Influenza Virus and its Relationship with Bacterial Otitis Media: A Review

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Abstract

Influenza virus is a common viral pathogen that can contribute to the progress of otitis media, particularly in children. The connection between influenza and otitis media primarily involves the virus's impact on the upper respiratory tract. Influenza infection can lead to inflammation and problems with the Eustachian tube, which disrupts normal the middle ear ventilation along with promotes fluid accumulation. This environment facilitates secondary bacterial infections or may allow direct viral invasion of the middle ear. Moreover, influenza weakens local immune defences, increasing susceptibility to ear infections. Clinical observations often show that otitis media occurs a few days following the start of flu signs such as fever, nasal congestion, and cough. Preventive measures, such as annual influenza vaccination, have been shown to reduce the incidence of otitis media through reducing its incidence and severity of influenza infections. Early diagnosis and appropriate treatment, based on if the etiologic is bacterial or viral, are essential for managing complications.

The different kinds of ear infections and the associated microorganisms that cause middle ear infections are discussed in this review paper. In order to identify ear infections, we describe the standard methods and clinical trials that employ them.

Keywords: Bacterial infection, Influenza Virus, Middle ear infection, Otitis media.

1. Introduction

All ages are susceptible to ear infections, although are more likely to get them. They are brought on by an infection, either bacterial or viral, that affects the middle, inner, or outer ear. In addition to the usual excruciating pain, the infection may also produce fever, transient hearing loss, or ear discharge. There are various types of ear infections, however the most typical ones are as follows: Otitis media acute (Prasad et al., 2020). A bacterial infection that causes a fluid accumulation causes Otitis media acute within the middle ear. Otitis media with effusion is far worse than Otitis media acute and causes an accumulation of fluid within the middle ear. Region Due to inflammation Tympanic membrane swelling is a sign of both types of otitis media. Because of this, clinically diagnosing Otitis media acute from Otitis media with effusion is challenging, the standard diagnostic method relies during the pneumatic otoscopy, considered "gold standard" for distinguishing between these two types (Lieberthal et al., 2013). Pneumatic otoscopes evaluate a movement of under pressure by producing the Tympanic membrane, A seal that is airtight, when fluid is added, the reaction will change accumulates in the rear the. Tympanic membrane, Besides the complex task of creating an airtight closure, the pneumatic otoscope cannot recognize the bacteria causing the infection or differentiate between viral and bacterial infections. Not distinguishing between acute otitis media from other type and/or bacterial and viral illnesses can result in antibiotic prescriptions, fostering drug-resistant microorganisms , As a result, There is a clinically unmet need for precise detection and identification of the bacteria causing otitis media ,The top three most common bacteria that cause these tow type of otitis media are *Moraxella catarrhalis* (Gram-negative), *Haemophilus influenza* "Gram-negative", and *Streptococcus pneumoniae* "Gram-positive" (Reid et al., 2009).

These bacteria are found in humans asymptomatically, Additionally, they mostly inhabit the upper respiratory tract. while sparsely populating the lower respiratory tract. Usually functioning as symbiotic partners, these bacteria shield the host from possible invasion by more harmful or pathogens resistant to antibiotics the primary cause of otitis media acute is collection of middle ear fluid, which creates an environment that is warm and moist that offers easy access and a favorable habitat for bacterial development (Ayala et al., 2017; Hall-Stoodley et al., 2006). Untreated acute otitis media can also cause acute mastoiditis, a bacterial infection that causes significant strain and incursion the mastoid cells in the ear's rear mastoid bone (Ludman & Bradley, 2012). Certain ear infections, such as herpes zoster of the ear infectious myringitis, and vestibular neuronitis, are brought on by viruses even though the majority of infections are brought on by bacterial invasion. The inflammation of the vestibular nerve, located in the inner ear, results in vestibular neuritis. The (**Figure1**), Show, healthy ear's eardrum appears pinkish gray, as seen in (**Figure 1b**), while the middle ear of an otitis media infection in (**Figure 1c**) has a red, protruding eardrum a (Ludman & Bradley, 2012).

