Otitis Media

Otitis Media Guideline Team

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Developed
November, 1997
Updated
May, 2002

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Patient population: Pediatric patients (>2 months old) and adults

Objectives: (1) Limit acute symptoms and suppurative complications caused by otitis media. (2) Decrease the incidence of hearing loss and its adverse effects on the development of speech and language. (3) Limit the development of antibiotic-resistant bacteria.

Key points

Diagnosis

- Distinguish between acute otitis media (AOM) and otitis media with effusion (OME) (see Table 1) in making therapeutic decisions.
- The presence of middle ear effusion should be determined by the combined use of otoscopy, pneumatic otoscopy, and tympanometry when necessary *[D*]*.

Antibiotic therapy of otitis media

- For isolated symptomatic episodes of AOM, the **antibiotic of choice is amoxicillin** (at a dose of 60-90 mg/kg/day div b.i.d. for 5-10 days). Treat AOM that is clinically unresponsive to amoxicillin after 72 hours of therapy with high-dose amoxicillin/clavulanate *[C*]*. Patients with persistent symptoms on high-dose amoxicillin/clavulanate should receive 1-3 doses of IM ceftriaxone *[C*]*.
- Antibiotic therapy can be deferred for many asymptomatic patients, and for most cases of OME *[D*]*.
- The use of macrolides for AOM should be avoided *[A*]*.
- Avoid multiple courses of empiric, broad-spectrum antibiotics *[D*]*.
- Routine prophylactic antibiotic therapy is not recommended for recurrent AOM.

Prevention of AOM and OME

- Offer annual influenza vaccination to all children with a history of recurrent AOM *[A*]*.
- Ensure that all infants receive the recommended pneumococcal conjugate vaccine *[A*]*.
- Avoid exposure to environmental smoke and group daycare (when feasible) for children with recurrent AOM or OME *[C*]*.
- Discontinue pacifier use in children with recurrent AOM and OME. Consider xylitol syrup or xylitol-containing chewing gum for children with recurrent AOM, depending on age *[A*]*.

Other Issues Addressed in the text

Special Populations

- Otitis media in infants 0–8 weeks old
- Otitis media in children with chronic illnesses
- Otitis media in adults

Special Situations

- Primary care management of tympanostomy tubes
- Cerumen removal
- Care of otorrhea

*** Levels of evidence for the most significant recommendations:**
A=randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel.

Clinical Background

Clinical Problem and Current Dilemma

Incidence

Otitis media is the second most common diagnosis made by pediatricians at sick patient visits. Approximately 30-60% of children have had at least one putative episode of acute otitis media (AOM) by age one, and 10-20% have had three or more. Approximately 80% have had at least one episode by age 3 years. With respect to otitis media with effusion (OME), approximately 80-90% will have had at least one episode of either AOM or asymptomatic middle ear effusion in the first year of life.

Variability in Diagnosis and Treatment

Despite the general familiarity with this common condition, a great deal of variability remains in diagnostic criteria, approaches to therapy, and follow-up.

Diagnosis. Practice guidelines, research studies, and common clinical practices vary significantly with respect to diagnostic criteria for acute otitis media.

(Continued on page 5)

Table 1. Diagnostic Definitions

Acute Otitis Media (AOM) (ICD-9-CM code 382.4)

- Middle Ear Effusion (MEE) - demonstrated by pneumatic otoscopy, tympanometry, air fluid level, or a bulging tympanic membrane

  plus
- Evidence of Acute Inflammation – opaque, white, yellow, or erythematous tympanic membrane or purulent effusion

  plus
- Symptoms of otalgia, irritability, or fever

Otitis Media with Effusion (OME) (ICD-9-CM code 381.4) MEE without symptoms of AOM (serous otitis media) with or without evidence of inflammation

Myringitis (ICD-9-CM code 384.00) Symptoms of acute inflammation plus tympanic membrane erythema without MEE (demonstrated by pneumatic otoscopy or tympanometry)

Table 2. Management of all children with AOM
Ibuprofen or acetaminophen to control pain

Management of purulent OME or minimally symptomatic AOM (viral, *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis*). Watchful waiting (or a single course of amoxicillin).

Uncomplicated AOM with symptoms (usually due to viruses, *S. pneumoniae*, *H. influenzae*, or *M. catarrhalis*). A single course of high-dose amoxicillin. If symptoms persist at 72 hrs, use a single course of high dose amoxicillin/clavulanic acid (A/C). Cefuroxime axetil, cefpodoxime proxetil, and cefdinir are alternative second line agents. If symptoms persist for several more days, consider 1-3 doses of IM ceftriaxone. Trimethoprim/sulfamethoxazole, azithromycin, and cefprozil are acceptable for children with allergy to amoxicillin. Antibiotics should be given for 10 days for infants and toddlers and for 5 days for age 2 and up.

AOM with significant systemic toxicity (e.g., high fever, malaise, vomiting, leukocytosis) *(viral, S. pneumoniae, group A strep)*. IM ceftriaxone or high dose amoxicillin; consider other etiologies. If significant symptoms persist at 72 hrs, consider tympanocentesis.

AOM with conjunctivitis (viral, sinusitis, *H. influenzae*). A single course of trimethoprim/sulfamethoxazole, amoxicillin / clavulanate, cefuroxime axetil, cefdinir, or cefpodoxime.

If eye discharge persists at 72 hrs: add quinolone opthalmic drops. If symptoms continue to persist, use a single course of high-dose amoxicillin clavulanate or tympanocentesis.

AOM with bronchitis. Treat with amoxicillin as above. Treat bronchospasm as indicated.

AOM with bronchiolitis (viral, *S. pneumoniae*, *H. influenzae*, or *M. catarrhalis*). Treat with amoxicillin as above.

Purulent otorrhea (*S. pneumoniae*, *H. influenzae*, *Staph. aureus*, *Pseudomonas aeruginosa*)**.** Otic toilet followed by ofloxacin or ciprofloxacin otic drops for 10 days. Consider amoxicillin for systemic symptoms.

