Update on eustachian tube dysfunction and the patulous eustachian tube

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Purpose of review

The purpose of this review is to summarize the recent knowledge on eustachian tube dysfunction and the patulous eustachian tube.

Recent findings

A clinically useful test for eustachian tube function is still lacking. Narrowing of the isthmus alone was demonstrated to be an insufficient cause of otitis media. Inflammatory mediators identified within the eustachian tube and middle ear cells were causally linked with otitis media with effusion. Increasing evidence was found that allergic disease and reflux may be two of the most important contributors of tubal inflammation causing otitis media with effusion. The adenoid size and proximity to the torus tubaris may also be important in considering which patients with persistent otitis media with effusion may benefit from adenoidectomy. Computed tomography scan has documented loss of soft tissue within the cartilaginous eustachian tube in patients with patulous eustachian tubes. An endoscopic approach to seal the tubal lumen has been found to be effective in relieving patulous symptoms.

Summary

These studies suggest that allergic rhinitis and gastroesophageal reflux should be investigated in patients with eustachian tube dysfunction. Adenoidectomy should also be considered in patients who have adenoids that obstruct the torus tubaris. Patients with a patulous eustachian tube may benefit from an endoscopic closure. Further research is needed to identify a clinically useful test for eustachian tube dysfunction.

Keywords

eustachian tube, eustachian tube dysfunction, eustachian tube testing, patulous eustachian tube

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Abbreviations

CT computed tomography
TVP tensor veli palatini

1068-9508

Introduction

This paper summarizes the recent publications on eustachian tube dysfunction and the patulous eustachian tube. A Medline search of recent articles published since April 2004 was performed using the keywords *eustachian tube*, *patulous*, *eustachian tube dysfunction*, and *eustachian tube testing*. Publications not written in English and articles that focused on malignant neoplasms were excluded from the current review. Studies that investigated otitis media were included only if the main focus of the article was on eustachian tube dysfunction. The subject matter has been organized in the following subtopics: anatomy, dynamic function and physiology, etiology, diagnostic testing, and treatment.

Anatomy

Several authors have studied the anatomy of the eustachian tube. Maheshwar *et al.* [1•] further defined the roof of the parapharyngeal space by performing anatomic dissections on 10 specimens. They found that the tensor veli palatini (TVP) fascia partitions the roof into an anterolateral and anteromedial compartment, which contains the cartilaginous eustachian tube. Further work is needed to determine whether variations in this fascial partition play a role in the dynamic function of the cartilaginous eustachian tube. Jen *et al.* [2•], analyzing temporal bone computed tomography (CT) scans, demonstrated a 92% incidence of peritubal cells opening directly into the osseous eustachian tube lumen in patients with pneumatized petrous apices. They hypothesized that this finding may account for persistent cerebrospinal fluid rhinorrhea after cerebellopontine surgery if these cells are not recognized and tubal obliteration is not performed sufficiently far into the lumen. Their findings are in agreement with temporal bone histology showing similar results by Saim *et al.* [3]. Abe *et al.* [4•] dissected 119 half-heads and examined the origin and insertion of the TVP muscle. They confirmed a number of earlier studies that there are two origins of the TVP muscle: at the cranial base and along the eustachian tube. In our own cadaver dissections, we have noted origin attachments of the TVP along the lateral cartilaginous lamina as well as the membranous antero-medial wall of the ET. Some specimens in our collection even showed TVP attachments to a large keel-like structure of the medial cartilaginous lamina close to the isthmus where the medial cartilage extends inferiorly around to the anterolateral wall. A very broad origin of the TVP can also occur. In the study by Abe *et al.* [4•], the principle insertion site passed into the palatine aponeurosis, again confirming

