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Recent Developments in the Treatment of Otitis Media with Effusion

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Abstract

The management of otitis media with effusion (OME) has received much attention recently as a result of, among other factors, the development of resistant bacteria and the finding of less long-term impact of middle-ear effusion (MEE) on development than previously believed. Guidelines have recently been published for the management of OME promoting more accurate diagnosis, particularly distinguishing acute otitis media from OME, and recommending the 'judicious' use of antibacterials. Today, more emphasis is being placed on prevention of disease by reducing risk factors and the development of vaccines. The identification of susceptibility genes may lead to better understanding of the pathogenesis of otitis media, which in turn may lead to the development of more innovative and satisfactory methods for prevention and treatment.

Otitis media is the most common disorder for which children and their families seek medical care next to the common cold.[1] The proper management of this disorder, which includes episodes of both acute otitis media (AOM) and otitis media with effusion (OME), has received much attention in recent years. Studies have suggested that otitis media has been overdiagnosed, and the short- and long-term effects on speech and language have been overemphasised leading to overtreatment. The worldwide development of resistant *Streptococcus pneumoniae* and other drug-resistant bacteria, which has been thought to be caused by overuse of antibacterials, has led to the recommendation of 'judicious' use of antibacterials in the treatment of otitis media.

1. Definition of Disease

The definition and terminology associated with otitis media is the source of much debate and results in much confusion when trying to compare various studies and reviews.[2] OME is generally defined as middle-ear effusion (MME) without the signs and symptoms of acute inflammation as found in AOM. Generally, AOM is characterised by rapid onset of the signs and symptoms of inflammation of the middle ear accompanied by MEE. Signs of inflammation include bulging or fullness of the tympanic membrane (TM), erythema of the TM and acute perforation of the TM with otorrhoea. Symptoms include ear pain (otalgia), irritability and fever. Sometimes it is difficult to distinguish between OME and AOM, as middle-ear disease can be thought of as a continuum.[3] However, it is important to make the correct diagnosis, since the treatment of the two types of middle-ear disease differs. This review discusses OME.

2. Diagnosis of Middle-Ear Effusion

Recognition of MEE during the physical examination requires the use of the pneumatic otoscope with an attached air bulb. To ascertain mobility of the TM, the physician must obtain a good, airtight seal between the speculum and the ear canal. Gentle application of air pressure via the hand-held bulb will reveal the extent of the mobility of the TM. Reduced or absent mobility of the eardrum during this procedure indicates loss of compliance of the TM either as a result of effusion behind the TM or increased stiffness because of scarring or thickening of the TM. Total absence of mobility of the TM may also be due to an opening in the eardrum caused by a tube or perforation.

The use of the tympanometer in the assessment of potential ear disease has been recognised as a valuable adjunct in the management of otitis media. When otoscopic findings are unclear or otoscopy is difficult to perform, tympanometry can be very useful in evaluating ear disease in children >6 months of age. This instrument, which uses acoustic immittance, provides measures such as peak compensated (static) admittance, tympanometric peak pressure, acoustic reflex and tympanometric width (a measure of gradient). A tympanogram is a plot of the immittance of the middle ear as a function of air pressure in the ear canal. Tympanometry can be combined with otoscopy to assess the status of the middle ear, particularly to determine the presence or absence of MEE and the presence or absence of a perforation of the TM.[4] Other methods of ascertaining middle-ear status have been investigated, including acoustic reflectometry[5,6] and ultrasound,[7] but no one method has been found to be completely accurate.

3. Medical Treatments

There has been a lot of interest in finding an efficacious nonsurgical treatment for OME.

