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Emerging techniques for otitis media

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Abstract
There is an immediate need for additional research into the pathophysiology of otitis media because it is still a leading cause of antibiotic prescriptions, surgeries, and outpatient visits in India. However, new therapies for the prevention and treatment of this disorder have not been developed. Acute otitis media, chronic otitis media, and tympanostomy tube implantation have all recently had new therapy recommendations released. This article discusses exciting new technology that are being studied for innovative methods to improve the diagnosis of otitis media. New insights into genetics and mucosal immunology have shed light on the pathophysiology behind otitis media propensity. Treatment options for this condition could improve greatly as a result of future research into changing these pathophysiologic underpinnings, maybe by means of trans tympanic medication delivery devices. New methods for studying the causes, symptoms, and treatments of otitis media have made great strides in recent years. Clinical practice is anticipated to include strategies aimed at substantially altering the illness's diagnosis and treatment during the next few years.

Keywords: Mucin MUC5B, optical coherence tomography, otitis media diagnosis, otitis media guidelines

Introduction
In otitis media (OM), an infection causes inflammation in the middle ear cleft and fluid to leak into the middle ear; this condition may occur with or without tympanic membrane rupture [1-2]. In India, the prevalence rates of ASOM range from 17–20%, CSOM from 7.8%, and OME from an unknown source [3]. Middle ear effusion (MEE) and sudden development of infection in the middle ear are symptoms of acute otitis media (AOM). Common symptoms include fever and otalgia, which are indicators of an infection. Chronic mucoid effusion without fever or otalgia is the hallmark of otitis media with effusion (OME) [4]. With 80% of children having had OME by the time they are 10 years old, it is clear that this ailment is rather common. Emergence of new-onset OME may occur when the inflammatory process subsides but MEE continues after an AOM [5]. The most prominent sign of chronic semi-otitis media (CSOM), which is defined as inflammation of the middle ear and mastoid cavity, is the presence of persistent or recurrent ear discharge via a ventilation tube or a hole in the tympanic membrane [6]. When CSOM affects the ossicles in the middle ear, it causes conductive hearing loss. It also increases the likelihood of neurological issues and sensorineural hearing loss, which is a kind of permanent hearing loss caused by damage to the inner ear [6]. This disease is more common in countries with low or medium incomes, while its incidence varies substantially among countries [7].

Aetiopathogenesis
Role of Eustachian tube
Extremely important is the fact that the ET continues to malfunction in newborns even after the first AOM assault has passed. The ET plays a vital role in determining the likelihood of AOM's recurrence since their main duties include protecting, cleaning, and ventilating the middle ears. The tensor velum platinum muscle contracts every time the middle ear deglutitive, allowing air to equalize with ambient pressure and ventilating the middle ear. When the external auditory tube (ETT) becomes clogged, a negative pressure rises inside the middle ear, leading to effusion and aspiration of secretions from the nose and throat. The ability of polymorphonuclear cells to destroy germs is diminished when there is inadequate ventilation, which leads to a decrease in PO2. The middle ear becomes infested with aerobic

and anaerobic microbes due to impaired clearance. When the ET becomes abnormally flaccid and less compliant, however, reflux otitis occurs [8-9]. In young children, ET dysfunction is a major problem because to the small diameter and horizontal orientation of the ET, which causes a high incidence of AOM and several relapses of each viral infection. Damoiseaux *et al*. [10] included 210 AOM patients less than 2 years old in their prospective study, and the poor long-term prognosis was explained by this.

