent drainage is, of course, diagnostic.

#### Technical diagnostic aids

In addition to clinical signs and symptoms, certain technical aids can assist in the diagnosis of AOM: tympanocentesis, tympanography, reflectometry, and pneumatic otoscopy.

Tympanocentesis is indicated when rapid bacteriologic diagnosis and antimicrobial susceptibility are necessary. This includes the treatment of children with underlying immune deficits, such as those receiving chemotherapy; children with mastoiditis, meningitis, or other intracranial complications; and children in whom two or three sequential courses of appropriate antimicrobial therapy have failed.

Tympanography is quite valuable in defining the presence of middle ear effusion, which is an absolute prerequisite for the diagnosis of AOM. However, tympanography can be difficult to perform, particularly in a young febrile or otherwise uncooperative child.

Obtaining a seal is often quite difficult, if not impossible, especially in children younger than 6 months of age.

Acoustic reflectometry has been advocated as a simpler way of establishing the presence of middle ear fluid. In contrast to tympanography, it does not require a seal and can also be performed through even a small opening in the cerumen in the external auditory canal. Acoustic reflectometry is a very useful diagnostic method and should become increasingly available over the next few years as it is improved and distributed more widely.

Pneumatic otoscopy is the most practical diagnostic modality for AOM. The pneumatic otoscope should be checked to assure that the bulb is current and the light is bright and white in color. If a yellow or orange bulb is used, the tympanic membrane will appear inflamed. The otoscope should be checked regularly to assure that there is appropriate pressure to move the tympanic membrane when it is pumped, that a tight seal can be applied, and that appropriate speculi are used to obtain a good seal in the external auditory canal.

#### An emphasis on diagnostic accuracy

One of the guidelines' main goals is to improve the accuracy with which clinicians evaluate the presence or absence of AOM. Pichichero and Poole<sup>2</sup> have shown clearly that a large proportion of children diagnosed with AOM instead have otitis media with effusion. As many as 50% of such cases are misdiagnosed or overdiagnosed as AOM.

Studies done in 1993 by Karma (reviewed in 1998 by Pelton<sup>5</sup>) examined tympanic membranes and used tympanocentesis to establish the presence or absence of infection. These studies identified certain findings that were highly correlated with AOM:

- A bulging tympanic membrane had a positive predictive value of 83% to 99%
- Distinctly impaired mobility in the presence of tympanic membrane fullness or bulging had a positive predictive value of 85% to 99%
- Redness of the tympanic membrane alone, without other findings, had a predictive value as low as 7%.

This demonstrates that the old paradigm,

Up to 50% of cases of otitis media with effusion are misdiagnosed as AOM

*“Chief complaint: earache; physical examination: red tympanic membrane; Rx: amoxicillin,”* is simply no longer adequate or acceptable. These guidelines now make it imperative that the position of the tympanic membrane and its mobility both be described when clinicians attempt to make a diagnosis of AOM.

## ■ HOW TO ADDRESS PAIN

### Principle 2:

The management of AOM should include assessment of pain. If pain is present, the clinician should provide treatment to reduce it.

A number of options for pain management are available in addition to acetaminophen, ibuprofen, and naproxen, including codeine, benzocaine drops, and myringotomy. Codeine may be used in certain cases, such as in older children, children who are not lethargic, children who are free of productive cough or wheeze, and children with reliable parents. The codeine may be given together with acetaminophen to provide further analgesic effect. Benzocaine drops have very marginal efficacy.<sup>6</sup> Myringotomy can be used for the child who is in extreme pain, as it provides almost immediate relief.

The utility of homeopathic medicines, osteopathic or chiropractic manipulation, and topical naturopathic agents requires confirmation. Use of home remedies such as putting warm oil in the ear canal (if otorrhea is absent), applying heat over the ear, and distraction have stood the test of time and offer little or no risk.