3.1 Decongestants/Antihistamines

A decongestant, with or without antihistamine, was a popular treatment for OME; however, clinical trials have shown that these medications are not efficacious.[8-11] In previous studies of OME at the Otitis Media Research Center here at Children's Hospital of Pittsburgh, PA, USA we found an oral decongestant-antihistamine combination had no efficacy either when given alone[12] or when given with an antimicrobial agent.[13]

3.2 Antibacterials

Antibacterials came into prominence as treatment for OME towards the late 1970's or early 1980's when studies showed the ineffectiveness of decongestant/antihistamine combination, at that time one of the most common treatments for OME. In addition, although thought to be sterile, studies showed that MEE from asymptomatic children with MEE contained bacteria.[14-16] In the study by Bluestone et al.,[16] *Haemophilus influenzae* was the most common organism found in OME aspirates (15%; 23% in AOM), followed by *Moraxella catarrhalis* (10%; 14% in AOM). *S. pneumoniae* was found in 7% of aspirates from children with OME and 35% of aspirates from children with AOM. A more recent study[17] that cultured MEEs at the time of tube insertion in 1999–2000 in Toronto, ON, Canada found *H. influenzae* in 17% of children, *M. catarrhalis* in 9.2% and *S. pneumoniae* in 5.5%. Overall, the three pathogens were isolated from 70% of AOM effusions compared with 32% of OME aspirates. Studies of chronic MEE from Japan and Finland also showed *H. influenzae* to be the most common pathogen isolated (20.2% and 8.0% of cultures, respectively) with *S. pneumoniae* accounting for 10.6% and 4.3%, respectively, and *M. catarrhalis* for 2.3% and 3.5%, respectively.[18] An even higher number of effusions are found to harbour bacteria when bacterial DNA is sought by polymerase chain reaction (PCR).[19,20] Post et al.[19] collected the MEE from 97 children with chronic OME (>3 months duration) who had all received multiple courses of antibacterials with no response. Using standard microbiological culture techniques, 22% of specimens grew *H. influenzae*, 5% grew *M. catarrhalis* and 5% grew *S. pneumoniae*. The percentages of total specimens that were culture-negative but PCR-positive for the various pathogens were *M. catarrhalis* 41%, *H. influenzae* 33% and *S. pneumoniae* 25%. Only 23% of effusions were negative for these bacteria by both culture and PCR.

Many studies of the efficacy of antibacterials have been reported.[21] Most studies show at least short-term efficacy of antibacterials. In our randomised, double-blinded, clinical trials of amoxicillin compared with placebo for OME,[13,22] we found resolution of effusion more often following treatment if patients were in the antibacterial-treated group but recurrence of effusion occurred in most patients within 3 months after completing treatment. Some antibacterials seemed to be more effective than others. In our study of amoxicillin, erythromycin + sulfafurazole (sulfisoxazole), and cefaclor compared with placebo, only amoxicillin was statistically significantly better than placebo, resulting in more children without MEE after treatment.[22] Other antibacterials, such as amoxicillin/clavulanic acid[23] and ceftibuten[24] proved to have no long-term advantage in clearing effusion compared with amoxicillin. The limited efficacy of antibacterial agents for OME has also been reported in several meta-analyses.[25-27]

3.3 Corticosteroids

Glucocorticosteroids have many effects that, at least theoretically, should make them efficacious for the treatment of middle-ear disease. The anti-inflammatory activity of corticosteroids derives from inhibition of phospholipase A_2 with the subsequent prevention of the formation of arachidonic acid and its metabolites;[28] this then prevents the synthesis of inflammatory mediators.[29,30] Corticosteroids have recently been shown to up-regulate transepithelial sodium transport in the middle-ear epithelium promoting the removal of fluid from the middle-ear space.[31] Also, corticosteroids have been shown to decrease mucin production *in vitro* by suppressing MUC5AC.[32] Although the relation of otitis media and allergy is unsettled, these actions of corticosteroids in lessening inflammation may ameliorate the allergic diatheses that are thought to be responsible for MEE.[33] Other proposed mechanisms of corticosteroid action are an increase in surfactant in the eustachian tube[34] and shrinkage of peritubal lymphoid tissue,[35,36] allowing for better tubal function.