Role of bacteria and virus

During the first year of life, newborns typically get RSV (respiratory syncytial virus). A prospective study [11] included 42 babies with bronchiolitis, ranging in age from 2 months to 24 months. Of them, 26 developed AOM either at enrollment or within 10 days, and 10 had OME. From the whole group of patients observed for three weeks, just six were able to avoid both AOM and OME. A more recent research corroborated these findings when it showed that 31% of patients with middle ear effusions that still contained RSV antigen returned after receiving effective treatment for their first episode of AOM [12]. Seventy percent of AOM patients may have microbes found in their middle ear fluid when the test is conducted [9]. The two most common types of bacteria found in human samples are *Streptococcus pneumoniae* and *Haemophilus influenzae* [13]. Important facts about the bacteria causing AOM could be revealed by nasopharyngeal aspirate culture [14–17].

Other risk factors

Due to their immature immune systems, young children are unable to combat encapsulated pathogens. Because of this, not only does ET dysfunction explain AOM's long duration, but too explains the significant likelihood of recurrence. Additional risk factors include being a smoker, having younger siblings in the household, and a family history of AOM. In a 1997 publication of a prospective study on 2,253 children aged 2 months to 2 years, these traits were found [18]. At the 12-month mark, 79% of patients had OME, whereas at the 24-month mark, 91% did. Lower socioeconomic status and frequent exposure to other children at home or at day care facilities were the most significant risk factors. The results were unaffected by breastfeeding or being around cigarette smoke.

Signs and symptoms of Otitis Media

Only half to two-thirds of children with AOM report experiencing ear discomfort, despite it being the most prevalent symptom [19, 20]. Preverbal children may experience ear pain more acutely if they are pulled, stroked, or held, if they cry for an extended period of time, or if their sleep or activity patterns alter [21]. Symptoms such as nausea, vomiting, fever, and lack of specificity do not differentiate between URTI and AOM in children [22]. MEE is critical for the diagnosis of AOM and OME; without it, neither disorder can be determined [21]. Overdiagnosis of AOM is common, and one reason for this is the difficulty in confirming MEE in primary care settings [23-25]. Possible causes of ear discharge or visible discharge in the external ear canal include acute otitis externa, chronic stenosis of the middle ear (CSOM), acute tympanic membrane perforation (AOM), or draining ventilation tubes (ASVT). One important feature that may be noticed by otoscopy to diagnose AOM is a bulge of the tympanic membrane [21].

Diagnostic Modalities

In order to diagnose AOM, an otoscopy is performed. To further assess the illness, a symptom severity scale may be used. Pneumatic otoscopy is the gold standard for diagnosing OME, with otomicroscopy and tympanometry rounding out the panel. Parents have the option to assess MEE using acoustic reflectometry. While otoscopy or otomicroscopy may detect CSOM-related tympanic membrane perforation, suctioning out ear discharge may be necessary for precise visualization. The main diagnostic method for OME is pneumatic otoscopy because to its strong diagnostic accuracy [26]. Due to the typical appearance of the tympanic membrane and the moderate or nonexistent nature of ear-related symptoms, otoscopy alone may fail to detect OME in the absence of a pneumatic bulb. Contrarily, pneumatic otoscopy helps avoid false diagnoses of OME caused by anomalies in the tympanic membrane surface that do not include MEE [26]. Pneumatic otoscopy improves diagnostic accuracy in comparison to otoscopy alone [28–29] and is a strong predictor of otomyositis media efficacy [20, 27]. The therapeutic uses of pneumatic otoscopy do, however, differ by locale. Training medical residents in pneumatic otoscopy is challenging [21], but it may be made better using a structured computer software that incorporates both static and moving images of the tympanic membrane [24]. Tympanometry enables the objective measurement of middle ear function as well as tympanic membrane movement [30]. When compared to pneumatic otoscopy, tympanometry has a lower specificity (50–75% vs. 80%), but it is just as sensitive (range: 90–94%) in diagnosing OME [31]. Although tympanometry is more successful and easier to use than pneumatic otoscopy in treating OM in children, problems with equipment cost and training make it difficult to implement in primary care settings [32]. Another measurement obtained by tympanometry is the amount of air in front of the probe. In children, this normally ranges from 0.3 to 0.9 ml. It is recommended to use a 1,000 Hz probe tone for newborns less than 6 months of age while doing tympanometry, since the 226 Hz tone is not responsive to MEE [33].

