

Acute Otitis Media: Why do we Need an Update?

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Updates are given when there is new information to disseminate. For this update on acute otitis media (AOM) we address the question, “Is the disease changing or is it just our concern over the consequences of our current treatment practice that leads us to desire an update on this topic?” Let’s look at several questions that will allow us to develop an answer to the first question.

One of the first things we need to determine is if AOM is an important topic to study. Otitis media is important because except for the common cold, otitis media is the most common disorder for which pediatric care is sought. It is also known that AOM leads the diagnosis list of indications for outpatient antibiotic therapy in the US. Further, almost all children in the US will have at least one ear infection diagnosed by 3 years of age. Therefore the topic of AOM is very significant and worthy of an update.

When trying to develop a reasonable treatment paradigm for the significant problem that is otitis media, we also need to look at why we treat AOM. The first of the reasons we treat AOM is to relieve the patient’s suffering by reducing the patient’s symptoms during an episode of AOM and to decrease the frequency of otitis media episodes. Beyond the consequences of the acute discomfort it is also a goal to avoid middle ear sequelae such as atelectatic drums and cholesteatoma. Another long term goal is to restore the hearing loss associated with otitis media with effusion (OME) and therefore prevent learning disabilities that result from hearing loss.

We also treat ear infections because AOM can cause potential damage to the patient acutely. Before antimicrobial therapy, AOM was associated with complications such as mastoiditis, epidural abscess and sigmoid sinus thrombosis, etc. Certainly such consequences are to be avoided if possible. Once antibiotic therapy was developed, it was therefore used in all cases of acute otitis media or possible acute otitis media. More recently the necessity of using antibiotic therapy for all possible cases of AOM has been brought into question as spontaneous resolution is high (60-80%) in children over 2 years of age when no antibiotic therapy is used. According to *Rosenfeld 2003*¹, 7-8 children with AOM would need to be treated with antibiotics to get one child to improve beyond the expected course of otitis media without antibiotic therapy. In the observed group that Rosenfeld reports on, mastoiditis incidence was lower than 0.25% when treated by observation and analgesics alone. Thus, even the reasons we treat AOM are conflicting and this leads to confusion about who should receive antibiotic therapy at all – remembering that all patients should have their acute pain addressed.

In order to better determine who should be treated, let us review the literature written about the natural history of the disease. Unfortunately even this is confusing as the meta-analysis presented in 2003 at IAPO meeting in São Paulo by Rosenfeld, showed no consistent definition of AOM in the studies he found that qualified for his evaluation. How can studies be compared if there is no consistent diagnosis of the problem or disease being evaluated? Even a recent Cochrane Review, looking at randomization of patients, blinding of evaluators and follow-up for complications of patients being treated with antibiotics versus patients treated with observation, no attention was given to how the diagnosis of AOM was made or what signs and symptoms were used to make the diagnosis. Further, the Dutch study that documented an observational approach to the treatment of AOM was based on family medicine providers observations without defined criteria of what qualified as AOM. This study did exclude children under two years of age, those with craniofacial abnormalities and the very ill. The conclusion by the Dutch was that children without antibiotic therapy did as well as children who were prescribed antibiotic therapy. We must be very careful before we conclude that no one needs antibiotics to treat AOM. Current information that is based on weak or inconsistent definitions may dilute the conclusions of any study. And occurs very often, many of the children in the studies diagnosed with AOM had instead, OME for which antibiotic therapy is not indicated.

So who do we need to treat with antibiotic therapy? We treat those who can be definitely diagnosed with an episode of acute otitis media. We also should consider antibiotic treatment for those who are immunologically immature and those prone to otitis media such as children with cleft palate, Down syndrome, achondroplasia, and others with skull base abnormalities.

But, what is AOM? Let's define AOM and compare that to OME. AOM is the rapid onset of symptoms and signs of an ear infection with inflammation in the presence of middle ear effusion. OME, on the other hand, is middle ear effusion in the absence of infection. This definition was first made by *Takata et al. in 2001*². Then in 2004 the American Academy of Pediatrics wrote a Clinical Practice Guideline on the diagnosis of AOM. According to the guideline, the diagnosis of AOM requires three things:

1. an acute onset of signs and symptoms
2. presence of middle ear effusion which can be appreciated by:
 - bulging of the tympanic membrane (TM)
 - limited or absent TM mobility or
 - = air fluid level or otorrhea
3. signs and symptoms of middle ear inflammation

The guideline does acknowledge that making the diagnosis of otitis media has some inherent uncertainty particularly because the history alone is insufficient. While it is true that ninety percent of children diagnosed with AOM present with fever, otalgia and excessive crying, 72% of patients presenting with the same symptoms do not have AOM. In addition, in order to make the diagnosis, not only do you need to see fluid, there must be specific signs of inflammation. Differentiating middle ear fluid in the absence of infection (OME) from middle ear fluid with

inflammation is difficult to distinguish (*Niemela 1994*)³. Furthermore, pneumatic otoscopy requires seeing nearly the entire TM. Physicians may not have adequate training or may not be able to safely clear ear canal cerumen to see the TM with the tools available to them in their office.