Results of trials of oral corticosteroids, alone[37-39] and in combination with an antibacterial agent,[40-45] generally suggest short-term efficacy. However, recurrence of MEE was common.[44,45] To avoid the systemic adverse effects of oral corticoste-

roids, other ways to deliver the drug have been tried. Torrey[46] reported the case of an adult with chronic OME managed by repeated injections of hydrocortisone directly into the middle ear space through the TM. Inhaled corticosteroids were found in one study to be not as effective as oral corticosteroids.[47] Intranasal corticosteroid was not found to be significantly better than placebo in two trials.[48,49]

3.4 Autoinflation

Insufflation of air through the eustachian tube in order to aerate the middle ear was popularised by Politzer over 100 years ago.[50] Variations on Politzer's device, an insufflation bulb and nasal applicator, have appeared through the years and have been used in patients with MEE.[51-55] These methods have had limited or no success in children, especially those with chronic effusion.

4. Surgical Interventions

For children with persistent OME or for children with frequent recurrences of OME in whom non-surgical approaches have been unsuccessful, surgical methods of prevention such as myringotomy with tube insertion and/or adenoidectomy should be considered.

4.1 Myringotomy with Tube Insertion

The efficacy of myringotomy with tube insertion for the management of OME has been the subject of many studies. Mandel et al.[56] reported the results of a 3-year clinical trial of 109 children, 7 months to 12 years of age, with OME of ≥2 months' duration who were unresponsive to medical management and who were randomly assigned to receive myringotomy alone, myringotomy with tube insertion or no surgery. Patients were stratified by the presence or absence of 'significant' hearing loss (pure-tone average >20dB bilaterally or >40dB unilaterally) and/or symptoms (vertigo or tinnitus). Those children without such hearing loss or symptoms were assigned to any of the three possible treatment groups but those with such hearing loss or symptoms were only assigned to myringotomy alone or myringotomy with tube insertion. During the first year, 53% of patients in the myringotomy alone group entered without hearing loss or symptoms and 59% of patients in the no surgery group met preset treatment failure criteria and underwent myringotomy with tube insertion. For children in the myringotomy alone group entered with hearing loss or symptoms, 67% met treatment failure criteria. A second study[57] designed to correct some of the design flaws of the first study and to extend the time until treatment failure involved 111 children with OME for at least 2 months and whose pure-tone averages bilaterally were ≤35dB. This study also found high rates of treatment failure in children in the myringotomy alone group (70%) and the no surgery group (56%). The percentages of time with MEE during the first year in the myringotomy alone, myringotomy with tube insertion and no surgery groups were 61%, 17% and 64%, respectively ($p < 0.001$). From these studies, it was concluded that myringotomy alone offered no advantage over no surgery in regard to percentage of time with effusion, number of AOM episodes and number of repeat surgical procedures, and myringotomy with tube insertion provided more disease-free time and better hearing than myringotomy alone or no surgery. Gates et al.[58] studied the effects of various surgical treatments in children 4–8 years of age with chronic OME; 127 children were randomly assigned to myringotomy and 150 were assigned to myringotomy with tube insertion. Compared with myringotomy alone, myringotomy with tube insertion provided less time with effusion, more time with better hearing and necessitated fewer surgical retreatments.

The previously mentioned studies[56,57] were performed at a time when it was considered 'unethical' to allow a child to have MEE for >2–3 months because of the associated hearing loss and the possible detrimental effects on speech and language development. A more recent study by Paradise et al.,[59] randomly assigned 429 children <3 years of age with persistent or recurrent OME to either prompt myringotomy with tube insertion or to myringotomy with tube insertion up to 9 months later. Eighty-five percent of children in the promptly treat-

ed group and 41 percent of children in the late treatment group had undergone myringotomy with tube insertion by 6 years of age. Concerning developmental testing at 6 years of age, there were no significant differences between the groups on 30 measures. Interestingly, in both the randomised clinical trial and in children randomly selected from those followed in the study but who did not meet criteria for randomisation, sociodemographic variables seemed to be the most important factors influencing developmental outcomes.