Follow up. Follow up should be scheduled at least monthly until middle ear effusion resolves.

Table 3. OME Management

OME Management. Children with documented OME should be followed monthly to document the persistence of MEE until clear. In many cases, it is difficult to know how long OME has been present. Thus, children with otitis media with effusion and documented language delays, school or behavior problems, and/or chronic medical conditions, should be referred promptly for audiologic evaluation regardless of the known duration of OME. If conductive hearing loss is found, otolaryngology referral is appropriate to consider management options. For children with uncomplicated OME, referral is appropriate when effusion has been present for 3-4 months.

A single course of high-dose amoxicillin/clavulanate is appropriate for OME that has been present 2-3 months.

Table 4. Recommended dosing

Approximate dose of amoxicillin 250mg/5cc or Augmentin ES 600mg/5cc to give amoxicillin 75-90 mg/kg div BID
Augmentin ES should be given with food!

Child's weight	Amoxicillin 250	Augmentin ES
5 Kg (11 #s)	3/4 tsp BID	2 ml BID
10 Kg (22 #s)	1 1/2 tsp BID	3/4 tsp BID
15 Kg (33 #s)	2 1/4 tsp BID	1 tsp BID
20 Kg (44 #s)	3 tsp BID	1 1/2 tsp BID
30 Kg (66 #s)	5 tsp BID	2 tsp BID
40 Kg (88 #s)	6 tsp BID	3 tsp BID
50 Kg (110 #s)	7 tsp BID	3 3/4 tsp BID

Table 5. Antibiotic Agents Used in the Management of AOM

Antibiotic (Brand Name)	Dose Peds	Cost[1] for 15 Kg Child for 10 days	Dose Adult	Cost for adult for 5 days	Advantages	Disadvantages	Clinical Role
Beta-lactam antibiotics							
Amoxicillin (Amoxil, Trimox)	60-90 mg/kg/day div BID	$8 gen	875 mg TID	$13 gen	Covers most pneumococcus Well tolerated	Beta-lactamase sensitive	First line in almost all situations
Amoxicillin/ clavulanate (Augmentin)	90 mg/kg/day div BID	$59	875mg BID	$37 gen	Covers most treatable pathogens	Increased diarrhea Expensive	First choice for amoxicillin failure
Cefuroxime axetil (Ceftin)	30 mg/kg/day div BID	$67	500 mg BID	$60 gen	Covers many pathogens	Fair pneumococcal coverage Unpleasant taste	Possible second line choice
Cefpodoxime proxetil (Vantin)	10 mg/kg/day div BID	$82	200 mg BID	$51	Covers many pathogens	Fair pneumococcal coverage Unnecessary gm neg coverage	Possible second line choice
Cefdinir (Omnicef)	14 mg/kg/day QD	$65	600mg QD	$41	Covers many pathogens	Fair pneumococcal coverage Excessive gm neg coverage	Possible second line choice
Cefprozil (Cefzil)	30 mg/kg/day div BID	$70	250 mg BID	$40	Good taste Moderate pneumococcal coverage	Beta-lactamase sensitive	Possible second line choice or first-line choice for amoxicillin allergy
Ceftriaxone (Rocephin)	50-75 mg/kg IM QD x 1-3 days	$141 (3 days)	1 g IM QD	$47 (one dose)	Broad reliable coverage	Parenteral Excessive gm neg coverage	1-3 doses for Augmentin failure
Other agents							
Trimethoprim / Sulfamethoxasole (Bactrim, Septra)	1 tsp/10 kg/dose BID 1 DS Tab BID	$14 gen	1 DS tab BID	$4 gen	Covers most H. influenzae Well tolerated	Risk of severe side effects Fair pneumococcal coverage	Possible first-line choice for amoxicillin allergy
Azithromycin (Zithromax)	Day 1: 10 mg/kg Day 2-5: 5 mg/kg	$29	500 mg x1, then 250 mg QD x 4d	$41	Covers atypical organisms Convenient	Fair coverage of relevant pathogens Less effective than Augmentin	Possible alternate choice for amoxicillin allergy; not appropriate for non-allergic patients

[1] Drug Costs – For brand drugs, Average Wholesale Price minus 10%. AWP from Amerisource Bergen Wholesale Catalog **4/03**. For generic drugs, Maximum Allowable Cost plus $3 from BCBS of Michigan MAC List, **1/27/03**

Table 6. Factors Influencing Surgical Decisions for OME and Recurrent AOM

Factor	Favors Surgery	Favors Alternatives to Surgery
Epidemiology		
Laterality of OME	Bilateral	Unilateral
Duration of OM	4 months or longer	Less than 3 months
AOM history	Recurrent AOM	Infrequent AOM
Daytime environment	Group day care	Home based care
Passive smoke	Frequent smoke exposure	No smoke exposure
Current season	Fall or early winter	Spring or early summer
Impact on child		
Physical symptoms	Ear pain, tugging, or pulling	Asymptomatic
Hearing	Bilateral hearing loss	Normal hearing
Speech and language	Speech delay or misarticulation	No speech impairment
Behavioral symptoms	Abnormal behavior	Normal behavior
School performance	Adversely affected	Unaffected
Miscellaneous		
Otoscopic appearance	TM retraction or collapse	Air bubbles or air-fluid level
Antibiotic tolerance	Multiple drug allergies	Antibiotics well tolerated
Baseline otitis media risk	High-risk population	Normal risk
Other indication for ENT surgery	Present	Absent

From Rosenfeld RM, Pediatric Clinics of North America 1996; 43(6):1175

Table 7. Clinical situations meriting consideration of subspecialty consultation or referral*

Acute otitis media

1. Emergent/Urgent referral. Any suspected complications such as meningitis (medical emergency) or other intracranial complications, facial weakness or paralysis, vertigo, or post-auricular swelling, redness, or displacement of the auricle (mastoiditis).**
2. Semi-urgent referral (2 to 3 days): Failure of antibiotic therapy with persistent severe signs and symptoms of AOM such as high fever or intractable pain (for consideration of diagnostic tympanocentesis).
3. Non-urgent referral: Perforation with persistent otorrhea.

