Otitis media: a review for the Family physician

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Otitis media (OM) is a serious healthcare concern worldwide. Acute otitis media is over-diagnosed. Symptoms are neither sensitive nor specific for the diagnosis of otitis media. Four characteristics of the tympanic membrane – position, mobility, color and degree of translucency should be evaluated and described in every examination. The most notable trends in the bacteriology of AOM during the past decade have been a rise in the proportion of patients infected with drug-resistant *S. pneumoniae* and an overall increase in beta-lactamase-producing *H. influenza* and *M. catarrhalis*. Antibiotic resistance to otogenic organisms occurs more frequently nowadays. Surgical management of otitis media is also discussed in this review.

Key words: Otitis media, infection, middle ear

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Introduction

Otitis media (OM) is a serious healthcare concern worldwide, not only because of the distress it causes the patient and the family but also because of the substantial economic burden it imposes on the health care system. Otitis media is defined as an inflammation of the middle ear, without reference to a specific etiology or pathogenesis. Because all pneumatized spaces of the temporal bone are contiguous, inflammation of the middle ear may also involve inflammation in the other three regions of pneumatization (mastoid, perilabyrinthine air cells, and petrous apex).[1]

Classification

The terms acute, sub acute, and chronic are recommended. Acute otitis media (AOM) is an inflammation of the middle ear that presents with a rapid onset of symptoms and signs of up to three weeks' duration. Chronic disease has had many synonyms, including serous OM, secretory OM, and 'glue ear', and implies middle ear fluid that has been present for three months or longer. The sub acute stage is the time in between. Recurrent AOM is defined as three episodes of otitis media within six months or four episodes within one year.[1]

Epidemiology

OM is one of the most common diagnoses made in the pediatrician's office. The direct and indirect costs of OM in the US were recently estimated to exceed $3.5 billion.[2] Otitis media is the most common reason for visits to pediatricians. The surgical placement of ventilating tubes for otitis media ranks as the second highest among the surgical procedures performed in children, circumcision being the most common. Also, inappropriate antibiotic treatment of the condition encourages the emergence of multidrug-resistant strains of bacterial pathogens.[3]

The incidence of OM has been well studied by Teele et al.[4], as well as by many other investigators. The incidence of OM increases after the newborn period (first 28 days). Teele found that by age 12 months nearly two thirds of all children had at least one episode of acute otitis media (AOM). By three years, 46% of children had three or more episodes of AOM. In this study, the highest incidence of AOM for both sexes was found in children aged 6 to 11

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months. Some investigators have also noted a second, lower peak between ages 4 and 5 years. The onset of AOM during the first year of life is important because the majority of children with multiple recurrences of AOM have their first episode before the age of 12 months.[1]

An epidemiological survey in Saudi Arabia was carried out with 9540 children aged up to 12 years to study the prevalence of acute otitis media and the rate of hearing impairment. A total of 100 (1.05%) were diagnosed with acute otitis media. The incidence was found to be higher among young children up to 4 years old and lower in the age group 8-12 years. Also it was found that the prevalence of AOM was higher among children whose parents were cousins compared with children of non-related parents. There is also evidence to indicate that poor socio-economic backgrounds and inadequate health services are associated with a higher rate of the condition.[5]

After an episode of AOM, there is a high incidence of persistent middle ear effusion (MEE) occurring. One study found that the mean duration of otitis media with effusion (OME) after AOM was 40 days. Shurin et al. reported that children who were younger than 24 months of age were 3.8 times more likely to have persistent MEE than those who were older.[6] They also found a higher incidence of persistent effusion in white children.

Varying distribution among sexes has not been found. Some studies have shown an increased preponderance in males when compared to females but others have challenged this finding, citing an equal distribution.[1]

Children in group daycare have been shown to be more likely to have OM as a complication of an upper respiratory tract infection when compared to those in home care. Niemala et al. found that the rate of tympanostomies and adenoidectomies was 59-67% higher for children below the age of three who were cared for at a daycare center.[7] Contributing factors for this increased incidence may include large numbers of children in close proximity and increased incidence of upper respiratory infections, with resultant frequent examinations by physicians.

