Otitis media (OM) is a serious healthcare concern in the US and worldwide, not only because of the distress it causes the patient and their family but also because of the substantial economic burden it imposes on the health care system. The direct and indirect costs of OM in the US were recently estimated to exceed $3.5 billion. Otitis media is the most common reason for visits to pediatricians. After circumcision, the surgical placement of ventilating tubes for otitis media is the most common surgical procedure performed in children. Also, inappropriate antibiotic treatment of the condition encourages the emergence of multidrug-resistant strains of bacterial pathogens.

It is likely that humans have always suffered from acute infection of the middle ear and its suppurative complications. Studies of 2600 year old Egyptian mummies reveal perforations of the tympanic membrane and destruction of the mastoid. Evidence of middle ear disease was also evident in skeletal material from a prehistoric Iranian population (1900 to 800 B.C.) Prior to the introduction of antimicrobial agents, otitis media either resolved spontaneously (via central perforation of the tympanic membrane or evacuation of the middle ear contents through the eustachian tube) or came to the attention of a physician who drained the middle ear by means of myringotomy. Purulent otitis media was a frequent reason for admission to a hospital. In 1932, purulent otitis media accounted for 27 percent of all pediatric admissions to Bellevue Hospital. Mastoiditis and intracranial complications were common.

Otitis media is defined as an inflammation of the middle ear, without reference to a specific etiology or pathogenesis. Because all pneumatized spaces of the temporal bone are contiguous, inflammation of the middle ear may also involve inflammation in the other three regions of pneumatization – the mastoid, perilabyrinthine air cells, and petrous apex.

Classifications

Classification of otitis media is currently based on the temporal sequence of the disease process (not severity). The terms acute, subacute, and chronic are recommended. Acute otitis media (AOM) is an inflammation of the middle ear that presents with a rapid onset of signs and symptoms, such as pain, fever, irritability, anorexia, or vomiting. Chronic disease implies...
middle ear fluid that has been present for three months or longer and has had many synonyms, including serous OM, secretory OM, and "glue ear". The subacute stage is the time in between. Unless the examiner knows the patient’s previous middle ear status, duration of disease can be very difficult to determine. However, prior clinical symptoms, combined with the use of tympanograms and audiograms can often help further delineation. 4

**Epidemiology**

As noted previously, OM is one of the most common diagnoses made in the pediatrician’s office, and its incidence may be increasing. This apparent increase may be due to an actual increase in the disease, increased vigilance on the part of pediatricians and other care providers, or a combination of the two. The incidence of OM has been well studied by Teele et al, as well as by many other investigators. The incidence of OM increases after the newborn period (first 28 days). Teele found that by age 12 months nearly two-thirds of all children had at least one episode of AOM. By three years, 46% of children had three or more episodes of AOM. In this study, the highest incidence of AOM for both sexes was found in children aged 6 to 11 months. Some investigators have also noted a second, lower peak between ages 4 and 5 years. The onset of AOM during the first year of life is important because the majority of children with multiple recurrences of AOM have their first episode before the age of 12 months. 4

There is a high incidence of persistent middle ear effusion (MEE) occurring after an episode of AOM. One study found that the mean duration of otitis media with effusion (OME) after AOM was 40 days. In a study by Shurin et al, it was shown that children who were less than 24 months of age were 3.8 times more likely to have persistent MEE than children who were older. They also found a higher incidence of persistent effusion in white children. 5

Varying distribution among sex has not been found, some studies have shown an increased preponderance in males when compared to females but others have challenged this, finding an equal distribution. A high incidence of middle ear disease has been shown in Eskimos, Native Americans, and in aboriginal children.

Children in group day care have been shown to be more likely to have OM as a complication of an upper respiratory tract infection when compared to those in home care. Niemala et al found that the rate of tympanostomies and adenoidectomies was 59-67% higher for children below the age of three who were cared for at a day care center. They also showed that when local authorities in Finland were obliged by law to arrange day care for all children under 3 years (beginning in 1990), the number of adenoidectomies performed on children at this age increased by 30%. 6 By the age of three, the risk of sustaining OM was similar for all types of child care situations. Contributing factors for this increased incidence may include large numbers of children in close proximity, increased incidence of upper respiratory infections with resultant frequent examinations by physicians, and increased parental awareness of illness with resultant examinations in an effort to decrease parental leave time from work. 4 This apparent harmful effect seems to be dependent on the number of children at the daycare center. The risk has been reported to be greatest at day care centers, lower in the different forms of family day care, and lowest among children who were cared for in their homes. The increased risk of AOM at larger day care centers is likely due to more exposures: each child brings to day care a microflora
acquired in the household. Therefore, the larger number of children at day care centers produces more chances for the introduction and dissemination of microorganisms compared to sites with a smaller number of children. 7

