Medscape

Acute Otitis Media

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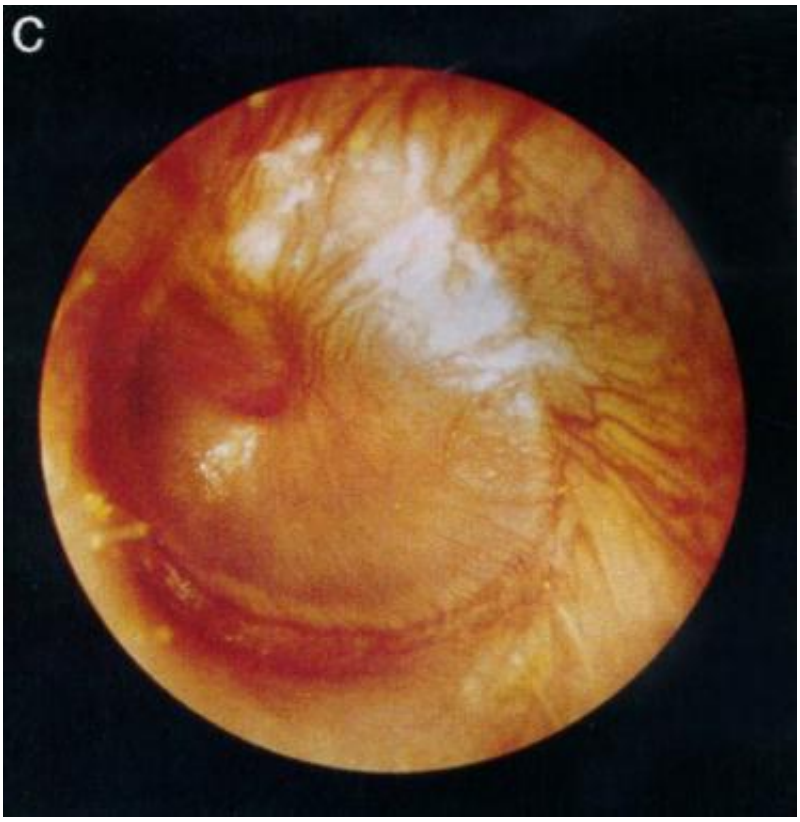
Overview

Practice Essentials

In the United States, acute otitis media (AOM), defined by convention as the first 3 weeks of a process in which the middle ear shows the signs and symptoms of acute inflammation, is the most common affliction necessitating medical therapy for children younger than 5 years.[1, 2, 3] See the image below.



Tympanic membrane of a person with 12 hours of ear pain, slight tympanic membrane bulge, and slight meniscus of purulent effusion at bottom of tympanic membrane. Reproduced with permission from Isaacson G: The natural history of a treated episode of acute otitis media. Pediatrics. 1996; 98(5): 968-7.

Signs and symptoms

Although the history of AOM varies with age, a number of constant features manifest during the otitis-prone years, including the following:

- Neonates: Irritability or feeding difficulties may be the only indication of a septic focus

- Older children: This age group begins to demonstrate a consistent presence of fever and otalgia, or ear tugging
- Older children and adults: Hearing loss becomes a constant feature of AOM and otitis media with effusion (OME); ear stuffiness is noted before the detection of middle ear fluid

Otalgia without hearing loss or fever is observed in adults with external otitis media, dental abscess, or pain referred from the temporomandibular joint. Orthodontic appliances often elicit referred pain as the dental occlusion is altered.

See Clinical Presentation for more detail.

Diagnosis

Pneumatic otoscopy is the standard of care in the diagnosis of acute and chronic otitis media. The following findings may be found on examination in patients with AOM:

- Signs of inflammation in the tympanic membrane
- Bulging in the posterior quadrants of the tympanic membrane may bulge; scalded appearance of the superficial epithelial layer
- Perforated tympanic membrane (most frequently in posterior or inferior quadrants)
- Presence of an opaque serumlike exudate oozing through the entire tympanic membrane
- Pain with/without pulsation of the otorrhea
- Fever

Testing

Testing in the acute phase is generally unhelpful, because all children with AOM have conductive hearing loss associated with the middle ear effusion. In addition, although tympanometry may assist in the diagnosis of middle ear effusion, this test is seldom necessary for the skilled pneumatic otoscopist.

Culture and sensitivity of a specimen from a fresh perforation or a tympanocentesis may be helpful.

Imaging studies

Radiologic studies are generally unnecessary in uncomplicated AOM. However, CT scanning may be necessary to determine if a complication has occurred. MRI might be more appropriate for diagnosing suspected intracranial complications.

Procedures

Tympanocentesis involves aspiration of the contents of the middle ear cleft by piercing the tympanic membrane with a needle and collecting that material for diagnostic examination.

Tympanocentesis should be performed in the following patients with AOM:

- Neonates who are younger than 6 weeks (and therefore are more likely to have an unusual or more invasive pathogen)
- Immunosuppressed or immunocompromised patients
- Patients in whom adequate antimicrobial treatment has failed and who continue to show signs of local or systemic sepsis
- Patients with a complication that requires a culture for adequate therapy

See Workup for more detail.

Management

Pharmacotherapy

Antibiotics are the only medications with demonstrated efficacy in the management of AOM; therefore, these agents are the initial therapy of choice. The antibiotic chosen should cover most of the common bacterial pathogens and be individualized for the child with regard to allergy, tolerance, previous exposure to antibiotics, cost, and community resistance levels. Duration of treatment may also be a consideration in the choice of antibiotic.[4]

Antibiotics used in the management of AOM include the following:

- Amoxicillin
- Amoxicillin/clavulanate
- Erythromycin base/sulfisoxazole
- Trimethoprim-sulfamethoxazole
- Cefixime
- Cefuroxime axetil
- Cefprozil
- Cefpodoxime
- Cefdinir
- Clindamycin
- Clarithromycin
- Azithromycin
- Ceftriaxone

Surgery

Surgical management of AOM can be divided into the following 3 related procedures:

- Tympanocentesis
- Myringotomy
- Myringotomy with insertion of a ventilating tube

Selection of the appropriate procedure results from evaluation of patient factors, surgeon factors, available resources, and urgency.

See Treatment and Medication for more detail.

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Background

In the United States, acute otitis media (AOM) is the most common affliction necessitating medical therapy for children younger than 5 years. The total annual cost to society for this disease and for otitis media with effusion (OME) runs into the billions of dollars. Yet, despite research into prevention and therapy, the costs of this disease continue to rise while the incidence remains unabated.

AOM is defined by convention as the first 3 weeks of a process in which the middle ear shows the signs and symptoms of acute inflammation. OME is defined as the presence of fluid in the middle ear with accompanying conductive hearing loss and without concomitant symptoms or signs of acuity. OME is classified as subacute when it persists from 3 weeks to 3 months after the onset of AOM and is classified as chronic thereafter.[1, 2]

The emergence of antimicrobial-resistant bacteria requires reevaluation of traditional management. Nevertheless, there is still a consensus that antibiotics are the initial therapy of choice for AOM. Surgical management of AOM can conveniently be divided into 3 related procedures: tympanocentesis, myringotomy, and myringotomy with insertion of a ventilating tube.

For patient education resources, visit the Headache and Migraine Center and the Oral Health Center. See also the eMedicineHealth articles Sinus Infection and Teething.

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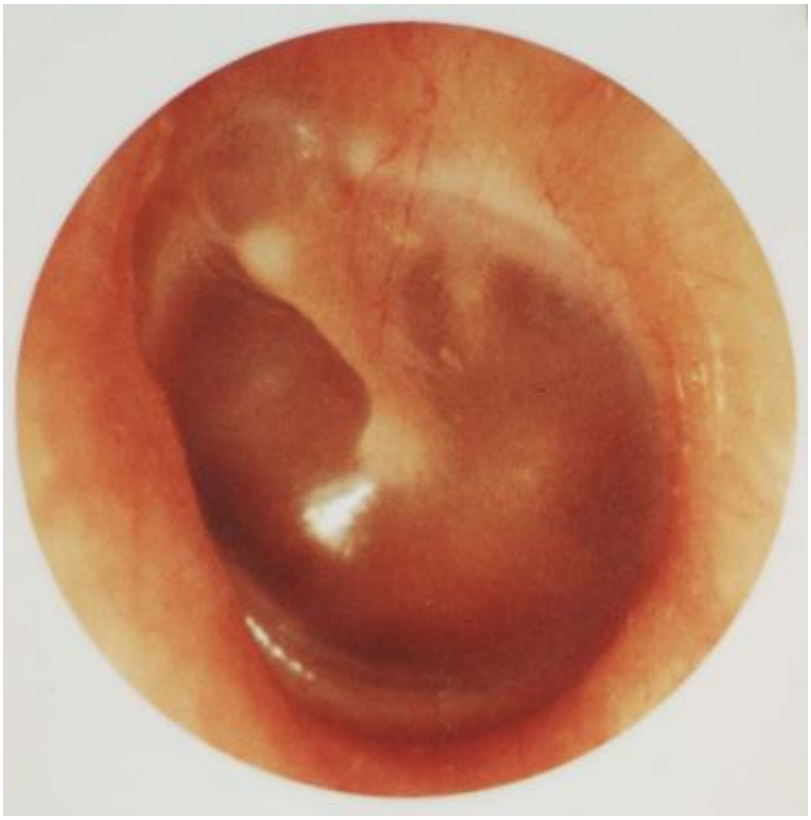
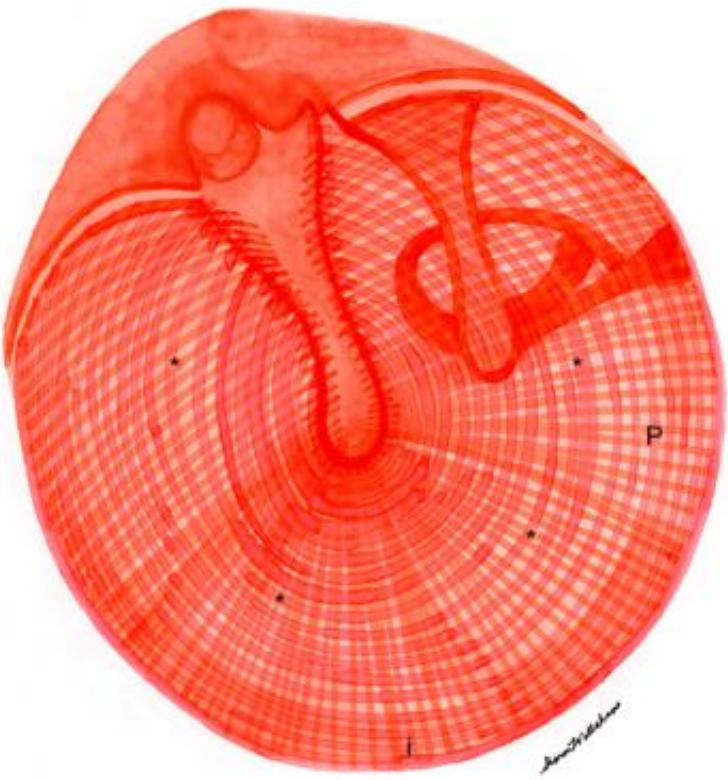
Anatomy

Incision of the tympanic membrane is primarily governed by the relations of the structures behind the membrane (see the images below). The tympanic membrane can be divided into quadrants with an imaginary line drawn vertically along the long process of the malleus and extending to the inferior annulus, along with a horizontal line at the umbo. Generally, it can safely be incised in all quadrants except the posterior superior section, behind which lie the incus and stapes, structures that might be injured inadvertently by incision in this area. The area above the pars tensa, the pars flaccida, should be avoided.



