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DISCERNING BETWEEN TYPES OF OTITIS MEDIA
AND THEIR EVIDENCE BASED TREATMENTS:
A REVIEW FOR THE AUDIOLOGIST

By

Hadassah Norowitz

A capstone research project submitted to the Graduate Faculty in Audiology
in partial fulfillment of the requirements for the degree of Doctor of Audiology,
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Abstract

DISCERNING BETWEEN TYPES OF OTITIS MEDIA AND THEIR EVIDENCE BASED TREATMENTS: A REVIEW FOR THE AUDIOLOGIST

By

Hadassah Norowitz

Advisers: Drs. Shlomo Silman and Michele B. Emmer

Otitis media is an inflammatory pathology of the middle ear and middle ear mucosa which accounts for the majority of cases of childhood hearing loss diagnosed by audiologists. However, considerable confusion exists regarding the distinction between otitis media with effusion, also known as middle ear effusion or “glue ear”, and acute otitis media, the quintessential ear infection. Since many children are referred for audiological evaluation in the process of determining the course of treatment and outcomes of treatment, audiologists must be knowledgeable of the evidence of efficacy for various treatment options as they field questions from parents with incomplete information from their physicians. Systematic reviews and guidelines for management of otitis media have been published repeatedly, but Berkman et. al (2013) contend that uncertainty remains among physicians regarding the comparative benefits and costs of the various treatment strategies, due to the lack of consensus on clinical and long-term functional outcomes of otitis media with effusion. The aim of this review is to present otitis media with effusion versus acute otitis media within the framework of their anatomy and pathophysiology; to address all methods currently used to treat otitis media with effusion and acute otitis media; and to propose a preferred way of treating middle ear effusion. A database

search was conducted to identify studies on otitis media and its treatments. Criteria for diagnosis as acute otitis media and otitis media with effusion were clearly established, and the evidence from relevant publications was critically analyzed. A remarkably favorable natural history for otitis media regardless of treatment was found, suggesting that many medical and surgical interventions are preemptively used despite their risks. Implications of this trend for those involved in the treatment and management of children with this pathology are discussed in this review.

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And to my Uncle Ian, may he rest in peace. He would have loved to read this.

This achievement belongs to us all.

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INTRODUCTION

Otitis media accounts for the majority of cases of childhood hearing loss diagnosed by audiologists. An ongoing relationship between pediatricians and otolaryngologists is formed as children are evaluated for symptoms of otitis media. However, considerable confusion exists regarding the distinction between otitis media with effusion, also known as middle ear effusion or “glue ear”, and acute otitis media, the quintessential ear infection. Since many children are referred for audiological evaluation in the process of determining the course of treatment and outcomes of treatment, audiologists must be knowledgeable of the evidence of efficacy for various treatment options. Many parents approach antibiotic use and tympanostomy tube insertion with fear and hesitation, while others trust the recommendations of their medical doctors and oblige to treatments which may be misguided. Doctors fail to educate their patients properly about their benefits and risks of treatment options. Systematic reviews and guidelines for management of otitis media have been published repeatedly, but Berkman et. al (2013) contend that uncertainty remains among physicians regarding the comparative benefits and costs of the various treatment strategies, due to the lack of consensus on clinical and long-term functional outcomes of otitis media with effusion. The aim of this review is to present otitis media with effusion versus acute otitis media within the framework of their anatomy and pathophysiology; to address all methods currently used to treat otitis media with effusion and acute otitis media among children through age 12 with no pre-existing conditions; and to propose a preferred way of treating middle ear effusion.

PHYSIOLOGY OF THE EAR

As sound travels through the different parts of the ear causing the process of hearing, an acoustical-mechanical function transitions into an electro-chemical one. The pinna of the outer ear acts as a funnel which delivers sound into the external auditory meatus. The lateral face of

the tympanic membrane registers the wave of sound pressure which causes a vibration, transmitting the sound to the adjoined ossicles of the middle ear: the malleus, incus and stapes. Through their mechanical action, the vibration acts upon the oval window to the cochlea of the inner ear. At this point, a pressure wave is sent through the bone-encased, fluid-filled cochlea. The pressure displaces the tonotopic basilar membrane at the regions specific to the comprising frequencies, thereby stimulating a complex response of chemical receptors which trigger electrical impulses corresponding to the pattern of sound. These encoded impulses are carried along from the auditory nerve to the auditory brainstem and cortex, where they are processed and finally perceived as meaningful sound.

The focal pathology of this paper, otitis media, is an inflammatory pathology of the middle ear and middle ear mucosa, behind the tympanic membrane. The middle ear cleft which houses the ossicles can be understood as a six-walled cavity whose integrity plays a vital role in the hearing function. In terms of its anatomic surroundings, the tympanic membrane is positioned laterally and the inner ear medially. The Eustachian tube is placed anteriorly, leading to the nasopharynx. Posteriorly are the mastoid air cells. The middle ear is lined by modified respiratory epithelium, which produces mucins that are normally transported down the Eustachian tube (Qureishi et. al, 2014). Other important nearby structures are the brain and meninges superiorly and the sigmoid sinus posteriorly. Any infection of the middle ear can spread to surrounding structures with serious results. Even in the absence of infection, the presence of a thick mucoïd or thin serous fluid within the middle ear space adversely affects the efficiency of transfer of sound from the tympanic membrane to the cochlea, resulting in a conductive hearing loss.

Worthy of specific mention is the eustachian tube, whose anatomic or physiologic abnormality is presumed to be the leading causative factor among children with recurrent episodes of acute otitis media or otitis media with effusion (Bluestone & Klein, 2007). The eustachian tube connects the distal middle ear to the proximal nasal cavity, palate, and pharynx, and it has three main physiologic roles. Firstly, it ventilates and regulates the pressure of the middle ear by equilibrating gas pressure in the middle ear with atmospheric pressure. The eustachian tube also serves to protect the middle ear, as a barrier to nasopharyngeal sound pressure and secretions. Secretions produced within the middle ear are drained by the eustachian tube into the nasopharynx, as another important role of the eustachian tube. Disruption within any of these systems can give rise to middle ear pathology. Concurrently, the eustachian tube functions most effectively when the systems both proximal and distal ends are also normal, and thus the functions of the eustachian tube must be considered in this context (Bluestone & Klein, 2007).

A healthy middle ear is maintained by the eustachian tube system's protective function. The structural and functional anatomy maintains a protective 'gas cushion' between the middle ear and mastoid gas cell system. The local immunological and mucociliary defense system of the respiratory epithelium in the eustachian tube lumen further clears secretions from the middle ear in a protective manner. Radiographic studies have demonstrated that the eustachian tube normally collapsed, with its tubal lumen closed off at rest. During swallowing, when the proximal end opens, liquid can enter this part of the tube, but it does not go into the middle ear because of the tube's narrow isthmus. In pathologic cases of middle ear disease, dye would reflux into the middle ear in some patients, especially during closed nose swallowing (Bluestone, 1971). In contrast, a healthy eustachian tube will perform its clearance function through its

passive closing process, beginning at the middle ear end of the tube and progressing towards the nasopharyngeal end, thus pumping out secretions (Bluestone & Klein, 2007).

The hearing function is most efficient when the gas pressure within the middle ear cavity is relatively balanced with the atmospheric pressure in the external auditory canal, because the tympanic membrane and middle ear compliance are optimal. Nearly ambient pressures are maintained in the middle ear due to the regular contractions of the tensor veli palatine muscle during swallowing: the muscle action pulls the eustachian tube open during swallowing, and thus air from the nose and throat can enter and ventilate the middle ear. Under normal physiologic conditions, relatively small changes in atmospheric pressure due to weather or elevation are equilibrated either to or from the middle ear, and they tend not to be noticeable (Doyle & Seroky, 1994). However, changes in equilibration can sometimes reach perceptible magnitude and become pathologic. Gas exchange between the non-collapsible middle ear/mastoid gas cell system and the mucosa occurs through a mucous membrane. Since a significant differential pressure exists between the microcirculation in the mucous membrane and the middle ear space at atmospheric pressure, the diffusion gradient can cause an underpressure in the middle ear cavity during equilibration.

Nature has dictated that even otologically normal children have less efficient eustachian tube function than do adults. A study in Sweden (Bylander, 1980) revealed that 35.8% of children could not equilibrate applied negative intratympanic pressure by swallowing, compared to only 5% of adults who were unable to accomplish this function. Weaker function was observed among the 3-6 year olds than among the 7-12 year olds. Many children with no apparent middle ear disease present with high negative middle ear pressure, likely due to this inefficient opening mechanism. Although Jerger (1970) proposed that the parameters for normal

resting middle ear pressure is between 0 and -100 daPa for symptomatic ears, Brooks (1969) suggested that the lower limit of the normal range of tympanometric peak pressures could be extended to 170 daPa for children who are otherwise asymptomatic. Nonetheless, even children with pressures outside this range have been reported normal, because high negative pressure does not necessarily indicate disease. It may simply indicate physiologic obstruction of the eustachian tube, wherein pressure regulation occurs only after an opening pressure is met by the nasopharynx-middle ear pressure gradient. Since the physiology between normal and abnormal is not fully understood, these children are generally still considered at risk for middle ear disease (Bluestone & Klein, 2007).

The incidence of otitis media decreases from infancy to adolescence, presumably due to improved eustachian tube function with increasing age (Bluestone & Klein, 2007). Just as anatomy differs between children and adults, so does the functional ability to open the eustachian tube during swallowing activity to equilibrate pressure between the middle ear and the nasopharynx. Aside from the effects of age on the eustachian tube function, posture is believed to affect the function of the eustachian tube, through the venous engorgement of the tube and reduced volume of air passing through the tube as body position reclines. Seasonal variation in children has also been observed, with better eustachian tube function in the summer and fall than in the winter and spring (Beery et. al, 1979).

OTITIS MEDIA: A WIDESPREAD DISEASE

Otitis media, literally defined as an inflammation of the middle ear, represents a significant group within otolaryngologic pathology. Although the different types of otitis media will be described as discrete diseases with a discrete set of clinical symptoms, signs, sequelae

and treatments, in reality there is a great degree of overlap between the different types, so that otitis media can be viewed as a continuum/spectrum of diseases (Qureishi et. al, 2014).

The etiology and pathogenesis of otitis media is agreed to be multifactorial, which fuses genetic, infectious (viral and bacterial), immunologic, environmental, social factors and Eustachian tube dysfunction (Bluestone & Klein, 2007). Factors of the host included an immature or impaired immune system; a familial predisposition; method of feeding, whether breast or bottle; sex; and race (Ramakrishnan et. al, 2007). Environmental factors include day-care attendance and smoking in the household. Anatomic and physiologic dysfunction contributing to otitis media consists of eustachian tube dysfunction and cleft palate or submucous cleft. Finally, allergy and infection play their own roles in the pathogenesis of OM.