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

There is data strongly suggesting a genetic susceptibility to OM. Variables associated with an increased risk of AOM include a sibling history of recurrent OM. Apache children living on the reservation as well as those who were adopted and living outside the Apache community have been studied. It was found that adopted Apache children had more episodes of acute otitis media than their non-Apache siblings and had an illness rate similar to that of Apache children who remained on the reservation. 3

Breast-feeding has been suggested as an important factor in prevention of respiratory tract infections and middle ear disease in infancy. Many studies have shown an inverse relationship between the incidence of middle ear disease and the duration of breast-feeding. 3 The mechanism of the protective effect of breast milk remains obscure. Data from a study of infants with cleft palate suggest that there is a factor in breast milk that is protective and is not due to the position or mode of feeding, as some have suggested. Two other studies indicate that breast-feeding had no effect on colonization of the nasopharynx with bacterial pathogens, indicating that the mechanism of protection relies on some immune-protective feature unassociated with prevention of colonization. 7

Passive smoke exposure has come under increased scrutiny as a risk factor for respiratory tract infections, including OM, because of pathological and physiological changes in the respiratory tract: goblet cell hyperplasia, mucus hypersecretion, ciliostasis, decreased mucociliary transport, and alteration of the immune defenses. Making use of the biochemical marker cotinine showed that high concentrations of serum cotinine were associated with an increased incidence of AOM and an increased duration of middle ear effusion following AOM. There is also an increased incidence of placement of tympanostomy tubes, chronic and recurrent OM, and otorrhea in children whose mothers smoked. 7

Many associated medical conditions predispose a child to OM. Cleft palate and craniofacial anomalies, especially if the midface is involved, appear to have an increased risk of OM. The incidence of middle ear disease does decrease somewhat after surgical repair of cleft palate but these children may continue to have frequent middle ear problems for years. There is an increased incidence of OM in children with congenital or acquired immune dysfunction (IgG subclass deficiency, AIDS, medications). Ciliary dysfunction frequently predisposes a child to OM (OM may be the first presenting sign of Kartagener’s syndrome). Edema of the nasopharynx and eustachian tube from prolonged nasotracheal intubation or nasogastric tube placement may lead to OM and sinusitis. Nasal obstruction from enlarged adenoids, sinusitis, and malignancy can also lead to OM. 4
Basic Science – Eustachian tube

The eustachian tube connects the middle ear and mastoid air cells to the nasopharynx. The nasal cavities and palate also constitute part of this system and may influence the function of the eustachian tube. In the adult, the anterior two-thirds of the tube are cartilaginous and the posterior third is bony; in the infant, the bony portion is relatively longer. In adults, the tube lies at an angle of 45 degrees in relation to the horizontal plane, whereas in infants this inclination is only 10 degrees.

The lumen of the eustachian tube is shaped like two cones, with the apex of each directed toward the middle. The aural orifice of the tube is oval, measuring 5 mm high and 2 mm wide in the adult. The nasopharyngeal orifice in the adult is a vertical slit at right angles to the base of the skull, but in the infant this opening is oblique owing to the more horizontal position of the cartilage. In the newborn, the nasopharyngeal orifice lies in the plane of the hard palate, but in the adult it is situated 10 mm above this plane. The middle portion, or isthmus, of the eustachian tube is not sharply constricted but is relatively long, with gradual widening at each end to form the aural and nasopharyngeal orifices. The diameter of the isthmus in the adult is 1 to 2 mm, but in the infant it is somewhat larger.

The mucosal lining of the eustachian tube is similar to mucosa elsewhere in the respiratory tract, including mucus-producing gland cells, ciliated cells, and plasma cells. The cartilaginous portion is similar to that of the nasopharynx and contains mucous glands. The mucosa in the bony portion of the eustachian tube is similar to that of the middle ear and contains both mucus-producing elements and ciliated cells.

Usually the eustachian tube is closed, but it opens during swallowing, yawning, and sneezing, permitting the air pressure in the middle ear to equalize with atmospheric pressure. This opening mechanism is muscular and involves the cartilaginous portion. The levator palatini, palatopharyngeus, internal pterygoid, and superior constrictor muscles have no influence on the patency of the orifice or the lumen of the tube. The tensor veli palatini is the only muscle related to active tubal opening. No constrictor muscle of the tube has ever been demonstrated, and closure has been attributed to the relaxation of the tensor muscle with passive return of the tubal walls to a condition of approximation. However, the internal pterygoid muscle may have some constrictor function.