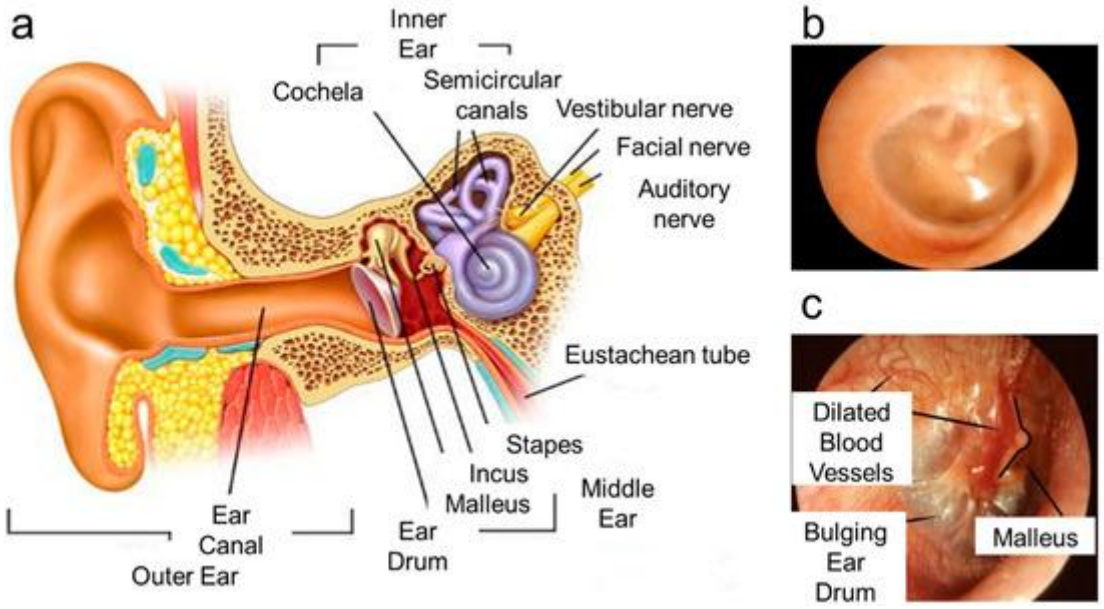

Figure 1: (a) (The human ear's structure), (b) A human ear in good health. (c) Human ear infection.

2- Types of ear infection and the related pathogens responsible for middle ear infection

There are three types of otitis media, acute otitis media, otitis media with effusion, and chronic otitis media with effusion.

2-1 Acute otitis media

Acute otitis media (AOM) is among the most common conditions that pediatricians treat. Approximately 50% of children will have had at least one ear infection by the time they turn two. Between the ages of three and twenty-four months, children are most at risk of developing AOM (Paul & Moreno, 2020).

Acute otitis media is often associated with a recent or continuing upper viral respiratory tract infection, generally known as a cold. This is due to the fact that upper respiratory tract illnesses can cause problems with the eustachian tube. The middle ear space and the sinuses are connected by the eustachian tube, which permits air to flow between Air can move between the middle ear area and the sinuses through a conduit called the eustachian tube (figure**2)**. When a child has a viral upper respiratory tract infection, the eustachian tube frequently becomes clogged with illness-related fluid or mucus. When there is a problem with the eustachian tube, A fluid buildup in the middle region of the ear might lead to an infection. Other risk factors for acute otitis media include atopy (including eczema, asthma, and seasonal allergies), exposure to tobacco smoke, daycare attendance, and a family history of it. Breastfeeding and abstaining from tobacco use have been shown to prevent the development of this kind of otitis media. The age and developmental stage of the kid can affect the symptoms of acute otitis media. The most particular symptom is ear pain. This pain is usually sudden and severe. When the infant or young child is asleep, it often wakes them up. However, symptoms alone are insufficient to diagnose it. (Paul & Moreno, 2020). Most cases of acute otitis media are caused by bacteria, although a third are caused by viruses, There for bacterial infections are caused by *Streptococcus pneumoniae*, which is followed by *Haemophilus influenzae, Moraxella*

catarrhalis, and a mix of species. Other germs can also be present in young newborns the relationship between middle ear and nose bacterial infections is not very strong (Worrall, 2007).

