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62 Otitis Externa, Otitis Media, and Mastoiditis

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SHORT VIEW SUMMARY

DEFINITION

Otitis Externa
- Otitis externa is an infection and inflammation of the external auditory canal.

Otitis Media
- Acute otitis media (AOM) is an acute illness marked by the presence of fluid in the middle ear and inflammation of the mucosa lining the middle ear space. Fluid may persist in the middle ear for weeks to months after appropriately treated AOM and is termed otitis media with effusion.

Mastoiditis
- Mastoiditis is infection and inflammation of the mastoid air cells and usually results from episodes of severe AOM.

EPIDEMIOLOGY

Otitis Externa
- Acute diffuse otitis externa or swimmer's ear occurs in hot humid weather.
- Invasive or malignant otitis externa occurs in diabetic, immunocompromised, and debilitated patients.
- Children are prone to place foreign objects in the external ear canal, which may cause maceration and infection of the skin lining the external canal.

Otitis Media
- Otitis media occurs at all ages, but the peak age group is children in the first 3 years of life.
- Children at risk for severe and recurrent otitis media are more frequently male, have a genetic predisposition to ear infections, and may be in large-group daycare exposed to frequent respiratory viruses and bacterial pathogens.

Mastoiditis
- The epidemiology of mastoiditis parallels that of otitis media.

MICROBIOLOGY

Otitis Externa
- The microbial microbiota of the external ear canal responsible for otitis externa is similar to that of skin elsewhere, including staphylococcal species and anaerobic bacteria.
- *Pseudomonas aeruginosa* is a frequent cause of swimmer's ear and malignant otitis externa.

Otitis Media
- *Streptococcus pneumoniae* and nontypeable *Haemophilus influenzae* are the most frequent bacterial pathogens in all age groups.
- *Moraxella catarrhalis,* group A *Streptococcus* and *Staphylococcus aureus* are less frequent causes of AOM.
- Respiratory viruses are frequent causes of AOM alone or associated with bacterial pathogens.

Mastoiditis
- The microbiology of mastoiditis is similar to that of AOM.
- Patients with persistent perforation of the tympanic membrane may have invasion of the mastoid by organisms present in the external ear canal, including *S. aureus* and *P. aeruginosa.*

DIAGNOSIS

Otitis Externa
- Acute localized otitis externa may occur as a pustule or furuncle that is visualized in the canal.
- Swimmer's ear is identified by edema, swelling, and erythema of the canal wall.
- Malignant otitis externa is associated with severe pain and tenderness of the tissues around the pinna and mastoid; pus may be present in the canal.

Otitis Media
- AOM is an acute illness with fluid in the middle ear and bulging or decreased mobility and inflammation of the tympanic membrane.

Mastoiditis
- The signs of mastoiditis include swelling, redness, and tenderness over the mastoid bone.
- The pinna is displaced downward and outward, and a purulent discharge may emerge through a perforation of the tympanic membrane.

THERAPY

Otitis Externa
- Swimmer's ear may be managed with gentle cleansing and irrigation of the external canal.
- Antibiotic solutions, including fluoroquinolone eardrops, are effective in localized infections.
- Systemic antimicrobial therapy, including activity against *P. aeruginosa,* is necessary to manage invasive external otitis media.

Otitis Media
- High-dose amoxicillin is the preferred drug for patients with AOM.
- If amoxicillin fails, amoxicillin-clavulanate or parenteral ceftriaxone is preferred.
- Some children with AOM improve without use of antimicrobial agents.
- Placement of tympanostomy tubes may be warranted for children with severe and recurrent episodes of AOM.

Mastoiditis
- Antimicrobial therapy is similar to that of AOM.
- Incision and drainage may be necessary when abscesses form in the mastoid air cells.

PREVENTION

Otitis Externa
- Patients should be dissuaded from placing foreign objects, including cotton-tipped applicators, in the external canal.

Otitis Media
- Chemoprophylaxis may be of value for prevention of episodes of AOM in children with severe and recurrent disease.
- Pneumococcal conjugate vaccines have been effective in reducing episodes of AOM due to vaccine serotypes.
- Influenza virus vaccines reduce the incidence of AOM during the winter respiratory season.

Mastoiditis
- Prevention is similar to that of AOM.

OTITIS EXTERNA

Infection of the external auditory canal (otitis externa) is similar to infection of skin and soft tissue elsewhere. Unique problems occur because the canal is narrow and tortuous; fluid and foreign objects enter, are trapped, and cause irritation and maceration of the superficial tissues. The pain and itching that result may be severe because of the limited space for expansion of the inflamed tissue. Infections of the external canal may be subdivided into four categories: acute localized otitis externa, acute diffuse otitis externa, chronic otitis externa, and malignant otitis externa. Reviews by Senturia and co-workers,[1] Hirsch,[2] and Rubin and Yu[3] provide more complete information.

Pathogenesis

The external auditory canal is approximately 2.5 cm long from the concha of the auricle to the tympanic membrane. The lateral half of the canal is cartilaginous; the medial half tunnels through the temporal

KEYWORDS

acute otitis media; amoxicillin; ceftriaxone; influenza virus vaccines; malignant otitis externa; nontypeable *Haemophilus influenzae;* otitis media with effusion; pneumococcal conjugate vaccines; *Pseudomonas aeruginosa; Streptococcus pneumoniae;* swimmer's ear

bone. A constriction, the isthmus, present at the juncture of the osseous and cartilaginous portions, limits the entry of wax and foreign bodies to the area near the tympanic membrane. The skin of the canal is thicker in the cartilaginous portion and includes a well-developed dermis and subcutaneous layer. The skin lining the osseous portion is thinner and firmly attached to the periosteum and lacks a subcutaneous layer. Hair follicles are numerous in the outer third and sparse in the inner two thirds of the canal. Cerumen and debris from epithelial cells accumulate in the canal and are extruded by normal cleansing mechanisms. On occasion, the material may become inspissated and obstruct the canal.

