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Current Concepts: Otitis Media in Children.

[Review Articles]

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Outline

- Definitions
- Acute Otitis Media
- Acute Otitis Media Unresponsive to Treatment
- Recurrent Acute Otitis Media
- Otitis Media with Residual Effusion
- Otitis Media with Persistent Effusion
- Conclusions
- REFERENCES

Graphics

- Figure 1
- Table 1

The frequency of otitis media is one of a number of factors causing physicians to seek out the most cost-effective clinical strategies for managing the condition. It is estimated that, by the time they reach two years of age, all the children in the United States currently under that age will have had a total of 9.3 million episodes of acute otitis media, [1] and that approximately 17 percent of children have three or more episodes during a six-month period [2]. Frequent episodes of otitis disrupt child-care arrangements and work schedules and generate parental anxiety and stress. The annual cost of the medical and surgical treatment of otitis in the United States is estimated at between $3 billion and $4 billion [3,4]. After circumcision, the surgical placement of ventilating tubes for otitis media is the most common surgical procedure performed in children. Finally, inappropriate antibiotic treatment of the condition encourages the emergence of multidrug-resistant strains of bacterial pathogens.

Definitionstoctoc

Infections of the ear are a spectrum of diseases involving the structures of the outer ear (otitis externa), the middle ear (otitis media), the mastoid process (mastoiditis), and the inner ear (labyrinthitis). Otitis media, an inflammation of the middle ear, is associated with a middle-ear effusion -- a collection of fluid inside the middle ear. Otorrhea is a discharge from the ear through a perforation in the tympanic membrane or through a surgically placed ventilating tube. Otitis media can be further classified by its associated clinical symptoms, otoscopic findings, duration, and complications.

Acute otitis media is an inflammation of the middle ear that presents with a rapid onset of signs and symptoms, such as pain, fever, irritability, anorexia, or vomiting [5]. Otitis media with effusion is characterized by the presence of an asymptomatic middle-ear effusion, [5] although it can be associated with a "plugged ear" feeling. Otoscopic findings of inflammation in acute otitis media may include decreased mobility of the tympanic membrane, which has a bulging contour that can be recognized because the visibility of the ossicular landmarks is impaired; a yellow or red color (or both); exudate; and bullae. Findings that suggest otitis media with effusion include visualization of air-fluid levels, serous middle-ear fluid, and a translucent membrane with diminished mobility. Otitis media with effusion can also be associated with negative pressure in the middle ear; negative pressure is suggested by the prominence of the lateral process, a more horizontal orientation of the malleus, and better mobility of the tympanic membrane when insufflation creates negative pressure.

Both acute otitis media and otitis media with effusion can be associated with a decrease in, or absence of, tympanic-membrane mobility, as seen with a flat, or type B, tympanogram and conductive hearing loss. The distinguishing characteristics of acute otitis media are the presence of symptoms and inflammation of the tympanic membrane. However, in acute otitis media, the symptoms are nonspecific and often result from viral upper respiratory infections. Therefore, the definition of acute otitis media is sometimes modified to include otoscopic findings of membrane inflammation, regardless of other symptoms. When it is thus defined, approximately one third of the cases of acute otitis media are not initially accompanied by fever, pain, irritability, or other nonspecific symptoms. When, in a child without symptoms, the tympanic membrane appears opaque, thickened, and scarred, it is difficult to distinguish acute otitis media from otitis media with effusion. However, in this situation, it may not be clinically important to distinguish these conditions. Bacterial pathogens can frequently be isolated from purulent, serous, and mucoid effusions regardless of the presence or absence of membrane inflammation or clinical symptoms [6,7].

Acute otitis media that is unresponsive to treatment is characterized by clinical signs and symptoms and otoscopic findings of inflammation that continue beyond 48 hours of therapy. Otitis media with residual effusion is characterized by the presence of an asymptomatic middle-ear effusion, without otoscopic signs of inflammation, 3 to 16 weeks after the diagnosis of acute otitis. After 16 weeks, this condition can be considered otitis media with persistent effusion. Otitis media with complications refers to damage to the structures of the middle ear, such as retraction pockets, adhesions, perforations, ossicular erosion, and cholesteatoma, as well as other intratemporal and intracranial problems.