However, only more recently has the functionally and structurally immature Eustachian tube, paired with an immature immune system emerged as the most important and probable causes of the increased incidence of otitis media in infants and young children. These young children often have a genetic predisposition which makes them more susceptible to otitis media. All of these factors render otitis media a common complication after a child is exposed to an upper respiratory tract infection (Bluestone & Klein, 2007).

Bluestone and Klein (2007) describe the pathogenesis of otitis media in children as a simple sequence of events. The patient first experiences an antecedent event, typically an upper respiratory tract infection, which produces congestion of the respiratory mucosa of the nose, nasopharynx, and eustachian tube. The congestion of the mucosa in the eustachian tube causes an obstruction of the tube's isthmus. This blockage causes negative middle ear pressure, which

leads to middle ear effusion. Once the mucosal secretions of the middle ear cannot drain properly through the eustachian tube, they accumulate in the middle ear.

THE ROLE OF THE EUSTACHIAN TUBE IN THE PATHOGENESIS OF OTITIS MEDIA

The physiologic roles of the eustachian tube are disrupted by various types of dysfunction. If the tube is too closed due to anatomic obstruction, the pressure regulation function within the middle ear will be impaired. An intrinsic obstruction of the eustachian tube can be due to inflammation secondary to infection or allergy (Bluestone et. al, 1977; Buchman et. al, 1994; Friedman et. al, 1983; McBride et. al, 1989). Extrinsic obstruction may arise from compression by a tumor or an adenoid mass. Acute or chronic inflammation, polyps, or a cholesteotoma due to middle ear disease may obstruct the eustachian tube at the distal end, near the middle ear. Obstruction of the tube's opening at the proximal end of the eustachian tube in the nasopharynx can likewise play a role even when the eustachian tube itself is patent and normally functioning. Adenoids, a foreign body, or a tumor can all impinge on the eustachian tube and anatomically obstruct the opening process required for pressure equilibration in the middle ear.

The eustachian tube may be functionally obstructed due to failure of the opening mechanism, when the tube is too floppy, when the tubal opening is inefficient, or when both defects are present. The most common manifestation is when the lumen of the cartilaginous portion fails to open during swallowing activity. Since infants have less cartilage in their eustachian tube, the lumen may not open when the tensor veli palatine contracts. An underdeveloped muscle may not be strong enough, and the small angle between the ear canal and eustachian tube further weakens the active opening process. Functional obstruction and

consequent inability to pressure regulate is considered to be one of the immature features of the infant tube (Bluestone & Klein, 2007).

The protective function of the eustachian tube becomes compromised when the tube is abnormally patent or relatively too short, when abnormal gas pressures develop at either end of the tubal system, or when there is a non-intact middle ear resulting in a loss of the middle ear gas cushion (Bluestone & Klein, 2007). If the eustachian tube lumen is excessively open, there is a free flow of air and nasopharyngeal secretions from the nasopharynx into the middle ear, resulting in reflux otitis media. A distensible tube resulting from a lack of stiffness will easily allow nasopharyngeal secretions to be insufflated into the middle ear. In this manner, infants and young children are more liable to force fluid (gas or liquid) into the middle ear by abnormally high positive nasopharyngeal pressure, during nose blowing, with Valsalva's maneuver, or during closed-nose swallowing, with even less pressure needed.

When the eustachian tube is relatively short, it effectually acts as if too open. In children under 7 years, the eustachian tube is significantly shorter compared to that of adults (Sadler-Kimes et. al, 1989). The shorter the tube, the more likely secretions can reflux into the middle ear, which may account for the troublesome otorrhea in infants and young children. When unphysiologic pressures develop at either end of the eustachian tube, the protective function may also suffer. When high negative pressure occurs in the middle ear, secondary an anatomic obstruction such as that during an upper respiratory tract infection, nasopharyngeal secretions may be aspirated into the middle ear.

In the presence of a normal eustachian tube, the middle ear/mastoid gas cell system must be intact in order to repel secretions through the eustachian tube. If the gas cushion is lost

through a non-intact middle ear/mastoid, the tube is effectively too open and nasopharygeal secretions can enter the middle ear. This is a consideration when there is a perforation of the tympanic membrane or a tympanostomy tube in place, and a surgeon is contemplating repair (Bluestone & Klein, 2007).

Rather than a primary cause for disease, an impaired mucociliary defense of the eustachian tube is related to a compromised ability in resolving middle ear effusions (Bluestone & Klein, 2007). However, if clearance of secretions is compromised and additionally high negative pressure is present, the fluid will become trapped in the middle ear and not allowed to drain. The pressure is only relieved once the suction is broken through spontaneous tympanic membrane rupture or through myringotomy, and then the fluid can drain. The Politzer method and Valsalva maneuver have had frequent success in clearing middle ear effusions in these instances, by relieving pressure through inflation of air through the eustachian tube.

Otitis media frequently occurs in allergic individuals (Draper, 1967), but the eustachian tube is presumably the affected site rather than the middle ear as the target organ. A particular study invoking a nasal challenge on allergic individuals produced adverse effects on eustachian tube function, but no otitis media in participants (Friedman et. al, 1983). Perennial allergic rhinitis, but not seasonal nasal allergy, has been correlated with otitis media with effusion (Passali et. al, 2005).

DISTINGUISHING BETWEEN TYPES OF OTITIS MEDIA: ACUTE OTITIS MEDIA AND OTITIS MEDIA WITH EFFUSION

According to the American Academy of Pediatrics (Lieberthal et. al, 2013), acute otitis media is defined as the rapid onset of signs and symptoms of inflammation in the middle ear. The hallmark symptoms of acute otitis media are fever and otalgia (Buchman et. al, 1995). Severe acute otitis media refers to acute otitis media with presence of moderate to severe otalgia or fever equal to or higher than 39 degrees Celsius, while nonsevere acute otitis media refers to acute otitis media with the presence of mild otalgia and a temperature below 39 degrees Celsius (Lieberthal et. al, 2013). Acute otitis media is considered to be uncomplicated when there is no otorrhea, which is discharge from the ear originating from the external auditory canal, middle ear, mastoid, inner ear, or intracranial cavity. Recurrent acute otitis media refers to 3 or more well-documented and separate acute otitis media episodes in the preceding 6 months or 4 or more episodes in the preceding 12 months with at least 1 episode in the past 6 months. Persistent acute otitis media occurs when features of middle ear infection persist during antibiotic treatment, or when the patient relapses within one month of treatment completion (Qureishi et. al, 2014).

In contrast, otitis media with effusion is defined as the collection of fluid in the middle ear; the signs and symptoms of acute inflammation or infection are absent (Perera et. al, 2013). Middle ear effusion refers to liquid in the middle ear, without reference to etiology, pathogenesis, pathology or duration (Lieberthal et. al, 2013). Prolonged effusion is commonly considered to be 3 months or more. The effusion may become infected secondarily due to an ascending infection from Eustachian tube into the middle ear cleft, which typically coincides with colds or minor upper respiratory infections. Sometimes, the infection may follow a sinus

infection or an episode of allergic rhinitis (Abdullah et. al, 2007). In these cases, otalgia can occur and recur frequently.

In actuality, there is lots of overlap between the types of otitis media, as children with one condition will often develop the other. In some cases acute otitis media precedes otitis media with effusion and in some otitis media with effusion precedes acute otitis media. Most cases of middle ear effusion occur after an episode of acute otitis media, with 67% of patients developing a middle ear effusion, typically for a mean duration of 23 days (Waseem et. al, 2014).

PATHOPHYSIOLOGY OF ACUTE OTITIS MEDIA

During an upper respiratory tract infection, the mucosa of the upper respiratory tract become congested, including the nasopharynx and eustachian tube. This anatomic obstruction leads to the development of negative middle-ear pressure. If prolonged, the viruses causing the primary infection and the potentially pathogenic bacteria that colonize the nasopharynx can be refluxed, aspirated, or insufflated into the middle ear through the Eustachian tube (Bluestone & Klein, 2007) and cause an acute otitis media. Middle ear effusion created by the infection accumulates due to the obstructed eustachian tube, and thus microbial pathogens can thrive and reproduce in the secretions, resulting in a suppurative and symptomatic otitis media.

As mentioned previously, anatomic or physiologic abnormality of the Eustachian tube is presumed to be the leading causative factor among children with recurrent episodes of acute otitis media or middle ear effusion. Children with recurrent acute otitis media were found to have significantly poorer active tubal function than controls with no history of acute otitis media, suggesting that recurrent acute otitis media is due to anatomic obstruction of the eustachian tube rather than a mechanical circumstance (Bluestone & Klein, 2007). Cytokine gene polymorphism is thought to have an effect on recurrence, particularly in children with allergic disorders (Joki-

Erkkila et. al, 2002). It is typical for infants and young children who have short and floppy eustachian tubes to reflux or insufflate nasopharyngeal secretions into the middle ear during a viral upper respiratory tract infection, or a cold.

Penicillin-resistant *S. pneumonia* is the most common cause of recurrent and persistent acute otitis media (Arrieta & Singh, 2007). Medical management of acute otitis media is actively debated in the literature, resulting from the dramatic increase in prevalence over the past 10 years caused by drug resistant *Streptococcus Pneumoniae* and beta lactamase producing *H influenza* or *M catarrhalis*, which are able to hydrolyze amoxicillin and some oral cephalosporins, leading to in-vitro resistance to these drugs (Waseem et. al, 2014). Empiric antibiotic therapy for this disease has become accordingly more complex, and opinions over first and second line therapies have emerged.

PATHOPHYSIOLOGY OF OTITIS MEDIA WITH EFFUSION

The etiology of otitis media with effusion is recognized to be multifactorial, including adenoid hypertrophy, infection (viral or bacterial), allergy, and environment and social factors (Abdullah et. al, 2007). Socioeconomic factors such as overcrowding, poor diet, and lack of healthcare have been implicated in the development of otitis media with effusion as well. Prevalence is higher among children from urban areas than rural areas. Male children, children fed with bottles during infancy as opposed to being breastfed, and children fed in a supine position rather than while held upright, are all at a greater risk for otitis media with effusion. Interestingly, high socioeconomic status in Malaysia was found to be associated with higher rates of otitis media with effusion, conceivably due to improved access to medical care among that class. Other factors such as race, premature delivery, passive smoking, allergy, asthma and family size had no influence on the prevalence of otitis media with effusion. It has been

repeatedly demonstrated that children who have persistent middle ear effusion have poor eustachian tube function (van Heerbeek et. al, 2001).