Healthy tympanic membrane.



Drawing of normal right tympanic membrane. Note outward curvature of pars tensa (*) of eardrum. Tympanic annulus is indicated anteriorly (a), inferiorly (i), and posteriorly (P). M = long process of malleus; I = incus; L = lateral (short) process of malleus.

Two other structures, the facial nerve and the round window, are generally protected from any but the clumsiest of surgeons, the former by its high position in the middle ear and the latter by the overhanging niche.

Tubes are generally placed anteriorly, either superiorly or inferiorly. Because the posterior segments are deeper and have more vibratory motion, posterior placement gives a greater dampening effect. Anteriorly, any incision should avoid exposure of the malleus, the malleolar ligament, and the annulus; such exposure creates a greater tendency for perforations to persist after extrusion of the tube.

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Pathophysiology

Obstruction of the eustachian tube appears to be the most important antecedent event associated with AOM. The vast majority of AOM episodes are triggered by an upper respiratory tract infection (URTI) involving the nasopharynx.

Viral and bacterial infection

The infection is usually of viral origin, but allergic and other inflammatory conditions involving the eustachian tube may create a similar outcome. Inflammation in the nasopharynx extends to the medial end of the eustachian tube, creating stasis and inflammation, which, in turn, alter the pressure within the middle ear. These changes may be either negative (most common) or positive, relative to ambient pressure.

Stasis also permits pathogenic bacteria to colonize the normally sterile middle ear space through direct extension from the nasopharynx by reflux, aspiration, or active insufflation.

The response is the establishment of an acute inflammatory reaction characterized by typical vasodilatation, exudation, leukocyte invasion, phagocytosis, and local immunologic responses within the middle ear cleft, which yields the clinical pattern of AOM.

In a minority of otitis-prone children, the eustachian tube is patulous or hypotonic. Children with neuromuscular disorders or abnormalities of the first or second arch are most likely “too open” and are therefore predisposed to reflux of nasopharyngeal contents into the middle ear cleft.

To become pathogenic in hollow organs, such as the ear or sinus, most bacteria must adhere to the mucosal lining. Viral infections that attack and damage mucosal linings of respiratory tracts may facilitate the ability of the bacteria to become pathogenic in the nasopharynx, eustachian tube, and middle ear cleft.

This theory might explain why viral antigens are commonly recovered from middle ear aspirates in children with AOM but the actual virus is only rarely isolated. Data have also been presented indicating that mucosal damage by endotoxins secreted by bacterial invaders may similarly enhance the adhesion of pathogens to mucosal surfaces.

Viral infection in the nasopharynx with subsequent inflammation of the orifice and mucosa of the eustachian tube has long been understood as part of the pathogenesis of AOM, although the complete role of the virus is not fully understood. Concurrent or antecedent URTIs are identified in at least a quarter of all attacks of AOM in children, but the virus itself seldom appears as the pathogen in the middle ear. Administration of trivalent influenza A vaccine has been shown to reduce the frequency of AOM during the influenza season.[5]

Viruses have been recovered with increasing frequency as techniques to identify them by direct culture and by indirect means (eg, enzyme-linked immunosorbent assay [ELISA]) have improved. On direct culture, the yield is less than 10%, with the respiratory syncytial virus (RSV) recovered most frequently; the influenza virus is a distant second. On ELISA, the presence of viral antigens is detected in approximately a quarter of middle ear aspirates; again, RSV is the virus most frequently detected by this method.

The presence of viruses in the middle ear effusion may influence the outcome of therapy for otitis media. Results of outcome studies have been mixed, ranging from no effect to evidence of prolongation of acuity and effusion when viruses are present in persons with AOM.

Immunologic factors

Immunologic activity may play a significant role in the frequency of AOM and its outcome. Although most research has focused on the immunologic aspects of OME, certain relations between AOM and the patient’s immune status have been demonstrated, as follows:

- Production of antibodies may promote clearance of a middle ear effusion after an acute attack
- Previous exposure or immunization may have a preventative role by suppressing colonization of the nasopharynx by pathogens
- The formation of antibodies during an attack may prevent or modify future attacks; unfortunately, antibodies to both Streptococcus pneumoniae and Haemophilus influenzae are of the polysaccharide type and the ability to produce them develops late unless conjugated to proteins
- Minor or transient immunologic defects may give rise to recurrent otitis media

Much attention has been focused on the immunoglobulins and the patient’s ability to form them. Immunoglobulin G2 (IgG2) and immunoglobulin G4 (IgG4) are responsible for immunity against polysaccharide antigens; deficiencies in the formation of these antibodies invariably lead to otitis media. Many patients with Down syndrome show decreased function of immunoglobulin A (IgA), IgG2, or IgG4, which partially explains their increased risk for chronic rhinitis and otitis media.

The immunologic aspects of AOM are not confined to the middle ear. The nasopharynx plays an important role in the pathogenesis of AOM, and immunologic modifications in this lymphoid tissue provide some protection from pathogens by preventing their adherence to mucosal surfaces. The presence of nasopharyngeal IgA antibodies to pneumolysin toxin released by pneumococcal autolysis appears to protect against invasion by healthy pneumococci.

On the other hand, not all immunoglobulins in the nasopharynx are protective. Bernstein describes the effects of immunoglobulin E (IgE) hypersensitivity or hyperimmune effects on the eustachian tube mucosa.[6] The allergic response in the nasopharyngeal end of the eustachian tube promotes stasis and the subsequent formation of a middle ear effusion.

Etiology

Viral pathogens

RSV is a large RNA paramyxovirus that is most commonly associated with bronchiolitis and pneumonia in very young persons, though it may cause acute respiratory disease in persons of any age group.[7, 8, 9] In northern climates, RSV is normally identified during annual epidemics in the winter and early spring, but it should be considered in any neonate with lethargy, irritability, or apnea, with or without otitis media. In older infants and children, respiratory symptoms are usually more prominent, making diagnosis easier.

RSV was identified early as a pathogen that appeared to create long-term pulmonary complications, primarily asthma, in as many as half of infants with bronchiolitis. RSV may be particularly lethal for children with congenital heart disease, cystic fibrosis, immunodeficiency, bronchopulmonary dysplasia, or prematurity of less than 37 weeks' gestational age.

RSV-specific intravenous (IV) immunoglobulin prophylaxis is recommended only for high-risk children. When treating a child with concomitant pneumonia or other systemic disease and otitis media, the practitioner must ensure appropriate diagnosis and management of all aspects of the child's illness. Drainage of the ear by tympanocentesis or myringotomy for culture and therapy may be necessary in some cases. Drainage is mandatory in neonates who are suspected to be in a septic state or in children who are immunosuppressed.

Bacterial pathogens

Pathogenic bacteria are recovered from the middle ear effusion in at least half the children with AOM, and bacterial DNA or cell wall debris is found in another quarter to a third of specimens previously classified as sterile. Four bacteria—namely, S pneumoniae, H influenzae, Moraxella catarrhalis, and Streptococcus pyogenes —are responsible for the majority of episodes of AOM in persons older than 6 weeks. Other bacteria recovered and implicated in AOM include Staphylococcus aureus, viridans streptococci, and Pseudomonas aeruginosa.

The emergence of resistance to antimicrobial agents is of increasing importance in the management of AOM and other bacterial illnesses.[10] The various mechanisms used by bacteria to confer this resistance will be delineated as the common pathologic agents linked to AOM are described.

Streptococcus pneumoniae

S pneumoniae is the most common etiologic agent responsible for AOM and for invasive bacterial infections in children of all age groups.[11] It is a gram-positive diplococcus with 90 identified serotypes (classified on the basis of the polysaccharide antigen), the frequency of which varies between age groups and geography. On direct culture, various studies have shown these bacteria to be responsible for 29-40% of isolates, but additionally pneumococcal antigens are recovered from approximately a third of those cultures classified as sterile.

Pneumococcal infections are probably responsible for at least 50% of AOM episodes. Serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F are responsible for most invasive pneumococcal disease in America; in ear aspirates from patients with AOM, serotypes 19 (23%), 23 (12.5%), 6 (12%), 14 (10%), 3 (8.5%), and 18 (6%) are isolated most commonly. The polyvalent pneumococcal vaccine confers immunity to approximately 85% of those serotypes responsible for AOM.

S pneumoniae was once susceptible to almost all common antibiotics, including penicillin G, erythromycin, and most sulfonamides. Alteration of the cell wall's penicillin-binding protein (the antimicrobial target) has led to the appearance of multidrug-resistant S pneumoniae (MDRSP), which is resistant to beta-lactam compounds, macrolides, and sulfonamides. Resistance rates as high as 40% have been reported for these 3 antimicrobial groups. Serotypes 6B, 9V, 14, 19A, 19F, and 23F have the highest frequency of penicillin resistance.

Ceftriaxone, cefotaxime, rifampin, and vancomycin still appear to have therapeutic efficacy, as does immunization with polyvalent pneumococcal vaccine for prevention. Unfortunately, polysaccharide antigens are not immunogenic early in life. To overcome this problem, conjugated antigens, in which the polysaccharide antigen is attached to a protein carrier, may be administered to induce production of antibodies to these polysaccharides. Some conjugated antigens (eg, vaccinations for H influenzae type b [Hib]) are in widespread use.