Acute Otitis Mediatoctoc

The steps in the diagnosis and management of acute otitis media are summarized in the algorithm in Figure 1. Several errors can lead to the overdiagnosis of this condition. These include a bias on the part of physicians and parents toward treating a sick child with antibiotics, a temptation to make the diagnosis without removing enough cerumen to visualize the tympanic membrane adequately, and a mistaken belief that a red membrane with normal mobility establishes the diagnosis. A red membrane can, in fact, be caused by a viral upper respiratory

tract infection, the child's crying, or efforts to remove cerumen. Even if the ear is examined with a pneumatic otoscope and an adequate view of the tympanic membrane is obtained, there are several reasons it may be difficult to assess the mobility of the membrane. These include an inadequate seal between the speculum and the ear canal, low light intensity, and a mistaking of the wall of the ear canal for the membrane. Placing a piece of rubber tubing 1/8 to 1/4 cm in width around the ear speculum, near its end, helps create an adequate pneumatic seal.

The most common bacterial pathogens in acute otitis media are Streptococcus pneumoniae and Haemophilus in-fluenzae, the pathogens most frequently associated with sinusitis and pneumonia [8]. Additional bacterial pathogens include Moraxella catarrhalis, Strep. pyogenes, Staphylococcus aureus, gram-negative enteric bacteria, and anaerobes. The nature of the relation between viral and bacterial infection is controversial. Since viruses have been identified as the sole infective agent in only 6 percent of the middle-ear aspirates obtained from children with acute otitis media, [9] viruses may promote bacterial superinfection by impairing eustachian-tube function and other host defenses, such as the respiratory epithelial-cell barrier.

Amoxicillin, trimethoprim plus sulfamethoxazole, and erythromycin plus sulfisoxazole are the antibiotics used initially for acute otitis media Table 1. Nevertheless, the effectiveness of antibiotics for this condition remains controversial. Placebo-controlled, randomized clinical trials of antibiotic treatment have been relatively small, typically involving fewer than 400 subjects, [10-18] and have had design problems [19,20]. Most of these clinical trials have compared two or more different antibiotics rather than one antibiotic with a placebo. Data correlating eradication of the organism with the clinical course of acute otitis media [21] suggest that only about one third of patients require antibiotics for the resolution of clinical signs and symptoms. In the other two thirds of treated children, symptoms resolve without eradication of the middle-ear pathogen [21]. Unfortunately, it is not possible to identify clinical criteria that distinguish the patients who require antibiotic therapy to eradicate the pathogen from those who do not.

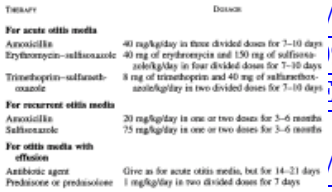

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Table 1.-Drugs Commonly Used for Acute Otitis Media, Recurrent Otitis Media, and Otitis Media with Effusion in Children

Pain usually continues for 8 to 24 hours after the initiation of antibiotic treatment. The most common treatment of pain, analgesics such as acetaminophen or ibuprofen, is often effective. Other options are topical eardrops containing benzocaine, glycerin, and antipyrine; for older children, analgesics containing codeine; and, if a bulging membrane is seen, relief of pressure with myringotomy or tympanocentesis. Topical therapy should be avoided when the eardrum has ruptured or is likely to rupture, because of the possibility of damaging middle-ear tissue. Unfortunately, the effectiveness of treatment for the pain of otitis has not been well studied, and the optimal method of management is not clear.

Those who favor withholding antibiotics are concerned that the unnecessary antibiotic treatment of otitis encourages the emergence of multidrug-resistant bacterial strains. The prevalence of strains of Strep. pneumoniae that are intermediately or highly resistant to penicillin, trimethoprim-sulfamethoxazole, or both is increasing throughout the United States [22]. The highly resistant strains are usually also resistant to third-generation cephalosporins [23].

Those who favor antibiotic treatment attribute the rapid decline in the incidence of mastoiditis and other complications of otitis in the late 1940s and 1950s to the introduction and widespread use of antibiotic therapy. In 1954, Rudberg compared the frequency of clinical mastoiditis in five different intervention groups involving 1365 patients with acute uncomplicated otitis media in Goteborg, Sweden [15]. The frequency of clinical mastoiditis was 17.3 percent (44 of 254) in the patients who were not treated, 1.5 percent (4 of 267) in the patients receiving sulfonamide, and 0 percent in the 333 patients receiving oral penicillin, the 275 receiving intramuscular penicillin, and the 236 receiving a combination of oral penicillin and sulfonamide.

