

Frequent Acute Otitis Media

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Recurrent acute otitis media (rAOM) is defined when the child experiences 3 or more episodes of acute otitis media (AOM) during six months or 4 or more episodes during one year with an intermediate period of at least 1 month between two consecutive episodes¹. It occurs in 5-30% of children with AOM^{1,2}. Frequent acute otitis media (fAOM), however, is not clearly defined but may be said to occur when the child experiences recurrent bouts of AOM with 1 month or less interval between completion of the antibiotic treatment and the next episode, and at least 4 or more episodes in a row. When first seen or referred, children with fAOM have been treated with multiple antibiotics usually starting with amoxicillin, then amoxicillin/clavulanate, cefuroxime, azithromycin or even an intramuscular cephalosporin, among others.

The age range of these children is between 10 months and 3 years although the majority of them are between 1 and 2 years of age. When faced with such a child, one should keep in mind 4 major points before deciding how to manage this disease:

1. What are the risk factors?

Risk factors should be recognized while taking the history in order to minimize or correct them, when possible. Risk factors may be **host-related** such as age, prematurity, gender, race, allergy, immune competence, genetic predisposition, presence of gastro-esophageal reflux and craniofacial abnormalities, or due to **environmental factors** such as upper respiratory tract infections, previous use of multiple courses of antibiotics to treat respiratory infections, day care, presence of siblings in day care, tobacco-smoke exposure, breast feeding, use of pacifier, low levels of vitamin D, seasonality and social economic status.^{3,4}

Although much has been discussed about the majority of these factors, some of them are obviously difficult or impossible to avoid or managed for the family. Others are curious observations such as the fact that thumb-sucking is not related with AOM whereas the pacifier is responsible for 25% of AOM during the first year of life⁵⁻⁷. A level of vitamin D less than 30 ng/ml has been recently related with AOM and rAOM^{8,9}. A level of vitamin D of 30 ng/ml was considered normal because lesser levels have been associated with changes in the parathormone levels as well as intestinal calcium transport.¹⁰

2. How are these ears being contaminated?

Assuming that there is no tympanic membrane perforation, it is important to recognize how these children are being contaminated and this includes, recurrent respiratory tract infections, presence of a sibling that is constantly or frequently infected, spending large part of the day in day care, aggressive frequent nose cleaning and the persistence of the bacteria in the nasopharynx. Frequent nasal cleaning

with saline flushes in the nose of these tiny children while laying down or even seated may force the infected rhinorrhea towards the Eustachian tube and later contaminate the middle ear.

3. Is the ear infected with the same bacteria or with a different one?

Several studies labeled recurrent AOM are in fact frequent AOM since the interval between episodes is less than a month¹¹⁻¹⁴. These studies show:

1. In patients with **complete eradication of middle ear pathogens by day 4 to 6** of antibiotic treatment, true relapses occur in only 28% of patients, however the lesser the time between the completion of the antibiotic treatment and the recurrence of AOM, the greater the possibility of a true relapse. As such, the occurrence of true relapse is 41%, 26%, 14%, 10% if the recurrent episode occurs within 1st, 2nd, 3rd or 4 weeks after the completion of the treatment, respectively^{11,12}. In this series, the majority of new episodes are due to a different pathogen.
2. Mostly early true relapses were caused by *Streptococcus pneumoniae*, and no cases of true relapse were seen by *Haemophilus influenzae* after 2 weeks of treatment.^{11, 12}
3. **Failure to eradicate pathogens from the middle ear during day 4 to 6** of antibiotic treatment is associated with clinical recurrences and in 66% of cases, these recurrences are caused by pathogens initially present in the middle ear effusion.¹³
4. With the advent of the pneumococcal conjugate vaccine PCV13, in a more recent study, *Haemophilus influenzae* is the major pathogen in AOM and rAOM¹⁴. As such, the first line antibiotic is amoxicillin/clavulanate. In this series, true bacteriologic relapse occurred in 40% of cases within a month of antibiotic completion, of which 77% were caused by *H. influenzae* and 23% by *S. pneumoniae*. In these cases, a new pathogen was found in 21, 4%, 33,3%, 41,2% and 57,1% at 1st, 2nd, 3rd and 4th week of completion of antibiotic treatment respectively. In this study, the relapse is more often caused by the same pathogen, specially if the time lapse between the completion of the treatment and the new episode is less than 3 weeks.

4. Where is the bacteria lodged in cases of fAOM?

In a large study in children aged 3 month to 3 years with AOM who completed antibiotic treatment for 10 days, 42% remained with *Streptococcus pneumoniae* in nasopharyngeal cultures¹². Of all those with AOM, 26% developed rAOM within 3 weeks of antibiotic treatment. In this study:

Within 3 weeks after completing 10 days of antibiotic treatment, of those who tested positive for pneumococcus in the nasopharynx, 32% developed another episode of AOM, as compared to 22% of those who tested negative for pneumococcus in the nasopharynx.

Middle ear effusion tested positive for pathogens in 81 % of the cases at the time of the recurrence of AOM, of which 50% were pneumococcus, 47% were *H. influenzae* and 3% were *M. catarrhalis*. Of those with pneumococcus in the middle ear effusion, 61% had positive nasopharyngeal cultures and 36% had negative na-

sopharyngeal cultures for pneumococcus. However, in 80% of cases the serotype of the pneumococcus in the nasopharynx and middle ear effusion was the same.