The microbial flora of the external canal are similar to the flora of skin elsewhere. There is a predominance of *Staphylococcus epidermidis, Staphylococcus aureus, Corynebacteria*, and, to a lesser extent, anaerobic bacteria such as *Propionibacterium acnes.*[4,5] Pathogens responsible for infection of the middle ear *(Streptococcus pneumoniae, Haemophilus influenzae*, or *Moraxella catarrhalis)* are uncommonly found in cultures of the external auditory canal when the tympanic membrane is intact.

The epithelium absorbs moisture from the environment. Desquamation and denuding of the superficial layers of the epithelium may follow. In this warm moist environment, the organisms in the canal may flourish and invade the macerated skin. Inflammation and suppuration follow. Invasive organisms include those of the normal skin flora and gram-negative bacilli, particularly *Pseudomonas aeruginosa.* Invasive otitis media is a necrotizing infection frequently associated with *P. aeruginosa.* The organism gains access to the deeper tissues of the ear canal and causes a localized vasculitis, thrombosis, and necrosis of tissues. Diabetic microangiopathy of the skin overlying the temporal bone results in poor local perfusion and a milieu for invasion by *P. aeruginosa.*

Clinical Manifestations and Management

Acute localized otitis externa may occur as a pustule or furuncle associated with hair follicles; the external ear canal is erythematous, edematous, and may be filled with pus and flakes of skin debris. *S. aureus* is the most frequent pathogen. Erysipelas caused by group A *Streptococcus* may involve the concha and the canal. Pain may be severe. Bluish-red hemorrhagic bullae may be present on the osseous canal walls and also on the tympanic membrane. Adenopathy in the lymphatic drainage areas is often present. Local heat and systemic antibiotics are usually curative. Incision and drainage may be necessary to relieve severe pain.

Acute diffuse otitis externa (swimmer's ear) occurs mainly in hot humid weather. The ear itches and becomes increasingly painful. The skin of the canal is edematous and red. Gram-negative bacilli, mainly *P. aeruginosa*, may play a significant role. A severe hemorrhagic external otitis caused by *P. aeruginosa* was associated with mobile redwood hot tub systems.[6] Gentle cleansing to remove debris, including irrigation with warm tap water should reduce symptoms; alternatively, hypertonic saline (3%) and cleansing with mixtures of alcohol (70% to 95%) and acetic acid may be used. . Hydrophilic solutions, such as 50% Burrow's solution, may be used for 1 to 2 days to reduce inflammation. A cotton wick may be of value in enhancing distribution of the ototopical agent when the canal is swollen. A 10-day regimen of a fluoroquinolone otic solution, such as ofloxacin[7] or ciprofloxacin-dexamethasone otic[8] or eardrops of neomycin alone or with polymyxin combined with hydrocortisone, are effective in reducing local inflammation and infection.

Chronic otitis externa is caused by irritation from drainage through a perforated tympanic membrane. The underlying cause is chronic suppurative otitis media. Itching may be severe. Management is directed to treatment of the middle ear disorder. Rare causes of chronic otitis externa include tuberculosis, syphilis, yaws, leprosy, and sarcoidosis.

Invasive ("malignant") otitis externa is a severe, necrotizing infection that spreads from the squamous epithelium of the ear canal to adjacent areas of soft tissue, blood vessels, cartilage, and bone[3,9] (see Chapter 221). Severe pain and tenderness of the tissues around the ear and mastoid are accompanied by the drainage of pus from the canal. Older, diabetic, immunocompromised, and debilitated patients are at particular risk. Life-threatening disease may result from spread to the temporal bone and then on to the sigmoid sinus, jugular bulb, base of the skull, meninges, and brain. Permanent facial paralysis is frequent, and cranial nerves 9, 10, and 12 may also be affected.[10] *P. aeruginosa* is almost always the causative agent (see Chapter 221). The extent of damage to soft tissue and bone may be identified and monitored by the use of computed tomography and magnetic resonance imaging.[3] Diagnostic tests for underlying disease should be instituted. The canal should be cleansed, devitalized tissue removed, and eardrops with antipseudomonal antibiotics combined with steroid instilled into the external auditory canal. Systemic therapy with regimens including activity for *Pseudomonas* spp. should be used for 4 to 6 weeks. The combination of ceftazidime, cefepime, or piperacillin with an aminoglycoside (gentamicin or tobramycin) should be considered.[10] Oral quinolones with activity against *Pseudomonas* spp., such as ciprofloxacin, have been effective therapy early in the course of invasive external otitis.[11]

Aspergillus species, particularly *A. niger*, may grow in the cerumen and desquamated keratinaceous debris in the external auditory canal, sometimes forming a visible greenish or blackish fluffy colony. Role of the mold in acute otitis externa is usually modest, if any, although, in the severely immunocompromised patient, *Aspergillus* can cause necrotizing otitis externa.[12] *Candida albicans* is a frequent cause of external otitis in children with chronic mucocutaneous candidiasis.