Acute Otitis Media Unresponsive to Treatmenttoctoc

Unresponsive acute otitis media is characterized by both clinical symptoms and otoscopic findings of membrane inflammation that persist after 48 hours of antibiotic therapy. This condition occurs in about 10 percent of children who are initially treated with a 10-day course of antibiotics. Unresponsive acute otitis media occurs more frequently when antibiotic therapy fails to eradicate pathogens than when the pathogens are eradicated. Organisms resistant to the initial therapy, however, can be identified in about one fifth of middle-ear aspirates obtained after therapy [24]. Eradication of a middle-ear pathogen by antibiotics within two to four days is less likely when both a virus and bacteria have been isolated from a middle-ear aspirate than when only bacteria are isolated [25]. Persistent symptoms and otoscopic findings of continuing inflammation are also associated with higher rates of isolation of virus from middle-ear aspirates [26].

Unresponsive acute otitis media in a child who has been treated initially with amoxicillin can be treated with trimethoprim-sulfamethoxazole or erythromycin plus sulfisoxazole, or the combination drugs can be given first and amoxicillin used as the second therapy Table 1. The sequential administration of these antibiotics provides excellent treatment for most middle-ear pathogens [27]. Trimethoprim-sulfamethoxazole and erythromycin plus sulfisoxazole cover most (beta)-lactamase-producing organisms resistant to amoxicillin, such as H. influenzae, M. catarrhalis, and many strains of Staph. aureus. Amoxicillin covers organisms resistant to trimethoprim-sulfamethoxazole, such as Strep. pyogenes, group B streptococci, and enterococci. Strep. pneumoniae resistant to multiple antibiotics will not be treated successfully by any of these regimens. Unfortunately, even more expensive drugs, such as third-generation cephalosporins and amoxicillin plus clavulanate, offer minimal additional coverage against these highly resistant pneumococcal organisms. Third-generation cephalosporins and amoxicillin plus clavulanate are mainly useful as antibiotics for children who are allergic either to amoxicillin or to antibiotics containing sulfa. If there is concern about associated bacteremia or about patient compliance, a child can be treated with an intramuscular injection of ceftriaxone [28]. Tympanocentesis should be performed if the patient appears to have sepsis. If unresponsive acute otitis media persists after a second or third course of antibiotics, myringotomy or

tympanocentesis may be a reasonable option in order to isolate the pathogen, drain the effusion, and identify the sensitivity pattern of the organisms.

The timing of follow-up visits depends on the child's response to therapy. Children should be reassessed when symptoms of acute otitis media continue beyond 48 hours or recur before the next scheduled visit. Children who become asymptomatic should have a follow-up visit three to six weeks after treatment begins. Follow-up visits for children with risk factors for treatment failure should take place two to three weeks after the initiation of therapy. These risk factors include an age of less than 15 months, a history of recurrent otitis media in the child or a sibling, and antibiotic treatment of otitis media within the previous month [27-30]. Parental judgment and observation will accurately identify children whose acute otitis media has resolved [29].

Recurrent Acute Otitis Mediatoctoc

Recurrent acute otitis media requiring antibiotic prophylaxis can be considered to exist when three new episodes of the condition occur within a six-month period. Antibiotic prophylaxis, with amoxicillin or sulfisoxazole Table 1, is effective in reducing the frequency of otitis episodes. A meta-analysis of nine randomized, controlled trials with a total of 958 subjects compared the rates of occurrence of acute otitis media in patients who received antibiotic prophylaxis and in a placebo group [31]. Although interpretation of these results is subject to the methodologic limits of meta-analyses, antibiotic prophylaxis reduced the frequency of new episodes of otitis by 44 percent. The mean difference was a decrease of 0.11 (95 percent confidence interval, 0.03 to 0.19) in the number of episodes of otitis per patient-month for patients who received antibiotics, as compared with controls.