Recurrent acute otitis media

1. Recurrent infections (over four documented infections in a year or three infections in six months).
2. Recurrent acute otitis media in a child with co-existing illnesses for which surgical treatment is desirable versus continued antibiotic therapy (e.g. immune deficiency, cystic fibrosis, sickle cell disease).
3. Recurrent infections with colonization with multi-resistant bacteria.
4. Recurrent infections and antibiotic allergies.

Chronic otitis media with effusion

1. Suspicion of hearing loss or history of language delay (audiology first).
2. Persistent middle ear effusion for 3-4 months.
3. Persistent tympanic membrane retraction or atelectasis.
4. Persistent abnormal tympanogram or audiogram.
5. All children with cleft palate, Down syndrome, or craniofacial malformations should be referred early rather than late.

Other

1. Cerumen impaction unresponsive to conservative management.
2. Suspicion of cholesteatoma.
3. Recurrent AOM or OME with history or symptoms of allergic disease.

*In many cases, primary care physicians will be able to manage these conditions without referral.

**Fluid in the mastoid air cells on CT scan or X ray, without clinical evidence of mastoiditis, is common with AOM and is not, in itself, an indication for referral.

Current Problem, continued

Most include the presence of middle ear effusion as an essential criterion. There is no consensus about the importance of signs of inflammation, tympanic membrane appearance, or clinical symptoms.

Use/overuse of antibiotics. Clinicians have years of experience treating middle ear disease with antibiotics. The favorable natural history of these conditions and the marginal impact of antibiotic therapy on outcome are underappreciated. Clinicians overestimate the extent to which clinical failure is due to antibiotic resistance, and overestimate the likelihood that second line medications will cover resistant organisms.

Referral process. Otolaryngology evaluation plays an important role in the management of recurrent AOM and persistent OME. However the ability of the surgeon to reach the most appropriate decision for the management of a given patient may be limited by a lack of historical information including previous antibiotic therapy and an accurate time course of middle ear disease.

Rationale for Recommendations

Diagnosis

Diagnostic criteria. See Table 1. Acute otitis media (AOM) is defined as the combination of middle ear effusion (MEE), signs of inflammation such as purulence, erythema, or a bulging tympanic membrane, and symptoms of fever, otalgia, or irritability in young children. In the absence of acute symptoms, a patient with MEE should be diagnosed with OME whether or not there are signs of acute inflammation. It is conceivable that some individuals with purulent effusion without symptoms (OME) or individuals with otalgia and TM erythema but no MEE (myringitis) are in the process of developing AOM with inflamed MEE and symptoms. However, given the marginal impact of antibiotics even for those patients with well-documented AOM, it is reasonable to defer treatment in patients with such questionable disease.

Diagnostic techniques. The basic question facing a clinician evaluating a patient's ears is whether or not MEE is present. If the presence or absence of MEE is less than clear, all available techniques should be used, including otoscopy, pneumatic otoscopy, and tympanometry.

Otoscopy. The most valuable technique for demonstrating the presence or absence of middle ear disease is the adequate visualization of normal landmarks. When the diagnosis of AOM is being considered, obstructing cerumen should be removed. The presence or absence of a light reflex is probably not a useful sign, and the tympanic membrane of a febrile or screaming child will sometimes appear reddened, even in the absence of middle ear disease. Even under ideal conditions using tympanocentesis as a gold standard for MEE, simple otoscopy has a sensitivity and specificity of only 74% and 60%, respectively for patients with OME. Middle ear fluid can be present even with normal landmarks. This highlights the importance of including pneumatic otoscopy and/or tympanometry in the assessment of the middle ear.

Pneumatic otoscopy. Brisk movement of the tympanic membrane with slight application of pressure is normal. If the tympanic membrane does not move perceptibly with application of slight positive or negative pressure, a middle ear effusion is likely. However, almost any eardrum will move if enough pressure is applied and excessive pressures can be painful. The major weakness of pneumatic otoscopy is the occasional difficulty of obtaining a good seal, especially in infants and in uncooperative children. This problem can be reduced by the use of appropriate ear specula. We recommend having a variety of reusable specula of different sizes, with and without rubber tips. Even under ideal conditions, the sensitivity and specificity of pneumatic otoscopy for MEE in a population undergoing tube placement is only 80-90%. A recent study demonstrated 50% accuracy among pediatricians and 70% among otolaryngologists on video pneumatic otoscopy.

Tympanometry/Acoustic reflectometry. Tympanometry and acoustic reflectometry can be valuable adjuncts to, but not a substitute for, otoscopy and pneumatic otoscopy. Tympanometry provides an important confirmation of middle ear fluid and is helpful for physicians honing their otoscopy skills. Tympanometry can also measure middle ear pressures and easily demonstrate the patency of myringotomy tubes by measuring increased external canal volumes. Tympanometry has a sensitivity and specificity of 70-90% for the detection of middle ear fluid, but depends on patient cooperation. Technical factors such as cerumen and probe position can lead to artifactual flattening of the tympanogram. The presence of a "normal" curve does not rule out the presence of air-fluid levels and effusion in the middle ear. However, together with normal otoscopy, a normal tympanogram is predictive of the lack of middle ear fluid. A "flat" tympanogram should be confirmed through repeated measurements, recording appropriate external canal volumes, and through correlation with pneumatic otoscopy. Acoustic reflectometry is also an appropriate approach for evaluating the presence of middle ear fluid, but, like tympanometry, it has imperfect sensitivity and specificity and must be correlated with the clinical exam.

Tympanocentesis. Tympanocentesis is the "gold standard" for demonstrating the presence of middle ear fluid and for identifying specific pathogens. This technique involves puncturing the pars tensa of the tympanic membrane under direct vision using a spinal needle attached to a vacuum trap. The major shortcomings of this procedure are that it is painful and, like any invasive technique, presents a risk for complications. These shortcomings can be minimized by the use of mechanical restraints and analgesic pre-medication. For patients with recurrent or severe symptoms, it might be appropriate to forego tympanocentesis and proceed directly to the placement of ventilation tubes in the operating room. Currently, the use of tympanocentesis is limited to research purposes at most centers. However, given the increasing

prevalence of antibiotic-resistant bacteria, it is possible that this technique will be used more frequently by primary care physicians in the future.