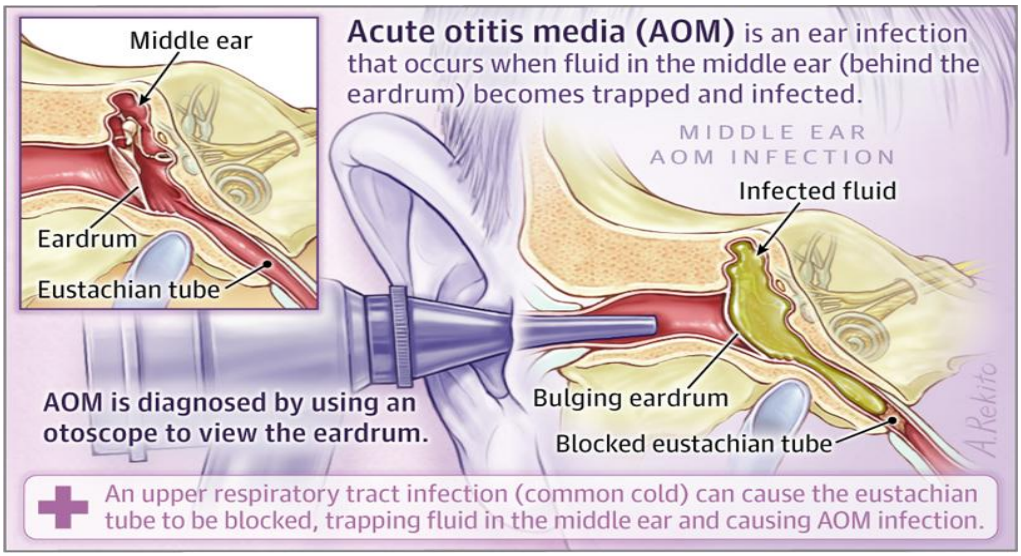

Figure 2: Acute otitis media (Paul & Moreno, 2020).

2-2 Otitis media with effusion

Is a prevalent condition in youngsters that is often asymptomatic, However, Otitis media with effusion (OME) can cause hearing loss that impairs a child's ability to develop their language and behavior, the diagnosis is mostly clinical and is based on otoscopy and, in some cases, tympanometry. Nasal endoscopy is advised only in situations of unilateral OME or when obstructive adenoid hypertrophy is suspected the presence of middle ear effusion at three-month intervals between visits is known as otitis media with effusion (Lieberthal et al., 2013). The disease known as "glue ear," or Otitis Media with Effusion, occurs when fluid builds up in the middle ear without any indications of an acute ear infection. Otitis media with effusion is distinguished by (Vanneste & Page, 2019) the existence of non-purulent fluid behind the eardrum; the absence of acute infection symptoms including fever, ear discomfort, or eardrum redness; Although it can happen to adults, it is most frequent in children ages 2 to 5. By the age of ten, many kids will have gone through at least one episode (Aarhus et al., 2015).

2-3 Chronic otitis media with effusion

Chronic otitis media with effusion (OME) or secretory otitis media (SOM) are the non-suppurative forms of otitis media with middle ear effusion. One of the most common ear conditions in children is Otitis media with effusion. Numerous factors, including eustachian tube dysfunction, viruses, allergens, bacteria, and their metabolites, are thought to be responsible for Otitis media with effusion. Gastroesophageal reflux disease (GER) is another potential cause of this condition. It is possible for gastric contents to reflux from the nasopharynx to the middle ear due to the angle between them, the immaturity of the eustachian tube in children and infants, and the supine position that newborns are often maintained in nasopharynx to middle ear (Agirdir et al., 2006).