The onset of otitis media with effusion typically follows a similar sequence of events as acute otitis media, but with a relatively asymptomatic acute onset. Bacterial isolates have been removed from ears with otitis media with effusion, but prolonged negative pressure in the middle ear often leads to a sterile middle ear effusion. The hydrops ex vacuo theory of middle ear effusion proposes that if the eustachian tube fails to open, the gas exchange from the middle ear into the microcirculation of the mucous membrane causes a middle ear underpressure, and transudation of effusion ensues (Bluestone & Klein, 2007).

When an upper respiratory tract infection lasts for a longer period, it can cause atelectasis of the tympanic membrane, sterile otitis media with effusion, or acute bacterial otitis media. Since the eustachian tube can still open in an ear with effusion, nasopharyngeal secretions can be aspirated, and thus the clinical result is otitis media with effusion combined with recurrent acute bacterial otitis media. The mucus which is commonly found in middle ears of children with otitis media with effusion may allude to an antecedent acute otitis media (Bluestone & Klein, 2007).

Persistent middle ear effusion is likely similar, whether resultant from infection or from prolonged negative pressure (Bluestone & Klein, 2000). Cytokines are stimulated, followed by pathways of inflammation which promote further effusion. Nitric oxide and free radicals have been implicated in the pathogenesis of persistent otitis media with effusion: as blood flow is increased within the mucous membrane, nitrogen is increased within the microcirculation of the mucosa, which results in further negative pressure. The infection caused by *Haemophilus influenzae* may change mucosal goblet cell density, which would simultaneously make the

middle ear cleft more susceptible to persistent effusion. This thickened effusion becomes trapped in the middle ear, as there is difficulty draining through the narrow mid-portion of the eustachian tube. If the mucociliary system and pumping action of the tube are also impaired, as they most likely would be, persistent middle ear effusion would be further perpetuated.

Chronic suppurative otitis media (without cholesteotoma) refers to the chronic stage following an episode of acute otitis media, in which there is continuous pus-like discharge through perforation of the tympanic membrane or tympanostomy tube (Bluestone & Klein, 2007). Since the tympanic membrane is not intact, the middle-ear gas cushion is lost, and pathogens from the nasopharynx are refluxed into the middle ear, further exacerbated in the presence of inflammation of the nose, nasopharynx, or paranasal sinuses. Initially, bacterial isolates resemble those extracted from behind an intact tympanic membrane or in acute otorrhea when tympanostomy tubes are inserted, such as *S. pneumoniae* and *H. influenza* (Mandel et. al, 1994). After the acute stage, *pseudomonas aeruginosa*, *staphylococcus aureus*, and other organisms from the external ear canal gain entry through the non-intact tympanic membrane into the middle ear, resulting in chronic infection. Alternatively, chronic suppurative otitis media can be caused while bathing and swimming, when organisms present in water infiltrate the middle ear cleft through the non-intact eardrum (Bluestone & Klein, 2007).

SEQUELAE OF OTITIS MEDIA

The most common clinical symptom of otitis media with effusion (Abdullah et. al, 2007) is conductive hearing loss approximating 25dB (Waseem et. al, 2014), which may be latent or overt and fluctuate in severity. In infants and young children, the hearing loss is usually latent, often presenting with co-morbid speech and language delay. The hearing loss may also stunt behavioral and academic development. The hearing loss can lead circumstantially to other

complications such as language delay, behavioral problems, and poor academic performance, which has given rise to many strategies advocated for medical treatment in patients with otitis media with effusion (Waseem et. al, 2014).

Auditory processing is also an area of concern, because otitis media with effusion can affect skills such as binaural auditory perception (Hall et. al, 1995) and speech recognition in noise (Schilder et. al, 1994), which eventually become a child's skills for overcoming classroom noise and successfully attending to the instruction. Normal hearing is required for normal auditory processing, but deficits in auditory perception can remain even when hearing is restored to normal, as with surgical intervention for middle ear effusion through tympanostomy tube insertion. Although a trial by Paradise et. al (2007, 2005) found no differences between early and delayed tube groups among children ages 6-9, and mild hearing loss among preschool children for periods of up to 9-12 months did not affect subsequent speech or language outcomes (Paradise et. al, 2001), generalizations from these findings will be reserved until this work can be replicated on new children with more serious middle ear disease (Berkman et. al, 2013).

Otitis media and hearing loss may affect long-term psychosocial outcomes (Hogan et. al, 2014). When looking at a nationally representative longitudinal study of two cohorts, abnormal/borderline psychosocial outcomes were more likely in a cohort aged 10-11 who experienced acute otitis media at age 4-5, while ongoing acute otitis media at age 0-1 did not predict poorer psychosocial outcomes. This finding reinforces the notion that suffering from recurrent otitis media specifically during a key developmental period has the potential to begin affecting and continuously impact on their ability to develop adequate language and literacy skills, as well as to learn and be included in group situations (Santrock, 2009).

The pre-school aged population of 4-5 years old who are affected with otitis media represents children with long-term hearing difficulty, or complications after years of recurrent pathology. Middle ear pathology is complicated by the fact that children with milder hearing problems have been reported to demonstrate the worst psychosocial health related quality of life and behavior scores (Wake et. al, 2004). In contrast to children with a language delay or permanent hearing loss, they are disadvantaged in terms of intervention, because their problems are perceived as minor. They are faced with subtle communication breakdowns, particularly in noisy environments such as classrooms and at home. These challenges are frequently misperceived as relational conflict (Hétu et. al, 1991), which is likely to impact on poorer psychosocial outcomes. Hogan (2014) proposed that management approaches for ear infections and hearing problems in young children should be expanded to address psychosocial needs.

Any amount of hearing loss creates an effective barrier against accessing the full auditory signal (Berkman et. al, 2013). As such, infants and toddlers are more susceptible to the negative effects that an otitis media with effusion-related hearing loss may pose, since they are learning the rules that govern language comprehension and production. Infant speech perception of the simple vowels /i/ and /u/ at 6 months of age was correlated with increased vocabulary at 18 and 24 months of age, compared to babies who could not discern those early sounds (Kuhl et. al, 2005). Since academic achievement is strongly predicted by early vocabulary development, these findings hold clinical considerations for children with otitis media with effusion.

Practitioners are concerned when the effusion reduces hearing because it may result in these functional limitations and have long term sequelae. Studies of children with otitis media have demonstrated abnormal vestibular function on moving platform posturography assessment and visually induced postural sway while the effusion was present (Bluestone, 2004). More

significantly, a study of 4-year old children by Casselbrant and colleagues (2000) with documented otitis media in the past but no middle ear effusion at the time of testing were found to have abnormalities of balance, which suggests that previous history of otitis media may result in a longer term balance dysfunction. Based on its short and long term sequelae, otitis media stands as an important disease group to study and understand. Furthermore, the prevalence and impact of otitis media may be even higher than previously thought, due to underestimation of ear-disease in infants and very young children.

PREVALENCE, AGE, COST, AND OTHER RISK FACTORS FOR OTITIS MEDIA

Otitis media is collectively recognized in the literature as the leading cause of morbidity in children, but its subtypes have differential effects on the population. Acute otitis media is most prevalent in early childhood, with peak incidence between 6 and 24 months (Waseem et. al, 2014). By age 3 more than 80% of children have been diagnosed. Immaturity of the immune system is believed to be a contributing factor to acute otitis media (Qureishi, 2014). In contrast, otitis media with effusion typically affects children between 3 and 7 years old. Otitis media with effusion can affect as many as 80% of children at some stage and is the most common cause of hearing impairment in the developed world (van Zon et. al, 2012). As of 2004, approximately 2.2 million new cases of otitis media with effusion were diagnosed annually in the US (American Academy of Family Physicians et. al, 2004). The relative decline in the incidence of otitis media after age 7 is attributed to the maturation of the Eustachian tube, which protects the middle ear from nasopharyngeal pathogens.

Current epidemiological trends in the United States have actually dipped below the target annual prevalence of otitis media diagnoses, which was set in the early 2000's at 294 per 1000 children (National Center for Health Statistics, 2011). Between 1997 and 2007, the annual prevalence of otitis media diagnoses in children younger than 18 declined from 345 to 247 per

1000 children, for an overall 28% decline (National Center for Health Statistics, 2011). This consistent decrease is believed to be related to the routine use of the pneumococcal conjugate vaccine among children, beginning after its licensure in 2000 (Zhou et. al, 2008). Although the incidence declined by 38% among children younger than 3 years between 1997 and 2007, the highest rates of otitis media are still represented by this age group (Klein et. al, 2008).

Anteunis et. al (1999) highlighted the low accuracy of parental recognition of otitis media in children less than two years, and it is uncertain whether the accuracy improves as children grow older. Middle ear effusion is notoriously asymptomatic, and acute otitis media often relies on the child's ability to communicate their otalgia, so parents may remain unaware of their child's pathology until age 4-5.

Acute otitis media is the most common infection for which antibiotics are prescribed in the United States (Hendley et. al, 2002). There are direct and indirect costs of treatment and time lost from school and work likely exceeding \$3 billion (Ahmed et. al, 2014). The routine prescription of antibiotics for acute otitis media ranges from 31% in the Netherlands to 98% in the USA and Australia (Scottish Intercollegiate Guidelines Network, 2003).

Prospective studies of twins and triplets have demonstrated a strong genetic component related to the amount of time with effusion, episodes of effusion and episodes of acute otitis media (Honjo et. al, 1979). Lack of breastfeeding is considered a risk factor, while breastfeeding for at least 3 months is protective (Ramakrishnan et. al, 2007). Studies of otitis media in infants with cleft palate who were fed breast milk through an artificial feeder have demonstrated a protective effect linked to the milk itself, and not simply from the suckling process (Swarts & Bluestone, 2003).

Children age 6 or older who experience otitis media with effusion are likely to be at different risk for negative impacts than those who experience otitis media with effusion as infants or very young children (Berkman et. al, 2013). The United States Agency for Healthcare and Research Quality (Berkman et. al, 2013) was not able to draw firm conclusions about the relative benefit of treatments as a function of age, but it has been suggested that including all children of studies may mask the benefits of treatment of individuals at varying ages.

Otitis media with effusion is more common among males. Daycare attendance increases the risk of contact with multiple children spreading bacterial and viral pathogens of acute otitis media (Ramakrishnan et. al, 2007). Exposure to cigarette smoke and air pollution has been linked to increased incidence of acute otitis media, especially if the parents smoke (Ramakrishnan et. al, 2007). Pacifier use is related to increased incidence of acute otitis media, and there is also increased incidence of acute otitis media in the fall and winter. There is an increased risk of antibiotic treatment failure for acute otitis media in children with more than one sibling living at home, among children who have previous antibiotic use, and among children with previous otitis media.