Symptoms severity scale for AOM

Several validated parent-reported symptom measures have been developed to assess the severity of AOM. There are seven items on the AOM Severity of Symptoms Scale (AOMSOS), and the answer possibilities range from "no," "a little," or "a lot" for the frequency of fever [34], irritability, trouble sleeping, trouble eating, ear pain, and ear tugging within the past twelve hours. Although children with normal ears may also exhibit some or all of these symptoms to varying degrees, the aggregate AOMSOS score may differentiate between children with and without AOM. One alternative measure of severity, the AOM Faces Scale (AOMFS), uses a seven-point scale with 1 representing no difficulty at all and 7 representing a major one [35].

Acoustic Reflectometry

The quantity of sound that is reflected off the tympanic membrane is measured by acoustic reflectometry; a higher reflectivity is associated with a higher chance of middle ear explosion (MEE) [36]. Compared to tympanometry, it has a number of benefits, such as being easy to use, not requiring a hermetic seal, and being available in an economical consumer form [37]. In order to keep tabs on their child's

middle ear health, parents may use these features. Other tests show that reflectometry is not as sensitive or specific. Due to its high specificity and negative predictive values, reflectometry is superior than tympanometry in eliminating MEE in children.

Image-Based Ultrasound

Optical coherence tomography (OCT) is a noninvasive imaging technique that detects changes in human tissues in real time. With a low-intensity light source, it creates 2D and 3D structure photographs with resolution on the micron scale. Because fluid particles scatter the imaging signal, the resulting image of reflected light may be utilized to determine fluid properties and differentiate between fluid and air [38].

Management

The misuse of antibiotics in modern times is leading to an increase in bacterial resistance. Antibiotics are prescribed by the American Academy of Pediatrics (AAP) for children less than 2 years old with a severe sickness (fever > 39.8 degrees, considerable otalgia, or toxic appearance) or a bilateral infection. Recent studies have shown that antibiotics are effective in alleviating symptoms and illnesses in these cases [39–40], with 10 days of treatment being better than 5 [41]. In cases when the patient's age exceeds 2, their otitis media is not severe, or if the diagnosis is uncertain, "watchful waiting" is recommended. The first line of treatment usually involves a high dosage of amoxicillin (90 mg/kg). If your kid is allergic to amoxicillin, there are two great oral cephalosporin alternatives: cefdinir and cefuroxime. If symptoms do not improve after 72 hours, it is recommended to administer injectable ceftriaxone or a high-dose of amoxicillin-clavulanate. As an alternative to cephalosporins, patients with severe type I penicillin allergies should use clindamycin (30-40 mg/kg daily, divided into three doses) [42]. When AOM keeps happening, myringotomy should be considered. The latest guidelines state that if a patient has had three episodes in the last six months or four events in the last year, and if a neurologist or otolaryngologist finds middle ear effusion (MEE) in either ear during the examination, tubes should be put [43]. After three months, OME usually improves without any further treatment. If MEE continues for more than three months, a referral to an otolaryngologist and a hearing test will be required. When OME persists for more than three months, surgical intervention may be necessary. This is particularly true for children who are at increased risk for other developmental delays, including Down syndrome, autism, late language acquisition, permanent hearing loss, craniofacial abnormalities, blindness, or any combination of these conditions. According to the guidelines made in 2016, children should be tested every three to six months until the MEE is no longer present. Antibiotics should not be given [26]. Other than placebo and spontaneous remission, no nonsurgical therapies for MEE have been shown to be more effective at this time. Therefore, new therapeutic approaches are urgently needed to lessen the surgical burden on young children. Infections, delayed speech development, hearing loss, and the risk of middle ear damage in the long run are all signs of chronic otitis media (COM) [44–46]. Research has shown that topical quinolones are more effective than topical antiseptics, systemic antibiotics, and no pharmaceutical treatment in eliminating CSOM-related auditory discharge in the short term (less than four weeks) [47-48]. The advantage of quinolones is that they are not ototoxic [49], however, there is currently equivocal data comparing the effectiveness of eardrops containing quinolones to those without [48]. Based on the little study that has been conducted, it seems that patients with CSOM would not have any greater benefit from a combination of systemic and topical antibiotics compared to topical antibiotics alone [47]. According to two reviews that compared two different autologous graft materials—i.e., temporalis muscle fascia tympanoplasty and cartilage tympanoplasty—to repair tympanic membrane perforation, the former resulted in fewer postoperative perforations and no differences in hearing. Novel, noninvasive treatments for otitis media may be on the horizon, thanks to recent advances in our knowledge of the immunologic pathways that drive the disease's growth. In order to describe MEE, unbiased large-scale proteome profiling was used, which revealed that the primary mucin glycoprotein found in COM effusions is MUC5B [52]. Also, several neutrophil extracellular traps (NETs) that connect with MUC5B were the primary macromolecular components of MEE [53]. Muc5b null mice have severe, spontaneous middle ear and upper airway infection [54], demonstrating that Muc5b is essential for defense of the middle ear and upper airway. Interestingly, there has been a recent association between mutations in the fucose transferase FUT2 gene and an increased chance of developing otitis media (55). This finding raises the idea that mucin glycosylation impacts innate immune responses in the middle ear. Although NETs and MUC5B serve as beneficial antimicrobial defense structures, it is crucial to promptly remove them from airway surfaces in order to prevent the harmful effects of inflammation [56-57]. In some cases, bacteria are able to persist despite bactericidal antibiotic treatment or elude immune responses because middle ear NETs may integrate into bacterial biofilms [58]. One new approach to treating chronic otitis media is to remove middle ear NETs using DNAse treatment [59].