earlier work. Secondary attachments were seen in some cadavers at the maxillary tuber and the palatoglossal arch. These findings suggest that if the hamulus is infractured during cleft palate surgery, the TVP function could be maintained by preserving the maxillary insertion. In a patient with bilateral cleft, Arnold *et al.* [5•] demonstrated an anomalous horizontal course of the eustachian tube. They found that the TVP muscle inserts at the posterolateral edge of the palatal cleft, whereas the levator veli palatini inserts at the medio-caudal edge. This finding supports earlier work that contraction of the levator palatini muscle may in fact cause eustachian tube obstruction rather than opening in patients with bilateral cleft palate. Finally, Bluestone *et al.* [6••] summarized the important contributions to the understanding of the anatomy and pathophysiology of middle ear disease since the Seventh International Symposium in Recent Advances in Otitis Media in June 1999. The references from this conference precede the dates of interest for this review, and the reader is referred to this excellent article as a review in itself.

Dynamic function and physiology

Cinamon [7•] used a plastic model of the middle ear and eustachian tube to examine its passive and dynamic properties. He found that eustachian tube obstruction by middle ear fluid may cause negative pressure in the middle ear even in the setting of an otherwise normally functioning eustachian tube. The ability to clear such fluid was dependent on the viscosity of the fluid, a finding confirming previous studies. Ghadiali *et al.* [8••] developed a computational technique using mid-cartilaginous images of the eustachian tube of normal adults to create a two-dimensional finite element model of the eustachian tube. Eustachian tube function was simulated by applying muscle forces in the appropriate direction where the muscle attached onto the soft tissue. In this model, they found that eustachian tube opening was highly dependent on the forces applied by the muscles and less dependent on the cartilage elastic properties. Kanick and Doyle [9••] studied a mathematical model of middle ear pressure regulation in the setting of atmospheric pressure changes. They documented buffering mechanisms that occur even in the presence of eustachian tube dysfunction. Such buffering mechanisms may include a hyper-compliant tympanic membrane and the mastoid space. These findings may explain why some patients with eustachian tube dysfunction do not experience barotrauma during cabin flight.

Four studies specifically examined gas exchange in the middle ear. Kanick *et al.* [10•] studied a mathematical model using morphometric measurements to estimate transmucosal gas diffusion in the middle ear. Similar compartmental exchange models have been successful in estimating pulmonary gas exchange; however, they found that this technique underestimates diffusion length, the distance that gas must diffuse across from the middle ear to the capillaries. They postulate that the main reason for this difference has to do with the relative uniformity and thinness of the alveolar walls compared with the variability and thickness of middle ear tissue. Kania *et al.* [11•] developed an experimental model in the rat ear to allow investigation of transmucosal gas exchange with variations of middle ear volume at constant pressure. Most prior animal studies have studied partial pressure differences as the main outcome measure. In their model, the eustachian tube was blocked by cauterizing it and then applying cyanoacrylate glue. A glass tube was then connected hermetically to the middle ear, allowing gas volume measurement. Their findings validated this model as a method for investigating transmucosal gas exchange.

Sade *et al.* [12•] used a plastic middle ear model to investigate how gas exchange would be affected by narrowing the isthmus of the eustachian tube. In their model, they found that there was no difference in gas exchange when the lumen of the eustachian tube was narrowed. Their conclusion was that tubal dysfunction could not be explained solely on the basis of the cross-sectional diameter of the isthmus and that other factors must be investigated. Yuksel *et al.* [13••], in a monkey model, investigated the role of nasal inflammation on N_2O gas exchange in the middle ear. They found that nasal challenge with prostaglandin, a known mediator of nasal inflammation, increases transmucosal inert gas exchange. They hypothesized that increased middle ear gas exchange, and therefore negative pressure generation, may contribute to otitis media in patients with nasal inflammatory conditions.