OTITIS MEDIA

Acute otitis media (AOM) is defined as an acute illness marked by the presence of middle ear fluid and inflammation of the mucosa that lines the middle ear space. Otitis media with effusion (OME) is defined by the presence of middle ear fluid without acute signs of illness or inflammation of the middle ear mucosa. It usually follows AOM but may also occur as a result of barotrauma or allergy. The peak incidence occurs in the first 3 years of life. The disease is less common in the school-aged child, adolescents, and adults. Nevertheless, infection of the middle ear may be the cause of fever, significant pain, and impaired hearing in all age groups. In addition, adults suffer from the sequelae of otitis media of childhood: hearing loss, cholesteatoma, adhesive otitis media, and chronic perforation of the tympanic membrane.

Three recent factors have and will alter the incidence, microbiology, and management of otitis media:

1. Introduction of the 7-valent conjugate pneumococcal vaccine (PCV7) in the United States in 2000 and the 13-valent vaccine (PCV13) in 2010 has reduced the number of episodes of vaccine serotype pneumococcal AOM and decreased the incidence of severe and recurrent disease.
2. Programs have been developed by the Centers for Disease Control and Prevention (CDC) and advocacy groups to inform health care workers and consumers about the appropriate use of antimicrobial agents and avoid use of these drugs for trivial, usually viral, respiratory tract infections, to decrease the selection of multidrug-resistant bacteria.
3. In 2004 and 2013, publication of management guidelines by the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP) presented criteria for managing AOM without antimicrobial agents.[13,14]

Interested readers are referred to the AAP/AAFP guidelines for management of AOM[13,14] and OME[15] and *Otitis Media in Infants and Children* by Bluestone and Klein.[16]

Epidemiology

By 3 years of age, more than two thirds of children have had one or more episodes of AOM, and one third have had three or more episodes.[17] The highest incidence of AOM occurs between 6 and 24 months of age. Subsequently, the incidence declines with age, except for a limited reversal of the downward trend between 5 and 6 years of age, the time of school entry. Otitis media is infrequent in adults, but the bacteriology and therapy are similar to those in children.[18]

Longitudinal studies have provided information about the characteristics of children who have recurrent and severe episodes of AOM.

The vast majority of children have no obvious defect responsible for severe and recurrent otitis media, but a small number have anatomic changes (cleft palate, cleft uvula, submucous cleft), alteration of normal physiologic defenses (patulous eustachian tube), or congenital or acquired immunologic deficiencies. An increased incidence of AOM occurs in children with Down syndrome.[19] Children with acquired immunodeficiency syndrome have a higher age-specific incidence of otitis media, beginning at 6 months of age, than uninfected children or children who initially were positive for human immunodeficiency virus antibody but who seroreverted.[20]

As is true for most infectious diseases of childhood, AOM occurs more often in males than in females. Correlation of the index child with severe or recurrent AOM in a sibling or parent identifies a likely genetic susceptibility. Proinflammatory cytokine gene polymorphisms and polymorphisms in immunoresponse genes were associated with recurrent AOM.[21,22] The age at the time of the first episode of AOM appears to be among the most powerful predictors of recurrent middle ear infections. Breast-feeding for 3 or more months is associated with a decreased risk of AOM in the first year of life. Race and ethnicity provide additional data, suggesting a genetic basis for recurrent middle ear infections; Native Americans, Alaskan and Canadian Eskimos, and Aboriginals have an extraordinary incidence and severity of otitis media.

The role of increased exposure to infectious agents and the importance of environmental pollutants have been identified in studies of the incidence of infection in group daycare and the effects of passive smoking on children. The introduction of infants into large daycare groups increases the incidence of respiratory infections, including otitis media. The daycare risk of infection is associated with the number of children in the facility. For children in large-group daycare, almost one episode of respiratory tract infections a month occurs during the first year of life, and AOM is a complication in about one third to one half of respiratory tract infections.[23] Children in daycare not only have more episodes of AOM than children in home care but have more severe disease, as measured by the need for more surgical procedures. A study of Pittsburgh children observed from birth through the second year of life noted that myringotomy and tympanostomy tube placements were performed in 21% of children in group daycare and in only 3% of children in home care.[24] Exposure to tobacco smoke documented by measuring a nicotine metabolite, cotinine, in saliva and urine, correlated with an increased incidence of new episodes of OME and the duration of effusion.[25] Kim and co-workers[26] have identified an association of invasive pneumococcal disease and otitis media with atmospheric conditions, air pollution (identified by levels of sulfur dioxide), and the isolation of respiratory viruses.

Pathogenesis

The middle ear is part of a continuous system that includes the nares, nasopharynx, and eustachian tube medially and anteriorly and the mastoid air cells posteriorly. These structures are lined with a respiratory epithelium that contains ciliated cells, mucus-secreting goblet cells, and cells capable of secreting local immunoglobulins.

Anatomic or physiologic dysfunction of the eustachian tube appears to play a critical role in the development of otitis media. The eustachian tube has at least three physiologic functions with respect to the middle ear: protection of the ear from nasopharyngeal secretions, drainage into the nasopharynx of secretions produced within the middle ear, and ventilation of the middle ear to equilibrate air pressure with that in the external ear canal. When one or more of these functions is compromised, the results may be the development of fluid and infection in the middle ear. Most episodes of AOM occur in the following sequence: congestion of the mucosa of the upper respiratory tract, often caused by a respiratory viral infection; swelling of the mucosa of the eustachian tube, progressing to obstruction of the tube at its narrowest section, the isthmus; secretions that are constantly formed by the mucosa of the middle ear accumulate behind the obstruction and if a bacterial pathogen is present, AOM may result. The pathogenesis of fluid that persists for weeks to months after episodes of adequately treated AOM or persistent OME remains uncertain. Recent studies have suggested that bacterial biofilms on the middle ear mucosa may play a role in chronic OME or OME.[27]

TABLE 62-1 Bacterial Pathogens Isolated from Middle Ear Fluid in Children with Acute Otitis Media, 1995-2003

BACTERIAL PATHOGEN	CHILDREN WITH PATHOGEN (%)* 1995-2000 (*N* = 399)	2001-2003 (*N* = 152)
Streptococcus pneumoniae	28	23
Haemophilus influenzae	25	36
Moraxella catarrhalis	3.5	3
Streptococcus, group A	1.5	1.3
None or nonpathogens	46	41

*Total percentages are more than 100% because of multiple pathogens per middle ear effusion.