## ■ TO OBSERVE OR NOT TO OBSERVE?

### Principle 3a:

Observation without antibiotics is an appropriate option for selected children with uncomplicated AOM based on diagnostic certainty, age, severity of illness, and certainty of follow-up

Observation without antibiotic therapy is an option clinicians may consider under certain circumstances, as outlined in Table 1. This principle is based on data generated over the last decades documenting the clinical resolution of otitis media among children given placebo or no therapy and on studies comparing response between children receiving

**TABLE 1**

### Observation vs antibiotic therapy: When to use each in children with acute otitis media (AOM)

AGE OF CHILD	IF DIAGNOSIS OF AOM IS CERTAIN	IF DIAGNOSIS IS UNCERTAIN
< 6 mo	Antibiotic	Antibiotic
6 mo–2 yr	Antibiotic	Antibiotic if severe illness; observe if nonsevere illness
2 yr	Antibiotic if severe illness; observe if nonsevere illness	Observe

placebo or no therapy and children receiving antimicrobials.<sup>7,8</sup> Questions have been raised about the validity of these data, since it was recognized that many of the children diagnosed with AOM may well have had otitis media with effusion, as previously noted. Also, many of the children studied belonged to relatively older age groups—older than 2 years in some cases, and older than 1 year in many cases—calling into question the validity of using observation alone in younger children. The median age of children with AOM is approximately 12 months, and since there is a large number of children with AOM around that age, the studies that involved those children should be considered the most appropriate for reference.

### Most patients will respond to symptomatic therapy

Looking at overall response rates, approximately two thirds of children with AOM will respond to symptomatic treatment alone at 24 hours, approximately 85% will respond at 2 to 3 days, and approximately 90% will respond at 4 to 7 days.<sup>7</sup> Treatment, when compared with symptomatic therapy, is more favorable in only 4% of children overall at 2 to 3 days; however, children under 2 years of age appear to be at a selective disadvantage, since observation alone fails in almost 25% of children in this age group with severe illness (see below).<sup>9</sup> As expected, there is no statistically significant difference between antimi-

**Observation without antibiotics may be considered under certain circumstances**

TABLE 2

**Microbiology of acute otitis media**

ORGANISM	CASES IN WHICH THE ORGANISM IS CAUSATIVE
<i>Haemophilus influenzae</i>	35%–50%
<i>Streptococcus pneumoniae</i>	25%–40%
<i>Moraxella catarrhalis</i>	5%–10%
Viruses	5%–15%
No growth of bacterial agents	1%–15%

crobial treatment and symptomatic therapy at 24 hours, given that 24 hours is required for antimicrobials to have an effect on the bacteria and for there to be a diminution in the inflammatory response, which is responsible for both the middle ear effusion and the discomfort that accompany AOM.

The observation option has certain limitations and certain provisions (Table 1). Patient age, certainty of the diagnosis, and severity of illness should determine the course of therapy. “Severe” illness is defined as illness in which the child’s temperature is 39°C or higher or there is moderate or severe otalgia. Children with mild ear pain and a temperature less than 39°C are considered to have “nonsevere” illness.

#### The microbiology of AOM translates to broad therapy choices

The antimicrobial therapy of AOM depends, of course, on the microbiology of the infection (Table 2). In recent years, there has been an appreciation of the rising incidence of nontypable *Haemophilus influenzae* as an etiology of AOM. At present, 35% to 50% of cases of AOM are caused by nontypable *H influenzae*, 25% to 40% by *Streptococcus pneumoniae*, and 5% to 10% by *Moraxella catarrhalis*.<sup>3</sup> A negligible number of cases are due to other bacteria. Viruses have been identified as the sole cause of infection in 5% to 15% of cases.<sup>10</sup> No growth of bacterial agents has been found in 1% to 15% of cases;<sup>3</sup> this finding may be attributable to AOM caused

TABLE 3

**Suggested antimicrobial therapy for acute otitis media**

- Amoxicillin 80 to 90 mg/kg/day in two divided doses for 5 to 10 days, depending on patient age
- For patients with non-type I or uncertain allergy to beta-lactams: cefdinir, cefuroxime, or cefpodoxime
- For patients with anaphylaxis or severe allergy to beta-lactams: azithromycin, clarithromycin, trimethoprim ± sulfamethoxazole, erythromycin-sulfisoxazole
- For patients with vomiting or uncertain compliance, ceftriaxone 50 mg/kg IM

by viral infection in early reports. Given this microbiology, a wide variety of antimicrobials are available for the treatment of AOM.