Inflammatory and infectious etiology

More than 600 articles were published on otitis media between April 2004 and April 2005. Of these articles, several focused on the role of the eustachian tube in the pathogenesis of otitis media. Nguyen *et al.* [14••] examined the cellular biology and cytokine profiles of the middle ear and torus tubaris in patients with otitis media. Middle ear fluid and nasopharyngeal biopsy specimens of atopic patients had higher levels of eosinophils, T lymphocytes, and Interleukin-4 (IL-4) $mRNA^+$ cells and lower levels of neutrophils and Interferon-gamma (IFN-γ) $mRNA^+$ cells compared with nonatopic patients. They conclude that in atopic patients, the allergic inflammation occurs on both sides of the eustachian tube. These findings support the concept of the middle ear as a component of the united airway in atopic patients. Lazo-Saenz *et al.* [15••] also found that patients with allergic rhinitis have a higher incidence of abnormal tympanograms compared with normal controls. Abnormal tympanograms were most frequently seen in children with allergic rhinitis under the age of 11 years. These latter two studies support the theory that environmental allergies may cause inflammatory changes and effusion in the middle ear.

With respect to gastroesophageal or laryngopharyngeal reflux causing eustachian tube dysfunction in children, Karkos *et al*. [16••] reviewed the current literature, which both supported and refuted this theory. They concluded that there was insufficient evidence to support the use of empirical antireflux treatment for the treatment of refractory middle ear effusions. Two studies looked at smoke exposure causing eustachian tube dysfunction. Effat [17•] examined *narghile* (water pipe) smoking, a common practice in Egypt, and found a higher incidence of attic retraction pockets compared with cigarette smokers. The increased negative intrapharyngeal pressure required to smoke with a *narghile* pipe was postulated as the cause. Da Costa *et al*. [18••] performed a case-controlled study of 750 children matched for age and sex. They found a higher incidence of otitis media in patients exposed to tobacco smoke, wood and charcoal smoke, short-term breast-feeding, and children living in overcrowded conditions. The findings of this study are consistent with earlier studies which have reported an association with parental smoking [19–21], upper respiratory tract infections [22,23], and short duration of breast-feeding [19,24,25].

Using a murine model of otitis media with effusion, Maeda *et al*. [26••] injected endotoxin derived from *Haemophilus influenza* into the middle ear. They found that eustachian tube blockage is essential for the induction of serous middle ear effusion and that the addition of endotoxin is associated with mucoid effusion, inflammatory cell infiltrate, and cytokine production. Lee *et al*. [27••] examined the antimicrobial activity of substances secreted by the eustachian tube and middle ear. They found that lysozyme and β-defensins can inhibit the growth of clinical isolates of otitis media pathogens. Wang *et al*. [28••] studied the protective effects of amifostine after irradiation in the middle ear with respect to Intercellular Adhesion Molecule 1 (ICAM-1) regulation. ICAM-1 is an intercellular adhesion molecule that mediates cell–cell adhesion by acting as a receptor for leukocyte surface antigens and is thought to play a role in early inflammation. They found that irradiation increased the expression of ICAM-1 in the middle ear mucosa and hypothesized that continuous ICAM-1 expression may cause eustachian tube stenosis.

Diagnostic tests and treatment

Straetemans *et al*. [29•] prospectively studied 136 children with a history of otitis media. The patients underwent three clinical tests of eustachian tube function and were followed over time to see which patients would develop recurrent otitis media. These tests were the forced response test, the pressure equalization test, and the sniff test. The forced response test assesses ventilatory function by gradually increasing the pressure in the middle ear until the eustachian tube opens. The pressure equalization test is a qualitative method to measure active eustachian tube function. Positive and negative pressures are applied to the middle ear, and the residual pressure is measured after several deglutinations. The sniff test is a measure of the capacity of the eustachian tube to protect the middle ear space against nasopharyngeal pressures. Patients are asked to sniff five times, and the middle ear pressure is recorded. They found that none of these tests were predictive of recurrent otitis media.