Etiology of AOM

Pathogens. AOM is usually a complication of an acute viral upper respiratory infection. Numerous large studies have documented the bacterial pathogens associated with the diagnosis of AOM and, in some cases, OME. The organisms *Streptococcus pneumoniae, Haemophilus influenzae* (non-typable), and *Moraxella catarrhalis* are consistently isolated from middle ear fluid in approximately 35%, 25%, and 15% of ears with AOM, respectively. A variety of bacteria, including Group A strep and *Staph. aureus* are isolated from approximately 15% of ears. Approximately 5% of ears have multiple pathogens. No bacterial pathogen is identified by tympanocentesis in approximately 20-30% of ears with clinical AOM.

A few studies have also sought evidence of viral infection. Respiratory viruses including RSV, rhinovirus, adenovirus, influenza virus, parainfluenza virus, and CMV are isolated from approximately 20% of middle ear samples cultured. Overall, evidence of viral infection is detected in almost 50% of children with AOM, half of whom have bacterial/viral co-infections

In cases of simultaneous infection with pathogenic viruses and bacteria, antibiotic responsiveness appears to be inferior to that of children with only bacterial infection, and microbiologic failure can occur despite clear in vitro sensitivity to the antibiotic used. Consequently, a second course of amoxicillin can effectively clear bacteria after the immune system has cleared the viral infection.

Chlamydia pneumoniae, a bacterial pathogen relatively insensitive to beta lactam antibiotics has been found in about 10% of middle ear specimens in some studies but not in others. The clinical significance of this finding remains unclear.

Risk factors for AOM

Age. Age is a significant predictor of AOM frequency, severity, and responsiveness to treatment. Infants and toddlers are more severely affected, and appear to be less responsive to therapy than older children. Consequently, clinicians should be cautious in extrapolating results from clinical trials involving older children to younger age groups.

Additional risk factors. Several specific risk factors for recurrent AOM and OME have been identified or are likely:

- Exposure to group day care with subsequent increase in respiratory infections.
- Exposure to environmental smoke or other respiratory irritants and allergens that interfere with Eustachian tube function.
- Lack of breast feeding.
- Supine feeding position.
- Use of pacifiers.
- Family history of recurrent AOM.
- Craniofacial abnormalities.
- Immune deficiency.
- Gastro-esophageal reflux.

Management

Principles underlying these guidelines

1. The risk of significant complications of middle ear disease should be minimized, including mastoiditis, meningitis, bacterial sepsis, intracranial abscess, prolonged symptoms of fever or irritability, and permanent hearing loss.
2. Selection of antibiotic-resistant pathogens due to antibiotic therapy should be avoided.
3. The impact of a course antibiotic therapy on the outcome of an episode of AOM is marginal at best. Clinical experience about the impact of treating middle ear disease can be misleading.
4. Antibiotic therapy should be reserved for those situations in which they are likely to have a positive impact on outcome.
5. Whenever possible, the choice of antibiotic should be based on interpretable clinical data, such as double tap clinical trials.

General management strategies.

Natural history. The clinical course of AOM is quite variable and clinical symptoms correlate incompletely with microbiologic status. Data from placebo controlled trials indicate that symptoms of AOM resolve spontaneously in 2-7 days in 80-90% of children depending on the population studied.

Impact of therapy. Patients should be informed that only 70% of episodes of AOM appear to be caused by bacteria, and that therefore, it is not surprising that at least 10-15% of these episodes will appear unresponsive to antibiotics no matter what agent is chosen. Approximately 25 children with symptomatic AOM will need to be treated in order to improve the symptomatic outcome at 3-5 days for one. Approximately 8 children would need to be treated to bring about complete clinical resolution (with the exception of serous OME) at 7-10 days. No significant difference is detected between groups at 7-14 days after diagnosis. Furthermore, the impact of antibiotic therapy is limited to its effect on the resolution of symptoms. There is no evidence that antibiotic therapy improves outcomes in asymptomatic patients.

The basic pathophysiology which determines whether or not a particular episode of AOM will respond to a given antibiotic is poorly understood. In general, the sensitivity of a particular bacterial isolate to a particular antibiotic *in vitro* significantly overestimates the microbiologic efficacy that can be expected in vivo. At least half of pathogenic bacteria recovered from the MEE of children who had failed clinically on amoxicillin are sensitive to this agent in vitro. For the 70% of children with positive bacterial cultures, 25% of those with persistent symptoms have actually cleared bacteria from the

MEE. Conversely, half of those who fail to clear bacteria from the MEE improve clinically. Thus, it is impossible to draw any reliable conclusion about bacteriologic efficacy from clinical outcome alone, and it is a mistake to attribute clinical failure to choice of the "wrong" antibiotic.

Severe suppurative complications of AOM are rare. Antibiotic therapy has no significant impact on persistence of effusion after AOM or time to recurrence.

Physicians are justifiably concerned that withholding antibiotics from children with AOM might result in increased complications. Population based studies indicate that the incidence of mastoiditis is doubled in countries such as the Netherlands where antibiotics are routinely withheld from children with symptomatic AOM. From placebo controlled trials, mastoiditis occurred in 0.5-1/1000 children with symptomatic AOM followed without antibiotic therapy. However, antibiotic therapy does not necessarily prevent acute mastoiditis. Several case series from the United States, Israel, and France have shown that acute mastoiditis is the first sign of acute otitis media in approximately 40-50% of cases, and occurs despite appropriate antibiotic therapy in another 40-50%. Few of the patients had had antibiotic therapy deferred. Thus, routine antibiotic therapy of all patients with AOM is unlikely to eliminate mastoiditis, and in the long run, might increase the frequency of mastoiditis by selecting for resistant organisms. In most cases acute mastoiditis will respond to parenteral antibiotic therapy without need for surgical intervention.