A retrospective study[60] evaluated risk factors for additional tube insertion in 2121 patients undergoing bilateral myringotomy and tube insertion. In 19.9% of the children, two or more tube insertions were performed. Patients younger than 18 months at the initial procedure were significantly more likely to have a second procedure (26.3% vs 15.9%; $p < 0.001$). Adenoidectomy was performed at the time of the initial tube insertion in 527 patients (24.5%). This reduced the probability of needing a second set of tubes (0.08 vs 0.24; $p < 0.001$). Also the probability of needing a third set of tubes was reduced when adenoidectomy was performed at or before the second set of tubes (0.15 vs 0.40; $p < 0.001$). The presence of craniofacial abnormalities and a family history of adenoidectomy, tonsillectomy or tube insertion increased the risk of subsequent tube insertions ($p < 0.001$). Sex and race were not risk factors for subsequent tube insertion.

Otorrhoea through a tube or perforation is a common problem after myringotomy with tube insertion and has been recorded in as many as 50% of children with tympanostomy tubes.[61] If untreated, it can develop into chronic suppurative otitis media. Several clinical trials have demonstrated that ototopical agents, such as ofloxacin otic suspension and ciprofloxacin/dexamethasone otic suspension are effective when acute otorrhoea occurs through a tympanostomy tube or perforation, even when no systemic antibacterial is given.[62-64] In a child who has severe systemic symptoms a systemic antibacterial should be added. The ciprofloxacin/dexamethasone combination has been shown to be superior to ofloxacin in resolving granulation tissue.[65] The use of other ototopical agents in patients with a nonintact TM has not been approved by the US FDA as they can be ototoxic, especially those that contain an aminoglycoside.

The sequelae of tympanostomy tube insertion in children with chronic OME followed for 8 years was reported by Daly et al.[66] 138 children (275 ears) followed for 3 years and 84 of these children (167 ears) followed for 8 years were evaluated in regard to TM myringosclerosis, atrophy, retraction pockets or perforations, hearing loss and static admittance. In general, the annual incidence of sequelae was greater at the 4–5 year follow up period compared with the 6–8 year follow up period. Whereas atrophy developed in 67% of the ears, myringosclerosis in 40% and perforation in 3% between the 3- and 8-year follow up evaluations, the annual risk of new sequelae declined considerably throughout the 3- to 8-year follow up period for most sequelae studied. However, atrophy and pars tensa/flaccida retraction were present in 55% of ears at the 8-year follow up, which may put children at risk for continuing middle ear problems during adolescence and adulthood. Johnston et al.[67] reporting the incidence of TM abnormalities in children in the previously cited trial[59] of prompt versus delayed tube insertion, found that children who underwent intubation had more segmental atrophy and tympanosclerosis at age 5 years than children who did not receive tubes. There was no significant relationship between hearing levels at 6 years of age and the presence or type of tympanic membrane abnormalities. A recent retrospective study of 507 children (1096 tubes) who underwent insertion of Armstrong bevelled grommet tympanostomy tubes reported that otorrhoea occurred in 93 (18.3%) patients and 10 (1.32%) persistent perforations that did not resolve spontaneously were noted after tube extrusion.[68]

A quality of life outcome study assessed the parents' appreciation of their child's general condition using the Otitis Media-6 scale before, after and retrospectively before tube insertion in a group of Dutch children 12–36 months of age.[69] The results from the retrospective assessment of the child's general condition prior to tube insertion indicated

that the parents underestimated the effects of otitis media before surgery. In particular, following tube insertion, parents were able to appreciate the extent of presurgical hearing loss.