Uzun [30••] studied 31 scuba divers who underwent 774 dives. Predive information on smoking history, septal deviation, otitis media history, rhinosinusitis history, Valsalva, Toynbee, nine-step inflation-deflation tympanometry, and mastoid pneumatization was analyzed to determine whether barotrauma could be predicted prior to diving. Their findings showed that eustachian tube dysfunction as demonstrated by inflation/deflation tympanometry and a small mastoid size is predictive of barotrauma during diving.

Egeli *et al*. [31••] compared the adenoidal-nasopharyngeal (AN) index to tympanograms. Measurements for the AN ratio were obtained from lateral neck films. The measurement of A is the distance from the point of maximal convexity of the adenoid pad to the anterior basiocciput. The measurement of N is the distance between the poster border of the hard palate and the antero-inferior edge of the sphenobasioccipital synchondrosis. The AN ratio is obtained by dividing the measurement of A with N. The authors found that an AN ratio of greater than 0.71 was associated with middle ear effusions and type C tympanograms. In other words, patients with a relatively large adenoid pad and shallow nasopharynx are more likely to have middle ear effusion or negative middle ear pressure. Antibiotic therapy was effective in reducing the adenoid size but did not reverse tympanometric values. In our own work, we have endoscopically observed that a relatively large adenoid does not need to cover the eustachian tube orifice to cause obstructive problems. During swallows, pharyngeal constriction and palatal elevation can squeeze a large adenoid pad against the postero-medial surface of the posterior cushion (torus tubaris) of the eustachian tube orifice and force the cushion anteriorly. Dilation of the tubal orifice may be prevented by this temporary obstruction by the posterior cushion.

Nguyen *et al*. [32••] investigated whether the position and size of the adenoid affects outcome in patients requiring pressure equalization tubes. Two groups of patients were studied: patient with adenoids abutting and not abutting the torus tubaris. Each group was made up of about 30 patients. Patients were randomized to tympanostomy tube insertion alone compared with tube insertion and adenoidectomy. Patients with abutting adenoids who underwent tube insertion alone had a 50% failure rate. When adenoidectomy was performed concurrently, the failure rate

decreased to 17% ($P < 0.05$). Patient with nonabutting adenoids had no difference in their failure rates with and without adenoidectomy (40% and 37%, respectively). This work again supports our endoscopic observations of adenoid compression of the tubal orifice to be a significant mechanism for tubal obstruction.

Uzun *et al.* [33•] compared fascia and cartilage tympanoplasty after cholesteatoma surgery. The authors investigated whether cartilage tympanoplasty after cholesteatoma surgery could reverse or improve eustachian tube dysfunction. Eustachian tube function was assessed by the nine-step inflation/deflation tympanometric test and the Toynbee test at follow-up examinations. While graft material did not correlate with outcome of eustachian tube function, patients with persistent eustachian dysfunction had better hearing results with cartilage tympanoplasty. Finally, Bluestone [34••] reported on otitis media research at Children's Hospital of Pittsburgh since 1969 with 256 references. The references are prior to the dates of interest of this review, so the interested reader is referred to the primary text.

Yung *et al.* [35••] reported on a prospective trial of a percutaneous mastoid vent for the treatment of chronic eustachian tube dysfunction. In this study, 23 participants were enrolled. The vent was created by making a small mastoid defect with a special drill bit. The vent was placed into the antrum and allowed to drain percutaneously through the mastoid defect. At 18 months of follow-up, 20 of 23 vents remained patent, and 13 of 17 atelectatic ears had become near normal. The advantage of this vent is that it demonstrates long-term patency and may remain patent longer than long-acting tubes. It also allows irrigation to ensure patency. This may be advantageous in patients who have problems with crusting. The disadvantage of this procedure is the greater risk of mastoid surgery and the cosmetic defect of having an exposed tube behind the ear.

