Chapter 4
Complications of Acute and Chronic Otitis Media

Nicholas J. Bennett, Scott R. Schoem, and Kyle Johnson

Introduction

Even though pediatric acute otitis media is very common, most children outgrow the underlying Eustachian tube dysfunction without any sequelae. However, a significant number will encounter mild or moderate degrees of complications with lingering effects into adulthood. These individuals will have permanent problems including hearing loss, speech articulation problems, eardrum perforation with occasional infections called otorrhea, and occasional pain and pressure issues due to lingering Eustachian tube dysfunction. A much smaller subpopulation will encounter serious or life-threatening intracranial complications.

In the preantibiotic era, complications of acute otitis media were very common with frequent hospital admissions due to intracranial complications such as meningitis, brain abscess and sigmoid sinus thrombosis. The incidence drastically decreased in the 1960s through the 1980s, only to re-emerge with the advent of antibiotic resistance and some degree of clinical complacency that antibiotics alone would cure acute mastoiditis. In nations with reduced access to adequate medical care, acute otitis media and mastoiditis leads to much higher complication rates and permanent disabilities.

This chapter discusses both common and uncommon complications of acute otitis media. The authors also introduce promising current and future research endeavors to alleviate Eustachian tube dysfunction.

N.J. Bennett, M.B.B.Chir., Ph.D.
Division of Infectious Diseases and Immunology, Connecticut Children's Medical Center, Hartford, CT, USA

S.R. Schoem, M.D.
Department of Otolaryngology, Connecticut Children's Medical Center, Hartford, CT, USA

K. Johnson, M.D. (✉)
Department of Otolaryngology, University of Connecticut School of Health Sciences, 263 Farmington Avenue, Farmington, CT 06030, USA
e-mail: Kjohnson@resident.uchc.edu

T.A. Valdez, J.G. Vallejo (eds.), *Infectious Diseases in Pediatric Otolaryngology*,
DOI 10.1007/978-3-319-21744-4_4

Normal Anatomy and Function

The middle ear is an air containing space in the temporal bone medial to the eardrum. The eardrum itself is approximately 1 cm square and is composed of 4 layers: squamous epithelium laterally, radial and circular fibrous layers, and mucosa medially. Attached to the medial surface of the eardrum is a chain of bony ossicles known as the malleus, incus, and stapes. The footplate of the stapes rests in the oval window of the cochlea [1]. Sound is conducted from the external world and the external auditory canal to the cochlea through mechanical vibration of the eardrum and ossicles. This mechanical energy is transduced into neural signals in the cochlea and conducted to the brain via the eighth cranial nerve [2]. This conduction of sound through the middle ear functions optimally when air in the middle ear space is at roughly the same pressure as air in the outside world. Unfortunately, the body tends to readily resorb air in any space in the body. Resorption of air in the middle ear leads to a negative pressure system, which then dampens vibrations in the eardrum and ossicles. The body overcomes this tendency to negative pressure in the middle ear with a valve connecting the middle ear space and the nasopharynx, known as the Eustachian tube. The Eustachian tube consists of a bony portion in the temporal bone that descends in a medial to lateral direction as it runs anteriorly from the temporal bone. The anteroinferior aspect of the Eustachian tube consists of a C-shaped cartilage connected to several muscles with a mucosal covering. The orifice of the Eustachian tube is closed in its resting position but opens during swallowing with contraction of the tensor veli palatini muscle, which is the primary dilator of the tube and attaches to the soft palate. Opening of the Eustachian tube orifice allows for air to enter and equalize the pressure of the middle ear space, allowing normal function of the auditory apparatus [3].

Importantly, the temporal bone is in close proximity to the skull base. The temporal bone is pyramidal in shape with its base located laterally and the apex located medially immediately adjacent to the cavernous sinus. The superior aspect of the temporal bone forms part of the floor of the middle cranial fossa, while the posterior wall of the temporal bone constitutes a large portion of the anterior floor of the posterior cranial fossa. Also along the posterior wall of the temporal bone is the sigmoid sinus. Anteriorly, the temporal bone connects to the sphenoid bone creating the roof of the infratemporal fossa. Also immediately anterior to the temporal bone lies the glenoid fossa where the temporomandibular joint articulates [1]. The parotid gland abuts the anterior aspect of the temporal bone at its lateral extent. In addition to the air containing middle ear space housed in the temporal bone, another space known as the mastoid resides posterior to the middle ear within the temporal bone. The mastoid is a usually aerated spaced with multiple air cells divided by bony septae. The mastoid connects with the attic or superior aspect of the middle ear space anteriorly through a space known as the aditus ad antrum. Thus aeration of the mastoid air cells is accomplished via appropriate function of the Eustachian tube as described above. The close proximity of these several structures to the temporal bone accounts for their involvement in complicated forms of otitis media as discussed below.

Pathophysiology

In some individuals, Eustachian tube function is insufficient to allow for consistent, sufficient aeration of the middle ear space. This is particularly true of young children, owing largely to the fact that their Eustachian tubes are shorter and oriented more horizontally than in adults, thus predisposing them to more frequent bouts of otitis media. The immature nature of young children also predisposes them to frequent viral upper respiratory infections [4]. Inflammation in the region of the nasopharynx from a URI leads to edema and swelling of the Eustachian tube orifice. This edema may temporarily worsen Eustachian tube function. When the Eustachian tube is unable to open for an extended period of time,

the air in the middle ear is absorbed to the point that negative pressure develops within the middle ear space, retracting the eardrum medially [5]. As this negative pressure builds, it allows for accumulation of serous fluid excreted by the mucosal cells lining the middle ear. The fluid can then become secondarily infected as the negative pressure in the middle ear provides a pressure differential to draw bacteria-containing secretions from the nasopharynx, leading to acute otitis media (AOM) [6]. Infection of the fluid leads to influx of white blood cells to combat the infection and release of inflammatory mediators. The increased cell count in the fluid leads to increased osmolarity of the fluid, leading to further influx of fluid into the middle ear space. However, given that the space is primarily fixed due to its bony confines, increased pressure in the middle ear space leads to bulging of the eardrum laterally. Stretching of the eardrum and inflammation of the mucosa are the primary causes of the symptoms of AOM. If left unchecked, the infection can spread posteriorly via the aditus ad antrum to involve the mastoid air space, leading to mastoiditis. Progression of AOM to include intracranial complications is most commonly believed to be due to hematogenous dissemination or direct extension through preexisting pathways from the temporal bone to adjacent structures [7]. Fortunately the routine use of antibiotics has made complications of otitis media much less common than they were in the pre-antibiotic era.

Microbiology

The microbiology of otitis media (OM) is similar to that of other respiratory tract infections, and almost exclusively the causative agents are either viruses or bacteria. Fungal infections are rare and are more typically seen in the context of chronic infections or otitis externa. Mycobacterial infections are very rare.