The tensor veli palatini muscle is composed of two bundles of muscle fibers divided by a layer of fibroelastic tissue. The bundles lie lateral to the eustachian tube, in a superficial-deep relationship to one another. The fibers of the superficial bundle run in an inferosuperior direction from their attachment in the inferior margin of the sphenoid bone, around the hamulus, to an attachment along the posterior border of the hard palate. The fibers of the deep bundle run from an inferolateral attachment in the fibroelastic layer to a superomedial attachment on the lateral membranous tubal wall, forming an acute angle with the wall. The tendinous portion of the deep bundle passes around the hamulus and inserts along the posterior margin.
The eustachian tube has at least three physiologic functions with respect to the middle ear – 1) protection from nasopharyngeal sound pressure and secretions, 2) clearance into the nasopharynx of secretions produced within the middle ear, and 3) ventilation of the middle ear to equilibrate air pressure in the middle ear with atmospheric pressure and to replenish oxygen that has been absorbed.

In the healthy state the middle ear and mastoid are protected from unwanted nasopharyngeal secretions by the anatomy of the eustachian tube system and by the middle-ear gas cushion. A TM that is not intact enhances liquid flow from the nasopharynx, because the middle-ear air cushion is altered. The middle ear gas composition is not identical to that of room air, oxygen is lower and carbon dioxide and nitrogen levels are higher.

Pathology

OM initially results in edema, capillary engorgement, and polymorphonuclear leukocyte infiltration into the lamina propria of the mucosa of the pneumatized spaces of the middle ear. Purulent exudate soon fills the spaces. Epithelial ulceration may occur, allowing granulation tissue proliferation, which may help to maintain the infection, obstruct drainage and ventilation, and enzymatically destroy bone. As the inflammation becomes more chronic, edema is replaced with fibrosis, and acute inflammatory cells are replaced with lymphocytes. Mucosal lamina propria proliferation of granulation tissue may form obstructive polyps. Respiratory epithelium in the protympanum and low cuboidal epithelium elsewhere are stimulated to become columnar and to increase the number of secretory goblet cells in the presence of infection. In more chronic inflammation, osteitis of the otic capsule, ossicles, and mastoid bone may occur. Absorption of the otic capsule can lead to fistula formation and invasion and obstruction of the inner ear. Partial or complete obstruction of the eustachian tube may occur secondary to fibrous and fibrocystic sclerosis. Massive edema of the mucosa can lead to polypoid changes and large polyps that can cause blockage of the eustachian tube and damage to the tympanic membrane and ossicles.

Factors involved in the development of acute otitis media include eustachian tube abnormalities, impaired immunity, viruses, inflammation and inflammatory mediators, and allergy.

Eustachian tube abnormalities play a major role in the development of acute otitis media. The normal functions of the eustachian tube are the regulation and equilibrium of pressure, protection and clearance of material from the middle ear. In many infants and children under the age of 7 years, there is an impaired opening mechanism in the eustachian tube. In American Indians and Down syndrome patients, the eustachian tube is always open and therefore, more prone to infection. In normal infants and children, Down syndrome patients, and in cleft palate, the eustachian tube is shorter than in adults and, thus, bacteria do not have to travel so far to cause infection. Active clearance of the middle ear may be reduced if the ciliary function of the mucosal cells is impaired by viral infections, such as influenza A, or bacterial toxins, such as pneumolysin produced by Streptococcus pneumoniae.

Children are known to have poorer local antibody responses than adults and studies have shown that children who are prone to otitis media have lower IgG2 levels than normal children and respond less well to pneumococcal antigens. Compared with normal children, children with
recurrent OM secreted low levels of cytokines, which are associated with the inflammatory response, into the nasopharynx. There were low levels of interleukin-1 (IL-1), IL-6, and tumor necrosis factor (TNF).

The inflammatory response is induced by endotoxin or other bacterial products, particularly cell-wall products, and also by local allergens. This leads to the release of cytokines, including TNF, IL-1, and IL-6, which then trigger the inflammatory response with release of prostaglandins and leukotrienes, which in turn attract and activate white blood cells. If dead bacteria are injected into the middle ear cavity, it has been shown that it will trigger the cytokines and the inflammatory response can still be detected in the middle ear fluid six weeks or more after effective antibiotic treatment. This may be one of the important mechanisms by which effusions persist in the middle ear following antibiotic treatment. Antibiotic treatment in itself leads to lysis of bacteria and release of bacterial cell wall material, which in turn is likely to exacerbate the inflammatory response.