On balance, these data support a strategy of deferring routine antibiotic therapy for asymptomatic patients or older patients with mild symptoms, or in patients in whom symptoms of AOM are overshadowed by symptoms of viral illness such as gingivostomatitis or gastroenteritis ("incidental AOM"). These individuals should be followed for clearance of effusion, and antibiotic therapy should be initiated if symptoms worsen.

Antibiotic choice. High dose amoxicillin is clearly the first choice of antibiotic therapy for almost all episodes of AOM. Dosing recommendations are listed in Table 4. In addition a subset of the antibiotics approved for AOM and OME are listed in Table 5 along with their dose, cost, advantages, disadvantages, and summary recommendations. With the exception of amoxicillin, none of these agents has been compared to placebo, and none has been shown to be superior to amoxicillin in randomized trials. The vast majority of clinical studies report a 20-30% symptomatic and microbiologic failure rate with every oral antibiotic tested. Even a ten-day course of high-dose amoxicillin clavulanate resulted in an 18% bacteriologic and 14% clinical failure rate at 10-12 day follow up.

Clinical failure, as defined by filling a second prescription within a week, is identical whether amoxicillin or more broad-spectrum agents, is chosen as initial therapy.

High-dose, short-course amoxicillin has been recently demonstrated to be less likely to select for penicillin-non-susceptible *S. pneumoniae* (PNSSP) than standard 10-day therapy and is not associated with any increase in side effects. In the event of documented amoxicillin allergy, reasonable choices include trimethoprim/sulfamethoxazole (TMP/SMX), azithromycin, and second-generation cephalosporins. Of these, TMP/SMX is the least expensive and is an effective agent for the treatment of antibiotic sensitive bacteria, particularly the HI often found associated with otitis/conjunctivitis syndrome. However, TMP/SMX has only fair coverage of GABHS and pneumococcus and can be associated with aplastic anemia and Stevens-Johnson Syndrome. Consequently, cost, risks, and benefits must be balanced when choosing among TMP/SMX, azithromycin, and cephalosporins.

It remains an open question whether the superior *H. influenzae* (HI) coverage of amoxicillin/clavulanate (A/C) justifies the choice of this agent as a first line agent. Assuming that 20% of AOM episodes are caused by HI and half of these isolates are beta lactamase positive, 10% of these episodes should respond preferentially to A/C compared to amoxicillin. However, half of these episodes would be likely to resolve spontaneously, and we suspect that the 5% theoretical advantage of A/C would not be detectable over the 15% failure rate observed with A/C, and would not justify the much greater cost and frequent complications of A/C.

Even in cases where parents are convinced "amoxicillin doesn't work for my child", amoxicillin is more likely to work than any oral cephalosporin. The few studies that have followed colonization with antibiotic-resistant pathogens have shown spontaneous clearance of resistant organisms after several months without antibiotics. Therefore, previous use of second line agents is not an indication for recurrent use of second-line agents.

Approximately 30-60% of clinical isolates of *S. pneumoniae* from children with AOM exhibit relative penicillin resistance (PNSSP) and approximately half of these exhibit resistance to multiple antibiotics. Pneumococcal penicillin resistance is always meditated by alterations in penicillin-binding proteins, never by beta-lactamase expression. In general, this resistance can be overcome by use of high dose oral amoxicillin or IM ceftriaxone. PNSSP are largely resistant to oral cephalosporins and 20% are fully resistant to trimethoprim/sulfamethoxazole (TMP/SMX) and 20% are resistant to macrolides. With respect to *H. influenzae*, 30-50% of HI isolated from children with AOM are amoxicillin resistant. This resistance is usually, but not always, mediated by beta lactamase and usually cannot be overcome by increasing amoxicillin dosing. Beta-lactamase positive HI (BLPHI) are generally sensitive to A/C, third generation cephalosporins, cefuroxime axetil, and in 85% of cases, TMP/SMX. BLPHI are resistant in vitro to cefaclor, loracarbef, and cefprozil in 26, 18, and 30% of isolates, respectively. It is for this reason cefaclor and loracarbef are not recommended. Cefprozil is included only because it maintains adequate pneumococcal coverage. Mixed infections of SP and HI occur in 10-20% of cases.

Clinical failure. In principle, beta lactamase positive HI (BLPHI) is the most likely middle-ear organism to persist despite adequate amoxicillin therapy. In reality, children with amoxicillin unresponsive AOM are 2-3 times more likely to be infected with PNSSP than BLPHI, or by mixed infections involving both bacteria. This fact emphasizes the importance of maintaining excellent coverage of PNSSP for patients with amoxicillin unresponsive disease. High-dose amoxicillin/clavulanate is the only oral agent with greater than 90% coverage of both PNSSP and HI and is our recommendation for the treatment of these patients. If significant symptoms persist, a 3-day course of parenteral ceftriaxone provided 97% clearance of PNNSP from children with previous antibiotic failure. In the event that significant symptoms persist despite such aggressive therapy, urgent tympanocentesis to guide therapy or placement of tympanostomy tubes may be indicated.

Although Ceftriaxone provides the best-documented coverage of otitis pathogens, concern exists about the potential of this agent to select highly resistant pathogenic bacteria. For this reason, the use of ceftriaxone should be limited to situations such as A/C failure or severe systemic symptoms, where parenteral therapy is indicated. Patients receiving ceftriaxone should be observed in the office for symptoms of anaphylaxis for at least 15 minutes after administration

Macrolides. Azithromycin and clarithromycin are theoretically excellent choices for the treatment of AOM and appear to have comparable clinical efficacy to other agents. However, a recent double-tap study demonstrated only a 55% bacterial clearance rate and a 30% clinical failure rate for azithromycin, even for bacterial isolates that are clearly sensitive to macrolides in vitro. Furthermore, numerous reports have been published describing patients who developed bacterial sepsis or meningitis while taking macrolides for AOM. In all cases, the organisms isolated from these individuals were macrolide resistant. Azithromycin is an appropriate choice in the event of amoxicillin allergy. Clarithromycin and erythromycin/sulfisoxazole offer no clinical advantages over azithromycin.