Acute otitis media and chronic otitis media with effusion which remain severe health and social issues, are among the most frequent reasons children between the ages of one and three visit the doctor. Up to 60% of children are estimated to have experienced at least one episode of Acute otitis media by the time they are seven years old. Numerous well-known conditions can either induce or exacerbate middle ear infections. The three most important ones are upper respiratory infections, allergies, and adenoids (Formanek et al., 2015).

3-Influenza Virus and Effect on Otitis Media

Among the most common infections disorders in children is Acute Otitis Media. According to reports, 86% of newborns experience an episode of acute otitis media by the time they are a year old, and 64% do so by the time they are six months old. Acute otitis media is frequently brought on by a viral illness, even though bacterial infections account for the majority of cases (Norhayati et al., 2017). It seems more likely that Acute otitis media, which is typically thought of as a bacterial illness, is a bacterial side effect of viral. However, a virus by itself can also cause it symptoms. The middle ear can occasionally become infected with the virus. Viral and bacterial interaction is noticeable when Both viruses as well as bacteria are present in the middle ear or when viral URI is still present when bacterial Acute otitis media is diagnosed the disease's negative effects result from increased and prolonged inflammation of the middle ear and postponed elimination of germs from the middle ear. (Chonmaitree, 2000) Numerous studies have demonstrated that the influenza virus by itself inflames the young mice's middle ear.

The development of bacterial otitis media may thus be significantly influenced by this inflammation (Short et al., 2011). Both bacteria and viruses can cause Acute otitis media, a middle ear infection, which is frequently unpleasant. A respiratory tract illness caused by a virus frequently precedes Acute otitis media and can cause germs to spread from the nasopharynx into the middle ear. (Winther et al., 2010). Influenza People are at risk of developing secondary infections with *Streptococcus pneumoniae*, Another name for the pneumococcus, due to Influenza A virus (IAV). Meningitis, pneumonia, sepsis, or otitis media are some of the symptoms of infections. (Short et al., 2013). Colonization by *S. pneumoniae* is typically temporary and asymptomatic. However, *S. pneumoniae* can spread to other parts of the body and cause illness when influenza A virus (IAV) is present (Kadioglu et al., 2008). revealed that IAV's suppression of the immune system can also make *pneumococcal pneumonia* more likely (McNamee & Harmsen, 2006).

The majority of new cases of Acute viral respiratory tract infections (VRIs) are temporally associated with otitis media. however, it is still unclear how much of these findings may be applied to other pneumococcal disease phenotypes, such as otitis media, Acute otitis media and otitis media with effusion are rather common side effects of respiratory virus infections in children, but they are far less prevalent in adults and adolescents. For example, among 2499 previously healthy adults and adolescents who developed acute influenza virus illness (Hayden, 2000).

Just 1.6% of patients experienced doctor-diagnosed ear infections that required medications. Pathogenic bacteria were found in 65% of MEFs that contained viruses, most frequently in conjunction with influenza virus (Hayden, 2000). The most common cause of pneumonia, sinusitis, and otitis media is *Streptococcus pneumoniae*. Ancestral influenza virus infections are the cause of many of these diseases. The purpose of this investigation was to ascertain

whether the influenza virus strain that preceded the bacterial challenge had an impact on the prevalence and kind of secondary pneumococcal infections. Any subtype of influenza virus boosted bacterial colonization of the nasopharynx in young ferrets infected with influenza virus and subsequently challenged with pneumococcus (Peltola et al., 2006). Influenza People are at risk of developing secondary infections with *Streptococcus pneumoniae*, also known as the pneumococcus, due to a virus (IAV).