Data modified from Casey JR, Pichichero M. Changes in frequency and pathogens causing acute otitis media in 1995-2003. Pediatr Infect Dis J. *2004;23:824-828.*

Microbiology

Bacteria

The bacteriology of otitis media has been documented by appropriate cultures of middle ear effusions obtained by needle aspiration. Many studies of the bacteriology of AOM have been performed. The results are remarkably consistent in demonstrating the importance of *S. pneumoniae* and *H. influenzae* in all age groups, but more recent studies, since the introduction of the pneumococcal conjugate vaccine, suggest that *H. influenzae* may replace *S. pneumoniae* as the most frequently isolated pathogen of AOM in children (Table 62-1).[28,29]

S. pneumoniae remains the most important bacterial cause of otitis media in most regions of the world. Relatively few serotypes are responsible for most disease, although there may be variation in serotypes in various regions of the world. The most common serotypes, in order of decreasing frequencies, were 19, 23, 6, 14, 3, and 18.[30,31,32] PCV7, introduced in 2000, contained serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F and was replaced in 2010 by PCV13, which added serotypes 1, 3, 5, 6A, 7V, and 19A. PCV7 was effective in reducing the incidence of AOM caused by vaccine serotypes.[33] Data are not yet available to determine the added benefit of PCV13. Otitis media caused by *H. influenzae* is associated with nontypeable strains in the vast majority of patients. In approximately 10% of cases, the otitis was caused by *H. influenzae* type B and was frequently severe and accompanied by bacteremia or meningitis. Type B is now rare because of the efficacy of the conjugate polysaccharide vaccine. Nontypeable strains of *H. influenzae* are a significant cause of otitis media in patients of all ages.[18] *H. influenzae* is the primary pathogen in the unique conjunctivitis-AOM syndrome.[34]

Moraxella catarrhalis has been isolated from approximately 10% of children with AOM[35] and is usually associated with a mild form of disease. Before 1970, almost all strains of *M. catarrhalis* were sensitive to penicillin. Today, most strains produce β-lactamase and are resistant to penicillin G, ampicillin, and amoxicillin.

S. aureus, including methicillin and multidrug-resistant strains, is an uncommon cause of AOM but may be associated with persistent otorrhea that follows insertion of tympanostomy tubes.[36]

During the preantibiotic era, AOM caused by group A *Streptococcus* (GAS) was a frequent cause of severe AOM, frequently complicated by mastoiditis and often associated with scarlet fever. For reasons unknown, AOM caused by GAS is now uncommon. A recent survey in Israel has identified GAS as being responsible for 3.1% of 11,311 episodes of AOM.[37]

Viruses

Virologic and epidemiologic studies have suggested that viral infection is frequently the initial event in the development of AOM.[38-42,43] Respiratory viruses have been isolated from the nasopharynx in up to 50% of children with AOM and have been detected in approximately 25% of middle ear fluids of children with AOM. Respiratory syncytial virus, influenza virus, enteroviruses, coronaviruses, and rhinoviruses were the most common viruses found in middle ear fluids.[38-41] Combined viral and bacterial infections are frequent and may be more severe than bacterial infection alone.[41,42,43] Chonmaitree and co-workers[42] have

noted that a higher proportion of patients with virus and bacteria in middle ear fluids fail to clear the bacteria 2 to 4 days after initiation of therapy, compared with the group who had bacteria alone.

Mycoplasma, Chlamydia, and Unusual Organisms

Mycoplasma pneumoniae was responsible for hemorrhagic bullous myringitis in a study of nonimmune volunteers inoculated with the organism.[44] However, the middle ear fluid of a large number of patients (771) has been studied, and *M. pneumoniae* was isolated in only one case.[45,46] Although mycoplasmas do not appear to play a significant role in AOM, some patients with lower respiratory tract disease caused by *M. pneumoniae* may have concomitant otitis media.

Chlamydia trachomatis is associated with acute respiratory infections in infants younger than 6 months and is a cause of acute infection of the middle ear in this age group. The organism has been isolated from middle ear fluid of infants with acute infection.[47]

Uncommon forms of otitis include diphtheritic otitis, tuberculous otitis, otogenous tetanus, otitis caused by *Mycobacterium chelonae*,[48] and otitis caused by *Ascaris lumbricoides* or Wegener's granulomatosis. Fungi are frequently associated with external otitis but rarely cause AOM; *Candida* and *Aspergillus* spp. have been isolated from middle ear fluids of immunodeficient patients who develop chronic suppurative otitis media.

Immunology

The middle ear is the site of a secretory immune system similar to those of other areas of the respiratory tract. Local and systemic immune responses occur in patients with acute or chronic OME. In the middle ear, immunologically active antigen interacts with immunocompetent cells in the lamina propria to produce a local immune response. The middle ear effusion that results from acute or chronic infection contains all the major classes of immunoglobulins, complement, cells, immune complexes of antigen and antibody, and various chemical mediators of inflammation. The role of these substances in the course of otitis media is uncertain. The immune response to various antigens may prevent subsequent infection, assist in clearance of fluid during the acute episode, or contribute to the accumulation and persistence of fluid in the middle ear cavity, which becomes the culture medium for the next infection.