A role for allergy in the etiology of OM has long been postulated, however, proving this association has been difficult. The allergic response may, at least, predispose the patient to MEE by congesting and obstructing the eustachian tube.

**Microbiology**

With the exception of *Moraxella catarrhalis* the list of bacteria causing OM has not appreciably changed for many years and appears to be similar worldwide. Approximately 30 to 35% of cases are caused by *Streptococcus pneumoniae*, 20 to 25% by nontypeable strains of *Haemophilus influenzae* and 10 to 15% by *M. catarrhalis*. The frequency of *M. catarrhalis* otitis appears to have increased in the last decade. The group A streptococcus causes acute middle ear infection in 2 to 4% of children and tends to occur in early spring. *Staphylococcus aureus*, gram-negative enteric bacilli, and other bacteria are found consistently but less frequently. In infants younger than 6 weeks of age, gram-negative bacilli cause about 20% of the AOM episodes. These organisms include *Escherichia coli*, *Klebsiella*, and *Pseudomonas aeruginosa*. Even in these very young infants, however, the most common organisms are still *S.pneumoniae* and *H.influenzae*. In the presence of an intact TM, the most likely source of the middle ear pathogens is the nasopharynx. Respiratory viruses may potentiate the possibility of nasopharyngeal colonization with bacteria, further increasing the incidence of OM.

In most studies 25 to 30% of middle ear fluid cultures are negative for bacteria, some of which are positive for viruses, including rhinovirus, adenovirus, influenza virus, parainfluenza virus, and respiratory syncytial virus (RSV). Recently viruses have gained increasing attention as possible copathogenic organisms in both acute and chronic OME and may help in the prolongation of middle ear effusion. For many years, physicians presumed that viral illness produced mucosal inflammation and edema resulting in eustachian tube dysfunction characterized by partial or complete obstruction of the passage and by accumulation of fluid in some patients. This was recently confirmed in a study of young adults with natural rhinovirus infection. Middle ear pressure changes were measured by a digital tympanometer at intervals during the illness of these subjects. Abnormal pressure occurred in 74% of patients with rhinovirus illness, more than half of these subjects had major pressure abnormalities.
frequency of subjects with abnormal middle ear pressures peaked on days 2 to 5 of illness, a time that coincides with the peak incidence of acute otitis media after onset of respiratory symptoms in infants and children. Acute OM has been documented in 20 to 50% of hospitalized patients with laboratory-confirmed respiratory viral infection.\(^\text{10}\) Also it has been shown that vaccination against influenza virus decreased the incidence of acute otitis media in infants and children. Much work has been done to determine the prevalence of various respiratory viruses in the middle ear during AOM so that attempts can be made to develop vaccines against the most prevalent organisms. Heikkinen \textit{et al} have found that RSV is the most commonly identified virus, being found in 74% of the middle ear isolates, followed by parainfluenza virus and influenza virus.\(^\text{11}\)

The most notable trends in the bacteriology of AOM during the past decade have been a rise in the proportion of patients infected with drug-resistant \textit{S. pneumoniae} and an overall increase in beta-lactamase-producing \textit{H. influenzae} and \textit{M. catarrhalis}. Before 1970 all strains of \textit{M. catarrhalis} were susceptible to penicillin and ampicillin. At the Pittsburgh Otitis Media Research Center the prevalence of beta-lactamase producing \textit{M. catarrhalis} progressively increased throughout the 1980s, so that by 1988 all strains were positive for beta-lactamase. The prevalence of beta-lactamase producing strains of \textit{H. influenzae} has also increased. From 1981 to 1986 the same group found a 17 to 34% increase in the annual prevalence of beta-lactamase positive strains. In the 1990s 45 to 50% of \textit{H. influenzae} strains recovered from AOM produce beta-lactamase.

There has been a profound increase in the prevalence of penicillin-resistant \textit{S. pneumoniae} in the 1990s, particularly in the pediatric population. As determined by broth microdilution, penicillin-susceptible organisms are characterized by a MIC <0.1 \(\mu\)g/ml; relative penicillin-resistance is defined as a MIC of 0.1 to 1.0 \(\mu\)g/ml; and high-resistance as >2.0 \(\mu\)g/ml. The incidence of penicillin-resistant \textit{S. pneumoniae} ranged from 1.8% in 1979 to 8% in 1982, with an average of 5% from 1979 to 1987. Since 1992, however, the incidence of penicillin-resistant \textit{S. pneumoniae} in younger children with invasive disease has dramatically increased to as high as 41% in some studies.\(^\text{9}\) More importantly when comparing children with recently treated AOM with those who had not received antibiotics within 3 days of culture, penicillin resistant pneumococcal strains were cultured from 44% vs 9%, respectively, and highly penicillin-resistant strains were cultured from 30% vs 2%, respectively. The majority of these penicillin-resistant strains were isolated from children younger than 24 months.