Transtympanic drug delivery

If children could be effectively medicated transtympanicly without undergoing surgery, systemic antibiotics, pain, or general anesthesia, the current treatment for AOM or COME would be much improved, if not revolutionized. When treating AOM, it is possible to topically apply higher doses of antibiotics to the middle ear without worrying about systemic adverse effects. Potentially available medications in COM or CSOM could target mucin viscosity, biofilms, or NETS. There have been several developments in the field of transtympanic drug delivery techniques in recent years. Perhaps the most well-established approach showing safety and effectiveness in chinchilla models is the application of chemical permeability augmentation agents to allow the filtration of drugs, such antibiotics, into the ear. A new approach has been published that demonstrates the active delivery of small molecules (or drugs) into the middle ear in ex-vivo mice [61]. Finally, a transtympanic method has been proposed by some researchers [62] that involves using magnets to propel magnetic nanoparticles encased in drugs across the tympanic membrane. In the next years, clinical trials will likely use one or more of these strategies.

Conclusion

Research into novel methods for the detection, evaluation, and treatment of otitis media has made great strides in recent years. Approaches of drastically altering the disease's diagnosis and treatment are anticipated to be implemented into clinical practice over the next several years.

References

1. Bluestone CD. Otitis media, atelectasis, and Eustachian tube dysfunction. Pediatric otolaryngology; c1990. p. 320-486.
2. Pratt-Harrington D. Galbreath technique: A manipulative treatment for otitis media revisited. Journal of Osteopathic Medicine. 2000 Oct 1;100(10):635-639.
3. Lazo-Sáenz JG, Galván-Aguilera AA, Martínez-Ordaz VA, Velasco-Rodríguez VM, Nieves-Rentería A, Rincón-Castañeda C. Eustachian tube dysfunction in allergic rhinitis. Otolaryngology: Head and Neck Surgery. 2005 Apr;132(4):626-629.
4. Duah V, Huang Z, Val S, *et al*. Younger patients with COME are more likely to have mucoid middle ear fluid containing mucin MUC5B. Int J Pediatr Otorhinolaryngol. 2016;90:133-137.
5. Chonmaitree T, *et al*. Viral upper respiratory tract infection and otitis media complication in young children. Clin. Infect. Dis. 2008;46:815-823.
6. Verhoeff M, Van Der Veen EL, Rovers MM, Sanders EAM, Schilder AGM. Chronic suppurative otitis media: A review. Int. J Pediatr. Otorhinolaryngol. 2006;70:1-12.
7. Monasta L, *et al*. Burden of disease caused by otitis media: systematic review and global estimates. PLoS ONE. 2012;7:e36226.
8. Bluestone CD, Klein JO. Otitis media with effusion, atelectasis, and Eustachian tube dysfunction. In: Bluestone CD, Stool SE (eds) Pediatric otolaryngology. Saunders, Philadelphia; c1983. p. 356-512.
9. Paradise JL. Otitis media in infants and children. Pediatrics. 1980;65:917-943.
10. Damoiseaux RA, Rovers MM, Van Balen FA, Hoes AW, De Melker RA. Long-term prognosis of acute otitis media in infancy: determinants of recurrent acute otitis media and persistent middle ear effusion. Fam Pract. 2006;23:40-45.
11. Andrade MA, Hoberman A, Glustein J, Paradise JL, Wald ER. Acute otitis media in children with bronchiolitis. Pediatrics. 1998;101:617-619.
12. Sagai S, Suetake M, Yano H, Yoshida M, Ohyama K, Endo H, *et al*. Relationship between respiratory syncytial virus infection and acute otitis media in children. Auris Nasus Larynx. 2004;31:341-345.