Diagnosis and Clinical Course

Acute otitis media is defined by the presence of fluid in the middle ear, along with signs or symptoms of acute illness and inflammation of the mucosa of the middle ear identified by erythema of the tympanic membrane. Signs and symptoms may be specific, such as ear pain, ear drainage, or hearing loss, or nonspecific, such as fever, lethargy, or irritability. Vertigo, nystagmus, and tinnitus may occur. Redness of the tympanic membrane is an early sign of otitis media, but erythema alone is not diagnostic of middle ear infection because it may be caused by inflammation of the mucosa throughout the upper respiratory tract. However, AOM may present with intense erythema of the tympanic membrane as the only otoscopic finding.[14]

The presence of fluid in the middle ear is determined by the use of pneumatic otoscopy, a technique that permits an assessment of the mobility of the tympanic membrane. The motion of the tympanic membrane is proportional to the pressure applied by gently squeezing and then releasing the rubber bulb attached to the head of the otoscope. Normal mobility is apparent when positive pressure is applied and the tympanic membrane moves rapidly inward; with release of the bulb and the resulting negative pressure, the membrane moves outward. Fluid or high negative pressure in the middle ear dampens the mobility of the tympanic membrane. Adjunctive techniques are available to confirm the results of otoscopic examinations and assist in the accuracy of diagnosis. Tympanometry uses an electroacoustic impedance bridge to record compliance of the tympanic membrane and middle ear pressure. This technique presents objective evidence of the status of the middle ear and the presence or absence of fluid.[49] Acoustic reflectometry measures sound reflectivity from the middle ear and is able to distinguish an air- or fluid-filled space. Spatial gradient analysis is correlated with the probability of middle ear effusion in children.[50] In addition to a professional model, a consumer model (Innovia Medical, Omaha, NE) is available that permits home monitoring of the development or persistence of middle ear fluid.

Fluid persists in the middle ear for prolonged periods after the onset of AOM, even though symptoms usually resolve within a few days after the initiation of antimicrobial therapy. About 70% of children with otitis media have fluid in the middle ear 2 weeks after the onset of disease, 40% still have fluid 1 month after the onset, and 10% still have fluid 3 months after the first signs of middle ear infection.[15]

Patients with middle ear effusion suffer from hearing loss of variable severity. On average, a patient with fluid in the middle ear has a 25-dB (pure-tone average) loss.[51] Because the development of speech, language, and cognitive skills is dynamic during infancy, when the incidence of AOM is highest, there is concern that any impediment to reception or interpretation of auditory stimuli might have an adverse effect. Children with histories of recurrent episodes of AOM score lower in tests of speech, language, and cognitive abilities than their disease-free peers.[52,53]

The results of microbiologic studies of middle ear effusions in patients with AOM are so consistent that the choice of antimicrobial agents may be based on knowledge of the bacteriologic characteristics of otitis media acquired from the many investigations, rather than on the results of cultures from other sites, such as the throat or nasopharynx (see Table 62-1). If the patient is toxic or has focal infection elsewhere, cultures of samples of the blood and of the focal infection are warranted. Needle aspiration of the middle ear effusion (tympanocentesis) to define the microbiologic characteristics of the infection should be considered in select patients—the patient who is critically ill at the onset, the patient who has not responded to initial antimicrobial therapy in 48 to 72 hours and is toxic, and the patient with altered host defenses (e.g., an immunologic defect, including the newborn infant).

Management

Acute Otitis Media

Antimicrobial Agents

The preferred antimicrobial agent for the patient with AOM must be active against *S. pneumoniae, H. influenzae*, and *M. catarrhalis.* Group A streptococci and *S. aureus* are infrequent causes of AOM and need not be considered in initial therapeutic decisions. Gram-negative enteric bacilli and methicillin-resistant *S. aureus* must be considered when otitis media occurs in the newborn infant, the patient with a depressed immune response, and the patient with suppurative complications of chronic otitis media. The antimicrobial agent should achieve concentrations in middle ear fluid above the expected minimal inhibitory concentration of the likely pathogens. Craig and Andes[54] have examined the relationship between bacteriologic cure in otitis media and serum and middle ear fluid concentrations for various antimicrobial agents. They found that a bacteriologic cure required the presence of serum concentrations above the minimal inhibitory concentration for at least 70% of the dosing interval.

There are now 19 antimicrobial agents approved by the U.S. Food and Drug Administration (FDA) for AOM. Amoxicillin remains the drug of choice for initial treatment because of its 25-year record of clinical success, acceptability, limited side effects, and relatively low cost. The drug is ineffective against β-lactamase–producing strains of *H. influenzae* and *M. catarrhalis.* The current incidence of amoxicillin-resistant *H. influenzae* and *M. catarrhalis* is not high enough to require a change in the initial therapy.

The recent recommendation of increasing the dosage of amoxicillin to 90 mg/kg/day achieves higher concentrations in middle ear fluid and further reduces the number of children in whom amoxicillin therapy will fail because of resistant pneumococci.[50] Alternatives to amoxicillin include amoxicillin-clavulanate, three sulfa-containing or trimethoprim-containing preparations (erythromycin plus sulfisoxazole, trimethoprim, and trimethoprim-sulfamethoxazole), two macrolides (azithromycin and clarithromycin), nine oral cephalosporins (cephalexin, cefaclor, cefixime, ceftibuten, cefprozil, cefpodoxime, cefuroxime axetil, loracarbef, and cefdinir), and one parenteral cephalosporin (ceftriaxone). Two topical fluoroquinolones, ofloxacin and ciprofloxacin-dexamethasone otic, are effective in children who have tympanostomy tubes and suffer acute otorrhea.