Patulous eustachian tube

Yoshida *et al.* [36••] examined 20 temporal bone CTs of patients with patulous eustachian tube and 25 normal controls. In the patulous eustachian tube group, the tubal lumen was patent throughout the cartilaginous portion ($P < 0.014$). They also found that the soft tissue corresponding to glandular tissue and Ostmann's fat was smaller in patients with a patulous eustachian tube. Kano *et al.* [37•] investigated the use of a novel audiometric test for assessing patulous eustachian tube. In this test, sound is presented to the nasopharynx and threshold testing is performed in the usual fashion. Threshold testing allows quantification of the severity of patulous eustachian tube and may be helpful to monitor patient progress. Orlandi and Shelton [38••] reported on eustachian tube occlusion in two patients with cerebrospinal fluid leak after lateral skull base or vestibular schwannoma surgery. Their endoscopic technique to cauterize the nasopharyngeal orifice and oversew it was successfully used on another cerebrospinal fluid leak case and one patulous eustachian tube case.

Conclusion

Several significant advancements made in the preceding year have increased our understanding of eustachian tube dysfunction and the patulous eustachian tube. The eustachian tube has a valve-like function within the cartilaginous portion where the mucosal surfaces are in apposition during the resting position. The tubal muscles must actively dilate the tubal valve open in order for adequate ventilation of the middle ear to occur. Failure of the valve to open adequately is likely responsible for a significant percentage of OME cases. Narrowing of the isthmus alone was demonstrated to be an insufficient cause for OME to occur. Active and passive exchange of middle ear gases occurs constantly within the middle ear, creating a continual trend toward negative pressure. The partial pressure of N_2 gas may be the driving force that determines how often the eustachian tube should open and ventilate the system.

Anatomic studies are increasing our knowledge of the active dilating muscles, the levator, and TVP. As CT and magnetic resonance imaging improve, these muscles may be better visualized even in real-time motion to improve our understanding of how they function or fail to function.

Inflammation of the tubal lumen is probably a major contributor to tubal dysfunction. Inflammatory mediators were identified within the eustachian tube and middle ear cells as causal links with OME. Research is needed to determine the etiology of these mediators and their mechanisms of action. Allergic disease, laryngo-pharyngeal reflux, persistent glue ear, sinusitis, Samter's (aspirin) triad, Wegener's disease, and other primary inflammatory disorders of the nasopharynx, eustachian tube, or middle ear can all be associated with otitis media, but the exact pathophysiology of middle ear effusion or infection remains to be elucidated. Increasing evidence was found that allergic disease and reflux may be two of the most important contributors to OME, causing tubal inflammatory responses that do not permit adequate dilation of the tubal valve. Inadequate tubal valve dilation may lead to increasing negative middle ear pressure with consequences of effusion, atelectasis, cholesteatoma, and other Otitis media complications. A great deal of research is still needed to explore these possible mechanisms of disease.

A clinically useful test for eustachian tube function is still lacking. Many tests will provide some objective measurements of the tube's opening process, but none to date have had any clinical relevance in predicting success for tympanoplasty or relief from OME. Current studies show that patients with persistent OME and large

adenoid size that abuts the posterior cushion (Torus tubaris) may benefit significantly from adenoidectomy.

The patulous eustachian tube is caused by incompetency of the tubal valve. It is a result of a longitudinal scaphoid defect in the antero-lateral wall of the cartilaginous tube's lumen that prevents complete closure of the valve. We have observed this defect endoscopically in all of our patulous tube cases, and there is now CT confirmation of these findings. An endoscopic approach to seal the tubal lumen has been found to be effective in eliminating cerebrospinal fluid rhinorrhea and relieving patulous symptoms. We developed an endoscopic approach for submucosal implantation of graft material to convert the concave defect into a normal convex bulge. This technique restores mucosal apposition, and we found that it relieves the patulous symptoms and preserves the tubal dilation function. Research is needed to determine the etiology of the patulous tube. Only a minority of our patients have identified pregnancy or weight loss as an etiology. Rheumatologic disorders, allergic disease, and reflux may also lead to atrophy of tubal tissues and cause patulous failure of the valve.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1 • Maheshwar AA, Kim EY, Pensak ML, *et al*. Roof of the parapharyngeal space: defining its boundaries and clinical implications. Ann Otol Rhinol Laryngol 2004; 113:283–288.
An anatomic study that looks at the boundaries of the parapharyngeal roof and cartilaginous eustachian tube.