Unlike \textit{H. influenzae} and \textit{M. catarrhalis}, \textit{S. pneumoniae} strains have yet to acquire the ability to make beta-lactamase. Instead pneumococci have developed penicillin-binding proteins of altered size and affinity for the penicillins. The penicillin binding proteins are enzymes that catalyze terminal stages of bacterial cell wall formation. When bound to penicillin the enzymes are inactivated, resulting in an altered cell wall structure and death of the organism. Additionally many resistant pneumococci are lysis-defective, meaning that they are tolerant in the presence of high concentrations of penicillin. The more altered penicillin-binding proteins an organism has, the more resistant it is to penicillin and other beta-lactam antibiotics. Additionally resistance to erythromycin and other macrolide antibiotics and to trimethoprim-sulfamethoxazole is common among penicillin-resistant strains. In many areas of the US, approximately two-thirds of the resistant strains have penicillin MICs of >0.06 to 1.0 \(\mu\)g/ml (intermediate resistance). The
remaining one-third are highly resistant (MIC > 1.0 \(\text{ug/ml}\)). The predisposing factors for resistant pneumococcal strains include age, previous beta-lactam antibiotic therapy, and day-care attendance. \textit{10}

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

In chronic suppurative OM the most frequently isolated bacteria is \textit{P. aeruginosa}. \textit{S. aureus}, \textit{Corynebacterium}, and \textit{Klebsiella} are also commonly isolated. Anaerobes may be more common in patients with cholesteatoma. The standard acute organisms are still found in the early stages of disease and may be the predisposing factor toward the chronic infection. \textit{4}

**Diagnosis**

For the clinician, the diagnosis of otitis media usually depends upon a high index of suspicion and the presence of symptoms, but primarily on the pneumatic otoscopic findings. The usual picture of acute otitis media is seen in a child who has an upper respiratory tract infection for several days and suddenly develops otalgia, fever, and hearing loss. Fever occurs in one-third to two-third of children with AOM, however a fever over 104 F (40 C) may be associated with bacteremia or a complication. Other associated signs and symptoms include irritability, lethargy, anorexia, vomiting, and diarrhea. Hearing loss will not be a complaint of the very young or even noticed by the parents. Otorrhea may come from the middle ear through an acutely perforated TM or through a preexisting tympanostomy tube or perforation. Less common signs and symptoms include tinnitus, vertigo, postauricular swelling, and facial paralysis. Older children more easily convey tinnitus and vertigo but parents may give a history of unsteadiness or clumsiness in the younger group.

Most children with chronic middle ear effusion are asymptomatic but some may complain of hearing loss and, less commonly, tinnitus and vertigo. In children the attention of an alert parent or teacher may be drawn to a suspected hearing loss. Older children will describe a frank hearing loss or, more commonly, a "plugged" feeling or "popping" in their ears. The symptoms are usually bilateral. Unilateral sins and symptoms or chronic middle ear effusion may be secondary to a nasopharyngeal neoplasm such as an angiofibroma or even a malignancy.

In the diagnosis of both AOM and OME, pneumatic otoscopy continues to be the gold standard. The TM should be evaluated for color, position, and mobility. An abnormal TM is frequently opaque and may appear yellow or blue (indicating MEE), dark red (indicating recent trauma or hemorrhage), or dark pink/lighter red (consistent with AOM or hyperemia of the TM caused by crying, coughing, or nose blowing). Mobility should be assessed and can reveal hypomobility of the TM, suggesting middle ear fluid; movement only with negative pressure, suggesting eustachian tube dysfunction; or no movement, suggesting perforation or tympanostomy tube. Evaluation of the TM can reveal other pathology such as retraction pockets, atelectasis, perforations, tympanosclerosis, or cholesteatoma.
It is also important to carefully examine the head and neck looking for associated congenital syndromes and craniofacial anomalies that can predispose to OM including cleft palate, Down syndrome, Treacher Collins, and hemifacial microsomia. Nasal polyps, severely deviated nasal septum, or a nasopharyngeal mass should be sought.