The incidence of OM parallels the incidence of upper respiratory tract infections, which are most prevalent during the winter months. OM is also common in the spring and fall, and least common during the summer. It has been found that MEE originating in the winter months appears to last longer than those occurring in the summer months.[1]

There is data strongly suggesting a genetic susceptibility to OM. Variables associated with an increased risk of AOM include a sibling history of recurrent OM.[8]

Breast-feeding has been suggested as an important factor in the prevention of respiratory tract infections and middle ear disease in infancy. Many studies have shown an inverse relationship between the incidence of middle ear disease and the duration of breast-feeding. The mechanism of the protective effect of breast milk remains obscure. Data from a study of infants with cleft palate[8] suggest that it is a factor in breast milk, and not the position or mode of feeding, as some have suggested, that is protective. Two other studies indicate that breast-feeding had no effect on colonization of the nasopharynx with bacterial pathogens, indicating that the mechanism of protection relies on some immune-protective feature unassociated with prevention of colonization.[9,10]

Passive smoke exposure has come under increased scrutiny as a risk factor for respiratory tract infections, including OM, because of pathological and physiological changes in the respiratory tract: goblet cell hyperplasia, mucus hypersecretion, ciliostasis, decreased mucociliary transport, and alteration of the immune defenses. There is also an increased incidence of placement of tympanostomy tubes, chronic and recurrent OM, and otorrhea in children whose mothers smoked.[9]

Many associated medical conditions predispose a child to OM. Cleft palate and craniofacial anomalies, especially if the midface is involved, appear to be related to an increased risk of OM. The incidence of middle ear disease decreases somewhat after surgical repair of cleft palate but these children may continue to have frequent middle ear problems for years. There is an increased incidence of OM in children with congenital or acquired immune dysfunction (IgG subclass deficiency, AIDS, medications). Ciliary dysfunction frequently predisposes a child to OM (OM may be the first presenting sign of Kartagener's syndrome).[1]

Edema of the nasopharynx and Eustachian tube (E.T.) from prolonged nasotracheal intubation or nasogastric tube placement may lead to OM and sinusitis. Nasal obstruction from

enlarged adenoids, sinusitis, and malignancy can also lead to OM.[1]

Physiology

The Eustachian tube has at least three physiologic functions with respect to the middle ear: 1) protection from nasopharyngeal sound pressure and secretions, 2) clearance into the nasopharynx of secretions produced within the middle ear, and 3) ventilation of the middle ear to equilibrate air pressure in the middle ear with atmospheric pressure and to replenish oxygen that has been absorbed.[1]

In the healthy state the middle ear and mastoid are protected from unwanted nasopharyngeal secretions by the anatomy of the Eustachian tube system and by the middle ear gas cushion. The Eustachian tube connects the middle ear and mastoid air cells to the nasopharynx. In the adult, the anterior two thirds of the tube are cartilaginous and the posterior third is bony; in the infant, the bony portion is relatively longer. In adults, the tube lies at an angle of 45° in relation to the horizontal plane, whereas in infants this inclination is only 10°. The nasopharyngeal orifice of the E.T. in the adult is a vertical slit at right angels to the base of the skull, but in the infant this opening is oblique owing to the more horizontal position of the cartilage. These factors predispose children to increased incidence of otits media.[1,8]

Diagnosis of Otitis Media

Every family physician is well aware of the diagnostic dilemma posed by an ill child who may or may not have acute otitis media. In even the most experienced hands, an adequate physical examination of the ears can be difficult to perform because of common problems such as cerumen blockage of the auditory canal, an uncooperative toddler, or because of inadequate visualization of the tympanic membrane due to low light output from old otoscope bulbs.[11]

Acute otitis media is over-diagnosed. Symptoms are neither sensitive nor specific for the diagnosis of otitis media; fever and ear pain are present in only one half of patients.[10] Many physicians rely on redness of the eardrum as the main diagnostic clue. Crying (and most young children cry when their ears are examined), removal of cerumen with associated irritation of the auditory canal and fever can all cause redness of the eardrum in the absence of middle ear infection. Most of all, when a parent brings a child to the physician because of irritability, rhinorrhea and fever, the temptation is great to see at least a little bit of redness or fluid behind the eardrum as justification for an antibiotic prescription.[11]

Four characteristics of the tympanic membrane – position, mobility, color and degree of translucency – should be evaluated and described in every examination. The normal tympanic membrane is in the neutral position (neither retracted nor bulging), pearly gray, translucent and responding briskly to positive and negative pressure, indicating air filled space. An abnormal tympanic membrane may be retracted or bulging, and immobile or poorly mobile to positive or negative air pressure. The color of eardrum is less important than the position and mobility. Therefore, the redness of the tympanic membrane alone does not suggest the diagnosis of acute otitis media.[11]