2 • Jen A, Sanelli PC, Banthia V, *et al*. Relationship of petrous temporal bone pneumatization to the eustachian tube lumen. Laryngoscope 2004; 114: 656–660.
A retrospective study of temporal bone CTs examining the incidence of peritubal cells opening into the eustachian tube lumen.

3 Saim L, McKenna MJ, Nadol JB Jr. Tubal and tympanic openings of the peritubal cells: implications for cerebrospinal fluid otorhinorrhea. Am J Otol 1996; 17:335–339.

4 • Abe M, Murakami G, Noguchi M, *et al*. Variations in the tensor veli palatini muscle with special reference to its origin and insertion. Cleft Palate Craniofac J 2004; 41:474–484.
Cadaveric study in 119 specimens examining the insertion and origin of the TVP muscle.

5 • Arnold WH, Nohadani N, Koch KH. Morphology of the auditory tube and palatal muscles in a case of bilateral cleft palate. Cleft Palate Craniofac J 2005; 42:197–201.
Autopsy study of the eustachian tube and associated muscles in a patient with bilateral cleft.

6 •• Bluestone CD, Hebda PA, Alper CM, *et al*. Recent advances in otitis media, 2: eustachian tube, middle ear, and mastoid anatomy; physiology, pathophysiology, and pathogenesis. Ann Otol Rhinol Laryngol Suppl 2005; 194:16–30.
The authors summarize the important contributions to the understanding of the anatomy and pathophysiology of middle ear disease since June 1999.

7 • Cinamon U. Passive and dynamic properties of the eustachian tube: quantitative studies in a model. Otol Neurotol 2004; 25:1031–1033.
Using a plastic model of the middle ear, mastoid, and eustachian tube, the authors show that intratympanic fluid alone may cause negative pressure in the middle ear.

8 •• Ghadiali SN, Banks J, Swarts JD. Finite element analysis of active eustachian tube function. J Appl Physiol 2004; 97:648–654.
The authors developed a computational technique using mid-cartilaginous images of the eustachian tube of normal adults to create a two-dimensional model of the eustachian tube.

9 •• Kanick SC, Doyle WJ. Barotrauma during air travel: predictions of a mathematical model. J Appl Physiol 2005; 98:1592–1602.
Investigators studied a mathematical model of middle ear pressure regulation in the setting of atmospheric pressure changes.

10 • Kanick SC, Doyle WJ, Ghadiali SN, *et al*. On morphometric measurement of oxygen diffusing capacity in middle ear gas exchange. J Appl Physiol 2005; 98:114–119.
Using morphometric measurements, the examiners attempt to estimate the oxygen diffusion capacity in the middle ear.

11 • Kania R, Portier F, Lecain E, *et al*. Experimental model for investigating transmucosal gas exchanges in the middle ear of the rat. Acta Otolaryngol 2004; 124:408–410.
This study investigates the use of a rat model to measure transmucosal gas exchange in the middle ear.

12 • Sade J, Cinamon U, Ar A, *et al*. Gas flow into and within the middle ear. Otol Neurotol 2004; 25:649–652.
Using a Perspex model of the middle ear, the investigators examine the relationship of the diameter of eustachian tube isthmus on gas exchange in the middle ear.

13 •• Yuksel S, Doyle WJ, Banks J, *et al*. Nasal prostaglandin challenge increases N(2)O exchange from blood to middle ear. Auris Nasus Larynx 2005; 32: 29–32.
In a monkey model, the investigators examine the role of nasal inflammation on N_2O gas exchange in the middle ear.