Common viruses that can cause otitis media include respiratory syncitial virus (RSV), influenza, parainfluenza, and metapneumovirus. Prophylaxis for RSV in the form of monoclonal antibody injections for at-risk infants reduces the rate of OM, as does influenza vaccination. Viral infections are generally self-limited and do not require treatment or preventative antibiotics "just in case". Secondary bacterial infections can and do occur. Even in cases where a viral cause is identified, it is wise to watch for signs of worsening infection and act accordingly.

The routine identification of causative organisms in the setting of OM is no longer done. This requires tympanocentesis, which is unlikely to be performed in the outpatient setting. Historically, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* were the predominant organisms responsible for OM. *S. pneumoniae* and some strains of *H. influenzae* are encapsulated organisms, with a polysaccharide coat that surrounds the bacterial cell and provides a degree of immune evasion. Younger children, in particular those under the age of two, are unable to mount a vigorous and lasting response to polysaccharide antigens. The ability to recognize and respond adequately to these bacteria improves with age, and above the age of 5 years the risk of serious infection is much lower. (See Chap. 3 for causes of Otitis Media in the era of PCV13.)

S. pneumoniae is a gram-positive coccus, often described as "lancet shaped" on gram stain, with a polysaccharide capsule. The capsule provides a degree of immune evasion as primary B cell responses against polysaccharides are blunted in the first few years of life. It is a predominant bacterial pathogen associated with respiratory tract diseases, such as OM, sinusitis, pneumonia, bronchitis, bacteremia and meningitis. There are over 90 capsular serotypes of *S. pneumoniae*, but the majority of invasive disease is caused by only a few strains.

H. influenzae is a gram-negative cocco-bacillus, which can appear pleomorphic on gram stain when grown in liquid media. It can also be encapsulated, with the more serious capsular type being *H. influenzae* type B. Non-typeable *H. influenzae* are less likely to cause invasive disease, but can still contribute to

OM and some lower respiratory tract infections, and in vaccinated children the non-typeable strains are likely to be the predominant type.

Moraxella catarrhalis is a gram-negative diplococcus, which often has a beta-lactamase enzyme present. Unlike the other two predominant pathogens, there is no evidence that it has a capsule to provide immune evasion. No vaccine exists for the organism, although it does appear that certain outer proteins are immunogenic. It is far less likely to cause serious invasive disease, such as bacteremia or meningitis. It is a cause of some cases of pneumonia and bronchitis.

Mycoplasma pneumoniae is an atypical bacterium that lacks a cell wall, and as such is intrinsically resistant to beta-lactam antibiotics. It is a cause of upper and lower respiratory tract disease, and in particular is known for causing a bullous myringitis. Mycoplasma infection is more common in those aged 5 and older, and may be due to it being commonly acquired in the school setting. There is no vaccine, but it is readily treated with macrolide antibiotics. Mycoplasma is not routinely cultured even if tympanocentesis is performed, due to the methods requiring prolonged incubation and microscopic examination, but PCR testing is available. Serology for mycoplasma IgM is sensitive but can be non-specific, and cold agglutinins may be a better test of acute disease [8, 9]. In general therapy for mycoplasma is empiric, as the time taken to obtain and confirm a diagnosis may be longer than the typical course of antibiotic therapy.

One aspect of the microbiology of OM is the formation of biofilms, which consist of mucus and bacterial flora, and which may provide protection from both the immune system and antibiotics. Non-pathogenic organisms that produce proteins that confer antibiotic-resistance may create a local environment in which antibiotic-susceptible organisms can flourish in the face of normally effective therapy. Biofilm formation has been shown to be common in those with chronic otitis media [10]. Staphylococcal species, including staphylococcus aureus and coagulase-negative staphylococcal species appear to be frequent isolates from biofilms although they are not a common cause of acute otitis media [11, 12].

The microbiology of OM favors the use of empiric narrow-spectrum therapy with beta-lactam antibiotics such as amoxicillin. Penicillin resistance in *S. pneumoniae* is mediated through a mutated penicillin-binding protein (PBP2x) and can be overcome with higher doses of antibiotic (80–90 mg/kg/day of amoxicillin, compared to 45 mg/kg/day in conventional dosing) [13]. Resistance in some strains of *H. influenzae* and Moraxella is through the production of a beta-lactamase enzyme that hydrolyzes the beta-lactam ring in penicillins, and can be overcome through the use of combination therapy with a penicillin and a beta-lactamase inhibitor such a clavulanic acid. Alternative agents may include oral cephalosporins with significant gram-negative activity such as second or third generation cephalosporins, although the oral bioavailability of these agents can be significantly less than that of amoxicillin. Macrolides such as azithromycin may have some activity, but resistance among pneumococcal isolates is relatively frequent and as such they would not be recommended as first-line agents. The fluoroquinolones, in particular levofloxacin, have excellent broad-spectrum activity against a wide range of respiratory pathogens, but should be used only as a drug of last resort in children due to concerns regarding side effects and the promotion of antibiotic resistance. The use of ciprofloxacin ear drops is a notable exception, as topical use may provide significant therapeutic effect while avoiding systemic side effects, particularly in cases of chronic OM with perforation.

Immune Deficiency

There are several immune deficiencies that predispose children to more frequent or severe OM, and frequent OM (more than eight in a year) may be the first sign of a problem with the immune system.

The most common problem is a defect in humoral immunity involving antibody responses. Naive B cells produce IgM, a pentameric molecule with high avidity but low affinity, as well as a surface IgD with identical antigen recognition to the secreted IgM. Antigen recognition, in particular in the context of concomitant T cell stimulation results first in a class-switch to one of the final immunoglobulin classes (IgG, IgA or IgE) and then a process of somatic hypermutation and affinity maturation to produce highly specific and effective antibodies.

The most serious antibody deficiencies involve a total loss of Immunoglobulin G (IgG). Bruton's Hypogammaglobulinemia is an X-linked disease where there is a total lack of B cells and as such no immune globulins are present. Children (almost exclusively boys) with Bruton's disease will present with frequent, recurrent infections including OM, but also more serious infections from pathogenic bacteria such as pneumococcal pneumonia or bacteremia. X-linked immunodeficiency with hyper IgM (XHIGM) is a class-switching failure and is due to a mutation in the T cell protein CD40-ligand. Children with mutations in the B cell protein CD40 may present with a similar phenotype but it is autosomal recessive. Children with hyper-IgM have absent IgG, IgA or IgE but develop very high levels of IgM as they age—IgM levels may be normal in infants and young children. They lack an ability to produce lasting immunity to infections, and in addition have a high risk of opportunistic infections from pneumocystis jirovecii and enterovirus. Without immune globulin replacement therapy these immune deficiencies are usually fatal in childhood.

IgG2 subclass deficiency is a specific isolated defect that predisposes the individual to infection from encapsulated organisms. IgG2 recognizes polysaccharide antigens as compared to the protein antigens recognized by IgG1 and IgG3, and because the predominant respiratory pathogens are pneumococcus and *H. influenzae*, infections from these organisms are then much more common. There will be no immunity to these organisms from either natural infection or from vaccination. IgG2 subclass deficiency can be treated with immune globulin replacement therapy to reduce the frequency and severity of infections.