Tympanometry provides additional information about actual pressure within the middle ear space. It measures the amount of sound reflected by the tympanic membrane and middle ear structures under varying conditions, and is a graphic representation of compliance changes. Various patterns are associated with normal, middle ear fluid, perforations or tympanostomies, retracted TMs, and stiff TM/middle ear systems. These data should, of course, be correlated with physical examination.[1,12]

Microbiology

With the exception of *Moraxella catarrhalis*, the list of bacteria causing OM has not appreciably changed for many years, and appears to be similar worldwide. Approximately 30 to 35% of cases are caused by *Streptococcus pneumoniae*, 20 to 25% by nontypeable strains of *Hemophilus influenzae* and 10 to 15% by *M. catarrhalis*. The frequency of *M. catarrhalis* in otitis appears to have increased in the last decade. The group A streptococcus causes acute middle ear infection in 2 to 4% of children, and tends to occur in early spring. *Staphylococcus aureus*, gram-negative enteric bacilli, and other bacteria are found consistently but less frequently. In infants younger than 6 weeks of age, gram-negative bacilli

cause about 20% of the AOM episodes. These organisms include *Escherichia coli*, *Klebsiella*, and *Pseudomonas aeruginosa*. Even in these very young infants, however, the most common organisms are still *S. pneumoniae* and *H. influenzae*.[13] Most studies show that 25 to 30% of middle ear fluid cultures are negative for bacteria. Some of the cultures are positive for viruses, including rhinovirus, adenovirus, influenza virus, parainfluenza virus, and respiratory syncytial virus (RSV). Recently viruses have gained increasing attention as possible co-pathogenic organisms in both acute and chronic OME, and may contribute to the prolongation of middle ear effusion. For many years, physicians presumed that viral illness produced mucosal inflammation and edema resulting in Eustachian tube dysfunction characterized by partial or complete obstruction of the passage and by accumulation of fluid in some patients. This was recently confirmed in a study of young adults with natural rhinovirus infection.[14] Middle ear pressure changes were measured by a digital tympanometer at intervals during the illness of these subjects. Abnormal pressure occurred in 74% of patients with rhinovirus illness, and more than half of these subjects had major pressure abnormalities. The frequency of subjects with abnormal middle ear pressures peaked on days 2 to 5 of illness, a time that coincides with the peak incidence of acute otitis media after onset of respiratory symptoms in infants and children. Heikkinen et al. have found that RSV is the most commonly identified virus, being found in 74% of the middle ear isolates, followed by parainfluenza virus and influenza virus.[15]

Bacterial Resistance

The most notable trends in the bacteriology of AOM during the past decade have been a rise in the proportion of patients infected with drug-resistant *S. pneumoniae* and an overall increase in beta-lactamase-producing *H. influenza* and *M. catarrhalis*.[12] There has been a profound increase in the prevalence of penicillin-resistant *S. pneumoniae* in the 1990's, particularly in the pediatric population. The incidence of penicillin-resistant *S. pneumoniae* ranged from 1.8% in 1979 to 8% in 1982, with an average of 5% from 1979 to 1987. Since 1992, however, the incidence of penicillin-resistant *S. pneumoniae* in younger children with invasive disease has dramatically increased, to as high as 41% in some studies.[13]

Antibiotic resistance occurs most frequently in patients who had recently been treated for acute otitis media. A 46% rate of penicillin-resistant *S. pneumonia* was found in patients recently treated for acute otitis media, with 33% of these strains being highly resistant.

The incidence of resistant pathogens is higher in children who attend day care facilities in the winter time and in children younger than two years of age.[12]

In the past, chronic MEE was thought to be sterile, but studies have shown a 30 to 50% incidence of positive middle ear cultures in children with chronic MEE, and polymerase chain reaction (PCR) testing has revealed that over 75% of the specimens are PCR positive for bacterial DNA. The most likely organisms are again, *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, and Group A streptococci.[1]

In chronic suppurative OM, the most frequently isolated bacteria are *P. aeruginosa*. *S. aureus*, *Corynebacterium*, and *Klebsiella* are also commonly isolated. Anaerobes may be common in patients with cholesteatoma. The standard acute organisms are still found in the early stages of disease and may be the predisposing factor toward chronic infection.[1]

Medical Treatment

There are many factors that should be considered in choosing an appropriate agent for treatment of acute otitis media. These include the activity of the drug against the usual otitic pathogens, safety, tolerance, ease of administration, the physician's experience, and cost.