Presumed to have a higher incidence of otitis media with effusion are certain races, including the American Indians and Eskimos, the Maori of New Zealand, natives of Guam, Greenland Eskimos, Australian aborigines and Laplanders (Abdullah et. al, 2007). Increased rates of otitis media with effusion in these races may reflect differences in access to health care, the socioeconomic status, and anatomic or biologic predisposition.

CLINICAL PRESENTATIONS AND DIAGNOSIS

ACUTE OTITIS MEDIA

According to the American Academy of Pediatrics (Lieberthal et. al, 2013), there is no gold standard for the diagnosis of acute otitis media, and accuracy is further complicated by the fact that acute otitis media has a spectrum of signs as the disease develops. There is considerable over-diagnosis of acute otitis media, which led the American Academy of Pediatrics to modify their diagnostic criteria in efforts of differentiating acute otitis media from otitis media with effusion. They cite an ill-understood premise in stressing the importance for clinicians to become proficient in distinguishing normal middle ear status from otitis media with effusion or acute otitis media: otitis media with effusion does not represent an acute infectious process that benefits from antibiotics. Improved diagnostics of middle ear status will avoid unnecessary use of antibiotics, which leads to increased adverse effects of medication and facilitates the development of antimicrobial resistance (Lieberthal et. al, 2013). According to their key action statements, clinicians should diagnose acute otitis media in children who present with moderate to severe bulging of the tympanic membrane or new onset of otorrhea not due to otitis externa. Clinicians should also diagnose acute otitis media in children who present with mild bulging of the tympanic membrane and recent (less than 48 hours) onset of ear pain (holding, tugging, and rubbing of the ear in a nonverbal child) or intense erythema of the tympanic membrane. Acute otitis media should not be diagnosed in children who do not have middle ear effusion, based on pneumatic otoscopy and/or tympanometry.

The pneumatic otoscope is the standard tool used in diagnosing otitis media, enhanced when a surgical head can be used to assist in cerumen removal from an infant's external auditory canal for improved visualization of the tympanic membrane (Lieberthal et. al, 2013). Pneumatic otoscopy enables evaluation of the contour of the tympanic membrane (normal, retracted, full,

bulging), assessment of its color (gray, yellow, pink, amber, white, red, blue), translucency (translucent, semi-opaque, opaque), and its mobility (normal, increased, decreased, absent). Clinical signs of acute otitis media on otoscopy include bulging or fullness of the tympanic membrane with loss of anatomic landmarks on visualization; opacification of the tympanic membrane regardless of color; erythema of the tympanic membrane; and abnormal tympanic membrane mobility on biphasic pneumatic otoscopy (Food and Drug Administration, 2012). If the tympanic membrane does not move perceptibly with applications of gentle positive or negative pressure, middle ear effusion is likely (Lieberthal et. al, 2013). The application of pressure will sometimes make an air-fluid interface behind the tympanic membrane more evident, which is diagnostic of middle ear effusion.

The latest criteria have been chosen to achieve high specificity, recognizing that less severe presentations of acute otitis media may be excluded (Lieberthal et. al, 2013). Prior definitions of acute otitis media lacked precision to exclude cases of otitis media with effusion, and diagnoses of acute otitis media could be made in children with acute onset of symptoms including severe otalgia and middle ear effusion, without other otoscopic findings of inflammation. The current guidelines endorses stringent otoscopic diagnostic criteria as the basis for management decisions. The combination of a “cloudy,” bulging tympanic membrane with impaired mobility was the best predictor of acute otitis media using a symptom based diagnosis in one particular study (Lieberthal et. al, 2013). Impaired mobility had 95% sensitivity and 85% specificity. Moderate to severe bulging of the tympanic membrane represents the most important characteristic in the diagnosis of acute otitis media, as bulging tympanic membranes have positive bacterial cultures 75% of the time. According to Dowell et. al (1998), 6-8 million courses of unnecessary antibiotic therapy have been prescribed annually due to misdiagnosis.

Pain is the major symptom of acute otitis media (Lieberthal et. al, 2013). Infants and younger children are more likely to present with non-localizing but noticeable signs of otitis media, while older children may be more likely to verbalize symptoms referable to the ear (Food and Drug Administration, 2012). Signs that may be observed in infants and younger children include head rolling, ear tugging, ear rubbing, fussiness or irritability, inconsolability, decreased appetite and sleep disturbance. Quantifiable symptoms in older children with acute otitis media include ear pain or earache, ear fullness and decreased hearing. Other clinical signs of acute otitis media included elevated body temperature or elevation in peripheral white blood cell count. Children may also commonly present with non-specific symptoms such as fever, headache, irritability, cough, rhinitis, listlessness, anorexia, vomiting, diarrhea, and pulling at the ears (Ramakrishnan, 2007).

According to Rosenfeld and Kay (2003), observational studies on the efficacy of treatments for acute otitis media are limited due to their low diagnostic certainty used in methodology. Literature basing diagnosis on non-pneumatic otoscopy and clinical symptoms are not considered to be reliable, while diagnostic certainty in the literature included methods such as tympanometry, pneumatic otoscopy, otomicroscopy, needle aspiration, or otolaryngologic referral.

OTITIS MEDIA WITH EFFUSION

As mentioned previously, otitis media with effusion refers to the condition where an asymptomatic fluid is present behind the tympanic membrane (Ramakrishnan, 2007). If the fluid persists behind an intact tympanic membrane in the absence of acute infection, it is termed chronic otitis media with effusion. The middle ear assessment described in the section of acute

otitis media beginning with careful pneumatic otoscopy is likewise used in examinations for middle ear effusion.

Tympanometry is highly useful in detecting middle ear effusion, with absence of tympanometric peak pressure (Type B) and low peak-compensated static admittance (Type As) often predictive of middle ear effusion (Abdullah et. al, 2007). In ears with effusion presenting with absent tympanometric peak pressure, compliance is equal over the whole pressure range and a peak is absent due to incompressible fluid within the middle ear and the resultant limited movement of the tympanic membrane. In ears with effusion presenting with low static admittance, the peak compliance indicated normal middle ear pressure while the shallow compliance suggested stiffness of the middle ear structures as induced by adhesions (Abdullah et. al, 2007). Absent tympanometric peak pressure has demonstrated the highest specificity for otitis media with effusion, while otoscopy and negative tympanometric peak pressure (Type C) have higher sensitivity but lower specificity for otitis media with effusion (Rosenfeld & Kay, 2003). Silman et. al (1992) and Silman & Emmer (1995) pointed out that measures of tympanometric width combined with acoustic reflex screening may reduce the number of false positive medical referrals, as the ipsilateral acoustic reflex will be absent in ears with middle ear effusion. In general, children between the ages of 3-7 years without significant history of middle ear disease will have static admittance >0.2 mmho and tympanometric width <150 daPa. Younger children and those with histories of middle ear disease may exhibit wider tympanograms (up to 250 daPa) even in the absence of middle ear effusion (American Academy of Audiology, 1997).

Otoscopically, the degree of retraction of the pars tensa is consistent with the negative middle ear pressure reducing the mobility of the tympanic membrane (Lieberthal et. al, 2013).

Atelectatic changes of the pars tensa and pars flaccida may even be present. As the tympanic membrane loses its color and translucency, its pathologic coloring may range from pale grey or amber, to a black or so-called “blue drum.” The membrane may present as thickened, dull and opalescent or thin and reflective. Fluid levels and air bubbles may be visualized within the middle ear cleft (Abdullah et. al, 2007).

A prospective, cross-sectional study on children in Malaysia aged 3-12 requiring surgery for chronic otitis media described the most common clinical and audiological profiles in that region (Abdullah et. al, 2007). The most common presenting complaint was hearing impairment (52%), followed by otalgia (18%), ear block (16%), and tinnitus (14%). Otosopic findings identified fluid in as many as 40% of the cases, followed by dullness (32%) and retracted tympanic membrane (28%). On audiometry, 48% of ears had moderate hearing loss, 32% had mild hearing loss, and 8% had severe hearing loss. Tympanometric profiles were characterized by absence of peak pressure (Type B) in 84% of ears and reduced compensated static admittance (Type As) in 12% of ears. Intraoperative findings during myringotomy revealed middle ear secretions (effusion) in only 76% of ears; 44% of these ears had mucoid effusion while 32% had serous effusion. None of the ears had purulent effusion.

Since the presentation of hearing loss is the most common symptom of otitis media with effusion (Abdullah et. al, 2007), the severity of the disease is often quantified based on pure tone audiometry. The progress and effects of treatment are also monitored by serial audiometry. Tympanometry effectively detects negative middle ear pressure, but since it is a screening tool, it cannot distinguish between a pressure change with or without middle ear effusion (Abdullah et. al, 2007). In actuality, transient improvement of otitis media with effusion followed by relapse occurs in 30-45% of children (Fiellau-Nikolajsen, 1979; Tos 1983), so improvement in

tympanometric peak pressure (Type C2) should not be equated with resolution (normal static admittance with normal tympanometric peak pressure; or Type A, with or without C1) (Rosenfeld & Kay, 2003).

The type of fluid suctioned from ears during myringotomy ranges from a thick mucus “glue-like” effusion to a thin serous fluid. These contents of the middle ear upon myringotomy have been analyzed, demonstrating that the viscosity is correlated with the concentration of mucin (Abdullah et. al, 2007). The prognostic value of middle ear aspirates is debated however. A study in Abdullah et. al (2007) suggested that recurrent cases of otitis media with effusion were correlated with different effusions resulting from various levels of enzymes and proteins. Another study insisted that the type of effusion found on aspiration before myringotomy had no predictive significance. Interestingly, not all patients who were diagnosed clinically with otitis media with effusion were found to have effusion present in the middle ear at myringotomy. Abdullah et. al (2007) states that this occurrence is common and cites the active debate in the literature on whether the exposure to nitrous oxide during general anesthesia is accountable for this phenomenon.

Chronic suppurative otitis media is persistent infection and resultant perforation of the tympanic membrane, through which otorrhea may flow (Bluestone & Klein, 2007). The patient may also present with thickened granular mucosa, polyps, and cholesteotoma in the middle ear. Additional bacteria may enter the middle ear through the hole in the tympanic membrane. This condition is diagnosed through history and examination not limited to otoscopy. The ear is first carefully cleaned, in order to visualize the tympanic membrane, attic, and for ruling out cholesteotoma. The examination may detect other sources of infection requiring treatment, such as the nose, paranasal sinuses, lungs or pharynx (Ramakrishnan et. al, 2007).