Hearing should be evaluated in any child with recurrent or persistent OM or for eustachian tube dysfunction for three reasons — 1) to document any sensorineural loss, 2) to document any conductive loss, and 3) to establish a baseline for later comparison and preoperative planning. Most children have screening audiograms before they enter school at age 4 to 5 years, but children who have recurrent or persistent disease, or in those with suspected hearing loss, should be evaluated earlier so that treatment and possible rehabilitation can begin as soon as possible. Tympanometry measures the amount of sound reflected by the TM and middle ear structures under varying conditions and is a graphic representation of compliance changes as the ear canal pressure is varied from – 200 to +200 mm H2O. Various patterns are associated with normal, middle ear fluid, perforations or tympanostomies, retracted TMs, and stiff TM/middle ear systems. This data should, of course, be correlated with physical exam. Acoustic reflexes can also be used in addition to these studies and can give information on the likelihood of a middle ear effusion. 3,4

Treatment

Since the different stages of otitis media are most frequently a continuum and since it is often difficult for the clinician to diagnose the precise stage of a patient’s illness accurately, the most common methods of managing these problems will be discussed as they relate to the specific condition.

Acute Otitis Media

Antimicrobials are the mainstay of therapy for acute otitis media. However, older children and adults with low grade or no fever and minimal or early signs of middle ear infection can be managed expectantly as long as follow-up evaluation can be assured at 24 to 72 hours. Since most clinicians rarely perform a tympanocentesis or myringotomy initially, the organism causing the otitis is usually not known with certainty before treatment begins. The recommended therapeutic dose of the antimicrobial should be administered for 10 days. During this period, the parents should be instructed to notify the clinician if the child fails to show a satisfactory clinical improvement. If there is persistence or recurrence of otalgia or fever, or both, then the child should be reexamined before the completion of the antibiotic course. There are many factors to consider in choosing an appropriate agent for treatment of acute otitis media. These factors include activity of the drug against the usual otitic pathogens, safety, tolerance, ease of administration, the physician’s experience, and cost. Most of the drugs approved for therapy of acute otitis media have activity against the common otitic bacterial pathogens, although variations exist among these drugs. For example amoxicillin(Amoxil) is ineffective against beta-lactamase producing organisms, trimethoprim-sulfamethoxazole(Bactrim or Septra) is not appropriate for group A beta-hemolytic streptococci, and cefixime(Suprax) and ceftibuten(Cedax) are less active in vitro against pneumococci than are the other commercially available oral cephalosporins. The ability of an antibiotic to achieve satisfactory concentrations
in middle ear fluid is also essential if prompt eradication of the organism from this space is to be accomplished. For example, amoxicillin concentrations in middle ear fluid are from 0.3 to 4.0 ug/ml after 15-mg/kg doses but increase to 2 to < 9 ug/ml after 45-mg/kg doses. The latter values should be effective for most intermediately resistant (MIC > 0.06 to 1.0 ug/ml) pneumococci and approximately one-third of resistant (MIC > 1.0 ug/ml) isolates. When vomiting or diarrhea become a problem with drug administration and absorption, ceftriaxone (Rocephin) at 50 mg/kg once IM should be considered as it compares favorably with standard 10 day courses in children with acute OM. It was found to eradicate _H. influenzae_ and _S. pneumoniae_ from the middle ear fluid cultures in all patients who underwent two tympanocenteses in one study.

There is no one preferred treatment for all infants and children with acute OM. Amoxicillin is favored by many for initial treatment because of its long history of safety and effectiveness. In communities where penicillin-resistant pneumococci are prevalent, larger dosages of amoxicillin (i.e. 60 to 90 mg/kg daily in two or three doses) should be effective. When disease is caused by beta-lactamase producing organisms, amoxicillin may not be clinically effective, in which case, amoxicillin-clavulanate (Augmentin), a cephalosporin, trimethoprim-sulfamethoxazole, or erythromycin-sulfa (Pediazole) could be used. Second generation cephalosporins provide good _in vitro_ activity against penicillin-susceptible _S. pneumoniae_ and group A streptococcus. The only oral cephalosporins possessing modest activity against relatively penicillin-resistant _S. pneumoniae_ are cefprozil (Cefzil), cefpodoxime (Vantin), and cefuroxime (Ceftin); however none possess _in vitro_ activity against highly penicillin-resistant _S. pneumoniae_. Recent data suggest that with the exception of cefuroxime (Ceftin), they often lack beta-lactamase stability against _H. influenzae_. In patients who fail to respond adequately to initial antibiotic therapy or have recurrent disease, amoxicillin-clavulanate (Augmentin), cefuroxime axetil (Ceftin), cefprozil (Cefzil), or ceftriaxone (Rocephin) can be considered for treatment. Selection of one of these agents or possibly one of the newer macrolides – clarithromycin (Biaxin) and azithromycin (Zithromax) – can be used.