IgA deficiency is a common finding (approximately 1 in 600 people) but in and of itself this may not actually pose a serious problem. IgA provides immunity at mucosal surfaces, being found in tears, saliva, breast milk and in the gastrointestinal tract. Those lacking IgA still have protection from serious encapsulated organisms through IgG subclass 2, so it may be prudent to test subclasses in those who are IgA-deficient. Isolated IgA deficiency is not amenable to immune globulin replacement therapy, and in fact those who are IgA-deficient often require low-IgA immune globulin products to avoid the risk of developing serious anaphylactic reactions through the development of anti-IgA IgE.

Children with Common Variable Immunodeficiency (CVID) present with recurrent or chronic respiratory infections, as well as chronic gastrointestinal complaints. They may have slightly low total IgG levels, or may even be within the normal range. They often have poor to absent responses to vaccinations, in particular the conjugated polysaccharide vaccines (pneumococcus and Hib). Some patients show an initial response to repeat vaccination, with a loss of immunity within 6–12 months. This is due to a defect in B cell memory, and in many instances may be a transient delay in the maturation of the immune system. Up to a third of children with recurrent OM may have a defect in polysaccharide immune memory [14], but how many of these go on to require long-term treatment for CVID is unclear.

Complement deficiencies are a collection of defects in the innate humoral immune system that can be broadly divided into early and late (terminal) complement deficiencies. Complement is particularly important in providing protection from encapsulated organisms, such as those that cause upper and lower respiratory tract infections. Children with terminal complement deficiencies are at a particular risk from invasive, recurrent infection with *Neisseria meningitidis*. Deficiency of the C3 or C4 components, which initiate the alternative complement pathway, is associated with recurrent upper and

sometimes lower respiratory tract disease. Mannose binding protein (MBP) is another initiator of the complement cascade and very low levels of MBP are associated with recurrent upper respiratory tract infections, in particular sinusitis. Due to the extremely rapid degradation of the complement components in the blood, there is no replacement option for routine prophylaxis. Protection from infections usually is provided by prophylactic antibiotics.

An important immune deficiency syndrome associated with recurrent OM is that of 22q11.2 deletion syndrome (also known as DiGeorge Syndrome, Velocardiofacial Syndrome, and Shprintzen Syndrome). 22q11.2 deletion is frequently associated with immunologic abnormalities, the most well-known being thymic aplasia and T cell lymphopenia. This may result, rarely, in a severe immune deficiency requiring thymic transplant, but more commonly the child has low absolute T cell numbers, with preserved T cell function and a normal ratio of CD4+ helper and CD8+ cytotoxic T cells. Many children with 22q11.2del have significant problems with OM in the early years of childhood, and interestingly this has little bearing on their future likelihood of immune deficiency or dysfunction. It appears to be primarily an issue with the anatomy of the ear. Children with 22q11.2del may have small, cupped pinnae, and narrow, tortuous outer ear canals. Presumably similar changes are found internally that affect the normal fluid drainage and pressure equalization of the middle ear. In addition, people with 22q11.2del have a particular problem with healing of the tympanic membrane, and even when they no longer have problems with infections they may have persistent perforations of the ear drum that last well into adulthood. Caution should be exercised in the placement of pressure-equalizing tubes in these patients as the surgical defect may become permanent.

Some children with 22q11.2del go on to develop a CVID-like immune deficiency with low IgG or poor vaccine responses, and long-term followup and monitoring with a specialist is recommended.

Very severe immune deficiencies involving absence of T cells, HIV infection, or severe-combined immune deficiency (SCID) more typically present with more severe or unusual infections than isolated OM, and in the absence of more serious issues patients and families can generally be reassured that these conditions can be ruled out.

In general, if there is a suspicion of an immune deficiency contributing to the frequency of a particular child's ear infections, consultation with an infectious disease specialist or immunologist is recommended.

Immunization

Childhood vaccinations to the common bacterial pathogens of childhood have led to significant reductions in the risk of invasive infection from these organisms.

The two main organisms that have proven to be amenable to vaccination are *S. pneumoniae* and *H. influenzae*. Both have polysaccharide capsules that assist immune evasion, and which infants and younger children have difficulty mounting an effective immune response to. Plain polysaccharide vaccines have much lower effectiveness in children under the age of 2 years. The covalent modification of the antigen through conjugation with a protein toxoid (either tetanus or diphtheria toxoid) engages T cell help to the B cell responses, and promotes B cell memory. Conjugate vaccines can also be boosted through repeated dosing, something that in plain polysaccharide vaccines is generally not possible, and which may in fact induce B cell anergy to the target antigen.

The conjugated polysaccharide vaccine against pneumococcus has led to dramatic reductions in the rates of serious disease. A 7-valent vaccine introduced in 2000 lowered infections due to S. pneumoniae in young children by 80–90 %. In the decade following that, there was a small but significant rise in non-vaccine strains causing disease. Two in particular, 19A and 6A, were associated with more invasive disease, a higher rate of *S. pneumoniae*-related hemolytic uremic syndrome [15], and higher

rates of antibiotic resistance. In 2010 a 13-valent vaccine was introduced that included these, and other serotypes, with the goal of addressing these issues. Early indications are that, at least in terms of invasive disease such as pneumonia, further gains have been realized.

The introduction of the conjugated Hib vaccine reduced infections by more than 99 %, with no sign of serotype replacement with other invasive strains. Much of the Haemophilus disease seen in the vaccine era is from non-typeable Haemophilus, and is far less serious.

Developmental Complications

Hearing Loss

Hearing loss is an important potential complication of otitis media, particularly in the chronic forms of the disease. Tympanic membrane perforations, chronic middle ear effusion, and erosion of the ossicles in the middle ear can all lead to conductive hearing loss. This occurs due to dampening of the vibrations as they travel through the eardrum and ossicles of the middle ear, in the case of chronic effusions, or frank disruption of the conductive system, in the case of ossicular erosion. Chronic suppurative otitis media (CSOM), in particular, is associated with permanent hearing loss in as many as half of patients affected with the disease, especially in developing nations where CSOM is more prevalent [16]. Formation of cholesteatoma (discussed below) can also lead to erosion through to the cochlea, leading to sensorineural hearing loss, although this is less common. In patients with less severe disease, the relationship between long term hearing loss and otitis media is less clear. Patients with middle ear effusions do suffer from a conductive hearing loss as long as the effusion is present [17]. However, studies have failed to definitively prove a long term hearing benefit to placement of PE tubes in children [18]. In fact, a Cochrane review in 2010 concluded that the hearing benefit obtained by the placement of PE tubes in children with documented hearing loss and otitis media with effusion was no better than the improvement in hearing that naturally occurs with age in children not treated surgically [19]. Therefore, according to the currently available body of literature, appropriately treated uncomplicated otitis media tends to have little lasting effect on a person's hearing. However, progression to chronic otitis media can have profound deleterious effects on hearing, particularly when diagnosis and treatment is delayed, such as in developing nations.