In theory, macrolides cover atypical organisms such as Chlamydia pneumoniae and Mycoplasma pneumoniae as well as the previously discussed otitis pathogens. However, it is uncertain to what extent these organisms are responsible for AOM and whether such infections benefit from treatment. On the other hand, it is clear that significant bacterial infections, such as pneumococcal pneumonia and bacteremia, are much more likely to be sensitive to amoxicillin than azithromycin, and macrolides should be avoided in situations where such infections are suspected.

Length of therapy. No study has yet defined the optimal length of antibiotic therapy. Several studies performed prior to the recent increase in penicillin resistance suggested that shorter courses of amoxicillin had efficacy comparable to ten-day courses. A more recent study of amoxicillin/clavulanate shows a trend to more frequent recurrence with five-day therapy. Shorter course antibiotic therapy should be reserved for children 2 and older without history of recent AOM.

Side effects of antibiotic therapy. Antibiotic therapy is frequently associated with side effects, primarily GI (5-20%) and cutaneous (allergic and diaper rash) (3-10%). Costs and inconvenience are always associated with antibiotic prescriptions. The increasing prevalence of antibiotic resistant bacteria is an ever-present concern. Rarer complications include systemic reactions, particularly to TMP/SMX, and the masking of serious infectious disease complications requiring specific therapy, e.g., partially treated meningitis or recurrent urinary tract infections.

It is likely that an oral fluoroquinolone will be approved for children in the next few years. We believe that use of quinolones should be reserved for patients with significant, recalcitrant symptoms or those with documented amoxicillin and cephalosporin allergies.

Treatment options for AOM. Treatment recommendations are outlined in Table 2. The decision to treat should be based on symptoms, since symptomatic improvement is the only outcome attributable to antibiotics in placebo-controlled trials of AOM. For children with purulent OME or minimally symptomatic AOM, it is reasonable to give parents a dated prescription for amoxicillin to be filled within a week at the parent's discretion if symptoms are worsening. In one randomized study, such an approach decreased the number of amoxicillin prescriptions filled by 70% and was well accepted and appreciated by parents. Alternatively, the clinician could defer therapy and ask the parent to call in the event of persistent symptoms to get a prescription over the phone. In either approach, parents would be spared an unnecessary follow-up visit.

When the diagnosis of AOM is in doubt (e.g., myringitis), the diagnosis of AOM should be deferred. Antibiotic therapy can be started empirically, if deemed clinically necessary, and early follow-up scheduled to refine the diagnosis.

High dose amoxicillin remains the agent of choice for almost every episode of AOM where antibiotics are indicated. Amoxicillin should be dosed at 60-90 mg/kg/day div BID times 5 days for children 2 and older. Second-line agents such as macrolides, trimethoprim/sulfa, and most cephalosporins have few advantages over amoxicillin, and in most cases, provide inferior coverage. For patients with persistent symptoms despite 3 days of amoxicillin therapy, the second line agent of choice is high-dose amoxicillin/clavulanate. Patients with continued symptoms should be treated with 1-3 doses of IM ceftriaxone or referred for urgent otolaryngologic consultation. Younger children probably benefit from a full ten day course of amoxicillin. Prolonged antibiotic therapy (>10 days) is almost never indicated.

Topical ofloxacin or ciprofloxacin/hydrocortisone, together with adequate otic toilet, is a valuable adjunct for the treatment of otorrhea, and usually obviates the need for systemic antibiotics.

Follow-up scheduling for AOM. Early clinical reevaluation is recommended for patients with AOM whose symptoms persist despite 3-5 days of antibiotic therapy. Early follow up is also important in very young children who might be unable to express their discomfort. Routine follow-up should be scheduled at 4-6 week intervals until clearance of MEE is documented, in order to identify children with persistent MEE (to allow the diagnosis of chronic OME) and to identify conditions with long term middle ear morbidity such as cholesteatoma, or atelectasis of the tympanic membrane.

Management options for recurrent AOM. The use of antibiotic prophylaxis for recurrent AOM is discouraged in most situations. Although early studies showed a small but statistically significant decrease in the frequency of recurrent AOM in patients receiving daily amoxicillin or sulfisoxizole vs. placebo (0.1-0.2 episodes per month decrease), a more recent study has failed to show such an effect. There are no data to predict the impact that the observed increasing prevalence of antibiotic resistance might have on the efficacy of prophylaxis. Furthermore, long term antibiotic prophylaxis has been shown to be a major risk factor for the acquisition of multi-resistant S. pneumoniae. TMP/SMX, cephalosporins, and macrolides are not FDA approved for long term prophylaxis. Sulfisoxizole is no longer available.

The placement of tympanostomy tubes can be considered for recurrent AOM on clinical grounds as described in Table 6. Tympanostomy tubes do not significantly reduce the rate of new episodes of middle ear disease, but they do convert individual episodes of AOM to episodes of tube otorrhea, with significantly less pain, less risk of suppurative complications, and less risk of hearing loss due to prolonged residual OME. Furthermore, tube otorrhea can be effectively treated with topical, rather than systemic, antibiotics, and will be less likely to contribute to increasing antibiotic resistance. Expectant management rather than tubes or long-term antibiotics is a reasonable option for children with recurrent acute otitis media without significant morbidity, i.e., hearing loss or abnormalities of the tympanic membrane such as retraction pockets or atelectasis.

Referral criteria for otolaryngology are summarized in Table 7. In all cases of recurrent AOM (and persistent OME) efforts should be made to seek and ameliorate predisposing factors such as exposure to tobacco smoke, group day care, supine feeding, and gastroesophageal reflux. Pacifier use should be discouraged. Breast feeding should be encouraged for future siblings. Influenza vaccine should probably be offered to children two years or older, since an episode of influenza would likely result in AOM, and each additional episode of AOM would then increase the likelihood that the child will require tubes. The use of xylitol containing chewing gum or xylitol syrup has been shown significantly decrease the risk of recurrent AOM.