#### NAVIGATING ANTIBIOTIC CHOICES

##### Principle 3b:

If the decision is made to treat with an antibiotic, amoxicillin remains the initial antibiotic of choice for most children

This recommendation is based on the recognition that amoxicillin is not only effective but also has a low incidence of side effects, is cost-effective, and, by virtue of its taste, helps to assure good compliance.

The suggested antimicrobial therapy for AOM is outlined in Table 3. High-dose amoxicillin (80 to 90 mg/kg/day) is to be given in two divided doses for 5 to 10 days, depending on patient age. Children who have uncertain allergy to beta-lactams or nonanaphylactic allergy are advised to take an oral cephalosporin, such as cefdinir, cefuroxime, or cefpodoxime. Although these three oral cephalosporins have equal microbiologic efficacy, there are no clinical studies comparing their efficacy. However, there is every reason to believe that they are equally effective clinically. Cefdinir is more palatable, as demonstrated in a palatability study in adults,<sup>11</sup> and thus is more likely to result in good compliance.

Observation alone fails in nearly 25% of children under 2 years of age with severe AOM



Children with a history of anaphylaxis or severe allergy to beta-lactams warrant treatment with one of the following: azithromycin, clarithromycin, trimethoprim-sulfamethoxazole, or erythromycin-sulfisoxazole.

#### Concerns about resistance guide amoxicillin dosing

The rationale for use of high-dose amoxicillin (80 to 90 mg/kg/day) is to provide drug levels in the middle ear fluid adequate to eradicate strains of *S pneumoniae* that are fully susceptible to penicillin as well as strains that are nonsusceptible, which represent approximately 25% of all pneumococci isolated from middle ear fluid nationally. The susceptibility pattern is geographically dependent, with some centers reporting nonsusceptibility in 60% of strains while others report it in as few as 15%. Moreover, one third to one half of nonsusceptible strains are highly resistant to penicillin.

Higher drug levels in the middle ear fluid will eradicate not only the susceptible organisms but also those of intermediate resistance, which are defined as pneumococci for which the minimum inhibitory concentration (MIC) of penicillin is between 0.12 and 1 µg/mL. Resistant organisms, for which the MIC is greater than 2 µg/mL, would also largely be eradicated by the higher doses, and there are few resistant organisms for which the MIC of penicillin is greater than 8 µg/mL.

Giving amoxicillin in two, rather than three, divided doses will assure yet higher middle ear fluid levels of the drug. The duration of therapy depends on patient age, and the guidelines reflect the fact that few data exist on short-course therapy in younger children. Thus, it is recommended that short-course amoxicillin therapy be limited to children 6 years of age or older, for whom 5 to 7 days may suffice.

#### Another option for selected children

For children who are vomiting or for whom compliance cannot be assured, ceftriaxone 50 mg/kg given as a single intramuscular dose can be considered appropriate therapy. In such cases, no additional oral therapy is required and, if conjunctivitis is present, no additional ocular therapy is required.

**TABLE 4**

#### Antimicrobial therapy for children who do not respond to initial management at 48 to 72 hours

- Amoxicillin-clavulanate 90 mg/kg/day in two divided doses (to 4 g),\* or
- Cefdinir, cefuroxime, or cefpodoxime, or
- Ceftriaxone 50 mg/kg intramuscularly or intravenously, three daily doses

\* Can be primary therapy for children with moderate to severe otalgia or fever  $\geq 39^{\circ}\text{C}$ .

#### ■ WHAT TO DO WHEN INITIAL MANAGEMENT FAILS

##### Principle 4:

Lack of response within 48 to 72 hours requires reassessment to confirm AOM. If confirmed in a child initially managed with observation, an antibiotic should be prescribed. If initial management was with an antibiotic, an alternative antibiotic should be prescribed.