14 •• Nguyen LH, Manoukian JJ, Sobol SE, *et al*. Similar allergic inflammation in the middle ear and the upper airway: evidence linking otitis media with effusion to the united airways concept. J Allergy Clin Immunol 2004; 114:1110–1115.
Investigators examine the cytokine and cellular profiles of the middle ear and nasopharynx in atopic patients, lending support for seasonal allergies as a cause of otitis media.

15 •• Lazo-Saenz JG, Galvan-Aguilera AA, Martinez-Ordaz VA, *et al*. Eustachian tube dysfunction in allergic rhinitis. Otolaryngol Head Neck Surg 2005; 132:626–629.
This study examines the incidence of abnormal tympanograms in patients with allergic rhinitis.

16 •• Karkos PD, Assimakopoulos D, Issing WJ. Pediatric middle ear infections and gastroesophageal reflux. Int J Pediatr Otorhinolaryngol 2004; 68:1489–1492.
Good review of the current data supporting gastroesophageal reflux as a cause of middle ear effusions in children.

17 • Effat KG. Otoscopic appearances and tympanometric changes in narghile smokers. J Laryngol Otol 2004; 118:818–821.
The study examined the otoscopic appearance of *narghile* smokers compared with cigarette smokers.

18 •• da Costa JL, Navarro A, Neves JB, *et al*. Household wood and charcoal smoke increases risk of otitis media in childhood in Maputo. Int J Epidemiol 2004; 33:573–578.
This is a case-controlled study of 750 patients that examined risk factors for eustachian tube dysfunction.

19 Rovers MM, Zielhuis GA, Straatman H, *et al*. Prognostic factors for persistent otitis media with effusion in infants. Arch Otolaryngol Head Neck Surg 1999; 125:1203–1207.

20 Owen MJ, Baldwin CD, Swank PR, *et al*. Relation of infant feeding practices, cigarette smoke exposure, and group child care to the onset and duration of otitis media with effusion in the first two years of life. J Pediatr 1993; 123: 702–711.

21 Kraemer MJ, Richardson MA, Weiss NS, *et al*. Risk factors for persistent middle-ear effusions: otitis media, catarrh, cigarette smoke exposure, and atopy. JAMA 1983; 249:1022–1025.

22 Persico M, Podoshin L, Fradis M, *et al*. Recurrent middle-ear infections in infants: the protective role of maternal breast feeding. Ear Nose Throat J 1983; 62:297–304.

23 Shimada J, Yamanaka N, Hotomi M, *et al*. Household transmission of Streptococcus pneumoniae among siblings with acute otitis media. J Clin Microbiol 2002; 40:1851–1853.

24 Fireman P. Otitis media and eustachian tube dysfunction: connection to allergic rhinitis. J Allergy Clin Immunol 1997; 99:S787–S797.

25 Chandra R. Prospective studies of breast feeding on the incidence of infection and allergy. Acta Paediatr Scand 1979; 68:691–694.

26 •• Maeda K, Hirano T, Ichimiya I, *et al*. Cytokine expression in experimental chronic otitis media with effusion in mice. Laryngoscope 2004; 114: 1967–1972.
Using a murine model of otitis media with effusion, the authors found that eustachian tube blockage is essential for the induction of serous middle ear effusion and that the addition of endotoxin is associated with mucoid effusion, inflammatory cell infiltrate, and cytokine production.

27 Lee HY, Andalibi A, Webster P, *et al*. Antimicrobial activity of innate immune
•• molecules against Streptococcus pneumoniae, Moraxella catarrhalis and nontypeable Haemophilus influenzae. BMC Infect Dis 2004; 4:12.
Authors examine the antimicrobial activity of secreted substances of the eustachian tube and middle ear. They found that lysozyme and β-defensins can inhibit the growth of clinical isolates of otitis media pathogens.