A heptavalent vaccine for S pneumoniae is now in widespread use and appears to have made an impact on the number of cases of invasive pneumococcal disease. This vaccine confers long-term immunity to 7 of the most common and invasive strains. Emerging evidence suggests that other serotypes are beginning to be recovered more frequently in ear and sinus infections. This might render the vaccine less useful in future years. In North America, this vaccine has now been replaced

by an updated 13-valent vaccine that contains conjugated antigenic material for 6 of those additional serotypes of the pneumococcus.

Haemophilus influenzae

In middle ear aspirates from patients with AOM, H influenzae is the second most frequently isolated bacterium and is responsible for approximately 20% of episodes in preschool children.[12] The frequency may be higher in otitis-prone children, older children, and adults who have received the pneumococcal vaccine.

A study by Martin et al looking at AOM cases between 1999 and 2014 in children aged 6-23 months found that, while nasopharyngeal colonization with S pneumoniae has reportedly decreased since pneumococcal conjugate vaccines (PCVs) were introduced, colonization with H influenzae in the study subjects initially increased before dropping back to levels seen prior to routine administration of 7-valent PCV (PCV7). The investigators obtained nasopharyngeal cultures from four cohorts of children with AOM. The first cohort was cultured in 1999-2000, before routine PCV7 use, while in the second (2003-2005) and third (2006-2009) cohorts, two or more doses of PCV7 were administered to 93% and 100% of children, respectively, and in the fourth cohort (2012-2014), 100% of the children received two or more doses of 13-valent PCV (PCV13). Nasopharyngeal colonization with H influenzae in cohorts 1, 2, 3, and 4 occurred in 26%, 41%, 33%, and 29% of children, respectively.[13]

The bacterium is a small, pleomorphic, gram-negative coccobacillus. Those bacteria encapsulated with a polysaccharide coating are classified into 6 distinct types (a-f); nonencapsulated types are referred to as nontypeable and are responsible for the great majority of AOM episodes. (The nonencapsulated strains have been subtyped biochemically and antigenically, but, to date, this classification has limited clinical application.)

Traditionally, Hib has been found responsible for most invasive illnesses attributed to these bacteria and for meningitis, epiglottitis, and septicemia. Hib accounts for only 10% of all episodes of AOM in which H influenzae is recovered. In areas of the world where the aforementioned Hib-conjugated vaccine is administered early in life, risks from this potentially lethal strain have greatly diminished.

Antimicrobial resistance in Hib is conferred almost exclusively (95%) by the formation of a single enzyme, triethylenemelamine 1 lactamase, which, in some series, is secreted by as many as 40% of all nontypeable strains. This resistance is overcome relatively easily by using blocking agents, extended-coverage cephalosporins, broad-spectrum macrolides, or sulfonamides.

H influenzae may participate more widely in head and neck infections than was once believed. One of the principal mechanisms is related to the ability of the bacterium to hide and recover from antibiotic action by forming a mucous complex known as a biofilm. Research has focused on enhancing penetration of or dissolving the protective biofilm.

Moraxella catarrhalis

In the mid-1970s, M catarrhalis was classified as nonpathogenic in middle ear infections, even though under its previous name, Neisseria catarrhalis, it constituted approximately 10% of all isolates from middle ear aspirates. At that time, M catarrhalis was almost universally susceptible to ampicillin-type penicillins. After 20 years and 2 name changes (from N catarrhalis to Branhamella catarrhalis to M catarrhalis), it is isolated in up to a quarter of children with AOM, and resistance to the ampicillin-type beta-lactams is almost universal.

M catarrhalis is a gram-negative diplococcus and is considered part of the normal flora of the human upper respiratory tract. Resistance is conferred by the secretion of multiple isoenzymes of lactamase, which may be plasmid or chromosomal in origin and which may be inducible (ie, present only in low levels until a substrate is provided). More than 1 isoenzyme may be secreted by a single bacterium.

At present, almost all forms are blocked by clavulanic acid, and most are still susceptible to sulfonamides, lactamase-stable cephalosporins, or broad-spectrum macrolides. M catarrhalis is often found to coexist with other airway pathogens. The lactamases (cephalosporinases) that M catarrhalis secretes may protect those other bacteria from antimicrobial agents to which the second target pathogen might ordinarily be susceptible.

A study by Chonmaitree et al of 367 infants (followed for 286 child-years) indicated that bacterial-viral interactions are associated with AOM, with such interactions between M catarrhalis and various respiratory viruses having been found in the report to affect the risk of upper respiratory tract infection and AOM.[14]

Streptococcus pyogenes

Although S pyogenes (a gram-positive coccus that constitutes the group A streptococci [GAS] in the Lancefield

classification), is still the fourth most commonly isolated bacterial pathogen from ears with AOM, it has shown a steady decline in frequency of recovery from the ear and in virulence over the past half-century. Similarly, a substantial decline in the major complications of streptococcal infection, rheumatic fever, glomerulonephritis, and scarlet fever has occurred.

S pyogenes may be associated with streptococcal toxic shock syndrome, which may include coagulopathy, soft tissue necrosis or fasciitis, desquamating rash, and liver or renal involvement.[15] It is primarily a pathogen of the pharynx, with more than 80 distinct M-protein strains identified. Currently, with the improvement in primary care and the availability of rapid identification tests, early aggressive treatment is normally instituted against this bacterium, which has shown minimal ability to develop resistance to antimicrobial agents.

Acute necrotic otitis media was associated with scarlet fever in the early 1900s; however, the condition was also associated with measles, pneumonia, and influenza. Generally, the patient was extremely ill with the systemic component of the disease and presented with a spontaneous perforation shortly after the onset of otalgia.

Early inspection of the ear would show the perforation to be moderate to large; within days, significant evidence of tissue necrosis would be observed, perhaps including the entire tympanic membrane, ossicles, the tympanic mucoperiosteum, or the bone of the mastoid air cells. The patient would demonstrate a marked conductive hearing loss, although sensorineural loss was not uncommon.

Pathologically, the ear showed a marked paucity of the normal vascular proliferation associated with an inflammatory reaction. Instead, a complete loss of the vascularity normally associated with vasculitis or toxin exposure occurred. Healing was never normal; tissue was replaced by epithelial invasion or scar tissue formation.

In industrialized societies, acute necrotic otitis media is now primarily of historic interest. The disease is still reported in aboriginal populations living in areas where modern medicine has not yet penetrated.

In the preantibiotic era, S pyogenes also appeared to be the organism most commonly recovered from patients with acute coalescent mastoiditis. In the 1990s, S pyogenes relinquished this distinction to S pneumoniae, but it remains a prominent pathogen when this disease is encountered in very young persons.

Other aerobes

Except in neonates and children with chronic disease, few other pathogens have been demonstrated in aspirates from the middle ears of immunologically intact individuals.

S aureus is rarely recovered, except in Japan, where studies indicate a somewhat higher incidence (up to 10%). Mycobacterium tuberculosis is most often associated with chronic otitis media but should be considered when a patient presents with painless otorrhea as an initial complaint and/or has multiple tympanic perforations. Any patient with a compromised immune system may be at risk for this opportunistic infection. Chlamydia pneumonia is an uncommon but significant pathogen in persons with AOM and responds only to macrolide therapy.

Anaerobes

Anaerobic bacteria have been recovered from the middle ears of children with AOM, but the data do not support a prominent role for these microorganisms in persons with otitis media, at least in the acute form. They may, however, play a greater role in chronic inflammation of the adenoid bed and biofilm formation. When recovered from ears of children with AOM, the anaerobic pathogen most often is not the sole pathogen cultured.

Common bacterial pathogens in neonatal period

In the perinatal period, the Escherichia coli, Enterococcus species, and group B streptococci are the etiologic agents most commonly responsible for sepsis and meningitis. These agents are often recovered from the middle ear, though the total percentage is probably less than 10% of neonates with AOM.

S pneumoniae remains the most common pathogen responsible for AOM in all age groups, including neonates. The nonencapsulated H influenzae and nontypeable varieties may be invasive in these infants and constitute the second most common pathogens recovered from the ear.

Because bacteremia is common in all neonates with AOM, tympanocentesis should be performed for both diagnosis and therapy in any infant with signs of AOM or generalized sepsis and any middle ear effusion. This should be part of any septic workup in neonates.

Risk factors

The following are proven risk factors for otitis media:

- Prematurity and low birth weight
- Young age
- Early onset
- Family history
- Race - Native American, Inuit, Australian aborigine
- Altered immunity
- Craniofacial abnormalities
- Neuromuscular disease
- Allergy
- Day care
- Crowded living conditions
- Low socioeconomic status
- Tobacco and pollutant exposure
- Use of pacifier
- Prone sleeping position
- Fall or winter season
- Absence of breastfeeding, prolonged bottle use

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Epidemiology

In the United States, 70% of all children experience one or more attacks of AOM before their second birthday. A study from Pittsburgh that prospectively followed urban and rural children for the first 2 years of life determined that the incidence of middle ear effusion episodes is approximately 48% at age 6 months, 79% at age 1 year, and 91% at age 2 years.[16]

The peak incidence of AOM is in children aged 3-18 months. Some infants may experience their first attack shortly after birth and are considered otitis-prone (ie, at risk for recurrent otitis media). A study by Megged et al found that 30% of pediatric patients who had neonatal AOM suffered from recurrent AOM later in childhood, compared with 10% of controls.[17]

In the Pittsburgh study, the incidence of AOM was highest among poor urban children. Differences in incidence between nations are influenced by racial, socioeconomic, and climatic factors.

Age-, sex-, and race-related demographics

Children aged 6-11 months appear particularly susceptible to AOM, with frequency declining around age 18-20 months. The incidence is slightly higher in boys than in girls. A small percentage of children develop this disease later in life, often in the fourth and early fifth year. After the eruption of permanent teeth, incidence drops dramatically, although some otitis-prone individuals continue to have acute episodes into adulthood. Occasionally, an adult with an acute viral URTI but no previous history of ear disease presents with AOM.

Definite racial differences exist in the incidence of AOM. Native Americans and Inuits have very high rates of acute and chronic ear infection, whereas African Americans appear to have a slightly lower rate than white children living in the same communities.

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Prognosis

Death from AOM is rare in the era of modern medicine. With effective antibiotic therapy, the systemic signs of fever and lethargy should begin to dissipate, along with the localized pain, within 48 hours. Children with fewer than 3 episodes are 3 times more likely to resolve with a single course of antibiotics, as are children who develop AOM in nonwinter months. Typically, patients eventually recover the conductive hearing loss associated with AOM.