Reassessment may be accomplished either by reevaluation in the office or, when the reliability of the observer is known to the physician and felt to be adequate, by telephone discussion. These telephone discussions should be well documented in the patient's chart.

Table 4 provides recommendations for appropriate therapy after failure of first-line therapy. Amoxicillin-clavulanate 90 mg/kg/day should be given in two divided doses up to 4 g. Because the clavulanate moiety causes the gastrointestinal adverse effects associated with this agent, if this higher dose of amoxicillin-clavulanate is used, it is recommended that the new 14-to-1 formulation, rather than the 7-to-1 formulation, be prescribed. This can also be accomplished by diluting amoxicillin-clavulanate with equal parts of amoxicillin. Alternative therapy includes the oral cephalosporins cefdinir, cefuroxime, or cefpodoxime, or ceftriaxone 50 mg/kg/day given intramuscularly or intravenously for three daily doses.

##### Further failure calls for tympanocentesis or cautious use of clindamycin

Children who do not respond to second-line therapy should be considered for tympan-

**Nonresponders to second-line therapy should be considered for tympanocentesis**

TABLE 5

### Strategies for preventing acute otitis media through risk-factor reduction

- Breast-feed rather than bottle-feed
- Eliminate supine bottle-feeding
- Eliminate exposure of the child to tobacco smoke
- Eliminate pacifier use
- Modify group day care activities
- Provide the child with influenza and pneumococcal conjugate vaccinations
- Have the child investigated for atopy and immunodeficiency

Overuse of clindamycin clearly will reduce its future utility

ocentesis, particularly if they have persistent symptoms that are concerning to the clinician, persistently high fever, or persistent severe pain. Therapy can then be adjusted on the basis of Gram stain results and subsequently fine-tuned on the basis of culture and susceptibility studies, which will, however, not become available for 48 to 72 hours.

If tympanocentesis is not available (or while the results of susceptibility studies are awaited), use of clindamycin should be considered. High-dose amoxicillin-clavulanate, as second-line therapy, will have eradicated not only the beta-lactamase-positive *H influenzae* and *M catarrhalis* but also *S pneumoniae* that may have escaped treatment during the first regimen using high-dose amoxicillin alone. Of the remaining organisms, the most likely would be highly resistant *S pneumoniae*, of which approximately 93% to 95% of organisms remain susceptible to clindamycin. Overuse of clindamycin clearly will reduce its utility in the future, so clinicians are cautioned to restrict its use only to children who do not respond to second-line therapy.

#### ADVICE FOR REDUCING THE RISK OF AOM

##### Principle 5:

Clinicians should encourage AOM prevention through reduction of risk factors

This includes encouraging breast-feeding over bottle-feeding, particularly among mothers who have had other children with recurrent AOM or who themselves had a history of

recurrent AOM (this also applies if the child's father had a history of recurrent AOM).

Elimination of supine bottle-feeding, elimination of exposure to tobacco smoke in the household, and elimination of pacifier use may also reduce the incidence of AOM.

For children who attend day care centers, particularly large centers, it may be ideal for the parents to seek smaller groups or eliminate day care entirely if their work schedules or economic conditions permit.

Influenza vaccination, either with the parenteral formulation<sup>12</sup> or with the new cold-adapted intranasal vaccine,<sup>13</sup> has been shown to reduce the overall incidence of AOM in children by approximately 30% during the influenza season. A more recent study, however, could find no efficacy of killed vaccine in preventing AOM during influenza season in children 6 to 23 months of age.<sup>14</sup> The recent recommendation by the Advisory Committee on Immunization Practice to immunize all children over 6 months of age with influenza vaccine eliminates the specific intent of using the vaccine for prevention of AOM.