28 Wang SZ, Chen ZC, McNamar JP, *et al*. The relationship between the pro-
•• tective effect of amifostine and decreased intercellular adhesion molecule 1 expression. Am J Otolaryngol 2005; 26:118–122.
The authors studied the protective effects of amifostine after irradiation in the middle ear. They found that irradiation increased the expression of ICAM-1 in the middle ear mucosa and hypothesize that continuous ICAM-1 expression may cause eustachian tube stenosis.

29 Straetemans M, van Heerbeek N, Schilder AG, *et al*. Eustachian tube function
• before recurrence of otitis media with effusion. Arch Otolaryngol Head Neck Surg 2005; 131:118–123.
Authors studied the forced response test, the pressure equalization test, and the sniff test to predict recurrent OME in children with a history of OME.

30 Uzun C. Evaluation of predive parameters related to eustachian tube dysfunction
•• for symptomatic middle ear barotrauma in divers. Otol Neurotol 2005; 26:59–64.
This study examines the predictive factors that lead to barotrauma during diving. A nine-step inflation/deflation tympanometry and a small mastoid size are predictive of barotrauma during diving.

31 Egeli E, Oghan F, Ozturk O, *et al*. Measuring the correlation between adenoi-
•• dal-nasopharyngeal ratio (AN ratio) and tympanogram in children. Int J Pediatr Otorhinolaryngol 2005; 69:229–233.
Authors compared the AN index with tympanograms and found that an increased AN ratio was associated with middle ear effusions and type C tympanograms.

32 Nguyen LH, Manoukian JJ, Yoskovitch A, *et al*. Adenoidectomy: selection cri-
•• teria for surgical cases of otitis media. Laryngoscope 2004; 114:863–866.
Authors investigated whether the position and size of the adenoids affect outcome of patients requiring pressure equalization tubes. They report on a prospective randomized trial and found that patients with adenoids abutting the torus tubaris benefit from adenoidectomy.

33 Uzun C, Caye-Thomasen P, Andersen J, *et al*. Eustachian tube patency and
• function in tympanoplasty with cartilage palisades or fascia after cholesteatoma surgery. Otol Neurotol 2004; 25:864–872.
Authors compared fascia and cartilage tympanoplasty with respect to eustachian tube function after cholesteatoma surgery.

34 Bluestone CD. Studies in otitis media: Children's Hospital of Pittsburgh-
•• University of Pittsburgh progress report – 2004. Laryngoscope 2004; 114: 1–26.
This is a review of otitis media research at Children's Hospital of Pittsburgh since 1969.

35 Yung MW, Bowdler D, Swan IR. The Yung percutaneous mastoid vent: re-
•• sults of a multicenter trial. Otol Neurotol 2004; 25:885–890.
Authors report on a percutaneous mastoid vent for the treatment of chronic eustachian tube dysfunction. At 18 months of follow-up, 20 of 23 vents remained patent, and 13 of 17 atelectatic ears had become near normal.

36 Yoshida H, Kobayashi T, Takasaki K, *et al*. Imaging of the patulous eustachian
•• tube: high-resolution CT evaluation with multiplanar reconstruction technique. Acta Otolaryngol 2004; 124:918–923.
This study examined temporal bones of patients with and without a patulous eustachian tube. In patients with a patulous eustachian tube, they found a patent cartilaginous eustachian tube at rest as well as a decreased volume of Ostmann's fat.

37 Kano S, Kawase T, Baba Y, *et al*. Possible new assessment of patulous eu-
• stachian tube function: audiometry for tones presented in the nasal cavity. Acta Otolaryngol 2004; 124:431–435.
Authors investigated the use of a novel audiometric test for assessing patulous eustachian tube. In this test, sound is presented to the nasopharynx, and threshold testing is performed in the usual fashion.

38 Orlandi RR, Shelton C. Endoscopic closure of the eustachian tube. Am J Rhi-
•• nol 2004; 18:363–365.
The authors report on one patient with a patulous eustachian tube and two patients with cerebrospinal fluid leak who successfully underwent closure of the eustachian tube using an endoscopic technique.