Middle ear effusion and conductive hearing loss can be expected to persist well beyond the duration of therapy, with up to 70% of children expected to have middle ear effusion after 14 days, 50% at 1 month, 20% at 2 months, and 10% after 3 months, irrespective of therapy.

In most instances, persistent middle ear effusion can merely be observed without antimicrobial therapy; however, a second course of either the same antibiotic or a drug of a different mechanism of action may be warranted to prevent a relapse before resolution.

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Presentation

History

The history of acute otitis media (AOM) varies with age, but a number of constant features manifest during the otitis-prone years.

In the neonate, irritability or feeding difficulties may be the only indication of a septic focus. Older children begin to demonstrate a consistent presence of fever (with or without a coexistent upper respiratory tract infection [URTI]) and otalgia or ear tugging. These latter symptoms are not entirely exclusive to AOM; teething pain or pharyngitis (particularly coxsackievirus infection) can mimic these symptoms.

In older children and adults, hearing loss becomes a constant feature of AOM and otitis media with effusion (OME), with reports of ear stuffiness noted even before the detection of middle ear fluid. Otalgia without hearing loss or fever is observed in adults with external otitis, dental abscess, or pain referred from the temporomandibular joint. Orthodontic appliances often elicit referred pain as the dental occlusion is altered.

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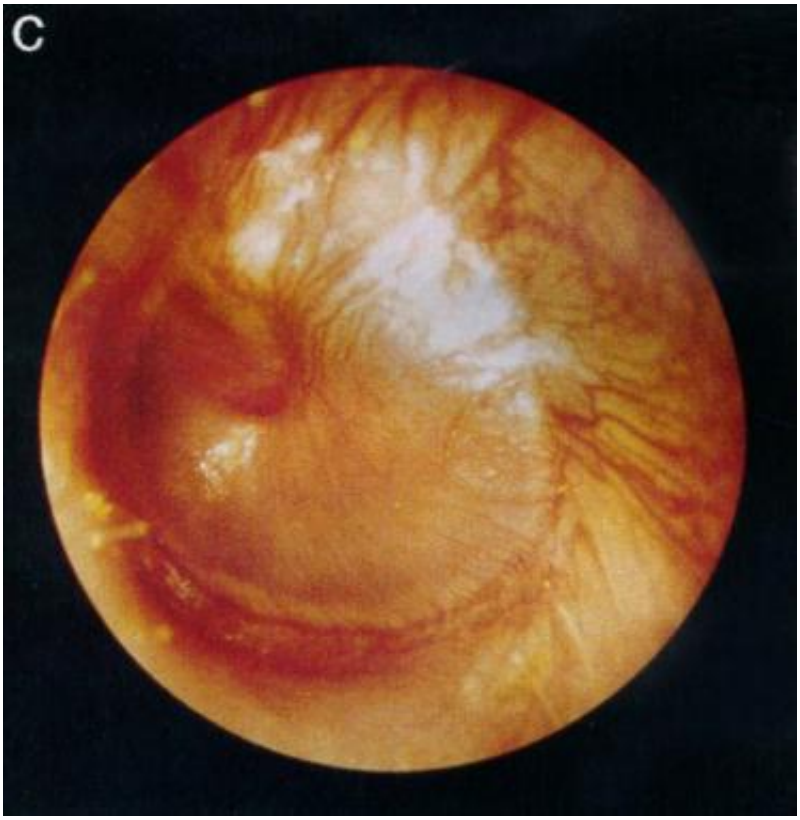
Physical Examination

There is no substitute for a thorough clinical examination. Pneumatic otoscopy is the standard of care in the diagnosis of acute and chronic otitis media. In AOM, the tympanic membrane normally demonstrates signs of inflammation, beginning with reddening of the mucosa and progressing to the formation of purulent middle ear effusion and poor tympanic mobility. The tympanic membrane may bulge in the posterior quadrants, and the superficial epithelial layer may exhibit a scalded appearance (see the image below).



Tympanic membrane of a person with 12 hours of ear pain, slight tympanic membrane bulge, and slight meniscus of purulent effusion at bottom of tympanic membrane. Reproduced with permission from Isaacson G: The natural history of a treated episode of acute otitis media. Pediatrics. 1996; 98(5): 968-7.

Perforation of the tympanic membrane is not unusual as the process advances, most frequently in posterior or inferior quadrants. Before or instead of a single perforation, an opaque serumlike exudate is sometimes seen oozing through the entire tympanic membrane.

With perforation and in the absence of a coexistent viral infection, the patient generally experiences rapid relief of pain and fever. The discharge initially is purulent, though it may be thin and watery or bloody; pulsation of the otorrhea is common. Otorrhea from acute perforation normally lasts 1-2 days before spontaneous healing occurs. Otorrhea may persist if the perforation is accompanied by mucosal swelling or polypoid changes, which can act as a ball valve.

Pneumatic otoscopy is an important diagnostic tool for differentiating AOM from acute bullous myringitis. The latter condition, in its purest form, manifests 10-14 days after a viral infection and causes severe localized otalgia without middle ear effusion.

The bullae or blebs may contain serous or hemorrhagic fluid and may extend onto the adjacent canal wall. Pain is relieved by puncturing the bleb. Similar blebs may occur in association with AOM. These patients demonstrate more systemic symptoms and continue to have pain associated with purulent middle ear effusion, which persists following rupture of the blebs.

It should be kept in mind that the findings described above apply to patients who are immunocompetent. Children who are immunosuppressed, particularly those undergoing chemotherapy, may not manifest the typical inflammatory responses. In these patients, the simultaneous appearance of systemic sepsis and a serous middle ear effusion might be the only indicators of AOM.

A finding of AOM does not relieve the practitioner of the responsibility to search for coexistent related or unrelated conditions. This responsibility is particularly important when antimicrobial agents are prescribed, in order to ensure appropriate simultaneous coverage of coexistent infections such as AOM with streptococcal pharyngitis or mycoplasmal pneumonia.

Transtympanic measurements of temperature in children with middle ear effusions have been shown to be inconsistent. Accordingly, body temperature should be measured by means of oral, rectal, or axillary methods.

Complications

The complications of AOM are classified by location as the disease spreads beyond the mucosal structures of the middle ear cleft. They may be categorized as follows:

- Intratemporal - Perforation of the tympanic membrane, acute coalescent mastoiditis, facial nerve palsy, acute labyrinthitis, petrositis, acute necrotic otitis, or development of chronic otitis media
- Intracranial - Meningitis, encephalitis, brain abscess, otitis hydrocephalus, subarachnoid abscess, subdural abscess, or sigmoid sinus thrombosis
- Systemic - Bacteremia, septic arthritis, or bacterial endocarditis

Danger signs of possible impending complications include (1) sagging of the posterior canal wall, (2) puckering of the attic, and (3) swelling of postauricular areas with loss of the skin crease.

Pediatric mastoiditis is a rare complication of AOM, with a study by King et al finding that nationally in the United States, between 2000 and 2012, the estimated incidence of pediatric mastoiditis peaked in 2006, at 2.7 cases per 100,000 population, and fell to its lowest point in 2012, at 1.8 cases per 100,000 population.[18]

A study of 177 children aged 6 months to 7 years suggested that recurrent episodes of AOM increase the risk of spontaneous tympanic membrane perforation (STMP). In addition, the study, by Marchisio et al, found a high frequency (50.8%) of nontypeable H influenzae in the middle ear fluid of patients with AOM with STMP, particularly in those with recurrent STMP. M catarrhalis and S pneumoniae (35.0% and 27.1% of cases, respectively) were the next most common bacterial pathogens found in AOM with STMP.[19]

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Diagnostic Considerations

In addition to the differential diagnosis, other problems to be considered include the following:

- External otitis
- Dental pain
- Temporomandibular joint pain
- Acute viral pharyngitis
- Trauma to the ear

Differential Diagnoses

- External Ear, Infections

Workup

Approach Considerations

Culture and sensitivity of a specimen from a fresh perforation or a tympanocentesis may be helpful.

Computed tomography (CT) may be necessary to determine if a complication has occurred; otherwise, imaging studies are unnecessary. Magnetic resonance imaging (MRI) might be more appropriate for diagnosing suspected intracranial complications.

All children with acute otitis media (AOM) have conductive hearing loss associated with the middle ear effusion; consequently, testing in the acute phase is probably unhelpful. Tympanometry may assist in the diagnosis of middle ear effusion but, for the skilled pneumatic otoscopist, is seldom necessary.

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Tympanocentesis

Tympanocentesis involves aspiration of the contents of the middle ear cleft by piercing the tympanic membrane with a needle and collecting that material for diagnostic examination. Normally, the hole is small enough to permit healing within 1 or 2 days.

Tympanocentesis should be performed in the following AOM patients:

- Neonates who are younger than 6 weeks (and therefore are more likely to have an unusual or more invasive pathogen)
- Patients who are immunosuppressed or immunocompromised
- Patients in whom adequate antimicrobial treatment has failed and who continue to show signs of local or systemic sepsis
- Patients who have a complication that requires a culture for adequate therapy

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Laboratory Studies

A study by Pichichero and Almudevar indicated that the presence of AOM caused by nontypeable H influenzae, as well as the disease's cure, can be determined from serum levels of S100A12 protein and interleukin-10 (IL-10).[20]

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Treatment

Approach Considerations

Acute otitis media (AOM) has been described as a self-limiting disease, provided that the patient does not develop a complication. This is an old description that has a renewed relevance. In the new millennium, practitioners are forced to learn the lessons of history because these may serve as our models of practice without effective antimicrobial agents. Nevertheless, for the time being, antibiotics remain the initial therapy of choice for AOM.

Other pharmacologic therapies have also been used to treat AOM. Analgesics and antipyretics have a definite role in symptomatic management. Decongestants and antihistamines do not appear to have efficacy either early or late in the acute process, although they may relieve coexistent nasal symptoms. Systemic steroids have no demonstrated role in the

acute phase.

Tympanocentesis and myringotomy are the procedures used to treat AOM. Certain patients require ventilation or drainage of the middle ear cleft for an extended period or have a history of repetitive attacks; these patients benefit from placement of a tympanostomy tube at the time of myringotomy.

Consultation is seldom necessary, although some otolaryngologists might be more comfortable having the pediatrician provide all the primary care.

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Antimicrobial Therapy

At present, a chorus of advocates recommends withholding antibiotic therapy for patients with AOM and following a “watchful waiting” or “wait and see” approach. As expected from long-known data, most children managed in this fashion do well, although a study from England observed an increase in the rate of mastoiditis in children that was, essentially, the inverse of the rate of decrease in prescriptions for acute otitis.