If the patient fails amoxicillin therapy, preferred regimens include the increased dosage of amoxicillin clavulanate (90 mg/kg/day in two doses) or intramuscular ceftriaxone (50 mg/kg once a day for 1 to 3 days). For children with severe and recurrent AOM, the use of tympanocentesis to identify the bacterial pathogen and susceptibility pattern may be necessary for choosing the most effective drug. For children with known and severe allergy to β-lactam antibiotics, a macrolide (erythromycin plus sulfisoxazole, azithromycin, or clarithromycin) is preferred, but trimethoprim-sulfamethoxazole may be useful in regions where pneumococcal resistance to this combination is not a concern.

Some children with AOM caused by a bacterial pathogen improve without the use of antimicrobial agents.[55-57] Howie and Ploussard[57] performed dual aspirates of middle ear fluid in children with AOM 2 to 7 days apart, with placebo given instead of an antibacterial drug. They found that 19% of middle ear fluids infected initially with pneumococci became sterile, and 48% of middle ear fluids infected initially with *H. influenzae* became sterile. The discrepancy between the proportion of infections becoming sterile after infection with the two bacterial species indicates that a simple mechanical effect (drainage of the infected fluid via a patent eustachian tube or a perforated tympanic membrane) was unlikely to be responsible for the microbiologic effect. It is more likely that a host mechanism, probably based on humoral or cellular immunity, acts preferentially to rid the infected ear of *H. influenzae* more frequently than *S. pneumoniae.*

The microbiologic results indicating that many children have AOM caused by a viral pathogen, and that some of the episodes of bacterial otitis media resolve without antibacterial drugs, prompted some European physicians to withhold antibiotic therapy from children with ear infections.[58,59] An option of observation of children with AOM rather than initial antimicrobial therapy is practiced extensively in Western Europe.[60] In 2004, the AAP and AAFP proposed a similar protocol for withholding antimicrobial therapy for children older than 2 years of age, whose diagnosis was uncertain, and who did not have severe disease (severe disease defined as moderate to severe otalgia or fever of 39° C [102.2° F] or higher).[13]

With appropriate antimicrobial therapy, most children with AOM are significantly improved within 48 to 72 hours. If there is no improvement, the patient should be reexamined. The child may have developed a new focus of infection or have received inadequate therapy.

Treatment of Otalgia

AOM may be painful due to pressure of the expanding abscess on the tympanic membrane. If pain is present, analgesic treatment should be considered. Acetaminophen or ibuprofen is effective analgesia for mild to moderate pain. Narcotic analgesia with codeine or its analogues is effective for severe pain but should be carefully considered because of risk of respiratory depression and altered mental status. Incision and drainage of the middle ear abscess by means of tympanostomy or myringotomy usually requires otolaryngologic support but provides immediate relief.[14]

Decongestants, Antihistamines, and Corticosteroids

Nasal and oral decongestants, administered alone or in combination with an antihistamine, are used extensively for the treatment of OME. The use of these drugs is based on the consideration that they reduce congestion of the respiratory mucosa and relieve the obstruction of the eustachian tube that results from inflammation caused by respiratory infection. The results of clinical trials, however, have indicated no significant evidence of efficacy of any of these preparations, used alone or in combination, for relief of signs of disease or a decrease in the time spent with middle ear effusion.[61,62]

Prevention of Acute Otitis Media

Prevention of severe and recurrent episodes of AOM includes chemoprophylaxis, use of bacterial and viral vaccines, and surgery.

Chemoprophylaxis

Chemoprophylaxis has been shown to be of value for the prevention of acute illness in children who have suffered from recurrences of middle ear infections. A variety of studies, including various antimicrobial agents and a placebo, have documented the efficacy of an antimicrobial agent in modified dosage in reducing the number of episodes of acute febrile illnesses caused by otitis media.[63,64] However, a modified dosage form of an antimicrobial agent may select resistant strains in the nasopharynx, and chemoprophylaxis should be considered only for children with severe and recurrent infections. Children should be considered for prophylaxis if they have had two episodes of AOM in the first 6 months of life or, in older children, three episodes in 6 months or four episodes in 1 year. Amoxicillin, 20 to 40 mg/kg, or sulfisoxazole, 50 mg/kg, may be administered once daily. Chemoprophylaxis may suppress symptoms of otitis media, but asymptomatic middle ear effusion may persist. The physician who chooses to use chemoprophylaxis to prevent acute recurrent disease must examine the patient at approximately 1-month intervals for middle ear effusion.

Because of concern for development of multidrug-resistant bacteria in patients receiving chemoprophylaxis, the 2013 guidelines of the AAP and the AAFP discourage chemoprophylaxis. The guidelines suggest prevention by placement of tympanostomy tubes, although it necessitates a surgical procedure and anesthesia.[14] Physicians must discuss with the parent the risk-benefit ratio of antibiotic prophylaxis versus surgery for prevention of further severe AOM.