It has been distressing to learn that residency programs in the United States have little formal training in otitis media. 41% of pediatric resident training programs have no formal training in otitis media and only 66% of family medicine residents are taught to use pneumatic otoscopy. A study was done that looked at the ability of physicians to correctly diagnose middle ear fluid as normal, AOM or OME from viewing pneumatic otoscopy videotapes. In this study, pediatricians correctly differentiated AOM, OME and normal, 50% of the time (range, 25-73%). They were able to identify an absence of normal in 90%, but overcalled AOM an average of 27% of the time mistaking OME for AOM. Are Ear, Nose and Throat specialists any better? On average, otolaryngologists gave a correct diagnosis 73% of the time (range, 48%-88%) and over diagnosed AOM 10%. Why is the otolaryngologist a little better? It was shown that otoscopy validated by tympanocentesis improves accuracy in diagnosing the presence or absence of effusion (*Kaleida 1992* and *Pichichero 2001*)⁴⁻⁵. So when an otolaryngologist evaluates an eardrum under the microscope and then places a myringotomy knife into the drum at the time of placing tubes s/he is training themselves to be a better otoscopist because the presence or absence of fluid is determined immediately. Therefore, we all have work to do to become better otoscopists if we want to diagnose otitis media accurately.

Now let's say we can accurately diagnose which patient truly has an ear infection. Does it matter how bad the ear infection is? Does every patient need to be treated with antibiotics? If they need antibiotics, which antibiotic is best?

In the Clinical Practice Guidelines of 2004, it was concluded that not every patient needs antibiotics but that every patient should have their symptoms of ear pain treated, especially in the first 24 hours of the acute episode. Specifics of pain treatment for otitis media have yet to be well studied, but options for otalgia therapies include (*Pelton 1998*)⁶:

- acetaminophen, ibuprofen
- home remedies: distraction, oil, warm, cold packs
- topical agents – benefit older children >5-6yrs
- homeopathic agents and
- narcotic analgesia.

Once pain is addressed, the next step in treating AOM is determining which patients require antibiotic therapy and which may be treated expectantly with a period of observation. Observation candidates are first stratified by age and then by disease severity. Therefore, children between six months and two years of age with non-severe illness **AND** uncertain diagnosis, or children over two years of age with non-severe symptoms **OR** uncertain diagnosis may have their antibiotic therapy delayed 48-72 hours. A policy of observation first requires stringent follow-up. Antibiotic therapy should be started if symptoms persist or worsen after the 2-3 day observation period. Children under six months considering

the immaturity of the immunologic system, are not candidates for observation and should be prescribed antibiotic therapy whether the diagnosis is certain or uncertain. Children between 6 months and two years of age should get antibiotics if the diagnosis is certain but may be placed into the observation group if the diagnosis is uncertain and the symptoms are not severe. Children older than two years may be placed in the observational group as if the diagnosis is certain but the symptoms are not severe or if the diagnosis is uncertain. Note that antibiotics are always indicated for a certain diagnosis and severe symptoms no matter what the age is.

So how can you know when symptoms are severe enough to warrant antibiotic consideration? My partner in Denver, Norman Friedman, published this year a scale that ranks symptom severity. The scale ranked from 1 (no problem) to 7 (extreme problem):

Symptoms scale from 1 to 7:

1. Not present/ Not a problem
2. Hardly a problem
3. Somewhat of a problem
4. Moderate problem
5. Quite a bit of a problem
6. Very much of a problem
7. Extreme problem

A second scale was developed that addresses otoscopy findings only.

Otoscopy severity scale, objective findings :

0: normal, or effusion without erythema

1: erythema only, no effusion

2: erythema, air/ fluid level, clear fluid

3: erythema, complete effusion, no opacification

4: erythema, opacification with air-fluid level or air bubbles, no bulging

5: erythema, complete effusion, opacification, and no bulging

6: erythema, bulging rounded doughnut appearance of the TM

7: erythema, bulging, complete effusion and opacification with bulla formation

When combined, the two scales were shown to have high reliability in ranking the severity of the child's ear infection. When you take the score of the symptom severity and add it to the score of the otoscopy findings a ranking of non-severe to severe can be made. If the scales together are lower than or equal to four, the patient is considered non-severe and may be treated with observation if they are over six months of age.

The two scales have been combined onto a 2-sided laminated cards that can be requested from dpmccorm@UTMB.EDU.

In summary, who needs antibiotics? Children under two years of age, children with associated anomalies or medical conditions, and children with severe symptoms and signs of AOM need antibiotic therapy for their ear infections.

Now that we know how to diagnose and ear infection and who needs them, which antibiotics shall we use?

In order to choose a particular antibiotic, we need to know which bacteria we are

treating. In otitis media, the most common bacteria is *Streptococcus pneumoniae*. The breakdown for the microbiology of AOM for 2004 in a Finland study (*Palmu 2004*⁷) is in **Table 1**.