A literature review by Thomas et al, which included scrutiny of evidence-based AOM recommendations, particularly those found in current American guidelines, concluded that the data used to compare the usefulness of prompt antibiotic therapy with 2-3 days of watchful waiting are not completely consistent. The investigators stated that controlled trials with well-defined endpoints are still needed to better address the question.[21]

A randomized, double-blind, placebo-controlled study indicated that in children with AOM, antimicrobial treatment may prove most beneficial for those with a severely bulging tympanic membrane, while initial observation may be the best course for children with a peaked tympanogram (A and C curves). The study involved patients aged 6 to 35 months.[22, 23]

Results from another randomized, placebo-controlled study indicated that antimicrobial treatment of AOM-related middle ear effusion is effective even in older children. In the Finnish study, of 84 children aged 6 months to 15 years, 50% of the patients were treated with antibiotics, with middle ear effusion resolving an average of 2 weeks earlier in these children than it did in patients who did not receive antibiotics. Reduction of mean duration of ear effusion by age was as follows[24, 25] :

- < 2 years: 8 days
- Age 2-6 years: 20 days
- >6 years: 1 day

General principles

Despite the advocates of watchful waiting, the overwhelming consensus is still that antibiotics are the initial therapy of choice for AOM, for 3 valid reasons:

- After the institution of antibiotic therapy, a marked decline in the suppurative complications of AOM is noted
- Practitioners cannot predict with certainty which patients will develop complications
- Studies have demonstrated that the use of antibiotics improves patient outcomes in both early and late phases of AOM

Some order has been brought to the discussions of antibiotic use under the auspices of the Centers for Disease Control and Prevention (CDC) and by the Agency for Health Care Policy and Research (AHCPR), both agencies of the US government. The CDC published 6 principles of appropriate antibiotic use in an attempt to bring precepts of good public health and responsible therapy to the discussion while minimizing the selection of resistant strains of bacteria within the community. These principles are as follows:

- Episodes of otitis media should be classified as AOM or otitis media with effusion (OME)

- Antimicrobials are indicated for treatment of AOM; however, diagnosis requires documented middle ear effusion and signs or symptoms of acute local or systemic illness
- Uncomplicated AOM may be treated with a 5- to 7-day course of antimicrobials in certain patients older than 2 years
- Antimicrobials are not indicated for the initial treatment of OME; treatment may be indicated if effusions persist for longer than 3 months
- Persistent OME after therapy for AOM is expected and does not require repeat treatment with antimicrobials
- Antimicrobial prophylaxis should be reserved for controlling recurrent AOM, defined as 3 or more distinct, well-documented episodes in 6 months or 4 or more episodes in 12 months

Choice of regimen

In the absence of culture results obtained from tympanocentesis, selection of an antibiotic should have the following 2 objectives:

- The antibiotic should cover most of the common bacterial pathogens (see Etiology)
- The antibiotic must be individualized for the child with regard to allergy, tolerance, previous exposure to antibiotics, cost, and community resistance levels

The duration of therapy is also empirically determined to some degree, and data indicate that significant numbers of children do not receive prescribed antibiotics beyond relief of acute symptoms. Traditionally, therapy is continued for 10-14 days; this is convenient for office scheduling, but it may not necessarily be more efficacious than 5 or even 2 days of therapy.

Short-duration therapy may not be appropriate in children younger than 2 years who appear prone to failure even after 14 days of therapy. Mandel showed that when an effusion-free ear was the prime objective, 20 days of antibiotic therapy achieved better outcomes than 10 days of therapy or placebo; however, after 90 days, no difference in the groups existed and recurrence was not prevented by the additional therapy.

Recommendations for administration of prescribed antimicrobials to treat AOM may differ from recommendations for the same antibiotic when used for soft tissue infections.

Pulse-dosing antibiotics, when administered for infections of hollow organs, such as the ear or sinuses, appear to be efficacious as a result of some more obscure antimicrobial mechanisms, increased compliance on the part of the patient or parent, and slower penetration into and removal from middle ear effusion.

Subminimal serum levels of antibiotics have been shown to disrupt adhesive bonds between bacteria and mucosal cell walls and to provide a postantibiotic effect, in which the reproduction of bacteria is disrupted for a period of hours after antibiotic exposure. Similarly, a leukocyte-enhancing action has been demonstrated at these low concentrations.

When antibiotics are used in this manner, marked variations are found in both the effectiveness of individual agents and the susceptibility of individual pathogens. Generally, beta-lactam antibiotics are most successful against gram-positive pathogens for both disruption of adhesion and postantibiotic effect.

Amoxicillin (or erythromycin-sulfisoxazole, in patients who are allergic to penicillin) remains the initial treatment of choice in children with AOM.

With the emergence of resistant strains, the practitioner may need to select an alternative antimicrobial regimen that includes either a broad-spectrum beta-lactamase–resistant cephalosporin or a combined formulation such as amoxicillin-clavulanate or trimethoprim-sulfamethoxazole. Combination therapy may help prevent the emergence of resistance by mutation, provided the pathogen is initially sensitive to both components (see Medication).

With the emergence of multidrug-resistant S pneumoniae (MDRSP), oral therapy consisting of amoxicillin and amoxicillin-clavulanate may have efficacy when the total amoxicillin dose reaches 80-100 mg/kg/d.

If a child does not respond to an antibiotic within 48 hours and concurrently develops local and systemic signs of toxicity, the pathogen may be resistant to the selected drug. Treatment options include an empiric change of antimicrobial agent or a drainage procedure with culture. In children with prolonged acute symptoms, failure to improve with antibiotic therapy

may indicate coexistent viral infection.

Tympanocentesis, Myringotomy, and Tympanostomy

Surgical management of AOM can conveniently be divided into 3 related procedures:

- Tympanocentesis
- Myringotomy
- Myringotomy with insertion of a ventilating tube

Indications for these 3 procedures may be diagnostic, therapeutic, or prophylactic. More than 1 indication for a procedure may have to be considered on a case-by-case basis. Selection of the appropriate procedure results from evaluation of patient factors, surgeon factors, available resources, and urgency. Each of these aspects must be examined to select that procedure that gives the optimal predicted outcome.

Tympanocentesis

Tympanocentesis, in its purest form, is a diagnostic procedure that gives the clinician access to acute or chronic middle ear effusions for culture and other evaluations. However, it can also be employed in a therapeutic setting. Additionally, tympanocentesis remains a valuable research tool in the evaluation of new antimicrobial agents for efficacy in AOM and for identification of host defense mechanisms or flaws in the middle ear immunochemistry.

Consider tympanocentesis in the following patients:

- Children who are immunosuppressed or immunocompromised
- Neonates with AOM (who are more likely to have an unusual or more invasive pathogen)
- Patients in whom antimicrobial therapy has failed and who continue to experience local or systemic signs of sepsis
- Patients who have had a complication of AOM in conjunction with attempts to recover the etiologic agent from other sites (eg, cerebrospinal fluid [CSF] or blood)

Generally, tympanocentesis is performed without anesthesia after sterilization of the ear canal with isopropyl alcohol or povidone-iodine solution. Insert a needle through the anterior portion of the tympanic membrane, and aspirate the contents of the middle ear into a sterile trap for identification of microbes and their properties.

A tympanocentesis may be converted to a myringotomy (see below) and rendered therapeutic by enlarging the hole in the tympanic membrane, often by spreading the edges with microalligator forceps or suction tip. Instilling antibiotic drops and suctioning the middle ear are possible through the myringotomy. Typically, the patient experiences prompt relief of local symptoms. Culture results must be obtained before extension of the incision.

Myringotomy

Myringotomy is the incision and drainage procedure for AOM. It is a product of technology that allows the illumination of the tympanic membrane, with or without magnification. A myringotomy may be an extension of a tympanocentesis (see above) or a separate incision of the tympanic membrane to provide drainage of the middle ear cleft to the ear canal.

In this procedure, the tympanic membrane is incised with a knife, and the resulting opening allows a fluid-filled middle ear to drain to the ear canal and the exterior. Depending on the size of the hole and the method used to create it, the tympanic membrane usually returns to normal within days to a few weeks.

A number of instruments, from knives to lasers, are available to perform this task, but the basic principles remain constant. The hole design, established either by size, by the application of material to retard healing, or by the type of initial tissue damage, is the primary factor in controlling how long the perforation remains open, which, in turn, is determined by patient need.

The use of a carbon dioxide laser in myringotomy on children with AOM has been promoted widely and directly to the consumer by the manufacturers of these instruments; proponents claim to have ushered in a new treatment for AOM without the use of antimicrobials. This approach is undoubtedly a boon for the otolaryngologist who is less technically adept, but to date, it has yielded little or no change in efficacy over standard myringotomy.

Myringotomy with ventilation tube

Some patients with AOM require ventilation or drainage of the middle ear cleft for an extended period (eg, patients with mastoiditis), whereas others may have a history of repetitive attacks. These patients benefit with the placement of a tympanostomy tube at the time of myringotomy. In most instances, general anesthesia or sedation is necessary in older children because topical anesthesia is relatively ineffective in acutely inflamed tympanic membranes.

Numerous tube designs are now available, each with its own weaknesses and strengths with respect to retention, reactivity, and complications. Selection of any tympanostomy tube design is governed by the length of time for which ventilation is likely to be needed. Tubes may be designed to permit tube placement for 6-9 months, for 9-18 months, or for longer than 2 years. Selection is also governed by the quality of the tympanic membrane's fibrous tissue and by patient need versus the increasing complication rates associated with prolonged ventilation.

With increasing antimicrobial resistance, surgical intervention in the form of tympanostomy tube placement can be expected to increase in the coming years, after having fallen into disfavor in the past 2 decades when resistance was less of a factor. In the author's practice, children younger than 15 months and those who attend day care centers are most likely to require surgery.

In a report on 248 pediatric patients who received tympanostomy tubes and postoperative otic drop therapy, Conrad et al found that tube occlusion occurred most frequently in patients with middle ear fluid and in those with longer time to postsurgical follow-up. The investigators, who conducted a retrospective medical record review, found that at first follow-up, one or both tubes were occluded in 10.6% of patients. Children with no serous fluid were found to be 3 times more likely to have unobstructed tubes than were children with fluid. It was also found that the chance of occlusion increased in relation to the amount of time that existed between surgery and follow-up.[26, 27]

Mastoidectomy

Mastoidectomy predates the extensive use of tympanic membrane incision, primarily because of the severity of the disease and the relatively frequent occurrence of spontaneous perforation in otitis-prone individuals. For example, in Eskimo communities of northern Canada, native Inuit are often found with large central perforations from chronic otitis.