4.2 Adenoidectomy for Otitis Media with Effusion (OME)

A study by Maw[70] begun in 1983, enrolling children 2–11 years of age with chronic OME, showed that adenoidectomy alone and tympanostomy tube insertion alone provided better results than no surgery, but the combination of the two surgical procedures provided better results than either alone.[71,72] The addition of tonsillectomy to adenoidectomy provided no additional benefit for middle ear fluid resolution. In the previously discussed study by Gates et al.[58] the children randomly assigned to the adenoidectomy plus myringotomy group (n = 130) and the adenoidectomy plus myringotomy with tube insertion group (n = 125) both had a lower percentage of time with effusion than those who received myringotomy with tube insertion alone (n = 129). Thus, based on these results, Gates et al.[58] recommended adenoidectomy plus myringotomy with or without tube placement as the 'first-line' procedure. In 1990, Paradise et al.[73] studied 213 children 1–15 years of age with recurrent AOM or OME who had previously had myringotomy with tube insertion. Children were randomly assigned to adenoidectomy or no adenoidectomy; myringotomy with tube insertion was also performed at the same time for specific indications. Of the 99 subjects who were randomised, there was a significant reduction in time with otitis media during the first 2 years in the children who underwent adenoidectomy compared with those who did not. For the remaining children followed but whose parents chose not to allow random assignment, the results favoured adenoidectomy compared with no adenoidectomy.

5. Guidelines for the Treatment of OME

In 1994 the US Agency for Healthcare Policy and Research developed a clinical practice guideline "Otitis Media With Effusion in Young Children".[27] This guideline was focused on children 1–3 years of age with no craniofacial or neurological abnormalities or sensory deficits. This guideline recommended use of pneumatic otoscopy for diagnosis, with tympanometry as an option. For initial management, observation or antibacterials were options but if, after 3 months, a child had significant hearing loss (bilateral hearing ≥20dB) a course of antibacterials or myringotomy with tube insertion were options. If after 3 months there was no significant hearing loss, observation or antibacterials were options, with myringotomy and tubes if the effusion did not resolve. Antihistamines, corticosteroids and tonsillectomy were not recommended at any time for OME, and adenoidectomy was not recommended for children 1–3 years of age because of lack of data proving efficacy.

The strengths and shortcomings of the guideline were highlighted in an article by Bluestone and Klein.[74] The reliance of the guideline on hearing status at 3 months to determine need for surgical resolution was considered a problem because of the lack of universal availability of hearing testing for young children, the lack of a universally accepted minimum hearing level necessary for normal development, and the known fluctuation in hearing levels in children with OME.[56] Also, other factors that might have played a role in the clinician's management decision for any individual patient were not considered, such as the appearance of the TM, previous surgery for otitis media, presence of speech/language delay, concurrent permanent hearing loss and the presence of vertigo. The recommendation of tympanostomy tubes only for bilateral chronic OME was also seen as a problem with these guidelines; other conditions such as chronic unilateral OME and frequently recurrent OME might also benefit from consideration of surgical management.

In May 2004, the American Academy of Family Physicians, the American Academy of Otolaryngology-Head and Neck Surgery, and the American Academy of Pediatrics Subcommittee on Otitis Media with Effusion felt that the previous OME guideline needed to be updated. In the new Clinical Practice Guideline on OME recommendations are evi-

dence-based and the guideline includes recommendations for children 2 months to ars with and without developmental disabilities or underlying conditions that predispose to OME and its sequelae.[75] The OME guidelines also include a grade based on quality of evidence. As in the previous guidelines, the updated guidelines recommend the use of pneumatic otoscopy not only for ascertaining the presence of MEE but also to distinguish OME from AOM. Being able to discriminate AOM, which in some instances may be treated with an antibacterial agent, from OME is particularly important now, with the emphasis on using fewer antibacterials. Antihistamines and decongestants were deemed ineffective for OME, as they were in the previous guideline and were not recommended for treatment. Previously, antibacterials were considered an 'option', but antibacterials and corticosteroids have not been found to have long-term efficacy and were not recommended for routine management of OME.

Both guidelines advise observation for at least 3 months before considering surgical treatment for children not at risk of speech or developmental delay, but the new guidelines allow for observation at 3- to 6-month intervals until the resolution of effusion, 'significant' hearing loss develops, or structural abnormalities of the tympanic membrane or middle ear develop. This willingness to extend the observation period comes from recent studies showing the lack of effect on later developmental outcomes in not-at-risk children.[76] Hearing testing is recommended when OME persists for ≥3 months or at any time that language delay, learning problems or a significant hearing loss is suspected in a child with OME, and language testing should be conducted for children with hearing loss. When a child becomes a surgical candidate, tympanostomy tube insertion is the preferred initial procedure; adenoidectomy should not be performed unless a distinct indication exists (nasal obstruction, chronic adenoiditis). If further surgical treatment is needed, adenoidectomy plus myringotomy is recommended, with or without tube insertion; tonsillectomy alone or myringotomy alone have not been found effective for the treatment of OME.