13. Leibovitz E, Satran R, Piglansky L, Raiz S, Press J, Leiberman A, *et al*. Can acute otitis media caused by *Haemophilus influenzae* be distinguished from that caused by *Streptococcus pneumoniae*? Pediatr Infect Dis J. 2003;22:509-515.
14. Libson S, Dagan R, Greenberg D, Porat N, Trepler R, Leiberman A, *et al*. Nasopharyngeal carriage of *Streptococcus pneumoniae* at the completion of successful antibiotic treatment of acute otitis media predisposes to early clinical recurrence. J Infect Dis. 2005;191:1869-187.
15. Samuelson A, Freijd A, Jonasson J, Lindberg AA. Turnover of non-encapsulated *Haemophilus influenzae* in the nasopharynges of otitis-prone children. J Clin Microbiol. 1995;33:2027-2031.
16. Spinola SM, Peacock J, Denny FW, Smith DL, Cannon JG. Epidemiology of colonization by nontypable *Haemophilus influenzae* in children: A longitudinal study. J Infect Dis. 1986;154:100-109.
17. Syrjanen RK, Herva EE, Makela PH, Puhakka HJ, Auranen KJ, Takala AK, *et al*. The value of nasopharyngeal culture in predicting the etiology of acute otitis media in children less than two years of age. Pediatr Infect Dis J. 2006;25:1032-1036.
18. Paradise JL, Rockette HE, Colborn DK, Bernard BS, Smith CG, Kurs-Lasky M, *et al*. Otitis media in 2253 Pittsburgh-area infants: prevalence and risk factors during the first two years of life. Pediatrics. 1997;99:318-333.
19. Shaikh N, *et al*. Responsiveness and construct validity of a symptom scale for acute otitis media. Pediatr. Infect. Dis. J. 2009;28:9-12.
20. Rothman R, Owens T, Simel DL. Does this child have acute otitis media? JAMA. 2003;289:1633-1640.
21. Lieberthal AS, *et al*. The diagnosis and management of acute otitis media. Pediatrics. 2013;131:e964-e999.
22. Laine MK, Tähtinen PA, Ruuskanen O, Huovinen P, Ruohola A. Symptoms or symptombased scores cannot predict acute otitis media at otitis-prone age. Pediatrics. 2010;125:1154-1161.
23. Rosenfeld RM. Diagnostic certainty for acute otitis media. Int. J Pediatr. Otorhinolaryngol. 2002;64:89-95.
24. Kaleida PH, *et al*. Mastering diagnostic skills: Enhancing proficiency in otitis media, a model for diagnostic skills training. Pediatrics. 2009;124:e714-e720.
25. Pichichero ME, Poole MD. Assessing diagnostic accuracy and tympanocentesis skills in the management of otitis media. Arch. Pediatr. Adolesc. Med. 2001;155:1137-1142.
26. Rosenfeld RM, *et al*. Clinical practice guideline: otitis media with effusion (update). Otolaryngol. Head Neck Surg. 2016;154:S1-S41.
27. Karma PH, Penttilä MA, Sipilä MM, Kataja MJ. Otoscopic diagnosis of middle ear effusion in acute and non-acute otitis media. I. The value of different otoscopic findings. Int. J Pediatr. Otorhinolaryngol. 1989;17:37-49.
28. Jones WS, Kaleida PH. How helpful is pneumatic otoscopy in improving diagnostic accuracy? Pediatrics. 2003;112:510-513.
29. American Academy of Pediatrics. Section on Infectious Diseases. A view through the otoscope: distinguishing acute otitis media from otitis media with effusion.
30. Onusko E. Tympanometry. Am. Fam. Physician. 2004;70:1713-1720.
31. Takata GS, *et al*. Evidence assessment of the accuracy of methods of diagnosing middle ear effusion in children with otitis media with effusion. Pediatrics. 2003;112:1379-1387.
32. Abbott P, Rosenkranz S, Hu W, Gunsekera H, Reath J. The effect and acceptability of tympanometry and pneumatic otoscopy in general practitioner diagnosis and management of childhood ear disease. BMC Fam. Pract. 2014;15:181.