Management options for OME. OME is a common consequence of AOM. MEE is expected to persist in 60% of children one month following a treated episode of AOM. MEE persists in 10% of cases three months after treatment. Similarly, prospective surveillance studies detect the presence of asymptomatic MEE in more than 20% of the infant-toddler population at a given time. Most of these episodes resolve spontaneously over a few weeks. 65% of all MEE of unspecified duration will resolve in 3 months without therapy. Antibiotic therapy will boost short-term resolution by about 15%. Systemic corticosteroid therapy significantly improves the short-term resolution of OME, however, such therapy has no long term impact on MEE and is, therefore, not recommended. No data supporting intranasal steroids exist.

There are two major reasons for concern about OME. First, OME frequently causes a mild to moderate conductive hearing loss. There is likely a subset of children for whom this hearing loss leads to behavioral disturbances or language delay and cognitive impairment. However, recent studies indicate that this effect is neither inevitable nor common. In fact, in one prospective study, the persistence of OME accounts for only 2-3% of the variance in language development.

In the case of otherwise healthy children under age 2, two randomized studies comparing immediate to delayed ventilation tube placement for prolonged OME failed to show any significant benefit of early ventilation tube placement on later language development. Less than half of patients for whom tube placement was deferred in one of these studies ended up getting tubes by age 3. However, if a child is exhibiting significant speech delay or behavioral disruption or suffers from some other cause of sensory or cognitive dysfunction, early tube placement is probably appropriate. Children with anatomic abnormalities such as a bifid uvula, cleft palate, or Down Syndrome are less likely to resolve their MEE spontaneously and should also be referred for early intervention. In order to serve those patients who will eventually need tubes in a timely manner, it is appropriate to refer any child with a 3-4 month history of documented OME.

The second important reason to be concerned about OME is the potential of prolonged negative pressure and MEE to cause permanent structural damage to the tympanic membrane or middle ear anatomy. Any child with apparent tympanic membrane atelectasis, retraction pockets, or middle ear masses should be referred for ENT evaluation without following for persistent effusion. Certainly, any child with MEE persisting more than a year should be referred for possible ventilation tube placement.

In some cases recurrent OME is a consequence of respiratory allergies. In individuals with history, family history, or physical findings of atopy, e.g., allergic rhinitis, shiners, chronic nasal obstruction, asthma, or eczema an allergy evaluation might be considered. Empiric antihistamine/decongestant therapy for OME per se is ineffective and not recommended.

Subspecialty referral. Possible criteria for subspecialty (otolaryngology, allergy, infectious disease) referral or consultation are listed in Table 6. In all cases, referral should be accompanied by a note from the primary care physician indicating either a specific question (i.e., does this child need tubes?) or indicating any preference for the management of the patient. It is acceptable to refer a patient for otolaryngologic evaluation for an opinion or for parental reassurance, even if the primary care physician does not believe that tympanostomy tubes are immediately necessary. Audiologic evaluation is also helpful for decision making and should be obtained together with otolaryngology referral for OME.

Special Circumstances

Special Populations

Otitis media in infants 0–8 weeks old. The preceding guidelines specifically exclude the treatment of AOM in young infants. This population is at increased risk of a severe or atypical outcome from suppurative AOM. Middle ear pathogens found in young infants include Group B strep, gram negative enteric bacteria, and *Chlamydia trachomatis*. Febrile young infants with apparent AOM should undergo a full sepsis work up as would be otherwise indicated. Consideration should be given to obtaining an ENT consultation for tympanocentesis. Initiation of empiric amoxicillin is probably acceptable for infants with URI and AOM who are otherwise well.

Otitis media in children with chronic illness. Several chronic medical conditions are associated with a predisposition to morbidity from otitis media including: craniofacial abnormalities, cleft palate (including submucus cleft), chromosomal abnormalities (especially trisomy 21), psychomotor retardation, gastroesophageal reflux, respiratory allergies, hearing loss of any etiology, visual loss, and acquired and congenital immune deficiencies. Management of these conditions is beyond the scope of this guideline, but early consideration of ENT referral in the event of recurrent AOM or persistent OME is recommended.

Otitis media in adults. The antibiotic guidelines regarding children can generally be applied to adults, although few clinical studies have been done. Smoking should be discouraged as a risk factor for any respiratory infection and AOM in particular. Oral or nasal steroids might be an appropriate option for adults with persistent MEE, particularly when associated with chronic nasal allergies. Any adult with a persistent (greater than 2 month) history of unilateral MEE should be evaluated for the presence of an underlying tumor of the nasopharynx or skull base. Otitis media in adults associated with a neck mass, difficulty swallowing, hoarseness, weight loss, double vision, vision loss, facial numbness, or other signs of cranial nerve dysfunction, should be considered to be caused by a skull base neoplasm until proven otherwise. Decongestants can be considered for rare instances (e.g. airplane flights), but in general are not considered useful. Antihistamines should be reserved for patients with allergic symptoms.

Special Situations

Primary care follow-up and management of tubes. Be familiar with the preferences of the surgeon to whom you refer patients, since he/she will likely be handling any complications of tube placement. Otolaryngologists vary in their recommendations regarding swimming, ear drainage, and other activities. There is no scientific evidence to support the efficacy of water precautions in preventing tympanostomy tube otorrhea.

Recommendations of the Division of Pediatric Otolaryngology at the University of Michigan Medical Center are summarized below.

Post-op irrigation. After the tubes are placed in the operating room, antibiotic ear drops are placed in both ears to irrigate the tubes. The parent is given the bottle to administer the drops for the next 2 to 3 days.

Ear drainage. Ear drainage may occur subsequently associated with an upper respiratory infection. The parent should clean the external ear with hydrogen peroxide on a cotton ball. Sulfa/steroid (Vasocidin) or quinolone drops should be used in the affected ear(s) two or three times a day until the drainage abates. Malfunctioning tubes should be treated with peroxide or vinegar/water irrigations.