The guidelines committee stressed that these guidelines were not intended to be the sole source of guidance in evaluating children with OME. Rather, they were intended to assist primary clinicians by providing a framework for clinical decision making. They were not intended to replace clinical judgment or establish protocols for all children with these conditions.

6. Prevention of Disease

The management of OME must also place strong emphasis on prevention, which includes avoidance of risk factors for OME and AOM (daycare, bottle feeding, use of a pacifier and tobacco smoke exposure),[77] the development of vaccines and the use of other strategies to prevent disease.

6.1 Vaccines

Recently, there has been strong interest in the development of bacterial as well as viral vaccines to prevent otitis media. A reduction in the frequency of AOM episodes would also affect the time a child spent with OME. Viral infection of the upper respiratory tract mucosa initiates a cascade of events that may lead to the development of AOM. Thus, most episodes of AOM could be regarded as a complication of a preceding or concomitant viral infection.[78] Studies have demonstrated a clinical association between respiratory viruses and AOM: the seasonal variation of AOM parallels that of upper respiratory tract infection (RTI),[79] the incidence of AOM is highest in the young children who experience 3–8 upper RTIs per year,[80] and during the first years of life boys appear to have more upper RTIs and a higher incidence of AOM than girls.[78] While bacterial vaccines are only able to prevent the bacterial complication of a viral infection, viral vaccines on the other hand act at an earlier stage in the pathogenesis of AOM. Thus, viral vaccines have the potential to prevent viral infections, thereby preventing the development of AOM by bacteria in the nasopharynx. Today, the influenza vaccine is the only commercially available viral vaccine to prevent RTI in the general population and can be administered parenterally as well as intranasally. This vaccine has

shown to be efficacious in preventing AOM in several studies.[81-83] One study did not show the vaccine to be efficacious; however, a low incidence of influenza A during the second year and enrolment of very young children who did not develop much disease are possible explanations for the poor protective effect found in this study.[84] Vaccines against respiratory syncytial virus[85] and other viruses are under investigation/development.

The most commonly isolated bacteria, using standard microbiological techniques, in the middle ear at the time of tympanostomy tube insertion are *H. influenzae*, *S. pneumoniae* and *M. catarrhalis*.[16] In 1983, the 23-valent polysaccharide vaccine against *S. pneumoniae* was licensed for use in the US. However, many of the pneumococcal serotypes in the polysaccharide vaccine are not immunogenic in children ≤2 years of age. By coupling purified capsular polysaccharide to various carrier proteins, infants and young children are able to be immunised.[86] A conjugate 7-valent vaccine against *S. pneumoniae* was developed and in 2000 this vaccine was recommended for universal use in children ≤23 months of age in the US.[87] A study from Kaiser Permanente in northern California, in children immunised at 2, 4, 6 and 12–15 months and followed up to 3.5 years of age, demonstrated that the conjugate pneumococcal vaccine reduced visits for otitis media by 7% and reduced otitis episodes by 5.8%. Recurrent otitis media was reduced by percentages that increased with otitis frequency, and tympanostomy tube insertion was reduced by 24% overall.[88] However, two recent studies of the effect of pneumococcal vaccine on OME have not found significant protection by this approach. Straetemans et al.[89] analysed data from the Finnish Otitis Media Vaccine Trial, a randomised, double-blind, controlled trial of heptavalent pneumococcal conjugate vaccine and found a weakly protective effect in children without older siblings. In a clinical trial designed specifically to look at the efficacy of pneumococcal vaccine for OME, van Heerbeek et al.[90] found no difference in recurrence of OME following spontaneous extubation (tubes inserted for chronic OME) in 2- to 8-year-old children immunised with heptavalent conjugate and 23-valent pneumococcal vaccines compared with those not immunised.