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

**Recurrent Acute Otitis Media**

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

Chemoprophylaxis with an antimicrobial agent. Sulfisoxazole, amoxicillin, ampicillin, and penicillin have been studied and used. This option appears to be decreasing due to the increased rate of penicillin-resistant _S. pneumoniae_ and beta-lactamase producing organisms. A recent meta-analysis showed a trend for better efficacy with sulfisoxazole than the other antibiotics in
studies with a high recurrent AOM rate. Intermittent antibiotic prophylaxis for recurrent AOM during upper respiratory tract infections is controversial. A US study with amoxicillin showed less efficacy for intermittent than continuous use, and a Finnish study showed a lack of efficacy for a 7-day course of amoxicillin-clavulanate given at the onset of an upper respiratory tract infection. 12

Myringotomy and tube insertion. Many parents choose not to employ a daily antimicrobial and may instead favor myringotomy and tympanostomy tube insertion. As long as the tubes are patent, studies have shown a decrease in the number and severity of episodes of AOM. This does not prevent the occurrence of recurrent OM with otorrhea, as up to 30% of children experience this. There is also the risk of persistent TM perforation, TM scarring, plugging of the tube, early extrusion, extrusion of the tube into the middle ear, and secondary infection around the tube. For children with particularly severe recurrent AOM, both prophylaxis and tube placement may be necessary. Myringotomy tubes are indicated in recurrent AOM, especially when antimicrobial prophylaxis fails to reduce the frequency, severity, and duration of attacks; minimum frequency of three or more episodes in 6 months or four or more episodes in 12 months with one being recent. 13

Adenoidectomy. Few studies have been performed but one study by Paradise et al found a significant difference in the attack rate of acute OM in children who had been randomized to received adenoidectomy in addition to tube placement in comparison to those who received tube placement alone. He found that during the first and second years of follow-up, 28% and 35% fewer episodes of AOM occurred in the study group versus the control. 4

Otitis Media with Effusion

Treatment of middle ear effusion should generally be considered for children with MEE of 3 months or longer since many studies have shown asymptomatic MEE associated with upper respiratory tract infections and resolving AOM. In addition to chronic MEE, the decision to treat can be affected by the following – 1) hearing loss, 2) discomfort, 3) frequent OME episodes, 4) vertigo or unsteadiness, 5) TM changes, 6) middle ear pathology, and 7) associated upper respiratory tract disease.

Among the medical options, only antimicrobial agents have been consistently shown to be of benefit. Antibiotics can be used here because there is evidence of persistent bacterial organism by both standard culture techniques and PCR, therefore, eradication of the organism may lead to resolution of the fluid. 4 There is controversy surrounding administration of a corticosteroid with or without an antibiotic. There is data showing that combination therapy with an antibiotic plus a corticosteroid improved the rate of clearance of effusions by 21% compared to antibiotic alone, and by 25% compared to placebo. There is other conflicting data in the literature so decision on corticosteroid use will be a matter of personal preference until more data is available. If combination therapy is used, a corticosteroid (prednisone, 1 mg/kg per day, given orally in two doses) can be administered for 7 days along with an antibiotic for 14 to 21 days. Children without a history of varicella who have been exposed to the virus in the month prior to treatment should not receive prednisone because of the risk of disseminated disease. 2
Surgical options are usually reserved for patients who do not improve with medical therapy and include myringotomy with tube insertion with or without adenoidectomy. Studies have shown an improvement in conductive hearing loss secondary to OME and a decrease in the amount of time spent with MEE. Gates et al described a 47% reduction in time spent with recurrent effusion in children who received adenoidectomy and tympanostomy tube placement (compared to a reduction of 29% in the tympanostomy only group) in a group of 4 to 8 year old children with OME. 18

Complications

The intracranial suppurative complications of otitis media are relatively rare today except in neglected cases. However, those that occur within the aural cavity and adjacent structures of the temporal bone are more common. Awareness of them is essential in management of children with otitis media, for even though many of the less serious conditions are not life-threatening, the quality of life may be severely affected. The aural and intratemporal complications and sequelae of otitis media include hearing loss, perforation of the TM, chronic suppurative otitis media, retraction pocket, acquired cholesteatoma, mastoiditis, petrositis, labyrinthitis, adhesive OM, tympanosclerosis, ossicular discontinuity and fixation, facial paralysis, cholesterol granuloma, infectious eczematoid dermatitis, and necrotizing otitis externa. 14

There has been an overall decrease in the incidence of suppurative intracranial complications of otitis media since the advent of antimicrobial agents. Today, these complications occur more often in association with chronic suppurative OM and mastoiditis, with or without cholesteatoma, than in association with acute otitis media. The middle ear and mastoid air cells are adjacent to important structures, including the dura of the posterior and middle cranial fossa, the sigmoid venous sinus of the brain, and the inner ear. Suppuration in the middle ear or mastoid, or both, may spread to these structures, producing the following complications: meningitis, extradural abscess, subdural empyema, focal encephalitis, brain abscess, lateral sinus thrombosis, and otitic hydrocephalus. 15

New Frontiers

There is much interest in the development of methods to prevent otitis media. Prevention rather than treatment would go a long way toward relieving human suffering and reducing its great financial impact on the health care system. Even a slight decrease in the incidence of OM would have a profound economic effect.