APPROACHES TO TREATMENT

THE NATURAL HISTORY OF OTITIS MEDIA: A CASE FOR WATCHFUL WAITING

The true efficacy of the various treatments for acute otitis media can only be judged when viewed in comparison to its natural history and spontaneous resolution. Rosenfeld and Kay (2003)'s seminal meta-analysis of published evidence provides quantitative estimates of natural history and serves as a benchmark study against which medical, surgical, or alternative therapies should be considered. Their data strongly suggested a favorable natural outcome for otitis media, with most children improving eventually irrespective of management. There has been repeated affirmation that otitis media is a self-limited disorder, and as such the function and role of nature needs to be balanced against potential therapeutic benefits.

Studies which investigate untreated otitis media are typically gleaned from a placebo group of a randomized trial studying another effect of some therapy. The placebo group is protected with close follow-up provisions to begin antibiotics for observation failures, typically after 48-72 hours. Meta-analysis data from randomized controlled trials (Rosenfeld & Kay, 2003) revealed that within 24 hours of diagnosis, 61% of children managed without antibiotics had symptomatic relief. Spontaneous resolution grew to 80% by 2-3 days. Complete clinical resolution, defined by the cessation fever, pain and otorrhea (but not middle ear effusion), was 70% at 7-14 days. Although one child in a placebo group developed meningitis, the incidence of suppurative complications in children managed without antibiotics (1 of 843, 0.12%) was comparable to that observed after initial antibiotic treatment (2 of 932, 0.21%). These findings are undoubtedly favorable for sporadic improvement of acute otitis media. However, the dilemma remains that it is impossible to identify from the onset the 20% likely to remain symptomatic (Rosenfeld & Kay, 2003).

A common finding after non-antibiotic management of acute otitis media was persistent asymptomatic middle ear effusion (Rosenfeld & Kay, 2003). Otitis media with effusion was heterogeneously reported in 41% of children at 4 weeks and 54% at 6 weeks, slowing to a homogenous 26% at 12 weeks. However, initial antibiotic therapy was not shown to alter the course of persistent otitis media with effusion after acute otitis media. Resolution rates were 59% by 1 month and 74% by 3 months.

Studies of the natural outcome of recurrent acute otitis media draw data from investigations studying the efficacy of antimicrobial prophylaxis (Rosenfeld & Kay, 2003). The control groups of children with recurrent acute otitis media are treated with standard antibiotic therapy for subsequent episodes, rather than long-term antibiotics. The outcome of interest is the natural prognosis for recurrence, rather than total resolution. Beginning with an average rate of ≥ 5.5 annual episodes of acute otitis media per child, the cumulative recurrence rate over a median observation period of 6 months was 2.8 annual acute otitis media per child. 41% of the children had no additional episodes of acute otitis media while on the placebo, and 83% have only 2 or fewer episodes. Only 17% of children remained otitis prone. However, many studies excluded children with baseline otitis media with effusion, immune deficiency, cleft palate, craniofacial anomalies, or Down syndrome. In those with underlying predisposing factors for acute otitis media or otitis media with effusion, spontaneous improvement is likely to be lower (Rosenfeld & Kay, 2003).

Rosenfeld's analysis (2003) offers optimistic outcomes for the majority of the population with high certainty, but he advises that population data does not equate results on the patient level. Without forgetting about the minority of the population who do not improve spontaneously, he advises that statistics cannot replace judgment in deciding who to treat and

who to observe. Nonetheless, there should be realistic treatment expectations based on best evidence synthesis. In light of this favorable evidence for natural resolution, the American Academy of Pediatrics (Lieberthal et. al, 2013) currently supports an initial observation period before initiating antibiotics. The child is monitored for 48-72 hours of “watchful waiting” in which only pain medications are utilized. After this stage, the child is re-evaluated and only then prescribed antibiotics if symptoms appear to persist or worsen. Clinical judgment is vital when selecting candidates for an initial observation period as opposed to initial antibiotic therapy. Patient-related factors such as age, co-existing conditions, other sensory deficiencies, socioeconomic class, parental language input, and sensory deprivation must be considered (Alper et. al, 2004) when predicting the natural history of otitis media.

Since Rosenfeld (2003) drew his data for acute otitis media from control groups of no therapy which ethically could not include very young children or those with very severe symptoms, it was admittedly not a random subset of children at risk for acute otitis media. Consequently, Rosenfeld (2003) cautioned that generalizations about the natural course of otitis media based on this study cannot be extended to all children aged 2 years or younger, particularly those with severe symptoms or high fever. When antibiotics are withheld from a young child, the risk of suppurative complications is relatively unknown and therefore an initial observation period is not appropriate. Prompt antibiotic therapy will be prescribed. For the rest of the population however, the Agency for Healthcare and Research Quality (Berkman et. al, 2013) evidence report on acute otitis media also concluded that suppurative complications were not increased if antibiotics were withheld but close follow-up was provided.

The natural history of otitis media with effusion is favorable as well, but with some variation by population and outcome (Rosenfeld & Kay, 2003). As mentioned previously,

almost 60% of effusions beginning after an episode of untreated acute otitis media resolve within a month, and close to 75% resolve by 3 months. Using a strict resolution criterion of conversion from absent tympanometric peak pressure (Type B tympanogram) to normal static admittance with normal tympanometric peak pressure (Type A tympanogram) for newly diagnosed cases of otitis media with effusion of unknown duration, the combined resolution rate was 20% by 3 months, growing to 72% by 6 months and 81% by 9 months. Since complete follow-up decreases with time, there is limited data available for outcomes beyond 12 months of observation. With otitis media with effusion of defined onset using a liberal criterion of tympanometric improvement from absence of tympanometric peak pressure (Type B tympanogram) to presence of tympanometric peak pressure (non-B tympanogram) in two different studies, resolution rates were dramatically higher: 67-72% by 1 month, 86%-95% by 3 months, and 98-100% by 6 months. For children with bilateral otitis media with effusion of known onset and persisting for 4 months or longer, resolution rates for one or both ears using liberal criterion were 16% by 1 month, 47% by 3 months and 65% by 6 months. Evidently, resolution rates in clinical practice will vary based on the definition of disease and outcome. In reality, the diagnostic criteria currently relied upon tend to be more liberal, using otoscopy or pneumatic otoscopy, with or without substantiation by tympanometry.

Otitis media with effusion is extremely dynamic, which affects a given child's odds for spontaneous resolution. When otitis media with effusion recurs over several years, episode duration seems to be similar, whether it is initial or recurrent (Hogan et. al, 1997). Prognosis of otitis media with effusion detected in May through August is most favorable, while otitis media with effusion detected September through February is the worst.

Initially, chronic otitis media with effusion resolves spontaneously in a manner similar to newly diagnosed cases of otitis media with effusion using strict criterion (Rosenfeld & Kay, 2003). By 3 months, 19% of ears with chronic otitis media with effusion no longer had effusions, rising to 25% by 6 months, and stabilizing at 31-33% at 1-2 years. Maw and Bawden (1994) reported longer term resolution rates using pneumatic otoscopy. There was 59% resolution at 4 years, 69% at 5 years, 85% at 7 years, and 95% at 10 years. On otoscopic findings however, untreated otitis media with effusion persisted for a median of 6.1 years. Abnormal tympanometric findings for untreated otitis media with effusion persisted for a median of 7.8 years.

Rosenfeld (2003) offered several mechanisms of spontaneous resolution for otitis media. The resolution of acute otitis media was related to the child's immune response and clearance of secretions through a patulous Eustachian tube. Although symptom relief may be evident, the complete clearance of middle ear effusions may be slowed because of persistent inflammation and mucosal edema. The trend for improvement in recurrent acute otitis media is typically gradual, and attributed to immune maturation, Eustachian tube growth, and regression from first clinical trial to a mean symptom state. He related the resolution of otitis media with effusion to a combination of drainage and absorption as the Eustachian tube matures, as well as the gradual reduction of the local immune response.

Influencing more favorable circumstances for the natural history of otitis media

Vaccines to prevent pneumococcal disease can decrease the incidence of acute otitis media (Jansen et. al, 2009). Additionally, they might be able to limit episodes of sinusitis and pharyngitis, which would otherwise further eustachian tube dysfunction and contribute to otitis media with effusion. The character of otitis media with effusion may change in the future as rates of vaccination rise, since bacterial infections will be largely diminished from the disease process

(Berkman et. al, 2013). For this reason, the American Academy of Pediatrics and American Academy of Family Practice (Lieberthal et. al, 2013) recommend the pneumococcal conjugate and annual influenza inoculations for all children according to updated schedules. Additionally, they advise clinicians to promote exclusive breastfeeding for 6 months or longer.

MEDICAL AND SURGICAL TREATMENT OPTIONS FOR ACUTE OTITIS MEDIA

The updated guidelines from the American Academy of Pediatrics and American Academy of Family Practice (Lieberthal et. al, 2013) proposed that acute otitis media management should begin with pain evaluation and treatment. Antibiotics should be prescribed for children at least 6 months old with severe signs or symptoms (moderate or severe otalgia or otalgia for 48 hours or longer or a fever) and in children aged 6-23 months with bilateral acute otitis media. Non-severe acute otitis media in children above age 2 may be managed with antibiotics, or with close follow-up and withholding antibiotics unless the child worsens or does not improve within 48-72 hours of symptom onset. The antibiotic of choice is Amoxicillin, unless the child received it within 30 days, has concurrent purulent conjunctivitis, or is allergic to penicillin. In those situations, an antibiotic prescription with additional B-lactamase coverage is indicated. If symptoms have not responded to initial treatment or worsened within 48-72 hours, the clinician should re-evaluate and consider a change in treatment (Waseem et. al, 2014).

The Centers for Disease Control and Prevention (CDC) has attempted to influence management recommendations for acute otitis media due to concerns about increasingly resistant strains of *S pneumonia* (Waseem et. al, 2014). They recommended using a higher dosage for first-line treatment, in order to achieve greater susceptibility of the bacteria. For the second-line therapy, after documenting true clinical failure of therapy after at least 3 days of treatment with high dose amoxicillin, the CDC suggested tympanocentesis in order to identify and guide

alternate antibiotic therapy through susceptibility testing of the etiologic bacteria. Since few primary care physicians routinely perform tympanocentesis in the office, a recommendation for empirical second-line administrations was issued, including high dose amoxicillin/clavulanate; oral cefuroxime axetil; and intramuscular ceftriaxone (injection). According to the FDA approval, these drugs penetrate at sufficient concentrations in the middle ear fluid for bacteriocidal action against the common pathogens in acute otitis media (including drug resistant *Streptococcus pneumoniae* and *H-influenzae*). However, several arguments have been made against this model of drug efficacy (Waseem et. al, 2014). First, although bacteriologic eradication guarantees clinical success, it is not actually needed in over 60% of patients, whose clinical success occurs even when bacteriologic eradication is not achieved. Eventually, almost all patients improve spontaneously. The CDC may have underestimated the efficacy of other antibiotics which concentrate intracellularly and have bacteriostatic action. The standards used to define bacterial killing have been questioned. Patient compliance and the associated factors of dosing frequency, duration of treatment, palatability, and drug cost were not addressed.