Contraindications for surgical therapy

Contraindications for incision of the tympanic membrane are relatively few in the presence of acute disease. In 25 years of practice, the author has twice managed to tap through "thick tympanic membranes" to find himself aspirating CSF from low-hanging and exposed dura (one associated with a porencephalic cyst). Neither resulted in a prolonged complication, but CSF may be obtained with considerably less excitement via lumbar puncture.

Patients with patulous eustachian tubes most frequently have persistent otorrhea after placement of tympanostomy tubes. Children with neuromuscular disease, unrepaired cleft palates, or Down syndrome are more prone to this outcome. Otorrhea may be the lesser evil when the child is septic or uncomfortable or when damage to the middle ear cleft is imminent. This contraindication is a relative one, and the parent must be informed of the risk and allowed to participate in the decision whether to proceed.

Complications of surgical therapy

Complications of tympanocentesis and myringotomy are few and rare in appropriately performed procedures in children with otherwise normal anatomy. They include the following:

- Immediate complications - Injury to the skin of the ear canal; injury to the ossicular chain
- Intermediate complications - Persistent otorrhea; persistent perforation; external otitis from persistent drainage; implantation cholesteatoma
- Long-term complications - Persistent perforation, with or without otorrhea; ear canal stenosis

The complications for myringotomy with ventilation tube placement are the same, with the addition of those related to the tube and to longer perforation.

With tubes of modern design, medialization is now quite rare. Some tube designs have a tendency to collect epithelial debris and inherently have a higher rate of cholesteatoma formation. As a rule, longer ventilation increases the likelihood of persistence of the perforation, the formation of aural polyps, and chronic otorrhea. Most of these complications are reversed by removal of the tube, with or without repair of the hole with a small myringoplasty.

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Prevention

Children with recurrent AOM have no effusion within the middle ear cleft between attacks of acute disease. Management of this condition is confined to either episodic management or preventive treatment.

In episodic management, each episode is considered a new attack and is treated with antibiotics; the patient is monitored until the episode resolves. Preventative treatment involves the administration of a conjugated heptavalent pneumococcal vaccine. Although the vaccine is intended to combat invasive effects in infants, immunized children have a reduced incidence of AOM, a reduced need for antibiotic therapy or tympanostomy tubes, and a reduced risk of invasion or hearing loss.[28]

Since the introduction of the heptavalent pneumococcal vaccine in 2000, researchers have found that nearly two thirds of invasive pneumococcal disease cases in young children have been caused by 6 serotypes that were not included in that vaccine. Those serotypes, along with the original 7, have been incorporated into pneumococcal vaccine valent-13 (Prevnar 13) that was approved in February 2010.

A study by Hasegawa et al indicated that the introduction of a heptavalent pneumococcal conjugate vaccine to Japan in 2009 significantly reduced the risk of AOM in infants and young children. The study, in which 614 parents were surveyed, found that, after adjustment for potentially confounding variables, the hazard ratio for AOM in vaccinated children was 0.33, with significant risk reduction in children between infancy and age 3 years and in young children over age 3 years. [29]

Similarly, a study by Tawfik et al indicated that since the introduction of pneumococcal vaccination, hospital admissions for pediatric AOM/complications of AOM in the United States have decreased in prevalence, as have admission rates for pediatric pneumococcal meningitis with AOM/complications of AOM. Using information from the Kids' Inpatient Database from between 2000 and 2012, the study found particularly sharp declines in admissions for children under age 1 years, from 22.647 to 8.715 per 100,000 persons, and for children aged 1-2 years, from 13.652 to 5.554 per 100,000 persons. [30]

A study by Kaur et al indicated that the introduction of 7-valent and 13-valent pneumococcal conjugate vaccine (PCV7 and PCV13) has reduced the prevalence of AOM in children aged 3 years or younger. The report found that out of 615 children, all of whom were vaccinated with PCV7 or PCV13, 60% suffered one or more episodes of AOM by age 3 years, and 24% experienced three or more episodes. In comparison, a 1989 study, conducted by Teele et al prior to the introduction of PCVs, found that by age 3 years, 83% of children followed experienced at least one episode of AOM, while 46% suffered three or more episodes. Kaur et al also attributed the change in AOM prevalence to more stringent criteria used to differentiate AOM from otitis media with effusion.[31, 32, 33]

If immunologic therapy to prevent AOM is to be found, however, vaccines that are effective against nontypeable H influenzae, as well as all serotypes of S pneumoniae, will have to be developed. Some progress is being made with the former.[34] As yet, however, no vaccine exists for nontypeable H influenzae. Correspondingly, research has been commenced on immunization against the common viruses that induce AOM—namely, respiratory syncytial virus (RSV), adenoviruses, influenza A and B viruses, and rhinoviruses.

Antibiotic prophylaxis is becoming less popular as resistant strains emerge. Amoxicillin and sulfisoxazole have both been used extensively. The former has better coverage against S pyogenes but may promote nasopharyngeal colonization with beta-lactam–resistant pneumococci and H influenzae. Reserve prophylaxis for otitis-prone children who are younger than 2 years or in day care and who have had 3 or more attacks in a 6-month period. Both amoxicillin and sulfisoxazole can cause serum sickness reactions.

A potential preventative measure is the natural sugar substitute, xylitol. Studies indicate that xylitol chewing gum, lozenges

or syrup may reduce the occurrence of AOM by as much as 25%.[35] However, a study by Danhauer et al suggested that most parents are unaware that xylitol can prevent AOM and would be unlikely to use it in their preschool- and kindergarten-aged children. Nonetheless, the investigators, who employed an Internet questionnaire, did find that parents who were previously aware of xylitol as a preventive and who had children with a history of AOM would be more likely to give it to their youngsters.[36]

Tympanostomy tube placement decreases episodes of AOM. Ventilation has been used more frequently when evidence of MDRSP exists. In the author's practice, resistance is noted most frequently in infants and children aged 6-14 months who are in day care.

Tympanostomy tubes are also beneficial in children with recurrent AOM and coexistent reactive airway disease and should be considered when recurrent episodes of AOM destabilize control of other systemic conditions. Examples include alterations in seizure thresholds, otitic hydrocephalus, or control of diabetes. Similarly, early tympanostomy tube placement might be considered for children with sensorineural hearing loss, speech development abnormalities, or learning dysfunction to give the child a consistent hearing model.

Control of nasal inflammation in children, whether caused by an allergy or by recurrent infection, appears to decrease the recurrence of AOM. Trials are being conducted to determine the efficacy of topical nasal steroids for decreasing middle ear disease, in an attempt to confirm anecdotal information that supports this treatment modality.

Some of the risk factors for AOM (see Etiology) can be removed by such efforts as altering child care arrangements, providing a tobacco-free living space, and stopping bottle use in children older than 1 year.

In children with recurrent AOM, adenoidectomy has demonstrated efficacy. However, determining which children will benefit from this treatment modality is not yet possible. Few pediatric otolaryngologists recommend adenoidectomy initially over tympanostomy tube placement alone, unless coexistent nasal symptoms are present. The procedure might be considered for older children who require replacement of their tympanostomy tubes. As additional information on the role of biofilm in the nasopharynx becomes available, the selection of candidates for adenoidectomy with or without tube placement is likely to improve.

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Long-Term Monitoring

Reexamine patients within 48 hours if no evidence of decreasing acuity manifests, if symptoms become more severe, or if a complication becomes evident. Otherwise, follow-up care is normally scheduled 10-14 days after the acute event.

Persistent middle ear effusion should be expected at the initial follow-up visit; statistically, only 30% of patients show complete resolution. In the absence of acuity, further treatment is unwarranted, but the patient should be scheduled to return at intervals until the effusion resolves. The author often gives parents an "emergency prescription" to be filled if the child with fluid in the middle ear develops acute symptoms prior to the next scheduled visit. In addition to decreasing off-hours calls, this provides the parent with a sense of security.

In a study of 1208 children, aged 6-24 months, Grindler and colleagues concluded that the health-related quality of life in children with recurrent otitis media was significantly worse than it was in healthy youngsters. In addition, in children with recurrent otitis media, myringotomy tube placement was associated with increased quality-of-life scores.[37]

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Guidelines

Guidelines Summary

Guidelines for the diagnosis and management of AOM have been issued by the following organizations:

- American Academy of Pediatrics (AAP)

- University of Michigan Health System (UMHS)

The American Academy of Pediatrics (AAP) released revised clinical practice guidelines for the diagnosis and management of uncomplicated AOM in children aged 6 months through 12 years in 2013.[38, 39] The updated recommendations, intended as a clinical decision-making framework for primary care physicians (PCPs), provide more rigorous diagnostic criteria intended to decrease unnecessary antibiotic use, as well as address therapeutic options, analgesia, prevention, and appropriate selection of antibiotics. They also discuss recurrent AOM, which was not covered in the previous guideline (2004).[38, 39]

The University of Michigan Health System published an update to its 2007 guidelines in 2013. A minor revision was released in 2014 to include information from the AAP that appeared after the publication of the guidelines.[40]

Diagnosis

Diagnostic action statements from the AAP guidelines include the following[38, 39] :

- AOM should be diagnosed when there is moderate to severe tympanic membrane bulging or new-onset otorrhea not caused by acute otitis externa
- AOM may be diagnosed from mild tympanic membrane bulging and ear pain for less than 48 hours or from intense tympanic membrane erythema; in a nonverbal child, ear holding, tugging, or rubbing suggests ear pain
- AOM should not be diagnosed when pneumatic otoscopy and/or tympanometry do not show middle ear effusion

The UMHS guidelines include the following recommendations[40] :

- Symptoms of pain or fever, together with an inflammatory middle ear effusion, are required to make a diagnosis of AOM
- The presence of middle ear effusion should be determined through the combined use of otoscopy, pneumatic otoscopy, and tympanometry when necessary

Treatment

AAP management-related action statements include the following[38, 39] :