33. Hunter LL, Preve BA, Kei J, Sanford CA. Pediatric applications of wideband acoustic immittance measures. Ear Hear. 2013;34(1):36S-42S.
34. Shaikh N, *et al*. Development and preliminary evaluation of a parent-reported outcome instrument for clinical trials in acute otitis media. Pediatr. Infect. Dis. J. 2009;28:5-8.
35. Friedman NR, *et al*. Development of a practical tool for assessing the severity of acute otitis media. Pediatr. Infect. Dis. J. 2006;25:101-107.
36. Combs JT, Combs MK. Acoustic reflectometry: spectral analysis and the conductive hearing loss of otitis media. Pediatr. Infect. Dis. J. 1996;15:683-686.
37. Erkkola-Anttinen N, Laine MK, Tähtinen PA, Ruohola A. Parental role in the diagnostics of otitis media: Can layman parents use spectral gradient acoustic reflectometry reliably? Int. J. Pediatr.
38. Monroy GL, Pande P, Nolan RM, *et al*. Noninvasive in vivo optical coherence tomography tracking of chronic otitis media in pediatric subjects after surgical intervention. J Biomed Opt. 2017;22:1-11.
39. Tahtinen PA, Laine MK, Huovinen P, *et al*. A placebocontrolled trial of antimicrobial treatment for acute otitis media. N Engl J Med. 2011;364:116-126.
40. Hoberman A, Paradise JL, Rockette HE, *et al*. Treatment of acute otitis media in children under 2 years of age. N Engl J Med. 2011;364:105-115.
41. Hoberman A, Paradise JL, Rockette HE, *et al*. Shortened antimicrobial treatment for acute otitis media in young children. N Engl J Med. 2016;375:2446-2456.
42. Siegel RM. Acute otitis media guidelines, antibiotic use, and shared medical decision-making. Pediatrics. 2010;125:384-386.
43. Rosenfeld RM, Schwartz SR, Pynnonen MA, *et al*. Clinical practice guideline: tympanostomy tubes in children. Otolaryngol Head Neck Surg. 2013;149:S1-S35.
44. Klein JO. The burden of otitis media. Vaccine. 2000;19(1):S2-S8.
45. Teele DW, Klein JO, Rosner BA. Otitis media with effusion during the first three years of life and development of speech and language. Pediatrics. 1984;74:282-287.
46. Johnson DL, McCormick DP, Baldwin CD. Early middle ear effusion and language at age seven. J Commun Disord. 2008;41:20-32.
47. Macfadyen CA, Acuin JM, Gamble CL. Systemic antibiotics versus topical treatments for chronically discharging ears with underlying eardrum perforations. Cochrane Database Syst. Rev. 2006;1:CD005608.
48. Macfadyen CA, Acuin JM, Gamble CL. Topical antibiotics without steroids for chronically discharging ears with underlying eardrum perforations. Cochrane Database Syst. Rev. 2005;4:CD004618.