Pneumococcal Vaccines

Polysaccharide pneumococcal vaccines have been evaluated for prevention of recurrences of AOM in children.[65-67] Children younger than 2 years of age had unsatisfactory responses to single-dose regimens, and the vaccine was of limited efficacy in prevention of AOM. A seven-valent conjugate pneumococcal polysaccharide vaccine, using a diphtheria toxin mutant (CRM 197) as the protein carrier (Prevnar, Pfizer Vaccines, Philadelphia, PA), was approved by the FDA in February 2000. The vaccine (PCV7) combined pneumococcal serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F and was demonstrated to be immunogenic in children as young as 2 months of age.[68] Antibody titers that were protective for prevention of invasive disease were achieved after doses administered at 2, 4, and 6 months but waned during the next 6 months, requiring a booster between the ages of 12 and 15 months.

PCV7 was effective in preventing vaccine-type invasive disease (97.4% efficacy in children immunized per protocol)[68] and pneumonia (18% decrease for radiographically identifiable disease), but the results were more modest for prevention of AOM.[32] The vaccine reduced the number of episodes of AOM by 7% and reduced the number of procedures for placement of ventilating tubes by 23%, as a reflection of recurrent episodes requiring placement of tubes. Bacteriologic efficacy of PCV7 was evaluated for prevention of AOM in Finnish infants.[69] Bacteriologic diagnosis was based on aspiration of middle ear fluids in patients with AOM who had completed the infant three-dose schedule (Table 62-2). Similar to a study in northern California, the vaccine reduced the incidence of AOM by 6%. The reduction in number of episodes of pneumococcal AOM was 34%, but the reduction in episodes caused by vaccine serotype disease was 57%. Of concern were

TABLE 62-2 Efficacy of PCV7 in Finnish Children with Acute Otitis Media (AOM)

END POINT	AOM EPISODES: PCV7 (*N* = 831)	AOM EPISODES: Control* (*N* = 831)	VACCINE EFFICACY POINT ESTIMATE (%)
Any AOM	1251	1345	6
Pneumococcal AOM	271	414	34
Vaccine serotypes	107	250	57
Cross-reactive serotypes	41	84	51
Nonvaccine serotypes	125	95	–33
Haemophilus influenzae AOM	315	287	–11
Moraxella catarrhalis AOM	379	381	–1

*Hepatitis B vaccine.

Data from Eskola J, Kilpi T, Palmu A, et al. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. N Engl J Med. *2001;344:403-409.*

increases in the number of episodes of AOM caused by nonvaccine organisms in children who received PCV7, a 33% increase in nonvaccine serotype pneumococcal AOM, and an 11% increase in episodes caused by *H. influenzae.* These data suggested that the vaccine was successful in reducing carriage of vaccine serotypes but that pneumococcal carriage was replenished with nonvaccine serotypes, which subsequently spread from the upper respiratory tract to the middle ear to cause AOM. An example of this serotype replacement is the emergence of multidrug-resistant serotype 19A, a strain not included in PCV7, as an increasing cause of invasive disease and otitis media.[70]

The 13-valent conjugate pneumococcal vaccine (Prevnar 13, Pfizer Vaccines, Philadelphia, PA) was introduced in 2010 and replaced PCV7 in the United States. In addition to the serotypes in PCV7, the additional serotypes, including types 1, 3, 5, 6A, 7V, and 19A were added. There are no data, as of May 2013, to assess the efficacy of PCV13 for prevention of AOM caused by the additional serotypes.

An 11-serotype vaccine with pneumococcal polysaccharides conjugated to a carrier protein D of nontypeable *H. influenzae* was developed by GlaxoSmithKline (GlaxoSmithKline Biologicals, Rixensart, Belgium). A clinical trial of the 11-serotype vaccine for efficacy in the prevention of AOM was conducted in the Czech Republic and Slovakia. The vaccine prevented 52% of AOM episodes caused by pneumococcal vaccine serotypes and 35% of episodes caused by nontypeable *H. influenzae.*[71] The vaccine was introduced as a 10-valent vaccine combining serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23 (Synflorix, GlaxoSmithKline Biologicals). The vaccine has been licensed in Europe and other regions but is not available in the United States.

The reasons why PCV7 was more effective in the prevention of invasive pneumococcal disease than in prevention of vaccine serotype pneumococcal AOM is uncertain, but it has been suggested that higher concentrations of serum antibody are necessary for the prevention of the local mucosal diseases such as AOM.

Respiratory Virus Vaccines

Because of the importance of respiratory viruses in the pathogenesis of AOM, viral vaccines could be of preventive value. Inactivated parenteral influenza virus vaccines were documented to decrease the incidence of AOM in children in daycare in Finland[72] and North Carolina.[73] A reduction of 30% of episodes of febrile otitis media was also reported in children after the administration of live-attenuated intranasal influenza vaccine.[74] Immunoprophylaxis against respiratory syncytial virus disease has progressed with the use of high-titer respiratory syncytial virus (RSV) immune globulin[75] and the introduction of palivizumab, an RSV monoclonal antibody immune globulin with high titers of neutralizing RSV antibody.[76] The RSV immune globulin, but not the monoclonal antibody, was effective in reducing the number of episodes of AOM.

Surgical Management

Surgical management of recurrent episodes of AOM and persistent effusion of the middle ear includes use of myringotomy, adenoidectomy, and the placement of tympanostomy tubes. Myringotomy, or incision of the tympanic membrane, is a method of draining middle ear fluid. Before the introduction of antimicrobial agents, myringotomy was the primary method of managing suppurative otitis media. Today, the use of myringotomy is limited to the relief of intractable ear pain, hastening resolution of mastoid infection, and drainage of persistent middle ear effusion that is unresponsive to medical therapy.