Speech Delay

Speech delay is an especially important concern in the pediatric population, as the first 2 years of life are a critical period for developing communicative abilities. During this time period, language development depends on exposure to language stimulus [20]. Hearing loss not corrected in the first several years of life is one major contributor to speech delay. However, the influence of recurrent acute otitis media (RAOM), particularly after the age of 2–3 years, on speech development is unclear. There is a theoretical possibility that any hearing loss during infancy or the toddler years, even if temporary, can have adverse effects on the development of speech and language. Multiple studies have attempted to evaluate the relationship between otitis media and speech development, with some finding a negative effect on speech development and others finding no effect. However, a recent meta-analysis failed to find sufficient evidence from well-designed studies to establish a clear and indisputable adverse effect of otitis media on speech development [21]. That meta-analysis noted that otitis media with effusion potentially has a very small to no effect on speech development, but the authors felt this modest effect may have in fact been an overestimation due to pooled studies failing to control for known confounding

factors such as low socioeconomic status. Fortunately, otherwise healthy children with uncomplicated otitis media, even when it is recurrent or persistent enough to warrant placement of tympanostomy tubes, do not appear to suffer from significant speech delay according to the currently available literature.

Intratemporal, Extracranial Complications

Eardrum Perforation

Typically, acute otitis media with rupture heals spontaneously without sequelae; however, repeated episodes of acute otitis media with rupture may result in persistent perforation. In addition, insertion of pressure equalizing ear tubes may lead to eardrum perforation with the rate of perforation depending on the size and construction of the tube (Fig. 4.1). The eardrum often has focal areas of myringosclerosis (scar plaques) or focal areas of retraction. Usually, these are visual findings on physician exam without any functional hearing deficit. Eardrum perforation should be distinguished from retraction. The advantage of eardrum perforation is protection against the slow, but steady negative pressure exerted against the undersurface of the eardrum leading to global retraction, permanent adhesive changes or development of cholesteatoma. Therefore, a perforation may be beneficial functioning as an ear tube without the appliance.

Several issues should be investigated before considering surgical closure of a long-standing eardrum perforation [22]. First, age plays a role. Closure at 5–6 years old, before the child may have outgrown Eustachian tube dysfunction, can lead to recollection of middle ear fluid and conductive hearing impairment, or retraction with potential ossicular erosion or cholesteatoma. Additionally, if the individual still has endogenous (not swimming related) ear infections with intermittent otorrhea, the perforation may well serve as an exit portal and be an asset rather than a liability.

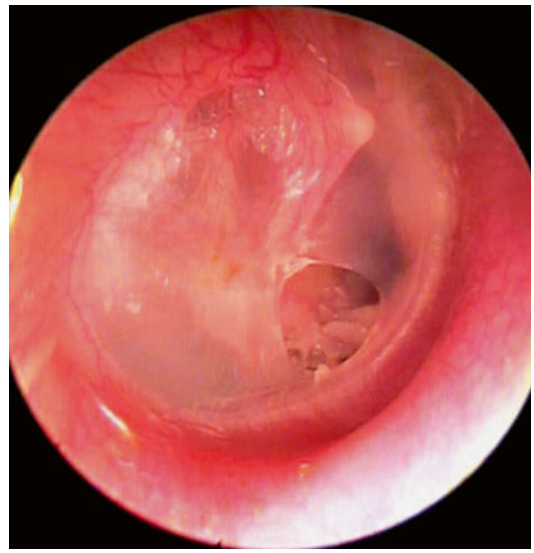

Fig. 4.1 Typical eardrum perforation following tympanostomy tube extrusion

The necessity of using a swim plug for eardrum perforation is controversial. Within the past two decades, recommendations have shifted from always using a plug to situational use depending on the type of water (pool, pond, lake, ocean) and depth of swimming [23]. Currently, most otolaryngologists recommend a plug for non-pool swimming and water exposure below 2–3 ft.

Surgical closure of persistent perforation is typically based on surgeon preference. However, a few guidelines are helpful. First, if the individual has a conductive hearing impairment greater than expected due to perforation alone, the ossicles should be examined as part of the procedure. This requires exploration of the middle ear (tympanoplasty) rather than attempt at closure of the perforation alone (myringoplasty). Second, even in the era of minimally invasive surgery, adequate exposure of the entire eardrum perforation and the size of the ear canal are important factors. If the ear canal accommodates only a 4or 4.5 mm speculum, enlargement of the ear canal or a postauricular approach may be necessary for success. Hearing results after tympanoplasty for perforation are not easily predictable [24]. Chronic middle ear disease may lead to acoustical changes that are not surgically correctable.

Adhesive Otitis Media

Consistent negative pressure due to ongoing Eustachian tube dysfunction acts as a vacuum on the undersurface of the eardrum leading to progressive eardrum retraction. When controlled early enough in the process via ventilation, the ear tube arrests the process. Without ventilation, ongoing severe negative pressure may lead to global retraction forming permanent adhesive scar bands from the undersurface of the eardrum to the ossicles and floor of the middle ear, collapse of the middle ear space and adhesive otitis media or "saran wrap" ear. Surprisingly, this may result in very minimal conductive hearing impairment if sound is conducted through the ossicles and oval window. However, in most cases, there is at least mild hearing impairment. The incus-stapes joint is often eroded and occasionally the stapes itself becomes eroded. Adhesive otitis media usually remains as a self-cleaning ear without formation of granulation tissue or cholesteatoma formation (Fig. 4.2).

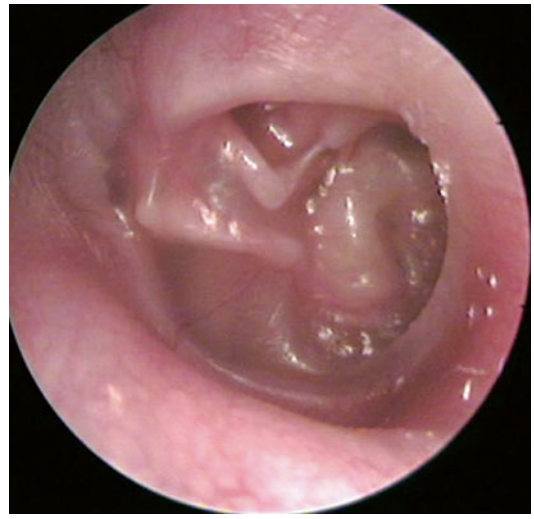

Fig. 4.2 Severe eardrum atelectasis after many years of Eustachian tube dysfunction

Treatment recommendations for this situation are controversial. Options include monitoring alone with periodic hearing assessment, placement of an ear tube through the eardrum for ventilation, placement of a subannular ear tube for ventilation [25, 26], and cartilage tympanoplasty [27, 28]. The use of transnasal balloon dilation of the Eustachian tube is currently experimental in adults.