The administration of antibiotics at the onset of symptoms of upper respiratory infection, rather than daily continuous prophylaxis, can also prevent episodes of otitis [32]. During the winter respiratory-infection season, however, the daily administration of prophylactic antibiotics appears to be a more effective strategy than beginning treatment only at the onset of symptoms of upper respiratory infection [33]. It is less clear whether there is a difference in the effectiveness of these approaches during the summer, when the frequency of otitis decreases.

Data are lacking on the relative effectiveness of different dosage schedules for prophylaxis (once a day vs. twice a day). There are also only limited data comparing the efficacy of different antibiotics in the prevention of recurrent otitis [34]. Antibiotic prophylaxis is at least as effective as ventilating tubes, if not more effective, in preventing new episodes [35,36]. In one study, the average rate of occurrence of new episodes of otitis was lower for children who received amoxicillin prophylaxis (0.60 new episode per child per year of treatment) than for children who received ventilating tubes (1.02) or placebo (1.08) [36]. The percentage of the treatment period during which a child had a middle-ear effusion, however, was lower for the children treated with ventilating tubes (6.6 percent) than for those treated with amoxicillin (10 percent) or placebo (15 percent) [36]. On the basis of such information, antibiotic prophylaxis for three to six months can be recommended as the initial approach to the prevention of episodes of recurrent otitis Table 1.

Active immunization is another approach to preventing recurrent otitis, but limited data on its effectiveness are available. Immunization strategies might be directed at viruses that cause acute

upper respiratory infections, as well as at bacteria. Vaccination against influenza during an epidemic of influenza A in Finland decreased the incidence of new episodes of otitis [37]. One multicenter clinical trial of a 14-valent pneumococcal vaccine showed that the vaccine reduced the number of new episodes in children with a history of recurrent otitis media [38]. Immunization with pneumococcal vaccine also reduced the number of episodes of otitis in children with recurrent otitis media who also had asthma [39]. A newly developed conjugate pneumococcal vaccine is being evaluated for its ability to prevent episodes of acute otitis media. In my view, it is reasonable to immunize children who have recurrent otitis with influenza vaccine and, in children over two years of age, with the pneumococcal vaccine (Pneumovax).

Otitis Media with Residual Effusiontoctoc

A concern about the negative effects of conductive hearing impairment on language development and academic functioning is the main reason to treat otitis media with residual effusion. The presence of an effusion is associated with a mild-to-moderate conductive hearing impairment of 20 dB or more [40]. There is a causal relation between severe (usually sensorineural) hearing loss, either congenital or acquired, and language development. However, a causal relation between the conductive hearing loss associated with otitis media and subsequent language development and learning has not been established. A recent clinical-practice guideline for otitis media published by the Agency for Health Care Policy and Research found "a weak association between otitis media with effusion early in life and abnormal speech and language development in children younger than 4 years" and "a weak association between [this condition] and delay in expressive language development and behavior (attention) in children over 4 years." [3]

The management options for otitis media with a residual effusion that remains present for a period of six weeks to four months include observation, antibiotics, and combination therapy with an antibiotic and a corticosteroid. Several meta-analyses [1,41,42] based on published reports of clinical trials of a corticosteroid plus an antibiotic, a corticosteroid alone, and an antibiotic alone found that treatment with an antibiotic alone or with an antibiotic plus a corticosteroid was more effective than treatment with placebo in clearing residual effusions. In one meta-analysis, the probability of cure for the groups (165 subjects) treated with the combination of a corticosteroid and an antibiotic was 63.6 percent (95 percent confidence interval, 56.3 to 71.0 percent); for the groups (674 subjects) treated with an antibiotic alone, it was 39.3 percent (95 percent confidence interval, 35.6 to 43.0 percent); and for the placebo groups (450 subjects), 15.1 percent (95 percent confidence interval, 11.8 to 18.4 percent) [1].

The guideline panel of the Agency for Health Care Policy and Research restricted its analysis to the initial phases of randomized, controlled clinical trials. Its data showed that combination therapy with an antibiotic plus a corticosteroid improved the rate of clearance of effusions by 25.1 percent (95 percent confidence interval, -1.3 to 49.9 percent) as compared with placebo, and by 21.4 percent (95 percent confidence interval, -1.4 to 42.6 percent) as compared with an antibiotic alone [3]. Because the results for combination therapy approached, but did not reach, significance when compared with placebo, the panel did not recommend corticosteroid therapy. However, the difference between combination therapy with an antibiotic plus a corticosteroid and either placebo or an antibiotic alone was significant. Therefore, considering all the evidence and pending the availability of data from additional clinical trials, it is my view that all three

options -- combination therapy with an antibiotic plus a corticosteroid, antibiotics alone, and observation without drug therapy -- should be considered.