Table 1. Microbiology for AOM

	Percent	Resistance
<i>S. pneumoniae</i>	50%	variable
<i>H. influenzae</i>	30%	35%
<i>M. catarrhalis</i>	15%	90%
Viral	(40%)	

Some of the variability in *S. pneumoniae* resistance is due to the use of vaccines. The Prevnar 7 covalent vaccine has been shown to decrease the 7 covered serotypes by about 34% but there was a rebound of non-covered serotypes by 33% in another Finnish study. *Pichichero 2006*⁸ in the US in 2005 studied the percent difference in *S. pneumoniae* and *H. influenzae* before and after Prevnar vaccine was introduced. In two geographically disparate locations the percent of AOM caused by *S. pneumoniae* dropped from 51 to 31%. Concomitantly the percent of *H. influenzae* increased from about 40% to more than 55%. These differences certainly affect the choice of antibiotic to eradicate pathogens. Vaccines can also have an indirect effect. The use of the influenza vaccine in Turkish children resulted in a decrease in OM visits by 11% in a study published in 2006.

But, how do we know the infection is bacterial? Ear infections certainly have been shown to be associated with viral infections affecting the upper respiratory tract. A bacterial infection may provide more specific ear findings such as earache or tugging.

With *S. pneumoniae*, the bulging of the ear drum can be severe, with high fever and leukocytosis. *H. influenzae* can be associated with conjunctivitis⁷⁻⁸.

Antibiotics are not without consequence, however. Some problems encountered with antibiotics are resistance, adverse drug reaction (20%), gastrointestinal problems, drug allergy (1 to 6%) and severe reaction (<0.5%). Things that contribute to resistance are: young age, day care, prophylaxis and geographic location.

Antibiotic use administered in the previous 30 days also increases resistance by selecting resistant organisms and eliminating normal nasopharyngeal flora as the presence of normal flora inhibits pathogenic growth.

So do you give antibiotic or don't you?

If you do give antibiotics when there is no real AOM infection, you risk selecting virulent organisms resulting in the recurrence of symptoms and infection. If you don't give antibiotics and there is infection, you risk prolonging symptoms and complications.

The ideal oral antibiotic should be effective in eradicating middle ear pathogens, be safe, be inexpensive, and have an acceptable taste. Unfortunately it seems often that the better tolerated the antibiotic, the less effective it seems to be. Let's look

at *H. influenzae* for example.

The table below (**Table 2**) shows the pharmacodynamic/pharmacokinetic (PK/PD) activity of antibiotics against beta-lactamase positive *H. influenzae*. The list runs from highest activity to lowest activity.

Table 2. Pharmacodynamic/pharmacokinetic (PK/PD) activity of antibiotics against beta-lactamase positive

Activity 	Highest Cefixime Ceftibuten Ceftriaxone
	Amoxicillin/clavulanate (Amox/Clav) Cefdinir Cefpodoxime proxetil Cefuroxime axetil Cefprozil
	Cefaclor Loracarbef Trimethoprim-sulfa (TMP/SMX)
	Azithromycin Clarithromycin
	Lowest Amoxicillin Erythromycin

H. influenzae.

The list for *Streptococcus pneumoniae* follows (**Table 3**):

Table 3. Comparative (PK/PD) activity of antibiotics against susceptible *S. pneumoniae*

Activity 	Highest Ceftriaxone
	Amoxicillin* Amoxicillin/Clavulanate* Ceftidininir Cefpodoxime axetil Clidamycin
	Azithromycin Cefaclor Clarithromycin Loracarbef Trimethoprim/sulfa
Lowest Cefixime Ceftibuten	

If we compare efficacy and tolerability of antibiotics listed in **Table 3**, however, it is seen that the more efficient the antibiotic the less tolerable it is (**Table 4**).

Table 4. Efficacy and tolerability

Relative Rank	Efficacy	Tolerability
Best	Ceftriaxone Amox/Clav ES Gatifloxacin Cefdinir	Amoxicillin Azithromycin Cefdinir Cefprozil
Better	Cefuroxime Cefpodoxime Cefprozil Amoxicillin	Gatifloxacin Amox/Clav
Good	Azithromycin TMP/SMX	TMP/SMX Cefpodoxime
Marginal		Ceftriaxone

Therefore the most ideal antibiotics at this time appear to be cefdinir or cefprozil if one is looking for both efficacy and tolerability. Amoxicillin is great for strep infection and quite tolerable but inactive against *H. influenzae*. Amox/Clav is highly effective but not well liked in taste tests. Ceftriaxone is used as injection and therefore while highly effective is painful to administer. Azithromycin is a well-tolerated antibiotic, which only requires one daily dose, and is currently recommended for beta-lactamase allergic patients. Fluoroquinolones are not FDA approved in the US for use in children and there is no other effective medication.

Conclusions

It does not seem that the disease is changing but hopefully our understand of what AOM is, and better ways of treating have changed.

1. The diagnosis of AOM should be based on the following: 1. acute symptoms, 2. the presence of effusion **and** evidence of inflammation on otoscopy.
2. Use the scale to determine overall severity of the patient's otoscopy findings and associated symptoms.
3. If it is necessary to treat with antibiotics, choose an antibiotic that is likely to help, not hurt.
4. Be willing to change your treatment as updates dictate.

References

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