Immunization with pneumococcal conjugate vaccine has been shown to reduce the incidence of AOM by varying degrees. Although the incidence of AOM caused by those serotypes present in the vaccine is significantly decreased, the overall effect of the vaccine on the incidence of AOM is quite limited. A large HMO study found a 6% reduction in the incidence of AOM,<sup>15</sup> a 7.8% reduction in the frequency of office visits due to AOM, and a 6% reduction in antibiotic prescriptions.<sup>16</sup> A subsequent Finnish study, while also noting a mean 6% reduction in AOM incidence, reported confidence intervals around the mean of less than 1.0, indicating the possibility of no efficacy at all.<sup>17</sup> Although the reduction in the overall incidence of single episodes of AOM is marginal, it is clear that the use of pneumococcal conjugate vaccine will reduce both the incidence of recurrent AOM (ie, five cases or more) and the incidence of the need for tympanostomy tubes by 20% to 25% annually.<sup>15,16</sup>

Children who have recurrent AOM should be investigated for allergy and immunodeficiency. However, children with immunodeficiency will rarely present with

recurrent AOM alone; they usually have an increased frequency and severity of other upper or lower respiratory tract infections and other infections.

Strategies for reducing risk factors for AOM are summarized in Table 5.

## ■ REFERENCES

1. Dowell SF, Marcy SM, Phillips WR, et al. Otitis media—principles of judicious use of antimicrobial agents. *Pediatrics* 1998; 101:165–171.
2. Pichichero ME, Poole MD. Assessing diagnostic accuracy and tympanocentesis skill in the management of otitis media. *Arch Pediatr Adolesc Med* 2001; 155:1137–1142.
3. Subcommittee on Management of Acute Otitis Media, American Academy of Pediatrics and American Academy of Family Physicians. Clinical practice guideline: diagnosis and management of acute otitis media. *Pediatrics* 2004; 113:1451–1465.
4. Marcy SM, Takata G, Shekelle P, et al. Management of acute otitis media. Evidence Report/Technology Assessment No. 15 (prepared by the Southern California Evidence-Based Practice Center under contract no. 290-097-0001). AHRQ publication no. 01-E010. Rockville, Md.: Agency for Healthcare Research and Quality; May 2001.
5. Pelton S. Otoscopy for the diagnosis of otitis media. *Pediatr Infect Dis J* 1998; 17:540–543.
6. Hoberman A, Paradise JL, Reynolds EA, et al. Efficacy of Auralgan for treating ear pain in children with acute otitis media. *Arch Pediatr Adolesc Med* 1997; 151:675–678.
7. Rosenfeld RM, Bluestone CD, eds. Evidence-Based Otitis Media. 2nd ed. Hamilton, Ont., Canada: BC Decker; 2003.
8. Rovers M, Schilder AGM, Zielhuis GA, Rosenfeld RM. Otitis media. *Lancet* 2004; 363:465–473.
9. 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; 87:466–474.
10. Heikkinen T, Chonmaitree T. Importance of respiratory viruses in acute otitis media. *Clin Microbiol Rev* 2003; 16:230–241.
11. Steele RW, Thomas MP, Begue RE. Compliance issues related to the selection of antibiotic suspensions for children. *Pediatr Infect Dis J* 2001; 20:1–5.
12. Clements DA, Langdon L, Bland C, et al. Influenza vaccine decreases the incidence of otitis media in 6- to 30-month-old children in day care. *Arch Pediatr Adolesc Med* 1995; 149:1113–1117.
13. 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.
14. Hoberman A, Greenberg DP, Paradise JL, et al. Effectiveness of inactivated influenza vaccine in preventing acute otitis media in young children: a randomized controlled trial. *JAMA* 2003; 290:1608–1616.
15. Black S, Shinefield H, Fireman B, et al. Efficacy, safety, and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. *Pediatr Infect Dis J* 2000; 19:187–195.
16. Fireman B, Black SB, Shinefield HR, et al. Impact of the pneumococcal conjugate vaccine on otitis media. *Pediatr Infect Dis J* 2003; 22:10–16.
17. Eskola J, Kilpi T, Palmu A, et al. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. *N Engl J Med* 2001; 344:403–409.

## ■ A ROLE FOR ALTERNATIVE MEDICINE?

No recommendations can be made at this time regarding complementary or alternative medicine for AOM, given the limited and controversial data currently available.

**Pneumococcal conjugate vaccine reduces rates of recurrent AOM and the need for tympanostomy tubes**