Chronic Otorrhea

Whereas some eardrum perforations remain clean and dry, others may intermittently drain mucopurulent infection [29]. If the ear drains only a few times each year and resolves within 1–2 weeks using antibiotic ear drops, then there is little concern. However, if the drainage persists longer than 3 weeks or resumes drainage soon after cessation, then the ear may have chronic infection within the mastoid cavity or chronically infected mastoid cholesteatoma. Some individuals may have small eardrum perforations with occasional otorrhea during upper respiratory infections. If drainage persists longer than 3 weeks, a bacterial and fungal culture should be obtained to help guide therapy.

For unremitting drainage, CT scan with contrast of the mastoid may help determine if long-term antibiotics or mastoidectomy may be beneficial. MRI is oversensitive for detection of mastoid disease and does not detect bony defects, as does CT scan.

Ossicular Erosion

Long-term Eustachian tube dysfunction with negative pressure or chronic drainage may lead to erosion of the incus-stapes joint and further erosion of both the incus and stapes bones leading to conductive hearing impairment [30, 31]. Yet, there are no prospective studies addressing how long this process takes to occur and when is the proper time of intervention to arrest this process. Moreover, cholesteatoma formation may erode the ossicles leading to conductive hearing impairment.

Ossicular erosion may occur by direct pressure exerted by the retracted eardrum, ongoing infection with inflammation or enzymatic bony destruction due to cholesteatoma. Commonly, the lenticular process of the incus is involved with incus-stapes disarticulation. Continuation of the process leads to stapes erosion. Usually, the malleus is spared.

Despite advances in technology, ossicular replacement with prostheses remains only moderately successful. Presence of the stapes bone leads to a higher success rate of ossicular reconstruction than with absence of the stapes [32–34].

Facial Nerve Paralysis

At any time, acute otitis media may cause acute facial nerve paresis or paralysis [35–37]. This is a direct toxic effect of the bacteria rather than an erosive process of the bone surrounding the nerve sheath. Facial nerve weakness is more likely if there is a natural bone dehiscence within the middle ear with a direct toxic effect on the nerve sheath. Treatment is urgent myringotomy with ventilation tube placement and culture-directed antibiotic therapy. Prompt therapy leads to over 95 % return of facial nerve function. However, delayed therapy may impair resolution of facial nerve weakness with residual permanent injury.

Cholesteatoma (Keratoma)

The term cholesteatoma is a misnomer and has no meaning. The term was coined in the 1850s when the thought was that this represented a growth or "oma" of cholesterin. Even though the proper term is "keratoma": meaning "skin growth," The literature continues to perpetuate the word cholesteatoma and it seems difficult to purge this from our lexicon (Figs. 4.3 and 4.4).

Acquired cholesteatoma may occur in several ways. Classically taught, focal eardrum retraction of the posterior half of the eardrum may extend to and beyond the incus and stapes bones with erosion of the ossicles [38] along with trapping of skin debris and formation of granulation tissue. If instead, or in addition, the posterior, superior portion of the eardrum called the pars flaccida retracts from the attic region behind to the antrum of the mastoid, this is termed an attic retraction cholesteatoma. An attic retraction cholesteatoma does not usually lead to ossicular damage unless there is a concurrent

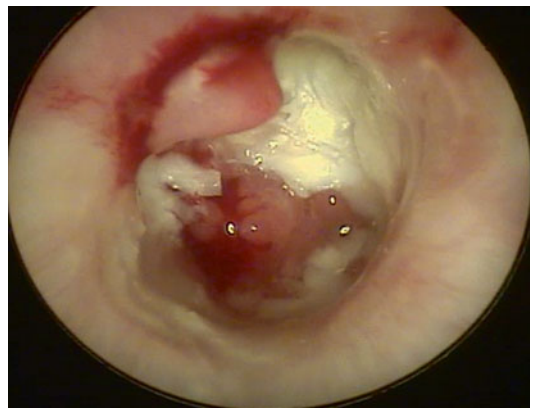

Fig. 4.3 Photo of middle ear cholesteatoma with granulation tissue

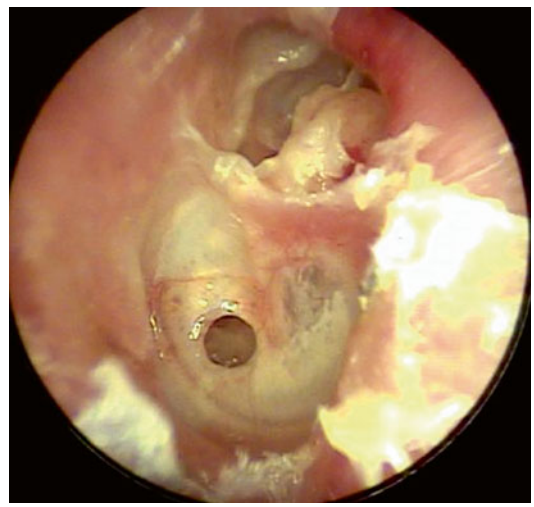

Fig. 4.4 Photo of attic retraction cholesteatoma and eardrum perforation

middle ear component tracking towards to incus and stapes. Other mechanisms of cholesteatoma formation include implantation of skin behind the eardrum after repeated eardrum rupture due to acute infection or occasionally due to a surgically created perforation as with ear ventilation tubes. Acquired cholesteatomas may remain clean and dry or may become chronically infected with mixed aerobic and anaerobic bacteria.

The cholesteatoma dissolves bone both by direct extension and by halisteresis (bone resorption through enzymatic destruction). This process may become very destructive with erosion of the bone separating the mastoid from the middle cranial fossa called the tegmen. The bone covering the floor of the mastoid may also erode with extension to the posterior fossa. Infection may then lead to intratemporal, intracranial complications. Treatment is surgical and may require several, staged surgeries for successful keratoma removal and ossicular reconstruction [39–42]. Pediatric ossicular reconstruction is less successful than in the adult population.

Acute Mastoiditis

An acute middle ear infection by definition leads to infection in the mastoid cavity via direct extension through the attic region of the middle ear, which is the portion of the middle ear cavity superior to the eardrum. Therefore, radiographically, the mastoid cavity will be expected to have infection just as the middle ear. However, an acute otitis media with radiographic fluid in the mastoid does not equate clinically with a diagnosis of acute mastoiditis. Rather, the diagnosis of acute mastoiditis depends on clinical findings. Early findings are fever, pain and erythema and edema behind the ear over the mastoid bone equating with the largest air cell of the mastoid called the antrum (Fig. 4.5). Next, as the mastoid diploic veins become engorged and develops venous congestion, the swelling increases pushing the conchal bowl of the ear outward and then downward (proptosis). Internally, the infection dissolves the trabecular network of bony partitions within the honey-combed mastoid cavity leading to coalescent mastoiditis. The cortex may then erode externally leading to a subperiosteal abscess and/or internally leading to an epidural abscess or brain abscess. A Bezold abscess develops when the

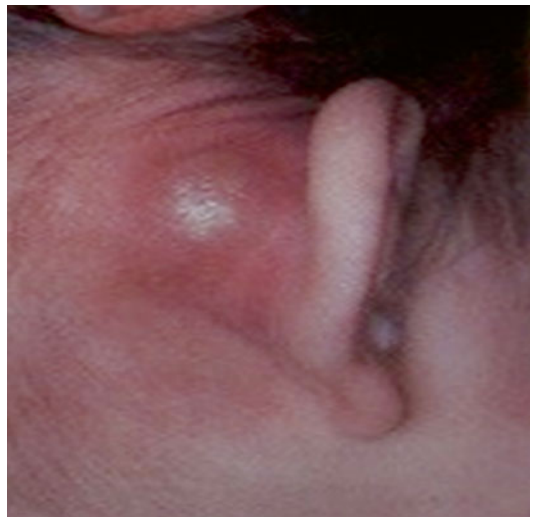

Fig. 4.5 Clinical photo of early mastoiditis

infection erodes through the mastoid tip into the neck. Gradenigo syndrome is the triad of deep unremitting ear pain, ear drainage and Cranial Nerve VI (abducens) paralysis.