49. Pappas S, *et al*. Topical antibiotic ear drops: are they safe? Int. J Clin. Pract. 2006;60:115-119.
50. Iacovou E, Vlastarakos PV, Papacharalampous G, Kyrodimos E, Nikolopoulos TP. Is cartilage better than temporalis muscle fascia in type I tympanoplasty? Implications for current surgical practice. Eur. Arch. Otorhinolaryngol. 2013;270:2803-2813.
51. Mohamad SH, Khan I, Hussain SS. Is cartilage tympanoplasty more effective than fascia tympanoplasty? A systematic review. Otol. Neurotol. 2012;33:699-705.
52. Preciado D, Goyal S, Rahimi M, *et al*. MUC5B is the predominant mucin glycoprotein in chronic otitis media fluid. Pediatr Res. 2010;68:231-236.
53. Val S, Poley M, Brown K, *et al*. Proteomic characterization of middle ear fluid confirms neutrophil extracellular traps as a predominant innate immune response in chronic otitis media. PLoS One. 2016;11:e0152865.
54. Roy MG, Livraghi-Butrico A, Fletcher AA, *et al*. Muc5b is required for airway defence. Nature. 2014;505:412-416.
55. Santos-Cortez RLP, Chiong CM, Frank DN, *et al*. FUT2 variants confer susceptibility to familial otitis media. Am J Hum Genet. 2018;103:679-690.
56. Cheng OZ, Palaniyar N. NET balancing: a problem in inflammatory lung diseases. Front Immunol. 2013;4:1.
57. Hong W, Juneau RA, Pang B, Swords WE. Survival of bacterial biofilms within neutrophil extracellular traps promotes nontypeable *Haemophilus influenzae* persistence in the chinchilla model for otitis media. J Innate Immun. 2009;1:215-224.
58. Juneau RA, Pang B, Weimer KE, *et al*. Nontypeable *Haemophilus influenzae* initiates formation of neutrophil extracellular traps. Infect Immun. 2010;79:431-438.
59. Hornton RB, Wiertsema SP, Kirkham LA, *et al*. Neutrophil extracellular traps and bacterial biofilms in middle ear effusion of children with recurrent acute otitis media–a potential treatment target. PLoS One. 2013;8:e53837.
60. Yang R, Sabharwal V, Shlykova N, *et al*. Treatment of *Streptococcus pneumoniae* otitis media in a chinchilla model by transtympanic delivery of antibiotics. JCI Insight. 2018;3:123415.
61. Kurabi A, Schaerer D, Chang L, *et al*. Optimisation of peptides that actively cross the tympanic membrane by random amino acid extension: a phage display study. J Drug Target. 2018;26:127-134.
62. Shapiro B, Kulkarni S, Nacev A, *et al*. Shaping magnetic fields to direct therapy to ears and eyes. Annu Rev Biomed Eng. 2014;16:455-481.

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