This study demonstrates that rAOM or fAOM are clearly associated with persistence of the bacteria mainly in the nasopharynx, but may persist in the middle ear effusion as well. These findings should also discourage the use of aggressive nasal cleaning with saline in children with rAOM or fAOM.

Evaluation and Treatment

Once a good history and physical is obtained and the risk factors are evaluated, including using lab tests, the therapeutical options should be equated. One should think about the ear and the nasopharynx as a whole since they are certainly interconnected in rAOM or fAOM. These include: 1) Avoiding or correcting risk factors, 2) attempting to eradicate the bacteria from the middle ear effusion and decrease the bacterial load from the nasopharynx if possible, 3) prevention of the recurrences and 4) surgery.

1. Avoiding or correcting risk factors including correction of gastro-esophageal reflux, avoiding aggressive nasal cleaning, evaluating and correcting food allergies, correcting low vitamin D levels, attempting to remove the child from the daycare for a while if that is feasible for the family, and avoid tobacco smoke exposure.

2. Attempting to eradicate bacteria from the middle ear and decrease bacterial load from the nasopharynx. The majority of these children, when referred to an otolaryngologist have already been subjected to multiple antibiotic treatments for the recurrences. As such, it may be assumed that the nasopharynx contains a large percentages of resistant bacteria. A few facts should be kept in mind:

In double paracentesis studies, the best results in eradication of bacteria from the middle ear at day 3-5 of antibiotic treatment were achieved by the use of amoxicillin/clavulanic acid with a higher amoxicillin concentration or with 3 doses of ceftriaxone.¹⁵

Changes in pneumococcal nasopharyngeal carriage vary in function of the antibiotic used. The least resistance promoting drug for the nasopharyngeal pneumococcus is amoxicillin¹⁶. Clindamycin increase this percentage from 9% to 22%, erythromycin from 13% to 30%, tetracycline from 13% to 31%¹⁷. The use of oral cephalosporins and azithromycin is probably a driver for multidrug resistance of pneumococcus, specially if children have been subjected to previous penicillin or macrolide treatments.¹⁸

In a 5 year study¹⁹ it was demonstrated that the yearly seasonal reduction in antibiotics in the warm months was significantly associated with a marked reduction in antibiotic resistance rates of pneumococcal isolates from middle ear effusions of children with otitis media.

Antibiotic treatment causes early and temporary changes in nasopharyngeal pneumococcal carriage as a function of the antibiotic use¹⁸. Intramuscular ceftriaxone causes a major reduction of colonization rates in the nasopharynx of pneumococcus which last only for 2-3 weeks²⁰.

The presence of a viral infection concomitant with a bacterial in the middle ear during AOM, decreases the penetration of amoxicillin in the middle ear effu-

sion^{21,22}. In a recent study²⁴, AOM is caused by viruses alone in 4%, bacteria alone in 27%, and by bacteria and viruses together in 66% of cases. Since most cases of AOM occur following a upper respiratory tract infection, these findings should be taken in consideration when prescribing amoxicillin, specially in recurrent or frequent AOM.

3. Prevention of recurrences – Other than the pneumococcal conjugate vaccine 13, the influenza vaccine has shown to decrease the rate of AOM of at least one episode over six months of follow up and a reduction in antibiotic use in vaccinated children²⁴. Immune modulation using oral bacterial lysates have shown benefit in reducing the number of respiratory tract infections in children.^{25,26}

4. Surgery

Surgical treatment for recurrent or frequent acute otitis media include myringotomy and tube placement alone or with adenoidectomy. The goal should be the control of the infection, prevent the occurrence of a permanent tympanic membrane perforation if possible, and correct speech delays if present, and avoid inner ear involvement either with the acute episodes or with the persistent middle ear effusion that follows. Studies summarized in the recent guidelines²⁷ demonstrate some advantages of the placement of tubes and adenoidectomy in the control of the disease. Adenoidectomy alone is not recommended. Placement of tubes are not recommended if there is no middle ear effusion²⁷. Since these children are very young, risks of the adenoidectomy should be considered and the possibility that tubes may have to be placed again at a later age. Recurrent placement of tubes has been associated with tympanic membrane changes such as retraction, perforation, tympanosclerosis and even cholesteatoma.²⁸

Based on these selective studies, the author prefers to adopt a conservative long term medical approach to fAOM prior to consider any surgery. This is due to the very young age of these children, to allow the removal of the adenoids at the time of tube placement if medical treatment fails, to decrease chances of recurrent tube placement to avoid tympanic membrane permanent changes. Other than avoiding and correcting risk factors, medical treatment may include long term antibiotic treatment with amoxicillin followed by oral immune modulation therapy using commercially available bacterial lysates, influenza vaccine in appropriate season and allowing a good summer season on vacation with their families in which these children are away from daycare, consume less antibiotics and grow a few months more. No other antibiotic is used for the long term treatment of the episode.

If all fails, or if the child becomes allergic to amoxicillin, surgery is considered, explaining to parents that a single set of tubes alone may bring only temporary relief and another set of tubes may be necessary with adenoidectomy at a later date if AOM or otitis media with effusion reoccurs when the first set of tubes fall off.

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