Enlarged adenoids may obstruct the orifice of the eustachian tube in the posterior portion of the nasopharynx and interfere with adequate ventilation and drainage of the middle ear. Studies of the use of adenoidectomy in children with prolonged effusions in the middle ear have identified in select children a beneficial effect in reducing the time spent with effusion.[77,78] Tympanostomy tubes resemble small collar buttons. They are placed through an incision in the tympanic membrane to provide drainage of fluid and ventilation of the middle ear. The placement of these tubes is now one of the most common surgical procedures in children. Criteria for the placement of tubes include persistent middle ear effusions unresponsive to adequate medical treatment over a period of 3 months and persistent negative pressure. Hearing improves dramatically after placement of the ventilating tubes.

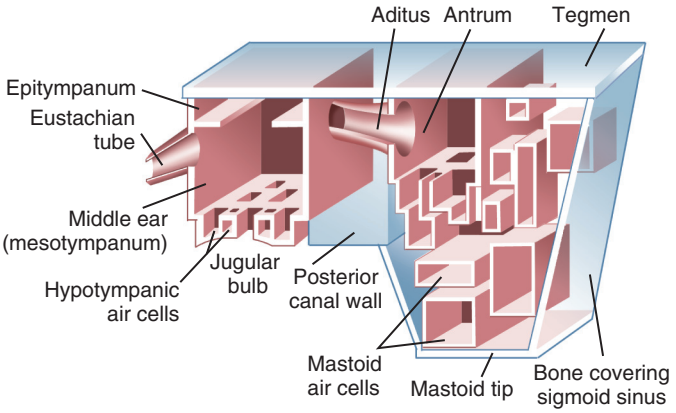

FIGURE 62-1 Diagrammatic representation of the anatomy of the middle and mastoid air cell system showing the narrow connection (aditus and antrum) between the two.

The tubes have also been of value in patients who have difficulty maintaining ambient pressure in the middle ear, such as occurs because of barotrauma in airline personnel. The liabilities of the placement of tubes include those of anesthesia associated with the procedure, persistent perforation, scarring of the tympanic membrane, development of cholesteatoma, and otitis media caused by swimming with ventilating tubes in place, but these occur infrequently.

MASTOIDITIS

The mastoid is the portion of the petrous temporal bone that lies superior to the middle ear cavity. The mastoid is filled with a system of interconnecting air-filled cells. The mastoid antrum serves as an open canal between the middle ear and mastoid air cells (Fig. 62-1). Thus, most cases of AOM with fluid filling the middle ear space are associated with some degree of inflammation of the mastoid air cells. The incidence of clinically significant mastoiditis, however, is low since the introduction of antimicrobial agents. Nevertheless, acute and chronic AOM still occur and may be responsible for significant morbidity and life-threatening disease.

Pathogenesis

At birth, the mastoid consists of a single cell, the antrum, connected to the middle ear by a small channel. Pneumatization of the mastoid bone takes place soon after birth and is extensive by 2 years of age. The clinical importance of the mastoid is related to contiguous structures, including the posterior cranial fossa, the middle cranial fossa, the sigmoid and lateral sinuses, the canal of the facial nerve, the semicircular canals, and the petrous tip of the temporal bone. The mastoid air cells are lined with modified respiratory mucosa, and all are connected with the antrum. Mastoiditis can occur at any age and may be particularly severe in older adults.[79,80]

Infection in the mastoid follows middle ear infection. Initially, there is hyperemia and edema of the mucosal lining of the air cells. Serous and then purulent exudate collects in the cells. Necrosis of bone caused by pressure of the purulent exudate on the thin bony septa follows. Coalescence of pus in contiguous areas results in abscess cavities.

The bacteriology of mastoiditis is the same as that of AOM, including *S. pneumoniae* and *H. influenzae* as the major pathogens. Patients with persistent perforation of the tympanic membrane may have invasion of organisms from the ear canal, including *Pseudomonas* spp. A pattern similar to the changes of pneumococcal isolates responsible for AOM since the introduction of PCV7 has also been identified in children with acute mastoiditis, including emergence of multidrug-resistant serotype 19A.[80]

Clinical Manifestations

Acute mastoiditis is usually accompanied by acute infection in the middle ear. During early stages, the signs are those of AOM with hearing loss, otalgia, and fever. Subsequently, swelling, redness, and

tenderness are present over the mastoid bone. The pinna is displaced outward and downward. A purulent discharge may emerge through a perforation in the tympanic membrane.

Chronic otitis media with mastoiditis can erode through the roof of the antrum, causing temporal lobe abscess, or extend posteriorly, causing septic thrombosis of the lateral sinus.

Diagnosis

Radiographs of the mastoid area may show a loss of sharpness of the shadows of cellular walls caused by demineralization of bony septa and cloudiness of areas of pneumatization caused by inflammatory swelling of the air cells. Computed tomography is helpful in delineating the extent of disease.

Cultures for bacteria from ear drainage fluid must be taken with care to distinguish fresh drainage fluid from material in the external canal. The canal must be cleaned and fresh pus obtained as it exudes from the tympanic membrane. If the tympanic membrane is not perforated, tympanocentesis should be performed to obtain material from the middle ear.

Management

The antimicrobial drugs of choice for acute infection are similar to those for AOM—antibiotics with activity against *S. pneumoniae* and *H. influenzae*. If the disease in the mastoid has had a prolonged course, coverage for *S. aureus* and gram-negative enteric bacilli may be considered for initial therapy until the results of cultures become available.

A mastoidectomy is performed when an abscess has formed in the mastoid bone. The procedure should be performed when antimicrobial agents have controlled sepsis.

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