If drainage does not resolve, the otolaryngologist should be contacted. Treatment options include changing drops to ofloxacin or ciprofloxacin/hydrocortisone drops, vinegar and water irrigations (using a 10 cc syringe and a cut off butterfly needle), or suction/debridement of the ear in the office. Oral antibiotics are not generally necessary (or useful) for the treatment of tube otorrhea but might be indicated for a child with systemic symptoms. Ear drainage in the absence of tubes might be secondary to otitis externa or to a tympanic membrane perforation and consideration should be given to topical therapy.

Prevention / management of water into ear in children with tubes. Many otolaryngologists advise their patients to use ear plugs with swimming, bathing, or washing hair. Others recommend simply using prophylactic ear drops after water exposure. Ear plugs sized to fit can be obtained through the otolaryngologist. Head bands or bathing caps can be worn alone or with ear plugs to help the plugs stay in place. Custom swim molds made by an audiologist may be recommended for children at high risk of otorrhea who swim frequently. Ear plugs are probably most important for swimming in lakes or unchlorinated water, where high bacterial counts or unusual organisms might be present.

Patients with tubes should follow up with otolaryngology every six months.

Cerumen removal. Home management includes hydrogen peroxide/water irrigations using a 10 cc syringe with a cut off

butterfly needle. It is reasonable to supply such a syringe to parents of children with impacted cerumen. Over the counter products are similar to peroxide but much more expensive. For hard impactions, a few drops of Auralgan or Colace syrup in the affected ear, followed 30 minutes later by irrigation, have both been shown to be effective.

Office management of cerumen impaction includes hydrogen peroxide/water or water irrigation by syringe or water-pik or debridement using a hand-held otoscope and curette. Referral to an otolaryngologist for removal of a moderate impaction is better tolerated than a lengthy visit for a severe impaction.

Patients with eczema, seborrheic dermatitis, or other skin disorders may actually have desquamating skin rather than cerumen obstructing the canal.

Information the Patient Needs to Know

Diagnosis

- **Acute otitis media.** AOM is an acute, symptomatic inflammation of the ear with fluid behind the eardrum.
- **Causes.** Either a bacterial infection or a viral infection of the ear can cause AOM.
- **Fluid without inflammation-URI's.** Fluid in the ear without symptoms of pain or fever is not the same as AOM. This can occur as a result of URI's ("colds").
- **Symptoms of AOM.** Common symptoms of AOM include irritability, poor sleep, loss of appetite, and fever. Ear-pulling is a poor predictor of AOM. Symptoms of teething or viral sore throats are often similar to AOM.
- **The diagnosis is complex.** The diagnosis of AOM or middle ear fluid can be very difficult and uncertain. Do not be surprised if different practitioners draw different conclusions from examining your child.

Natural history

- **Self-curing.** Most ear infections get better without antibiotic therapy.
- **Middle ear fluid.** Middle ear fluid persists for at least two months following an episode of AOM.

Treatment

- **Symptom treatment.** Fever reducing medications are effective in reducing the symptoms of AOM.
- **Antibiotics**
  - -- **Not always effective.** Ear infections caused by viruses or antibiotic resistant bacteria will not get better in the short term no matter what oral antibiotic is prescribed.
  - -- **Not always necessary.** Most ear infections resolve on their own. The more mild the symptoms, the more likely that the infection will resolve without antibiotics.
  - -- **Amoxicillin.** Amoxicillin is usually more effective and has fewer side effects than other antibiotics. Previous use of broad-spectrum antibiotics does not indicate their need in subsequent episodes.
  - -- **Take all of the prescription.** Finish the recommended course of antibiotics. (If you run out of medication after five days of therapy and symptoms are resolved, it is probably not necessary to fill another prescription.)
  - -- **Not for persisting middle ear fluid.** Additional antibiotics add little to speeding the clearance of middle ear fluid following an episode of AOM.
  - -- **Not for URI's.** Using antibiotics in children with URI's does little to speed the resolution of symptoms or decrease the rate of AOM. It is associated with increased risk of antibiotic resistance.

Follow-Up

- If symptoms persist after 72 hours. Patients should return for reevaluation if symptoms persist or worsen after 72 hours of oral therapy.

Prevention

- **Day care, smoke, pacifier use.** Exposure to day care, pacifier use, and tobacco smoke significantly increase the risk of AOM, OME, and symptoms of upper respiratory infection. Hand washing can be helpful in limiting spread.
- **Immunizations.** The conjugated pneumococcal vaccine, Prevnar, reduces the risk of ear infections slightly. Children with recurrent ear infections should probably get an annual influenza vaccine.
- **Xylitol.** Xylitol-containing chewing gum significantly decreases the risk of recurrent ear infections. However, the use of such gum should be balanced by the risk of choking, especially in younger children, and children should not be allowed to chew gum when physically active.
- Ear infections are not generally contagious, and children with isolated AOM can return to school whether or not they are receiving antibiotics.

Strategy for Evidence Search

The literature search for this project was conducted in two phases. The team began with the results of the literature searchs performed for Evidence-Based Otitis Media (Rosenfeld and Bluestone, 1999) and for Management of Acute Otitis Media: Evidence Report/Technology Assessment Number 15 (Agency for Healthcare Quality and Research, 2000). To supplement these searches with more recent findings, the team then conducted a search of literature published on Medline prospectively using the major keywords of: since 1/1/98, human, English language, clinical trials, and guidelines. Terms used for specific topic searches within the major key words included: acute otitis media, otitis media with effusion, recurrent otitis media, etiology and natural history, diagnosis (signs and symptoms, hearing loss, otoscopy, pneumatic otoscopy, tympanometry, tympanocentesis, audiogram), treatment (antibiotic therapy, adjunctive therapy, myringotomy, laser tympanostomy),

cerumen impaction, otorrhea. Detailed search terms and strategy available upon request. The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent information available to expert members of the panel, including abstracts from recent meetings and results of clinical trials. Negative trials were specifically sought. The search was a single cycle. Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Disclosures

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

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