The development of a vaccine against nontypeable *H. influenzae* is also in progress. Difficulty in finding a common antigen among the multiple strains has delayed the development of a commercially available vaccine. Gu et al.[91] reported the results of a phase I study of a lipooligosaccharide-based conjugate vaccine for nontypeable *H. influenzae* in adults that showed some promise; the authors stated that a phase II study in children was planned. Another study using recombinant P6, an outer membrane protein found in all *H. influenzae*, showed protection against otitis media in mice.[92]

7. Other Approaches

Many parents rely on homeopathic treatment of their child's otitis media, more than most paediatricians are aware. There are many difficulties in designing adequate randomised clinical trials of this type of treatment, including lack of standard homeopathic treatments, need for clinicians with the required expertise in both homeopathy and definitions and diagnosis of middle-ear disease, and the selection bias possible as a result of the differing demographics of parents who choose homeopathy versus standard medical care.[93,94] Harrison et al.[95] reported a randomised, nonblinded trial of individualised homeopathic treatment compared with 'standard' treatment (autoinflation with or without 'low-dose' antibacterials) in 33 children 18 months to 8 years of age with OME. Audiometry at 12 months suggested a better outcome in the homeopathy group. At present, there are no methodologically sound randomised trials of the efficacy of homeopathic treatment for OME.

The role of gastro-oesophageal reflux disease (GORD or GERD) in OME is unknown. Rozmanic et al.[96] reported that 15 (56%) of 27 children with either chronic OME or recurrent AOM and no reflux-related symptoms had pathological GORD on 24-hour continuous oesophageal pH monitoring. Tasker et al.[97] found evidence of pepsin/pepsinogen in 59 (91%) of 65 thick mucoid MEE samples from children undergoing myringotomy for OME.

The concentrations of pepsin/pepsinogen were up to 1000 times that in serum, leading the authors to conclude that this was evidence of reflux. On the other hand, El-Serag et al.[98] published their case-control study of 1980 children between the ages of 2 and 18 years with the diagnosis of GORD (from their hospital's database and not further defined) compared with 7920 children without the diagnosis of GORD. In this population, otitis media was inversely associated with GORD (2.1% vs 4.6%).

Results from epidemiological, anatomical, physiological, immunological but maybe most convincingly twin and triplet studies[99-101] have indicated that there is a genetic predisposition to otitis media. Daly et al.[102] reported finding possible genetic locations on chromosomes 10q, 19q and 3p involved with susceptibility to otitis media. At the Ear, Nose and Throat Research Center at Children's Hospital of Pittsburgh, PA, USA, we are in the process of conducting a study enrolling 500 families with at least two children who have had tympanostomy tubes inserted to identify susceptibility genes using a three-stage gene-mapping methodology. The identification of susceptibility genes for otitis media will allow future development of molecular assays which can be used as a tool to determine whether or not a child is at increased risk for otitis media. Also, this knowledge may lead to a better understanding of the pathogenesis of otitis media which in turn may lead to the development of more innovative and satisfactory methods for prevention and treatment.

8. Conclusions

The management of otitis media is continually evolving. As bacterial resistance has increased, the clinicians' diagnostic skills in distinguishing OME from AOM have become even more important. With the lack of evidence of developmental problems resulting from chronic effusion and the lack of non-surgical therapy with long-term effects on OME status, clinicians are becoming more comfortable with longer observation periods of children with OME before resulting to surgical treatment. When surgical therapy is decided upon, the practice at our institution is to employ myringotomy with tube insertion as the first procedure in a child without airway obstruction, with adenoidectomy as a later procedure if surgery is warranted because of recurrent effusion. Vaccines to prevent infection with bacteria and viruses involved in the pathogenesis of otitis media are on the horizon, and results of studies to define the genes involved with otitis media susceptibility may provide new directions for treatment and prevention of disease.

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