The incidence of acute mastoiditis has declined since introduction of the heptavalent pneumococcal conjugate vaccine (PCV7) in 2000 [43, 44]. However, the clinician must guard against a false sense of security regarding the efficacy of intravenous antibiotic therapy alone, without prompt surgical intervention to arrest the infectious process, especially in the presence of intracranial complications [45, 46].

Intratemporal, Intracranial Complications

The overall incidence of intracranial complications has declined dramatically. However, masked symptoms and signs may lead to a false sense of security with delayed therapy or undertreatment. The clinician needs to be keenly aware of circumstances that warrant concern including deep unremitting ear pain, vertigo and only partial response to antibiotic therapy.

Advances in imaging technology have greatly enhanced the ability to make critical, life-saving decisions quickly. Magnetic resonance imaging with vascular flow studies help pinpoint the site and extent of disease.

Meningitis

The incidence of bacterial meningitis has greatly decreased in well-vaccinated populations. Vaccination with PCV 7 and PCV 13 has been instrumental in reduction of pneumococcal meningitis, with reductions in the order of 80–90 %, almost exclusively in vaccine serotypes [47].

Meningitis is a medical emergency, requiring immediate initiation of intravenous, broad-spectrum antibiotics (typically a third generation cephalosporin in combination with vancomycin to cover for resistant pneumococcus). It is a rare complication of otitis media and more typically occurs through hematogenous spread, subsequent to initial invasion of the retropharyngeal tissues by the pathogenic bacteria that are common oral flora. Meningitis can occur secondary to infection in adjacent structures, such as the frontal or mastoid air sinuses, and in that setting the onset may be sudden and catastrophic.

Although the diagnosis can be made clinically it usually requires a lumbar puncture be performed to obtain cerebrospinal fluid (CSF) for analysis, gram stain, and culture. Bacterial meningitis typically has high white cell counts in the CSF (1000's per microliter) with a neutrophil predominance, low glucose and high protein. Bacteria may or may not be visible on gram stain, but usually grow readily from fluid cultures. Antibiotic therapy should not be delayed for results, and in fact should ideally not be delayed by the attempts to perform the lumbar puncture. If the lumbar puncture cannot be performed quickly, empiric therapy followed by subsequent attempts to obtain CSF for analysis is the standard of care.

The duration of treatment varies by pathogen—from as short as a week for Neisseria meningitides to 3 weeks or more for enteric organisms. Consultation with an infectious disease specialist is recommended.

There is a risk of sensorineural hearing loss secondary to bacterial meningitis, and all patients who have meningitis should have a hearing test performed at the end of therapy.

Epidural Abscess

Acute mastoiditis may lead to an epidural abscess via direct extension of infection through natural dehiscences of bone to either the middle or posterior fossa. The most common site is extension through the tegmen bone separating the mastoid cavity from the middle cranial fossa (Figs. 4.6, 4.7 and 4.8). The presenting symptom is deep seated, throbbing pain from dural traction. Neurosurgical consultation should be obtained. When small, the abscess will usually resolve with mastoidectomy and culture directed intravenous antibiotics. When extensive, the intracranial abscess may require neurosurgical drainage [48].

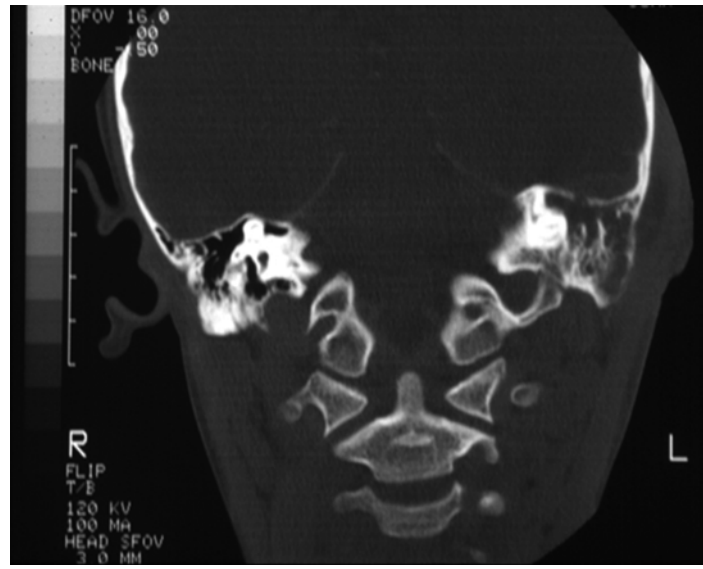

Fig. 4.6 CT scan of bony erosion of tegmen that separates mastoid from middle cranial fossa