Most of the drugs approved for therapy of acute otitis media are effective against the common otitic bacterial pathogens, although variations exist among them. For example, amoxicillin (Amoxil) is ineffective against beta-lactamase producing organisms, trimethoprim – sulfamethoxazole (bactrim or septra) is not appropriate for Group A beta-hemolytic streptococci, and cefixime (suprax) and ceftibuten (Cedax) are less active in vitro against pneumococci than are the other commercially available oral cephalosporins.[13]

There is no single preferred treatment for all infants and children with acute OM. Amoxicillin is favored by many for initial treatment

because of its long history of safety and effectiveness. When disease is caused by beta-lactamase producing organisms, amoxicillin may not be clinically effective, in which case, amoxicillin-clavulanate (Augmentin), a cephalosporin, trimethoprim-sulfamethoxazole, or erythromycin-sulfa could be used.[13]

Second generation cephalosporins provide good in vitro activity against penicillin-susceptible *S. pneumoniae* and group A. streptococcus. The oral cephalosporins possessing modest activity against relatively penicillin-resistant *S. pneumoniae* are cefprozil (Cefzil), cefpodxime (Vantin), and cefuroxime (Ceftin); however none possesses in vitro activity against highly penicillin-resistant *S. pneumoniae*. Recent data suggest that with the exception of cefuroxime (Ceftin), they often lack beta-lactamase stability against *H. influenzae*.[13]

In patients who fail to respond adequately to initial antibiotic therapy or have recurrent disease, amoxicillin-clavulanate (Augmentin), cefuroxime axetil (Ceftin), cefprozil (Cefzil), or ceftriaxone (Rocephin) can be considered for treatment. One of these agents or possibly a newer macrolides such as clarithromycin (Klacid) or azithromycin (Zithromax) can be used.[14]

While 10 days of administration is standard in North America, and 5 to 7 days of administration standard in Europe, several studies have found that 3, 5, and 10 days are equally effective as judged by initial response and short-term and long-term outcomes.[16,17] The recommended therapeutic dose of the antimicrobial should be administered for 10 days. During this period, the parents should be instructed to notify the clinician if the child fails to show a satisfactory clinical improvement. If there is persistence or recurrence of otalgia or fever, or both, then the child should be re-examined before the completion of the antibiotic course.[13]

Management options other than routine antimicrobial administration produce good results. Symptomatic care with analgesics and observation should be offered with the option of starting antimicrobial therapy if symptoms persist or worsen. A telephone contact or office visit on the following day should be arranged for children younger than two years, and at 3 days for older children. Parents who accept management without antibiotics need assurance of access to physicians if prompt improvement is not evident.[18]

After an appropriate course of a usually effective antimicrobial therapy, most children are clinically well, but up to 50% will have persistent middle ear fluid. Several options can be considered, although many of them have not proved to be consistently significantly more effective than observation. These options include 1) another course of the same antimicrobial but for a longer time, 2) another course of a different antimicrobial, 3) topical or systemic decongestants and/or antihistamines, 4) topical or systemic steroids, 5) Eustachian tube/middle ear inflation, and 6) observation. If the patient is symptomatic, effusion may appear later because the condition may take up to three months to resolve.[1]

Recurrent Acute Otitis Media

Children who experience recurrent AOM but who do not have persistent middle ear fluid can be considered for the following options:

1. CHEMOPROPHYLAXIS WITH AN ANTIMICROBIAL AGENT

Sulfisoxazole, amoxicillin, ampicillin, and penicillin have been studied and used. This option appears to be decreasing due to the increased rate of penicillin-resistant *S. pneumoniae* and beta-lactamase producing organisms.

A recent meta-analysis showed a trend for higher efficacy with sulfisoxazole than the other antibiotics in studies with a high recurrent AOM rate. Intermittent antibiotic prophylaxis for recurrent AOM during upper respiratory tract infections is controversial.