If combination therapy is selected, a corticosteroid (prednisone, 1 mg per kilogram of body weight per day, given orally in two doses) can be administered for 7 days along with an antibiotic (trimethoprim-sulfamethoxazole or an alternative) for 14 to 21 days Table 1. Crushed prednisone tablets can be added to jelly to camouflage the bitter taste of the medication. Children without a history of varicella who have been exposed to the virus in the month before treatment should not receive prednisone because of the risk of disseminated disease. The side effects of prednisone given for otitis media are similar to those seen in children with asthma who are treated with short courses of steroids. These include increased appetite, fluid retention, occasional vomiting, and, in rare cases, marked changes in behavior. If the residual middle-ear effusion resolves, either unilaterally or bilaterally, the child should be followed up monthly. Antibiotic prophylaxis with low doses of amoxicillin (20 mg per kilogram per day, given given either once or twice daily) or sulfisoxazole (75 mg per kilogram per day, given either once or twice daily) should be administered for three months to prevent a recurrence [43,44].


Otitis Media with Persistent Effusiontoctoc

For the treatment of a two-year-old child who has otitis media with effusion, ventilating tubes should be considered only if the effusion has persisted for at least four months and if a documented bilateral hearing impairment of 20 dB or more is present, according to the national clinical-practice guidelines [3]. The decision to place ventilating tubes, as well as the timing, should depend on the developmental and behavioral status of the child as well as on the parents' preference. Children who have otitis media with persistent effusion have a higher incidence of abnormalities such as cholesteatoma, adhesive otitis, retraction pockets, atrophy of the tympanic membrane, and persistent membrane perforations than children without a history of persistent effusion [45,46]. For example, in one study, membrane atrophy was present in 11 percent of children with a history of persistent otitis media and attic retraction was present in 8 percent, as compared with 3 percent and 1 percent, respectively, of children without persistent otitis [45]. Unfortunately, there is no way to identify the small proportion of children with persistent otitis in whom there will be damage to the middle ear. More important, the insertion of ventilating tubes does not prevent damage from occurring [46].

The main reason for surgery in children with persistent otitis is to restore normal hearing, and thereby promote language development and reduce the risk of behavioral problems. Surgical options include the placement of ventilating tubes and adenoidectomy if it is thought that enlargement of the adenoids is interfering with eustachian-tube function. Adenoidectomy cannot be recommended for children under four years of age, because data are not available on its efficacy in this age group, [47-49] although some otolaryngologists advocate its use for such children in selected circumstances. Adenoidectomy for otitis media in the absence of signs of upper airway obstruction is usually considered only if a child has a complication from ventilating tubes, such as persistent otorrhea or intrusion of a tube into the middle-ear space, or if the patient requires multiple reinsertions of the tubes [49]. Tonsillectomy combined with adenoidectomy is no more effective than adenoidectomy alone in treating persistent effusions [48] and is therefore not recommended in the clinical-practice guidelines [3]. The mortality rate associated with a

combined tonsillectomy and adenoidectomy varies from 0.004 to 0.006 percent, [50,51] and the rate of local hemorrhage that requires treatment from 0.49 to 4.00 percent [52,53]. Children with a submucous cleft palate should not have an adenoidectomy because of the risk of velopharyngeal insufficiency and speech impairment.

Conclusions toctoc

The diagnosis and management of otitis media in children remain challenging and controversial. The differing ability of families to cope with a child with recurrent or persistent otitis media and the lack of data that show a causal relation between conductive hearing impairment and subsequent behavior problems or delays in language development (or both) require the clinician to solicit and to consider parental preferences in treatment.

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Figure 1.-An Algorithm for the Diagnosis and Management of Otitis Media in Children. Risk factors for the failure of treatment are an age of less than 15 months, a history of recurrent otitis media in the patient or a sibling, and antibiotic treatment of otitis media within the previous month