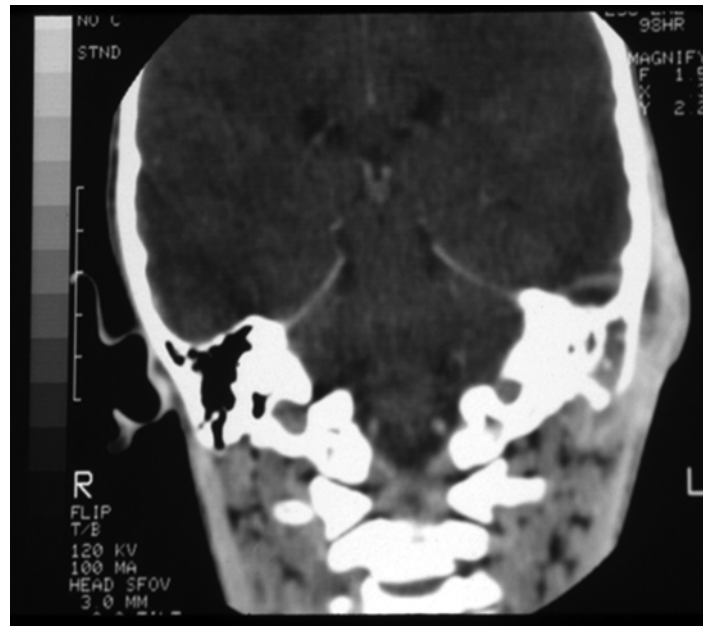

Fig. 4.7 CT scan from same patient of epidural abscess

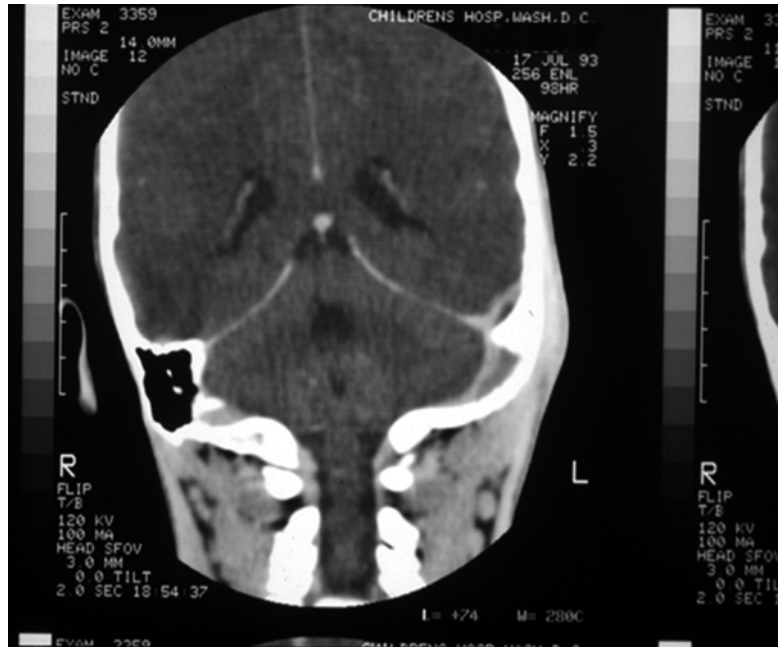

Fig. 4.8 CT scan from same patient of sigmoid sinus thrombosis

Sigmoid Sinus Thrombosis

In the preantibiotic era, sigmoid sinus thrombosis was a more frequent complication of acute mastoiditis. The classic sign of "picket fence" fever referred to the wide swings in temperature with high fever followed by resolution, and then resumption of high fever repeating the cycle. Although sinus thrombosis is still seen, the symptoms and signs are often muted by use of oral antibiotics and fever-reducing medications. Deep pain, fever, and high white blood cell count are cardinal features. When assessing for acute mastoiditis, CT scan with contrast may indicate suspicion for sinus thrombosis. A more conclusive follow up study is magnetic resonance imaging with venography.

Both medical and surgical therapy options are controversial. Surgically, some experts advocate only performing a mastoidectomy whereas others recommend uncapping the bone overlying the sinus, incising and evacuating clot from the sinus. Duration of intravenous antibiotic therapy also varies. In addition, opinions vary on whether anticoagulation therapy is required and for how long to treat based on risk of clot propagation and stroke [49].

Labyrinthitis

Labyrinthitis occurs when infection spreads through either the round window or oval window of the middle ear into the inner ear. This may lead to vertigo, sensorineural hearing loss or both [45, 48]. Myringotomy with culture may help guide antibiotic therapy and ventilation tube placement may speed up the recovery.

Brain Abscess

True brain abscess extends through the tegmen and dura into the temporal lobe, or via the sigmoid sinus into the posterior fossa [46, 48]. An infected cholesteatoma may also erode through the dura into the brain. Clinical presentation may include high fever, vertigo, seizures, severe headache, irritability and lethargy. More worrisome signs include visual field deficits, papilledema and hydrocephalus. Urgent and aggressive medical and surgical therapy is required.

References

1. Anson B, Donaldson J. Surgical anatomy of the temporal bone. 3rd ed. Philadelphia: Saunders; 1981.
2. Geisler CD. From sound to synapse. Oxford: Oxford University Press; 1998.
3. Cunsolo E, Marchioni D, Leo G, Incorvaia C, Presutti L. Functional anatomy of the Eustachian tube. Int J Immunopathol Pharmacol. 2010;23(1 Suppl):4–7.
4. Bluestone CD, Swarts JH. Human evolutionary history: consequences for the pathogenesis of otitis media. Otolaryngol Head Neck Surg. 2010;143(6):739–44.
5. Rettig E, Tunkel DE. Contemporary concepts in management of acute otitis media in children. Otolaryngol Clin North Am. 2014;47(5):651–72.
6. Rovers MM, Schilder AG, Zielhuis GA, et al. Otitis media. Lancet. 2004;363(9407):465–73.
7. Harker LA. Cranial and intracranial complications of acute and chronic otitis media. In: Snow JB, Ballenger JJ, editors. Ballenger's otorhinolaryngology head and neck surgery. 16th ed. Hamilton: Decker; 2003. p. 294–316.
8. Qu J, et al. Accuracy of IgM antibody testing, FQ-PCR and culture in laboratory diagnosis of acute infection by Mycoplasma pneumoniae in adults and adolescents with community-acquired pneumonia. BMC Infect Dis. 2013;13:172.
9. Shankar EM, et al. Serosurveillance of acute Mycoplasma pneumoniae infection among HIV infected patients with pulmonary complaints in Chennai, Southern India. J Infect. 2006;53(5):325–30.
10. Gu X, Keyoumu Y, Long L, Zhang H. Detection of bacterial biofilms in different types of chronic otitis media. Eur Arch Otorhinolaryngol. 2014;271(11):2877–83.
11. Zhao AS, et al. Impact of 13-valent pneumococcal conjugate vaccine on otitis media bacteriology. Int J Pediatr Otorhinolaryngol. 2014;78(3):499–503.
12. Casey JR, Adlowitz DG, Pichichero ME. New patterns in the otopathogens causing acute otitis media six to eight years after introduction of pneumococcal conjugate vaccine. Pediatr Infect Dis J. 2010;29(4):304–9.
13. Dagan R, et al. Bacteriologic and clinical efficacy of high dose amoxicillin/clavulanate in children with acute otitis media. Pediatr Infect Dis J. 2001;20(9):829–37.
14. Sharma SK, Casey JR, Pichichero ME. Reduced serum IgG responses to pneumococcal antigens in otitis-prone children may be due to poor memory B-cell generation. J Infect Dis. 2012;205(8):1225–9.
15. Bannerjee R, et al. Streptococcus pneumoniae-associated hemolytic uremic syndrome among children in North America. Pediatr Infect Dis J. 2011;30(9):736–9.
16. Jensen RG, Koch A, Homøe P. The risk of hearing loss in a population with a high prevalence of chronic suppurative otitis media. Int J Pediatr Otorhinolaryngol. 2013;77(9):1530–5.
17. Rovers MM, Stratman H, Ingels K, et al. The effect of short-term ventilation tubes versus watchful waiting on hearing in young children with persistent otitis media with effusion: a randomized trial. Ear Hear. 2001;22(3):191–9.
18. Khodaverdi M, Jørgensen G, Lange T, Stangerup SE, Drozdziewizc D, Tos M, Bonding P, Caye-Thomasen P. Hearing 25 years after surgical treatment of otitis media with effusion in early childhood. Int J Pediatr Otorhinolaryngol. 2013;77(2):241–7.
19. Browning GG, Rovers MM, Williamson I, Lous J, Burton MJ. Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. Cochrane Database Syst Rev. 2010;10, CD001801.
20. Tonn CR, Grundfast KM. What an otolaryngologist should know about evaluation of a child referred for delay in speech development. JAMA Otolaryngol Head Neck Surg. 2014;140(3):259–65.
21. Roberts JE, Rosenfeld RM, Zeisel SA. Otitis media and speech and language: a meta-analysis of prospective studies. Pediatrics. 2004;113(3 Pt 1):e238–48.
22. James AL, Papsin BC. Ten top considerations in pediatric tympanoplasty. Otolaryngol Head Neck Surg. 2012;147(6):992–8.
23. Derkay CS, Shroyer MN, Ashby J. Water precautions in children with tympanostomy tubes. Am J Otolaryngol. 1992;13(5):301–5.