When treating children with acute otitis media, compliance, duration of therapy, and cost are extremely important issues that must be considered amidst recommendations (Waseem et. al, 2014). The most influential factors for compliance seem to be the frequency of dosing, palatability of the agent, and duration of therapy. Less frequent doses are more appealing than more frequent ones which interfere with daily routines. Shorter duration of therapy, such as 5-7 days versus 10-14 days, also promotes compliance but should only be used when equal clinical efficacy is expected. Above all, palatability will determine compliance in young children.

Benefit from antimicrobial treatment is not widespread across children, either because their etiology of disease may not be bacterial, or because their immune systems clear the

infection without use of a drug (Waseem et. al, 2014). Since no clinical criteria exist to distinguish these children who do not require antibiotic therapy, practitioners generally do not withhold initial antimicrobial therapy for proven cases of acute otitis media. However, due to an increasing awareness of the pathophysiology of disease among parents and practitioners, there has been a rise in observation-only approach in emergency departments with less parental anxiety (Waseem et. al, 2014). The wait-and-see approach should be chosen on the basis of joint decision-making with the parents and with a safety mechanism in place to give antibiotics if symptoms do not improve in 48-72 hours. It is important to note that an initial period of observation is not associated with a greater risk of complications when compared to those receiving immediate treatment (Marcy et. al, 2001).

In cases of recurrent acute otitis media, prophylactic antibiotics are not recommended, due to concerns about long duration of antibiotic exposure and potential side effects (Rosenfeld et. al, 2013). Rather, tympanostomy tubes are the preferred option to minimize the number of acute otitis media episodes, especially when antimicrobial prophylaxis fails. However, it is important to recognize that these management options for acute otitis media are only effective for as long as the antibiotics are taken, or for the duration of tympanostomy tube stay time, respectively (Qureishi et. al, 2014). A gap in the literature exists as to whether the treatments for otitis media with effusion reduces recurrent acute otitis media, which is another crucial outcome for parents and providers even when hearing and other functional outcomes do not show an effect.

MEDICAL AND SURGICAL TREATMENT OPTIONS FOR OTITIS MEDIA WITH EFFUSION

Many clinical questions still exist regarding the best treatment approach for chronic otitis media, with insufficient evidence to provide confident answers. The majority of the literature uses a narrow scope to define interventional outcomes: reduced otitis media with effusion or improved hearing (Berkman et. al, 2013). The Agency for Healthcare Research Quality comparative effectiveness review (Berkman et. al, 2013) found only a few studies which examined language development and behavior problems, and a few quality of life outcomes. They discovered no studies which focused on parental and patient satisfaction with care or health care utilization. Little is known about these important broader outcomes, which would otherwise allow superior guidance of individualized treatment decisions. In situations of uncertainty, Berkman et. al (2013) state that clinicians must synthesize recommendations in clinical practice guidelines, their experience and expert opinion, and individual patient and family-level shared decision making.

Another shortcoming in the literature on treatments for otitis media with effusion is that studies do not consistently examine harms. The Agency for Healthcare Research and Quality review (Berkman et. al, 2013) revealed a lack of uniform assessment standards for the same treatment, and even a lack of consistent indices used by investigators to report on the same measure. These deficiencies in methodology prevent quantitative summaries from being performed, and conclusions are not easily reached regarding long-term effects of otitis media with effusion due to lack of standardized instrumentation and outcome measures. For any given comparison, time-frames are rarely uniform, which further prevents generalizations to be made through a proper meta-data analysis.

Otitis media with effusion is unlike many other medical diagnoses because nearly all cases of otitis media with effusion will resolve with time, with no intervention (Berkman et. al, 2013). Even though the disease is highly prevalent, it is transient in most children and does not require medical or surgical intervention unless it becomes chronic (Bluestone, 2004). The question for intervention therefore becomes whether shortening the patient's time with effusion will improve other important outcomes (Berkman et. al, 2014). The current guidelines in the United States and the United Kingdom recommend a 3-month period of observation with serial audiometry and assessment of the degree of hearing loss and the impact on a child's development before determining the need for treatment. These guidelines recommend either ventilation tube surgery or hearing aids, although guidelines are not always followed (Daniel et. al, 2013). Neither intervention is without associated risks, and both approaches are ultimately reliant upon the natural resolution of the predisposing factors for otitis media with effusion, as can be expected in the majority of children with increasing age (Qureishi et. al, 2014).

Two major therapeutic approaches have emerged in response to this endemic, which resolve the majority of cases either on their own or in combination. Drug therapy and surgical treatment are considered the framework for management options. Drug therapy encompasses antimicrobials, antihistamine-decongestants, intranasal and systemic steroids, nonsteroidal anti-inflammatory drugs, mucolytics, and aggressive management of allergic symptoms. Surgical treatment refers to myringotomy with or without intubation, associated or not with adenoidectomy. As time passes and traditional treatments reveal their shortcomings, delayed treatment, autoinflation, and complementary and alternative medicine are also becoming increasingly appealing.

Of the medical options, only antimicrobial therapy provides measurable benefits (Waseem et. al, 2014). However, antimicrobial therapy for otitis media with effusion presents as a murky option, as no clinical guidelines or consensus recommendations suggest which antimicrobials to use as first-line agents for otitis media with effusion. Selection of an antibiotic agent is dependent upon the clinician's proficiency, as it must be individualized to the patient based on prior experience, age, sex, and daycare attendance in order to limit further failures and antibiotic resistance. Studies of prolonged treatment in patients with otitis media with effusion show no advantage in therapies that last longer than 10 days (Waseem et. al, 2014).

Oral and intranasal steroids have been repeatedly proven to be ineffective as treatment for otitis media with effusion (Berkman et. al, 2013) in both the short term and the long term, either with the addition of antibiotics or without. They are not currently recommended in any major guidelines, nor are they approved by the U.S. Food and Drug Administration for treating children with otitis media with effusion. The current guidelines from the American Academy of Pediatrics actually recommend against the use of oral and intranasal steroids in treating otitis media with effusion in children (Lieberthal et. al, 2013). The risks of steroid administration have been found to outweigh potential benefits. For some reason, these pharmaceutical agents are still a commonly used intervention even though they have not demonstrated additional benefit. However, one study by Rosenfeld (1996) reported that surgery was avoided or postponed for 6 months in 25% of children treated with steroids. Therefore, steroid administration may have a use in children who are not good surgical candidates. The steroid regimen is typically oral prednisone or prednisolone for 5-7 days, administered in combination with a beta-lactam antibiotic (Waseem et. al, 2014).

When otitis media with effusion is unresponsive to medical therapy, or when middle ear effusion persists more than 12 weeks, the patient is typically referred to an otolaryngologist to discuss surgical options in conjunction with further medical therapies. Early surgical interventions such as tympanocentesis may be performed by primary care physicians, but more invasive procedures require an otolaryngologist (Waseem et. al, 2014). Evidence shows that surgical interventions decrease time with effusion compared with watchful waiting, and that tympanostomy tubes improves hearing in the short term (Berkman et. al, 2013).

Tympanocentesis is defined as the surgical puncture of the tympanic membrane with needle aspiration of fluid from the middle ear, with proper analgesia given to the patient 30 minutes before the procedure (Shaikh et. al, 2011). By identifying pathogens in the specimen of fluid obtained, antimicrobial therapy can be customized for the patient. Tympanocentesis is indicated when a patient with otitis media is seriously ill or appears toxic. It may be indicated following unsatisfactory response to antimicrobial therapy, or if the otitis media is associated with a confirmed or potential suppurative complication. This procedure will also be performed in cases of otitis media in a newborn, sick neonate, or patient who is immunologically deficient, any of whom may harbor an unusual organism (Waseem et. al, 2014)

Myringotomy is an operation which is typically performed under general anesthesia. An antero-inferior radial incision is made into the tympanic membrane and all fluid is removed using suction, thereby relieving the pressure caused by an excessive buildup of fluid and draining all pus from the middle ear (Smith & Greinwald, 2011). A ventilation tube is typically then placed at the incision site through the eardrum, to keep the middle ear aerated for a prolonged time and to prevent reaccumulation of fluid. Children are typically discharged well on the next

day (Abdullah et. al, 2007). Children with tympanostomy tubes can usually swim or bathe without specific precautions such as earplugs or headbands (Waseem et. al, 2014).

Without the insertion of a tube, the incision usually heals spontaneously in two to three weeks. Depending on the type, the tube is either naturally extruded in 6 to 9 months after placement (Qureishi et. al, 2014) or removed during a minor procedure (Smith & Greinwald, 2011). Beverley Armstrong is credited for having introduced the vinyl tube in 1954 (Rimmer, 2007), making today's most common surgical procedure of childhood over 70 years old. Ventilation tubes are alternatively referred to as grommets, tympanostomy tubes, and pressure equalization tubes.

Most guidelines recommend consideration of tympanostomy tube placement in children with bilateral otitis media with effusion lasting greater than three months, after an unresponsive trial of antibiotic therapy. When the otitis media with effusion is unilateral, the consideration point for tympanostomy tubes will be at 6 months duration, if there is evidence of tympanic membrane structural abnormality secondary to otitis media with effusion or if the patient has recurrent acute otitis media. However, careful observation would be sufficient if hearing is normal in the affected ear and there is no evidence of the above criteria (Waseem et. al, 2014). The current trend by clinicians is to refer patients with prolonged effusion and a mild to moderate hearing loss to otolaryngologists for placement of tympanostomy tubes. If the child's duration of otitis media with effusion does not meet criteria for chronic disease but its cumulative duration over the year is considered excessive, tympanostomy tube insertion is recommended (Waseem et. al, 2014). Tympanostomy tubes are also recommended for children who experience eustachian tube dysfunction not relieved by medical treatment, even in the absence of middle ear effusion, as other symptoms could include fluctuating hearing loss,

disequilibrium, tinnitus, autophony, and severe retraction pocket threatening cholesteotoma. Clinicians are also swifter to intervene surgically when otitis media with effusion has persisted due to the physiological and developmental possibility that a conductive hearing loss could worsen speech and language outcomes, either in the short term or in the long term (Berkman et. al, 2013). When unilateral or bilateral otitis media with effusion is unlikely to resolve quickly, children at risk for developmental difficulties may benefit from tympanostomy tubes (Waseem et. al, 2014), such as those children with permanent hearing loss, speech-language or developmental delay/disorder, autism spectrum disorder, Down syndrome, craniofacial disorders, and cleft palate.