At present, the vaccine approach seems to hold the greatest promise for ultimate prevention of OM. In addition to the bacterial vaccines, vaccines against the most common viruses predisposing to OM may also prove valuable in the prevention of OM. The multifactorial etiology of AOM constitutes a serious problem in the development of a vaccine. It is not certain whether even a highly effective vaccine against the main pathogens responsible for AOM would decrease its overall incidence when there are so many contributing factors to the pathogenesis of AOM. Despite these concerns there is much interest and hope in the development of these vaccines.
_S. pneumoniae_ is the most common bacterial agent in AOM, so several pneumococcal vaccine trials of AOM prevention have been reported. While the number of episodes of AOM caused by serotypes immunogenic in the children were reduced, these studies did not show convincing reduction in the total incidence of AOM, because the immunogenicity of most serotypes was poor in children under two years of age. However, they did find that a good serum antibody response is followed by type specific protection from middle ear infection. Therefore, if it is possible to overcome the lack of immunogenicity of the polysaccharide antigens in infants, prevention of OM due to _S. pneumoniae_ is a realistic goal. Several polyvalent pneumococcal conjugate vaccines are currently under development and a few have entered clinical trials.

Nontypeable strains are responsible for a vast majority of episodes of AOM caused by _H. influenzae_. As the nontypeable strains are without a polysaccharide capsule, in comparison to _H. influenzae_ type b, a different approach must be taken toward vaccine development. Several indirect lines of evidence suggest that serum bactericidal antibody is associated with protection from infection. Therefore, an antigen that generates serum bactericidal antibodies holds promise as being capable of generating a protective immune response.

_M. catarrhalis_ has been recognized as an important pathogen in OM only during the last decade. Therefore, work on this bacterium lags behind that on _S. pneumoniae_ and _H. influenzae_. Several outer membrane protein antigens with potential as vaccine candidates have been identified. One problem has been that _M. catarrhalis_ is exclusively a human pathogen and it has been difficult to develop an animal model because the organism does not survive in many animal species. As strategies for prevention of infections caused by _S. pneumoniae_ and _H. influenzae_ are developed, the relative importance of _M. catarrhalis_ in the etiology of AOM may increase.

The well established role of viruses in the pathogenesis of AOM justifies the consideration of viral vaccines in the prevention of AOM. About 150 immunotypes of identified viruses, 100 of which are rhinoviruses, account for URI’s. Studies on the structure of rhinoviruses indicate that the prospects for development of an effective rhinovirus vaccine are poor. However, if children could be protected against the most common viruses predisposing to AOM (respiratory syncytial virus, influenza A virus, adenovirus, and parainfluenza viruses), a profound impact on the incidence of AOM could be anticipated. Several investigators have studied the role of influenza vaccine and shown a decrease in the incidence of OM during the influenza season. Some authorities are now recommending influenza vaccine starting at 6 months of age to those at higher risk of OM. Recent work by the UTMB Pediatric department found that RSV is the principal virus invading the middle ear during AOM and intranasal RSV vaccines to protect both the upper and lower respiratory tract are being developed. 1, 11, 16

Finally, xylitol, a widely used sweetening substitute for sucrose, has been evaluated for a role in the prevention of AOM. Xylitol is shown to have a preventive effect on dental caries by inhibiting the growth of _S. mutans_, a bacterium responsible for caries. Xylitol has also been shown to inhibit the growth of _S. pneumoniae_ in growth media. Using xylitol chewing gum, syrup, and lozenges versus controls, a group of investigators found that all three decreased the number of days that the study children were on antimicrobials secondary to OM. They found that the xylitol chewing gum and syrup led to a significant reduction in the occurrence of AOM among the children at day care centers (40% reduction for gum and 30% reduction for syrup,
respectively). These effects are thought to be explained by its local inhibitory effects on the growth of pneumococci and the inhibition of the adhesion of both pneumococci and *H. influenzae* in the nasopharynx. 17

---

**Bibliography**


Posted 11/02/1999