24. Kent DT, Kitsko DJ, Wine T, Chi DH. Frequency-specific hearing outcomes in pediatric type 1 tympanoplasty. JAMA Otolaryngol Head Neck Surg. 2014;140(2):106–11.
25. Cloutier JF, Arcand P, Martinez J, Abela A, Quintal MC, Guerguerian AJ. Subannular ventilation tubes: retrospective study. J Otolaryngol. 2005;34(5):312–6.
26. Elluru RG, Dhanda R, Neely JG, Goebel JA. Anterior subannular T-tube for prolonged middle ear ventilation during tympanoplasty: evaluation of efficacy and complications. Otol Neurotol. 2001;22(6):761–5.
27. Friedman AB, Gluth MB, Moore PC, Dornhoffer JL. Outcomes of cartilage tympanoplasty in the pediatric population. Otolaryngol Head Neck Surg. 2013;148(2):297–301.
28. Velepic M, Starcevic R, Ticac R, Kunjundzic M. Cartilage palisade tympanoplasty in children and adults: long term results. Int J Pediatr Otorhinolaryngol. 2012;76(5):663–6.
29. Van Dongen TM, van der Heijden GJ, Freling HG, Venekamp RP, Schilder AG. Parent-reported otorrhea in children with tympanostomy tubes: incidence and predictors. PLoS One. 2013;8(7), e69062.
30. Guo Y, Liu Y, Lu QH, Zheng KH, Shi LJ, Wang QJ. CT two-dimensional reformation versus three-dimensional volume rendering with regard to surgical finding in the preoperative assessment of the ossicular chain in chronic suppurative otitis media. Eur J Radiol. 2013;82(9):1519–24.
31. Choi SA, Kang HM, Byun JY, Park MS, Yeo SG. Analysis of differences in facial nerve dehiscence and ossicular injury in chronic otitis media and cholesteatoma. Acta Otolaryngol. 2014;134(5):455–61.
32. Berenholz LP, Burkey LM, Lippy WH. Short- and long-term results of ossicular reconstruction using partial and total plastipore prostheses. Otol Neurotol. 2013;34(5):884–9.
33. Wolter NE, Holler T, Cushing SL, Chadha NK, Gordon KA, James AL, Papsin BC. Pediatric ossiculoplasty with titanium total ossicular replacement prosthesis. Laryngoscope. 2014;125(3):740–5. doi:10.1002/lary.24896.
34. Hess-Erga J, Moller P, Vassbotn FS. Long-term hearing result using Kurz titanium ossicular implants. Eur Arch Otorhinolaryngol. 2013;270(6):1817–21.
35. Pelligrini S, Gonzalez Macchi ME, Sommerfleck PA, Bernaldez PC. Intratemporal complications from acute otitis media in children: 17 cases in two years. Acta Otorrinolaringol Esp. 2012;63(1):21–5.
36. Elliott CA, Zalzal GH, Gottlieb WR. Acute otitis media and facial nerve paralysis in children. Ann Otol Rhinol Laryngol. 1996;105(1):58–62.
37. Evans AK, Licameli G, Brietzke S, Whittemore K, Kenna M. Pediatric facial paralysis: patients, management and outcomes. Int J Pediatr Otorhinolaryngol. 2005;69(11):1521–8.
38. Mohammadi G, Naderpour M, Mousaviagdas M. Ossicular erosion in patients requiring surgery for cholesteatoma. Iran J Otorhinolaryngol. 2012;24(68):125–8.
39. Diom ES, Cisse Z, Tall A, Ndiaye M, Pegbessou E, Ndiaye IC, Diallo BK, Diouf R, Diop EM. Management of acquired cholesteatoma in children: a 15 year review in ENT service of CHNU de FANN Dakar. Int J Pediatr Otorhinolaryngol. 2013;77(12):1998–2003.
40. Edfeldt L, Kinnefors A, Stromback K, Kobler S, Rask-Andersen H. Surgical treatment of paediatric cholesteatoma: long-term follow up in comparison with adults. Int J Pediatr Otorhinolaryngol. 2012;76(8):1091–7.
41. Shirazi MA, Muzaffar K, Leonetti JP, Marzo S. Surgical treatment of pediatric cholesteatomas. Laryngoscope. 2006;116(9):1603–7.
42. McRackan TR, Abdellatif WM, Wanna GB, Rivas A, Gupta N, Dietrich MS, Haynes DS. Evaluation of second look procedures for pediatric cholesteatomas. Otolaryngol Head Neck Surg. 2011;145(1):154–60.
43. Tamir SO, Roth Y, Dalal I, Goldfarb A, Marom T. Acute mastoiditis in the pneumococcal conjugate vaccine era. Clin Vaccine Immunol. 2014;21(8):1189–91.
44. Halgrimson WR, Chan KH, Abzug MJ, Perkins JN, Carosone-Link P, Simoes EA. Incidence of acute mastoiditis in Colorado children in the pneumococcal conjugate vaccine era. Pediatr Infect Dis J. 2014;33(5):453–7.
45. Maranhao AS, Andrade JS, Godofredo VR, Matos RC, Penido NO. Intratemporal complications of otitis media. Braz J Otorhinolaryngol. 2013;79(2):141–9.
46. Sun J, Sun J. Intratemporal complications of chronic otitis media. Eur Arch Otorhinolaryngol. 2014;271(11):2923–6.
47. Mvint TT, et al. The impact of 7-valent pneumococcal conjugate vaccine on invasive pneumococcal disease: a literature review. Adv Ther. 2013;30(2):127–51.
48. Isaacson B, Mirabal C, Kutz Jr JW, Lee KH, Roland PS. Pediatric otogenic intracranial abscesses. Otolaryngol Head Neck Surg. 2010;142(3):434–7.
49. Ulanovski D, Yacobovich J, Kornreich L, Shkalim V, Raveh E. Pediatric otogenic sigmoid sinus thrombosis: 12 year experience. Int J Pediatr Otorhinolaryngol. 2014;78(6):930–3.