The American Academy of Otolaryngology-Head and Neck Surgery Foundation issued a guideline in July 2013 on the use of tympanostomy tubes in children aged 6 months to 12 years with otitis media (Waseem et. al, 2014). They acknowledge that many children with otitis media with effusion improve spontaneously, especially when effusion is present for less than 3 months. They recommend against surgery for children with a single episode lasting under 3 months. Age-appropriate hearing evaluation must be performed before surgery and for all children with persistent otitis media with effusion. Tympanostomy tubes should be offered to children with impaired hearing and bilateral otitis media with effusion lasting over 3 months, but surgery is more justifiable when there are associated symptoms such as vestibular symptoms, school or behavioral problems, ear discomfort, or lower quality of life. They actually advised against the use of tympanostomy tubes in cases of recurrent acute otitis media without middle ear effusion. However, tympanostomy tubes are recommended in cases of persistent middle ear effusion in order to prevent future incidence of acute otitis media and to facilitate treatment of acute otitis media with ear drops instead of oral antibiotics.

Based on a “small and uneven body of evidence,” the Agency for Healthcare Research and Quality (Berkman et. al, 2013) ultimately concluded that tympanostomy tubes decreases effusion and improves hearing over a short period of time relative to myringotomy alone, watchful waiting, or delayed treatment. Children with a history of otitis media with effusion prolonged greater than 3 months are more likely to demonstrate resolution of effusion for up to 2 years after the procedure (Berkman et. al, 2013). The marginal benefit with respect to hearing thresholds is observed up to six months after tube placement. Nonetheless, shorter periods of time may be important for the youngest children (under age 3) who are still developing their speech and language skills. Results specific to this group are sorely lacking in the literature (Berkman et. al, 2013).

In other words, as more time passes from the point of tympanostomy tube insertion, differences in hearing and effusion become smaller and less significant. Overall, differences have not been found in speech, language, and functional outcomes. In practice however, parents often request tympanostomy tubes because they hope that it will minimize the time that their children are ill and in pain (Berkman et. al, 2013). It remains to be proven whether this intervention or other treatment options affect these outcomes.

Tympanostomy tubes are more likely to decrease the time with persistent middle ear effusion, with strong evidence to support effects on middle ear effusion lasting more than 1 year, and moderate evidence to support effects on middle ear effusion lasting more than 2 years, compared to watchful waiting or delayed treatment. Although the practice of referring for tympanostomy tubes is widespread, the Agency for Healthcare Research and Quality (Berkman et. al, 2013) found no evidence of differences in long-term functional outcomes of quality of life

between subjects who had tympanostomy tube placement and those who had only watchful waiting for otitis media with effusion.

When comparing effectiveness among types of tympanostomy tubes, the length of the tube seems to have a direct effect on how long the tube is retained in the ear. Otitis media with effusion recurrence at 1 year or longer was higher in the shorter term tympanostomy tubes (Berkman et. al, 2013). There was no effect on hearing outcomes based on design, placement technique, or material. Evidence of effect on clinical outcomes other than hearing was insufficient to demonstrate differences.

Ventilation tube insertion is associated with a number of risks (Berkman et. al, 2013), including purulent otorrhea (10%-26%), myringosclerosis (39%-65%), retraction pockets (21%), and persistent tympanic membrane perforations (3%). Perhaps the most alarming risk pointed out by Schmidt (1990) is death from general anesthetic complications, estimated at 1 per 5,000 to 10,000 procedures. The tympanostomy tubes designed to be retained in the ear for a longer period of time are more effective in limiting recurrence of otitis media with effusion (Berkman et. al, 2013), but they are also related to a higher risk for persistent tympanic membrane perforations (up to 24%) (Vlastarakos et. al, 2007). One trial of short term tubes reported that 20-25% of children required a second set of tubes within 2 years (Daniel et. al, 2012). There is insufficient evidence to state which routine of insertion yields the best reduction of effusion with the least harms, nor is it known whether these outcomes differ for younger versus older individuals (Berkman et. al, 2013). The age at which untreated effusion is most deleterious for the child is also uncertain (Berkman et. al, 2013). Additionally, since the tubes manage but do not cure the underlying otitis media with effusion, fluid may return to the middle ear once the tubes extrude.

The worldwide rate of chronic suppurative otitis media has been found to be a problem not only in developing nations, but also in industrialized countries, because of the rising popularity of tympanostomy tube surgery. Appropriate treatment of acute otorrhea is recommended to prevent chronic disease. Chronic suppurative otitis media without cholesteatoma is usually prevented by timely and effective treatment of otorrhea that is associated with attacks of acute otitis media (Bluestone 2004).

Concerns regarding outcomes in the long term are complicated by the fact that effusions resolve in the overwhelming majority of patients without intervention. However, it is unknown how long a mild to moderate hearing loss can be present before effecting negative impact on a child. It is also crucial to consider the developmental stage of the child in this equation, because outcomes may differ at varying points in a child's growth. It is interesting to note that a series of studies by Paradise et al. (2005) found no difference in long-term functional outcomes between preschool children who delayed 9-12 months in insertion of tympanostomy tubes after otitis media with effusion onset with a mild hearing loss, compared to those who underwent earlier insertion. However, it is unknown whether a toddler is able to tolerate the same degree of hearing loss without compromising their language development. As alluded to previously, studies comparing tympanostomy tubes to other surgical or non-surgical treatments do not consistently document the type of tympanostomy tube used, which also limits the conclusions which can be made about those comparisons (Berkman et. al, 2013).

Adenoidectomy refers to the surgical removal of the adenoids from the back of the nasal cavity. The adenoids belong to the infection-fighting lymphatic system, but are generally considered to be a vestigial organ beyond the age of 1. The procedure is performed under general anesthesia and was originated by William Meyer in 1867. Although adenoidectomy is normally

associated with obstructive sleep apnea, it is often considered for children with recurrent otitis media previously treated with tympanostomy tubes, either alone or combined with tonsillectomy (Brietzke & Gallagher, 2006). Surgery for adenoidectomy is more invasive, which raises concern that it may threaten more serious complications than tympanostomy tubes. However, there is limited evidence which details or estimates this risk (Berkman et. al, 2013).

Less is known about long-term outcomes of adenoidectomy, particularly with respect to functional outcomes (Berkman et. al, 2013). Adenoidectomy is thought to have a role in preventing recurrent otitis media with effusion, but due to associated risks it is typically not recommended as a primary treatment of otitis media with effusion, unless there are frequent or persistent upper respiratory infections (Qureishi et. al, 2014). When assessing the probability of otitis media with effusion resolution at 6 months and 1 year follow-up, adenoidectomy is superior to no treatment in improving resolution. However, effects on hearing are mixed. Adding adenoidectomy to myringotomy seems to enhance time with effusion and hearing outcomes at 24 months (Berkman et. al, 2013), and some evidence suggests that adding adenoidectomy to tympanostomy tubes may provide further benefit as well. Studies are lacking comparing adenoidectomy alone to tympanostomy tubes alone. Relative to myringotomy, adenoidectomy alone is an effective treatment for middle ear effusion. Adenoidectomy added to tympanostomy tubes offers superior outcomes to tympanostomy tubes alone. There is no difference in hearing outcomes when tympanostomy tubes or myringotomy is added to adenoidectomy, compared to adenoidectomy alone (Berkman et. al, 2013).

With respect to chronic suppurative otitis media, the definitive management is usually surgical. A variety of techniques are available to repair the tympanic membrane and remove infection. However, conservative treatment consisting of regular aural toilet followed by the use

of antibiotics, antiseptics and topical steroids (Marchisio et. al, 2013) is sometimes appropriate, serving the aim of reducing bouts of recurrent discharge, infection, and therefore associated hearing loss (Woodfield & Dugdale, 2008). Medical management alone is based on patient choice, the absence of surgical options, when the effected side is the only hearing ear, or when the risks of surgery outweigh its benefit (Qureishi et. al, 2014).

ALTERNATIVE TREATMENT OPTIONS FOR OTITIS MEDIA

Autoinflation is a technique which opens and forces air through the eustachian tube by raising pressure in the nose (Perera et. al, 2013). This is accomplished by forced exhalation with a closed mouth and nose; blowing up a balloon through each nostril; use of an anesthetic mask; or a Politzer device. The goal is to introduce air into the middle ear via the eustachian tube, which will equalize the pressure and allow better drainage of effusion (Perera et. al, 2013). In the 1800's, Jean-Marc Gaspard Itard in France and Adam Politzer in Austria were the first to discuss the treatment of otitis media by addressing the permeability of the Eustachian Tube itself, and alterations which could control the development of middle ear disease. Their objective was not only to open the eustachian tube, but to normalize it. Unlike other methods of transtympanic drains of middle ear effusion, autoinflation techniques promote more permanent effects by targeting the pathogenic origin of middle ear effusion: the immaturity of the eustachian tube and its dysfunction. Mechanically, the opening of the eustachian tube acts to balance the pressure in the tympanic cavity as well as rehabilitate the periuvular musculature by increasing its tone (Saga et. al, 2009). Studies have suggested that transtympanic drainage alone has limited lasting effects, because it lacks this direct action component. Consequently, autoinflation techniques should be considered a viable alternative to conventional methods. This procedure is not typically used in the United States, but it offers an alternative noninvasive treatment strategy in older children. It has been increasing in popularity as a non-pharmacological approach.

Several methods of autoinflation have been proposed, since its advent. The Valsalva maneuver was the first recorded technique for pressurization of the middle ears, which was developed by Antonio Valsalva in the 1700's. The patient pinches his nostrils closed and pressure is increased in the chest. He then attempts to blow out of the closed nostrils while the cheek muscles are kept tight. This is generally considered the easiest and most intuitive of the techniques, but there are some discomforts with prolonged efforts.

The Politzer maneuver is the original concept of a medical procedure that aerates the middle ear by blowing air up the nose during the act of swallowing, thereby insufflating the Eustachian tube. The Politzer bag, devised by its namesake in 1863, is a soft rubber bulb with a tube that is inserted into the nose to increase air pressure in the nasopharynx while swallowing. The physician instructs the patient to swallow, and when the patient swallows he squeezes the bag. However, this technique had some engineering shortcomings due to the lack of control over amount of air pressure applied into the ear and the trouble coordinating with children between insertions of the air pressure and swallowing. Future devices were improved upon and modeled based on the original concept of Politzerization.