- AOM management should include pain evaluation and treatment
- Antibiotics should be prescribed for bilateral or unilateral AOM in children aged at least 6 months with severe signs or symptoms (moderate or severe otalgia or otalgia for 48 hours or longer or temperature 39°C or higher) and for nonsevere, bilateral AOM in children aged 6-23 months
- On the basis of joint decision-making with the parents, unilateral, nonsevere AOM in children aged 6 -23 months or nonsevere AOM in older children may be managed either with antibiotics or with close follow-up and withholding of antibiotics unless the child worsens or does not improve within 48-72 hours of symptom onset
- Amoxicillin is the antibiotic of choice unless the child received it within the previous 30 days, has concurrent purulent conjunctivitis, or is allergic to penicillin; in these cases, clinicians should prescribe an antibiotic with additional β-lactamase coverage
- Clinicians should reevaluate a child whose symptoms have worsened or not responded to the initial antibiotic treatment within 48-72 hours and change treatment if indicated
- In children with recurrent AOM, tympanostomy tubes, but not prophylactic antibiotics, may be indicated to reduce the frequency of AOM episodes
- Clinicians should recommend pneumococcal conjugate vaccine and annual influenza vaccine to all children according to updated schedules
- Clinicians should encourage exclusive breastfeeding for 6 months or longer

The UMHS guidelines concur overall with those of the AAP and include the following additional treatment recommendations[40] :

- When antibiotic therapy is deferred, facilitate access to antibiotics if symptoms worsen (ie, a "back-up" prescription given at visit)
- Amoxicillin is the first choice of antibiotic therapy; if amoxicillin is contraindicated, azithromycin is the appropriate first-line therapy
- For AOM that is unresponsive to amoxicillin after 72 hours of therapy, administer amoxicillin-clavulanate or azithromycin
- Patients with significant, persistent symptoms on high-dose amoxicillin-clavulanate or azithromycin may respond to intramuscular ceftriaxone; the decision to use ceftriaxone should weigh the negative impact it will have on local antibiotic resistance

The American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) offers the following guidance on the use of tympanostomy tube insertion for children with AOM[41] :

- Tympanostomy tube insertion should not be performed in children with recurrent AOM who do not have middle ear effusion (MEE) in either ear at the time of assessment for tube candidacy
- Bilateral tympanostomy tube insertion should be performed in children who have unilateral or bilateral MEE at the time of assessment for tube candidacy
- Educate caregivers of children with tympanostomy tubes regarding the expected duration of tube function, recommended follow-up schedule, and detection of complications
- Clinicians should prescribe topical antibiotic eardrops only, without oral antibiotics, for children with uncomplicated acute tympanostomy tube otorrhea
- Encourage routine, prophylactic water precautions (use of earplugs or headbands; avoidance of swimming or water sports) for children with tympanostomy tubes

The French Society of Otorhinolaryngology (SFORL) issued clinical practice guidelines for the use of nonsteroidal antiinflammatory drugs (NSAIDs) in pediatric ENT infections in September 2019.[42]

In uncomplicated pediatric ENT infections, such as acute otitis media, tonsillitis, upper respiratory tract infections, and maxillary sinusitis, NSAIDs are indicated at analgesic doses (eg, ibuprofen 20-30 mg/kg/day) in combination with acetaminophen (in the following circumstances:

- The pain intensity is determined to be medium (ie, a visual analogue scale [VAS] score of 3-5 or "Evaluation Enfant Douleur" [EVENDOL] child pain score of 4-7) and insufficiently responsive to first-line acetaminophen (residual VAS ≥3 or EVENDOL ≥4)
- Pain is moderate to intense (VAS score 5-7 or EVENDOL score 7-10)

When combined, acetaminophen and ibuprofen should be taken simultaneously every 6 hours.

NSAIDS should not be prescribed to pediatric patients with severe or complicated ENT infections.

NSAIDs should be suspended in patients with infections that have unusual clinical presentations in terms of duration or symptoms.

NSAIDs should not be given for more than 72 hours.

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Medication

Medication Summary

Antibiotics are the only medications with demonstrated efficacy in the management of AOM. Most antibiotics can be administered once or twice daily to improve compliance and to avoid the necessity of sending medication to school or day care centers. The following list excludes medications that have reduced activity against common pathogens or that have significant adverse effects without other redeeming features to warrant inclusion.

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Antibiotics

Class Summary

Empiric antimicrobial therapy must be comprehensive and should cover all likely pathogens in the context of the clinical setting.

Amoxicillin (Amoxil, Trimox, Wymox)

DOC for management of AOM. Interferes with synthesis of cell wall mucopeptides during active multiplication, resulting in bactericidal activity against susceptible bacteria.

Amoxicillin/clavulanate (Augmentin)

Combination drug that includes a blocking agent (clavulanic acid).

Erythromycin base / sulfisoxazole (E.E.S. 400)

Doses supplied in 200 mg/5 mL (erythromycin) and 600 mg/5 mL (sulfisoxazole). Widely used for individuals who are penicillin-sensitive. Well absorbed from GI tract but best administered on full stomach to avoid GI upset.

Trimethoprim/sulfamethoxazole (Bactrim, Bactrim DS, Septra, Septra DS)

Inhibits bacterial growth by inhibiting synthesis of dihydrofolic acid.

Cefixime (Suprax)

By binding to one or more of the penicillin-binding proteins, arrests bacterial cell wall synthesis and inhibits bacterial growth.

Cefuroxime Axetil (Ceftin)

Second-generation cephalosporin that maintains gram-positive activity of first-generation cephalosporins; adds activity against Proteus mirabilis, H influenzae, E coli, Klebsiella pneumoniae, and M catarrhalis.

Condition of patient, severity of infection, and susceptibility of microorganism determine proper dose and route of administration.

Cefprozil (Cefzil)

Binds to one or more of the penicillin-binding proteins, which, in turn, inhibits cell wall synthesis and results in bactericidal activity.

Cefpodoxime (Vantin)

Indicated for management of infections caused by susceptible mixed aerobic-anaerobic microorganisms.

Cefdinir (Omnicef)

Third-generation cephalosporin indicated for treatment of uncomplicated skin infections.

Clindamycin (Cleocin HCl)

Lincosamide for treatment of serious skin and soft tissue staphylococcal infections. Also effective against aerobic and anaerobic streptococci (except enterococci). Inhibits bacterial growth, possibly by blocking dissociation of peptidyl t-RNA from ribosomes, causing RNA-dependent protein synthesis to arrest.

Clarithromycin (Biaxin)

Inhibits bacterial growth, possibly by blocking dissociation of peptidyl t-RNA from ribosomes, causing RNA-dependent protein synthesis to arrest.

Azithromycin (Zithromax)

Broad-spectrum macrolide antibiotic. Absorption markedly reduced when taken with food.

Ceftriaxone (Rocephin)

Third-generation cephalosporin. Manufacturer has heavily promoted IM use of this drug to physicians and directly to the public for routine treatment of AOM. Subsequently, MDRSP resistance has emerged, making this less effective in many communities. Author believes this drug is best reserved for IV use for management of severe infections. Avoid widespread use for AOM.

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Questions & Answers

Overview

Which viruses are typically found in the middle ear of patients with acute otitis media (AOM)?

What is the role of immunology in the pathogenesis of acute otitis media (AOM)?

What is the role immunoglobulins in the pathogenesis of acute otitis media (AOM)?

What is the role of respiratory syncytial virus (RSV) in the etiology of acute otitis media (AOM)?

Which bacteria are etiologic agents in acute otitis media (AOM)?

What is the role of S pneumoniae in the etiology of acute otitis media (AOM)?

What is the role of H influenzae in the etiology of acute otitis media (AOM)?

What is the role of M catarrhalis in the pathogenesis of acute otitis media (AOM)?

What is the role of S pyogenes in the pathogenesis of acute otitis media (AOM)?

Which bacteria are less common causes of acute otitis media (AOM)?

What is the role of anaerobic bacteria in the etiology of acute otitis media (AOM)?

Which bacteria are associated with acute otitis media (AOM) in neonates?

What are the risk factors for acute otitis media (AOM)?

What is the incidence and prevalence of acute otitis media (AOM) in the US?

In which age groups is acute otitis media (AOM) most prevalent?

How does the prevalence of acute otitis media (AOM) vary among races?

What is the prognosis of acute otitis media (AOM)?

Presentation

Which history findings suggest acute otitis media (AOM)?

How is acute otitis media (AOM) diagnosed?

What does a finding of tympanic membrane perforation indicate in acute otitis media (AOM)?

How is acute bullous myringitis differentiated from acute otitis media (AOM)?

Which comorbidities must be identified before treatment of acute otitis media (AOM) is initiated?

How should temperature be measured in children with suspected acute otitis media (AOM)?

What are the potential complications of acute otitis media (AOM)?

Which findings are signs of impending complications of acute otitis media (AOM)?

How often is mastoiditis a complication of acute otitis media (AOM)?

What is the role of recurrent acute otitis media (AOM) in spontaneous tympanic membrane perforation (STMP)?

DDX

Which other conditions should be considered in the workup of acute otitis media (AOM)?

What are the differential diagnoses for Acute Otitis Media?

Workup

Which tests may be performed in the workup of acute otitis media (AOM)?

What is the role of tympanocentesis in the diagnosis of acute otitis media (AOM)?

When is tympanocentesis indicated in the workup of acute otitis media (AOM)?

Which serum testing results are used to direct treatment of acute otitis media (AOM) caused by nontypeable H influenzae?

Treatment

What are the treatment options for acute otitis media (AOM)?

When should antibiotic therapy be initiated for treatment of acute otitis media (AOM)?

How effective is antibiotic therapy for acute otitis media (AOM)?

Why are antibiotics the initial therapy for treatment of acute otitis media (AOM)?

What are the CDC guidelines for the use of antibiotics for treatment of acute otitis media (AOM)?

What is the basis of antibiotic selection in the treatment of acute otitis media (AOM)?

What is the duration of antibiotic therapy for the treatment of acute otitis media (AOM)?

What is the role of pulse-dosing antibiotics in the treatment of acute otitis media (AOM)?

What is the role of subminimal serum antibiotics in the treatment of acute otitis media (AOM)?

Which antibiotic is the initial treatment of choice for acute otitis media (AOM)?

What are the treatment options for antibiotic-resistant acute otitis media (AOM) infections?

Which surgical procedures are performed in the treatment of acute otitis media (AOM)?

What is the role of tympanocentesis in the management of acute otitis media (AOM)?

When is tympanocentesis indicated in the treatment of acute otitis media (AOM)?

How is tympanocentesis performed in acute otitis media (AOM)?

How is a tympanocentesis converted to a myringotomy during treatment for acute otitis media (AOM)?

What is myringotomy?

How is a myringotomy performed in the treatment of acute otitis media (AOM)?

When are tympanostomy tubes indicated in the treatment of acute otitis media (AOM)?