A US study with amoxicillin showed lower efficacy for intermittent than continuous use, and a Finnish study showed a lack of efficacy for a 7-day course of Amoxicillin-clavulanate given at the onset of an upper respiratory tract infection.[19]

2. MYRINGOTOMY AND TUBE INSERTION

Many parents choose not to employ a daily antimicrobial and may instead favor myringotomy and tympanostomy tube insertion. Studies have shown a decrease in the number and severity of episodes of acute otitis media as long as the tubes are patent.[18]

3. ADENOIDECTOMY

Few studies have been performed, but a significant difference has been observed in the attack rate of acute otitis media in children who had been randomized to receive adenoidectomy in addition to tube placement, in comparison to those who received tube placement alone. During the first and second years of follow-up, 28% and 35% fewer episodes of acute otitis media occurred in the study group than in the control.[17]

Conditions that may be associated with otitis media, e.g. sinusitis, nasal allergy, immune deficiency, ciliary dysfunction and nasopharyngeal pathology (enlarged adenoid) should be ruled out and treated.[1]

Antibiotics recommended for the treatment of acute otitis media[10]
Penicillins
Amoxicillin
Amoxicillin-clavulanate (Augmentin)
Sulfa-based combinations
Erythromycin-sulfisoxazole (pediazole)
Trimethoprim-sulfamethoxazole (Bactrim – Septra)
Macrolide
Azithromycin (Zithromax)
Clarithromycin (Klacid)
Second-generation cephalosporins
Cefaclor (Ceclor)
Cefprozil (Cefzil)
Cefuroxime axetil (Ceftin)
Loracarbef (Lorabid)
Third generation cephalosporins
Cefdinir (Omnicef)
Cefixime (Suprax)
Cefpodoxime proxetil (Vantin)
Ceftibuten (Cedax)
Ceftriaxone (Rocephin)

Surgical Treatment

INDICATIONS FOR TYMPANOSTOMY TUBE INSERTION

1. Chronic middle ear effusion that is relatively asymptomatic and does not respond to medical management, and has persisted for at least three months when bilateral, or six months when unilateral. Insertion at an earlier time would be reasonable when there is significant hearing loss, speech or language delay, or severe retraction pocket, or disequilibrium/vertigo, or when tinnitus is present.
2. Recurrent acute otitis media, especially when antimicrobial prophylaxis fails to prevent frequent, severe, and long-lasting disease. Minimum frequency for considering tympanostomy tube insertion would be three or more episodes during the previous six months.
3. When a supportive complication is suspected or present. Insertion of a tympanostomy tube at the time of tympanocentesis/myringotomy can provide more prolonged drainage and aeration of the middle ear cleft.
4. Eustachian tube dysfunction, even in the absence of middle ear effusion, when the patient has persistent or recurrent signs and symptoms that are not relieved by medical treatment. These symptoms may include hearing loss (usually fluctuating), disequilibrium, vertigo and tinnitus.

Conclusion

Many children with acute otitis media do not benefit from antimicrobial therapy because the etiology of their illness is not bacterial, or the infection is cleared by the immune system without the use of a drug. At present, we do not have clinical criteria for distinguishing which children are in need of antibiotic therapy for acute otitis media.[6]

A change in treatment approach will require education of both parents and physicians, but it would be expected to reduce costs and adverse effects from medication and contribute to reducing the development of bacterial resistance without compromising outcomes.[18]

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CME Questions

After you have completed reading the above article, take the test given below. Circle T (True) or F (False) in the answer sheet on page 90 to show the correct answer to each question. Questions 21 to 30 are related to the content in this article.

21. Acute otitis media (AOM) is defined as inflammation of the middle ear that presents with a rapid onset of symptoms and signs up to five weeks' duration.
22. Children in group day care have been shown to be more likely to have acute otitis media.
23. Breast-fed babies are more prone to middle ear disease than bottle-fed babies.
24. Passive smoke exposure is considered as a risk factor for otitis media.
25. Crying, cerumen removal, and fever can all cause redness of the tympanic membrane in the absence of any disease.
26. A red tympanic membrane alone does not indicate a diagnosis of acute otitis media.
27. Safety, tolerance, eases of administration, cost, and activity of antimicrobial drug against usual otitic pathogens should be considered in choosing an appropriate agent for treatment of acute otitis media.
28. The first line of medical management of acute otitis media is injectable cephalosporin.
29. Myringotomy and tube insertion are indicated for children with chronic middle ear effusion that persisted for at least three months when bilateral or six months when unilateral and does not respond to medical treatment.
30. Antibiotic resistance occurs most frequently in children who attended day care facilities or recently treated for acute otitis media.