The EarPopper, developed by Shlomo Silman in 1999 (Silman & Arick, 1999) is a handheld, battery-operated device which releases a controlled volume of air according to the user's age, hearing loss, and amount of fluid in the ear. The device is intended for users aged 4 and older, and it can be used by the patient without medical supervision. Parents are instructed to administer the EarPopper twice daily, alternating nostrils. The total duration of air flow is under one second, and the control under specified parameters ensures the safety of the device. Using the EarPopper, middle ear effusion resolved in 74% of cases compared to only 26% in the control group (Arick & Silman, 2005). In the follow up study on cases not resolved through

initial therapy, the treatment period with the device was extended for another 3-4 weeks, leading to an increase from 74% to 84% overall success with the EarPopper (Silman et. al, 2005). As of 2007, the cost of in-patient tube insertion including myringotomy was \$22,930 (Russo et. al, 2010). In contrast, the cost of the commercially-available, home version EarPopper is currently \$169 (EarPopper website). Given its favorable efficacy, by beginning a trial period with an autoinflation device and reserving surgical intervention of PE tubes as a last resort, economic impact if more commonly adopted could be tremendous.

Another common method of autoinflation is Otovent treatment. The Otovent balloon is inserted into the nostril, and the user blows into the balloon. Air then blows back into the nose while the user swallows. The maneuver is typically performed three times daily. Blanshard et. al (1993) demonstrated significant improvement in pneumatic otoscopy and tympanometry among children who were on the waiting list for ventilation tube insertion. Compliance of over 70% was needed in order to observe improvement in middle ear effusion, which underscored the need to utilize this therapy regularly under supervision. However, there is generally limited acceptability to its users, as the mechanism is cumbersome, unpleasant, and difficult to use. Additionally, there is a possibility that bacteria can be forced from the nasopharynx into the middle ear during this procedure (Bluestone et. al, 1996).

Autoinflation devices are a simple mechanical means of improving otitis media with effusion. Although evidence is conflicting regarding the specific duration of use needed for a significant effect, findings broadly support a beneficial effect of autoinflation on the clinical resolution of middle ear effusion at least in the short term (Perera et. al, 2013). Beneficial outcomes are mostly in the area of tympanometry and composite outcomes, while autoinflation does not consistently appear to improve pure-tone audiometry thresholds. Nonetheless, outcome

measures for treatments of otitis media are beginning to be extended to quality of life measures which are important to parents and children, and may prove to be a worthy realm of benefit served by autoinflation.

A Cochrane Review (Perera et. al, 2013) concluded that use of autoinflation in the short term is favorable at 1 month and at 2 months, but given the small number of studies and the lack of follow-up, the long-term effects cannot be determined. It is also acknowledged that the type of device used may be critical in ascertaining the benefits of autoinflation. In Perera et. al (2013), Politzerisation was suspected to be more effective than the classic Otovent device or carnival blower with a balloon attached, but comparisons were made difficult due to different entry criteria used in the various studies.

As mentioned previously, compliance, duration of therapy and cost are important issues that must be considered amidst recommendations for otitis media. Because of the low cost and absence of adverse effects, the Cochrane Collaboration (Perera et. al, 2013) recommends that it is pragmatic to consider autoinflation whilst awaiting natural resolution of otitis media with effusion. They encourage the ongoing evaluation of such interventions in the primary care setting, with increased awareness and the ability to instruct and educate parents and children in their use. Anecdotally, the only adverse events for autoinflation appeared to be pain in select children when undertaking autoinflation and that continued enthusiasm for the procedure can diminish over time (Perera et. al, 2013). There is also some concern regarding the need for adherence, and whether children and parents will be willing to tolerate the inconvenience of the procedure. The most significant improvement tends to be noticed in those who have a high compliance for the duration of the treatment, which is why additional research is needed on

trends in compliance and adverse events, as well as evidence on how to attain good compliance (Perera et. al, 2013).

In response to the major concern of possible developmental sequelae over the course of otitis media with effusion, there is no current treatment that is proven to affect speech and language development, including tympanostomy tubes (Browning et. al, 2010). Although no studies on autoinflation currently address these outcomes, the Cochrane Collaboration (Perera et. al, 2013) concedes that there is a real possibility that watchful waiting without intervention may have similar long-term outcomes to any other intervention. As with any other valid drug therapy used to treat otitis media, specific characteristics of individual cases may cause treatment failure. Customarily, surgery would be opted for in those cases.

The Agency for Healthcare Research and Quality (Berkman et. al, 2013) planned to include Complementary and Alternative Medicine in its review, but failed to locate any studies which met its criteria. As such, there is no evidence regarding the efficacy of these treatments. Nonetheless, there has been increasing interest in the public in alternatives to surgical interventions or traditional medical management. There is an ongoing and potentially promising randomized controlled trial that is investigating the benefit of dietary modifications in treating patients with otitis media with effusion, which proposes an inclusion of a food allergy assessment into the standard treatment options for chronic otitis media with effusion in children. When indicated, subsequent dietary modifications in addition to standard surgical procedures would be taken. The role of adenoidectomy in this approach, if of any benefit, is also being studied (Berkman et. al, 2013).

Gastric reflux may play a role in otitis media with effusion, given the presence of high pepsin, a component of stomach fluid, in the middle ear fluid of children with chronic otitis media with effusion (McCoul et. al, 2011). The treatment of children who have otitis media with effusion with anti-reflux medications is currently being evaluated, but the risks associated with anti-acid use in children will need to be incorporated into treatment decisions (van der Pol et. al, 2011).

AUTHOR'S CONCLUSIONS ON A PREFERRED METHOD OF TREATING OTITIS MEDIA

According to Rovers (2008), the “ideal treatment for otitis media should be preventive or curative, widely available, non-toxic, and rapidly effective at clearing the effusion, and would have a sustained effect.” This cannot begin without improved physician awareness and an improved dialogue with their patients. Considerable misunderstanding of the condition and the pathophysiology currently leads to inappropriate and ineffective treatment attitudes. After a careful diagnosis has been established, evidence is needed to support treatment decisions. Moving forward, trends in treatment should be consciously based on the modern understanding of the distinct disease processes of acute otitis media and otitis media with effusion. In this manner, medical and surgical treatments will be more accurately guided, treatment options will be presented honestly on an individualized basis, and there will be increased confidence in a conservative approach.

As verified in Rosenfeld and Kay (2003), antimicrobials have a proven efficacy for acute otitis media, but excellent outcomes are also attained in children with an initial observation period. Relief experienced by prophylactic treatment for recurrent acute otitis media is often similar to the relief of children whose intervention was delayed for 6 months. Although 3 months

of documented otitis media with effusion are typically recommended before otherwise healthy children undergo surgery, a relative increase of 30-50% in spontaneous resolution was observed if this period was extended to 6 months. Only periods of observation longer than 6 months were consistently unsatisfactory.

Compared to watchful waiting, tympanostomy tubes is promptly effective in reducing effusion and improving hearing (Berkman et. al, 2013). However, their enhanced effect is limited by virtue of the nature of middle ear effusion, which usually resolves even if left untreated. The Agency for Healthcare Research and Quality (Berkman et. al, 2013) acknowledged this finding even when including those who received tympanostomy tube intervention after an unsuccessful period of watchful waiting, indicating that the benefit is short-lived even in more severe cases.

In light of these findings, a delayed treatment approach at least up to 6 months is justifiable in many cases which currently receive formulaic pharmacological or surgical intervention despite their associated risks. If utilized indiscriminately, repeated antibiotic use can lead to decreased appetite, failure to thrive, and a longer term resistance even on a population level. When surgery is opted for excessively, children are exposed to the risks of unneeded anesthesia and require numerous follow-up appointments which result in school and work absences and ultimately become resentful. As the leading advantage of undergoing surgery, the prompt improvement in hearing offered by tympanostomy tubes may not be absolutely necessary if the child is being closely monitored and developing well. The study by Paradise et. al (2005) is encouraging in that no differences were found between early and delayed tube groups among children ages 6-9. However, there is an admittedly differential risk on development based on the child's age over the course of effusion, and it appears as though preschool children age 3-4 may be the most susceptible to deleterious effects of conductive hearing loss. Nonetheless, a parent

can compensate for the temporary hearing loss by holding their younger child closer to them when speaking, and by arranging for preferential seating in the classroom for improved access to the teacher's voice.

On the basis of joint decision-making, watchful waiting is arguably the appropriate course of treatment for a large percentage of patients with otitis media. Of course, to denounce antibiotics completely would be to revert to a pre-antibiotic era (Lieberthal et. al, 2013); and to shun surgical interventions would also disservice the part of the population who require stop-gap measures, such as those children who have co-existing conditions. Knowing how to differentiate the various prognoses for otitis media will allow us to direct the treatment appropriately and reserve interventions for those children at risk for a prolonged course of disease. As mentioned, the status of a child's hearing, speech, overall development, school performance and quality of life should always be considered when choosing a prolonged observation period.

The evidence regarding developmental delay specifically associated with untreated otitis media in the short term is highly uncertain and leaves room to believe that the long-term outcomes are similar regardless of the treatment course. Due to the prevalence of tympanostomy tube insertion as a treatment for otitis media and since the root cause of pathology is now recognized to be eustachian tube dysfunction in most cases, it seems prudent to allow patients the option to habilitate this aspect before surgery is recommended. In contrast to the traditional methods which only treat the symptoms of otitis media with effusion, autoinflation techniques target the underlying cause in efforts of providing more lasting effects. Not only do Politzerization devices help empty the fluid contents of the middle ear, but they also strengthen the muscles of the Eustachian tube. By the adopting these practical techniques at home, the improvement noticed over the period of watchful waiting holds even greater potential.

Based on this author's clinical experience at a well-known pediatric audiology practice in New York with numerous cases of otitis media encountered daily, the overwhelming majority of parents are resistant to surgery. They are improperly educated about the procedure by their doctors, with tympanostomy tubes threatened from an early stage. Even when informed of their child's moderate hearing loss, parents try to postpone procedures for as long as they can. They often cite home remedies that have been informally recommended to them to avoid surgery, including ear drops and vitamins with unlikely claims. It has become apparent that some parents are determined and desperate for at least a trial period with a conservative treatment before settling for an aggressive one. Based on promising evidence and personal experience, autoinflation techniques which have indeed been substantiated would be excellent candidates and very well-received by the general population if they were routinely recommended by physicians. Families with a significant history of otitis media could even use autoinflation devices preventatively, given the genetic component of the disease and trends evidenced in families. The very same attribute that causes susceptibility in the immature eustachian tube also enhances its permeability in rehabilitation. Finally, given the incidence of otitis media worldwide, these portable devices could be utilized in underdeveloped countries for a fraction of the cost of any other treatment available.

Given the vast room for improvement, it is no coincidence that otitis media investigators, including otolaryngologists, pediatricians, specialists in pediatric infectious disease, allergy, and immunology, research scientists, biostatisticians, audiologists, and speech pathologists have recently been identified as being in the 99th percentile of NIH awardees over the past 25-year period. It is with great hopes that papers such as this one will refine the presentation of the

disease as well as the available evidence on its treatments, in efforts of improving management methods to best serve our patients with otitis media.

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