Why is the placement of tympanostomy tubes likely to increase as a treatment for acute otitis media (AOM)?

What factors increase the risk of tympanostomy tube occlusion in acute otitis media (AOM)?

What is the role of mastoidectomy in the treatment of acute otitis media (AOM)?

When is surgery contraindicated for acute otitis media (AOM)?

What are possible surgical complications in the treatment of acute otitis media (AOM)?

What are the treatment options for recurrent acute otitis media (AOM)?

Which vaccines have reduced the incidence of acute otitis media (AOM) in children?

Which vaccines are being investigated for prevention of acute otitis media (AOM)?

When is antibiotic prophylaxis indicated in the management of acute otitis media (AOM)?

What is the role of xylitol in the prevention of acute otitis media (AOM)?

How effective is a tympanostomy tube in the management of acute otitis media (AOM)?

Does control of nasal inflammation affect recurrence of acute otitis media (AOM)?

Which risk factors for acute otitis media (AOM) can be mitigated?

What is the role of adenoidectomy in the treatment of acute otitis media (AOM)?

When should patients with acute otitis media (AOM) be reexamined after initiation of treatment?

What findings are expected at a follow up visit for acute otitis media (AOM)?

Does acute otitis media (AOM) affect a child's quality of life?

Guidelines

What are the AAO-HNSF guidelines for the use of tympanostomy tubes in the treatment of acute otitis media (AOM)?

Which organizations have released treatment guidelines for acute otitis media (AOM)?

What are the AAP diagnostic guidelines for acute otitis media (AOM)?

What are the UMHS diagnostic guidelines for acute otitis media (AOM)?

What are the AAP treatment guidelines for acute otitis media (AOM)?

What are the UMHS treatment guidelines for acute otitis media (AOM)?

Medications

Which medications are used in the treatment of acute otitis media (AOM)?

Which medications in the drug class Antibiotics are used in the treatment of Acute Otitis Media?

emedicine

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References

1. Rettig E, Tunkel DE. Contemporary concepts in management of acute otitis media in children. Otolaryngol Clin North Am. 2014 Oct. 47 (5):651-72. [Medline]. [Full Text].
2. Minovi A, Dazert S. Diseases of the middle ear in childhood. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2014. 13:Doc11. [Medline]. [Full Text].
3. Danishyar A, Ashurst JV. Otitis, Media, Acute. 2018 Jan. [Medline]. [Full Text].
4. Sakulchit T, Goldman RD. Antibiotic therapy for children with acute otitis media. Can Fam Physician. 2017 Sep. 63 (9):685-7. [Medline]. [Full Text].
5. Clements DA, Langdon L, Bland C, Walter E. Influenza A vaccine decreases the incidence of otitis media in 6- to 30- month-old children in day care. Arch Pediatr Adolesc Med. 1995 Oct. 149(10):1113-7. [Medline].
6. Bernstein JM. The role of IgE-mediated hypersensitivity in the development of otitis media with effusion. Otolaryngol Clin North Am. 1992 Feb. 25(1):197-211. [Medline].
7. American Academy of Pediatrics. Respiratory syncytial virus. Red Book: Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, Ill: 2006. 560-566.
8. Arola M, Ruuskanen O, Ziegler T, et al. Clinical role of respiratory virus infection in acute otitis media. Pediatrics. 1990 Dec. 86(6):848-55. [Medline].
9. Arola M, Ziegler T, Ruuskanen O. Respiratory virus infection as a cause of prolonged symptoms in acute otitis media. J Pediatr. 1990 May. 116(5):697-701. [Medline].
10. Block SL. Causative pathogens, antibiotic resistance and therapeutic considerations in acute otitis media. Pediatr Infect Dis J. 1997 Apr. 16(4):449-56. [Medline].
11. American Academy of Pediatrics. Pneumococcal infections. Red Book: Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, Ill: 2006. 525-537.
12. American Academy of Pediatrics. Haemophilus influenzae infections. Red Book: Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, Ill: 2006. 310-3318.
13. Martin JM, Hoberman A, Shaikh N, et al. Changes Over Time in Nasopharyngeal Colonization in Children Under 2 Years of Age at the Time of Diagnosis of Acute Otitis Media (1999-2014). Open Forum Infect Dis. 2018 Mar. 5 (3):ofy036. [Medline]. [Full Text].
14. Chonmaitree T, Trujillo R, Jennings K, et al. Acute Otitis Media and Other Complications of Viral Respiratory Infection. Pediatrics. 2016 Mar 28. [Medline].

15. American Academy of Pediatrics. Group A streptococcal infections. Red Book: Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, Ill: 2006. 610-620.

16. Paradise JL, Rockette HE, Colborn DK, et al. Otitis media in 2253 Pittsburgh-area infants: prevalence and risk factors during the first two years of life. Pediatrics. 1997 Mar. 99(3):318-33. [Medline].

17. Megged O, Abdulgany S, Bar-Meir M. Does Acute Otitis Media in the First Month of Life Increase the Risk for Recurrent Otitis?. Clin Pediatr (Phila). 2018 Jan. 57 (1):89-92. [Medline].

18. King LM, Bartoces M, Hersh AL, Hicks LA, Fleming-Dutra KE. National Incidence of Pediatric Mastoiditis in the United States, 2000-2012: Creating a Baseline for Public Health Surveillance. Pediatr Infect Dis J. 2018 Mar 27. [Medline].

19. Marchisio P, Esposito S, Picca M, et al. Prospective evaluation of the aetiology of acute otitis media with spontaneous tympanic membrane perforation. Clin Microbiol Infect. 2017 Jan 19. [Medline].

20. Pichichero ME, Almudevar A. Serum cytokine biomarkers accurately predict presence of acute otitis media infection and recovery caused by Haemophilus influenzae. Int J Pediatr Otorhinolaryngol. 2016 Apr. 83:200-4. [Medline].

21. Thomas JP, Berner R, Zahnert T, et al. Acute otitis media-a structured approach. Dtsch Arztebl Int. 2014 Feb 28. 111(9):151-60. [Medline]. [Full Text].

22. Tahtinen PA, Laine MK, Ruohola A. Prognostic Factors for Treatment Failure in Acute Otitis Media. Pediatrics. 2017 Sep. 140 (3):[Medline].

23. Basco WT. Predicting Treatment Failure in Kids With AOM. Medscape. 2017 Nov 27. [Full Text].

24. Boggs W. Antimicrobial Treatment of Acute Otitis Media Shortens Duration of Middle Ear Effusion. Medscape. May 9 2014. [Full Text].

25. Tapiainen T, Kujala T, Renko M, et al. Effect of Antimicrobial Treatment of Acute Otitis Media on the Daily Disappearance of Middle Ear Effusion: A Placebo-Controlled Trial. JAMA Pediatr. 2014 May 5. [Medline].

26. Barclay L. Postop Tympanostomy Tube Obstruction Common. Medscape Medical News. Jul 11 2014. [Full Text].

27. Conrad DE, Levi JR, Theroux ZA, et al. Risk Factors Associated With Postoperative Tympanostomy Tube Obstruction. JAMA Otolaryngol Head Neck Surg. 2014 Jul 10. [Medline].

28. Fireman B, Black SB, Shinefield HR, et al. Impact of the pneumococcal conjugate vaccine on otitis media. Pediatr Infect Dis J. 2003 Jan. 22(1):10-6. [Medline].

29. Hasegawa J, Mori M, Showa S, et al. Pneumococcal vaccination reduced the risk of acute otitis media: a cohort study. Pediatr Int. 2015 Jan 23. [Medline].

30. Tawfik KO, Ishman SL, Altaye M, Meinzen-Derr J, Choo DI. Pediatric Acute Otitis Media in the Era of Pneumococcal Vaccination. Otolaryngol Head Neck Surg. 2017 Mar 1. 194599817699599. [Medline].

31. Frellick M. Vaccines Have Changed the Epidemiology of Acute Otitis Media. Medscape Medical News. 2017 Aug 7. [Full Text].

32. Kaur R, Morris M, Pichichero ME. Epidemiology of Acute Otitis Media in the Postpneumococcal Conjugate Vaccine Era. Pediatrics. 2017 Aug 7. [Medline]. [Full Text].

33. Teele DW, Klein JO, Rosner B. Epidemiology of otitis media during the first seven years of life in children in greater Boston: a prospective, cohort study. J Infect Dis. 1989 Jul. 160 (1):83-94. [Medline].

34. Hong W, Peng D, Rivera M, Gu XX. Protection against nontypeable Haemophilus influenzae challenges by mucosal vaccination with a detoxified lipooligosaccharide conjugate in two chinchilla models. Microbes Infect. 2010 Jan. 12 (1):11-8. [Medline].

35. Azarpazhooh A, Limeback H, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. Cochrane Database Syst Rev. 2011 Nov 9. 11:CD007095. [Medline].

36. Danhauer JL, Johnson CE, Baker JA, et al. Will Parents Participate in and Comply with Programs and Regimens Using Xylitol for Preventing Acute Otitis Media in Their Children?. Lang Speech Hear Serv Sch. 2015 Feb 4. [Medline].

37. Grindler DJ, Blank SJ, Schulz KA, et al. Impact of otitis media severity on children's quality of life. Otolaryngol Head Neck Surg. 2014 Mar 13. [Medline].

38. Barclay L. Pediatric ear infection: updated AAP treatment guidelines. Medscape Medical News. February 25, 2013. Available at http://www.medscape.com/viewarticle/779817. Accessed: March 5, 2013.

39. [Guideline] Lieberthal AS, Carroll AE, Chonmaitree T, Ganiats TG, et al. The diagnosis and management of acute otitis media. Pediatrics. 2013 Mar. 131(3):e964-99. [Medline]. [Full Text].

40. University of Michigan Health System (UMHS). Otitis media. April 2013. Available at http://www.med.umich.edu/1info/FHP/practiceguides/om.html.

41. [Guideline] Rosenfeld RM, Schwartz SR, Pynnonen MA, et al. Clinical practice guideline: Tympanostomy tubes in children. Otolaryngol Head Neck Surg. 2013 Jul. 149 (1 Suppl):S1-35. [Medline]. [Full Text].

42. Truffert E, Fournier Charrière E, Treluyer JM, Blanchet C, Cohen R, Gardini B, et al. Guidelines of the French Society of Otorhinolaryngology (SFORL): Nonsteroidal anti-inflammatory drugs (NSAIDs) and pediatric ENT infections. Short version. Eur Ann Otorhinolaryngol Head Neck Dis. 2019 Sep. 136 (4):289-294. [Medline].