Pneumonia, sepsis, meningitis, or otitis media are all possible signs of infection. The question of whether IAV-induced immunosuppression or the activation of an abnormal immune response causes subsequent pneumococcal illness is still up for debate. (Cripps et al., 2005). *Pneumococcal-influenza* virus coinfections in children most frequently result in otitis media, which can cause irreversible hearing loss and deadly meningitis. According to studies conducted in the chinchilla, IAV's capacity to alter neutrophil activity promoted secondary pneumococcal otitis media, indicating that the development of disease may be influenced by, immunosuppression brought caused by a virus instead of inflammation Secondary otitis media, on the other hand, might be primarily unrelated to immunosuppression brought on by IAV and instead stand in for the viral NA's. capacity to cleave sialic acid and reveal receptors for pneumococcal adhesion (Tong et al., 2002). Otitis media happens when the tube connecting the ear to the neck swells for a variety of reasons, such as the common cold, trapping fluids inside the ear and creating an ideal environment for the growth of bacteria that cause ear infections. This makes otitis media easier because babies' and young children's ears are small and prone to blockage. Although the majority of ear infections don't have any lasting effects, the following dire outcomes can arise from recurrent ear infections (Jamal et al., 2022).

4- **Advanced Techniques for the Identification of Otitis Media**

In clinical settings, an otolaryngologist's most common tool for diagnosing issues related to ear pain is an otoscope. Coloration, transparency, and the existence of liquid in the tympanic membrane are the main factors analyzed in the middle ear. (Worrall, 2007). Most of the time, patients are prescribed oral or topical antibiotics, which, while effective in treating pain, cause the illness to reoccur because bacteria have evolved to become resistant to these drugs. Frequent usage of antibiotics and bacterial biofilms have been shown to contribute to the rise in antimicrobial resistance.

(Nazzari et al., 2015; Principi et al., 2003). The develop of an antibiotic-encapsulated hydrogel with chemical permeability enhancers to improve the antimicrobial therapy and drug efficacy when administered to the tympanic membrane through the external auditory canal of the ear (Yang et al., 2016). The hydrogel formulation successfully removed AOM from the Haemophilus influenzae bacteria in a chinchilla mode. Medications would cover a whole course of antibiotics with a single dosage, increasing patient adherence, preventing antibiotic overdosage, and eventually lowering recurrent adverse effects. (Figure 3a) (left) depicts a standard otoscope, whereas Figure 3a (right) displays a Cell Scope otoscope that is compatible with iPhones. According to Monroy et al., an otoscope's sensitivity and specificity for diagnosing otitis media were almost 70% (Monroy et al., 2015).

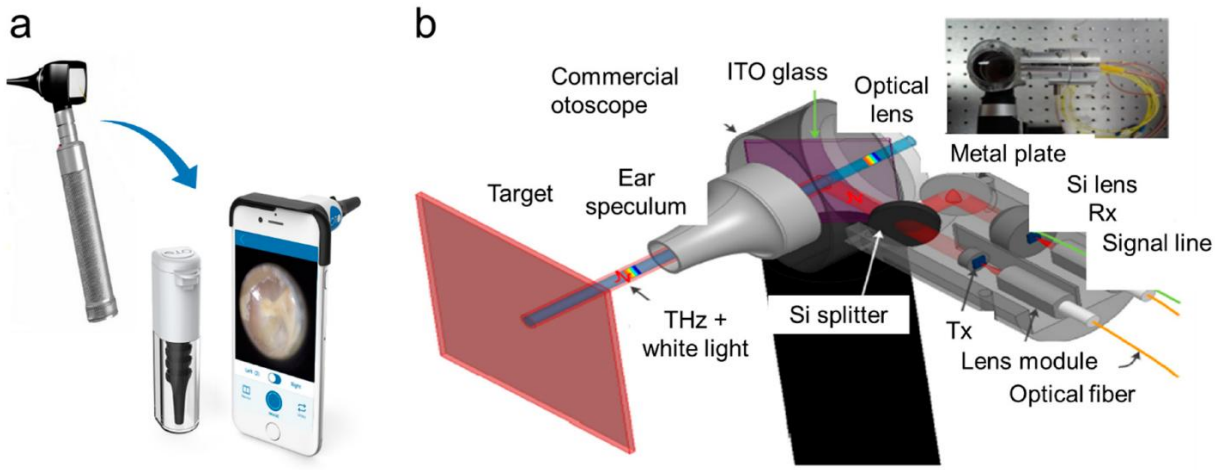

Figure 3: Clinically available tools to detect middle ear infection. (a) Cell Scope; (b) terahertz otoscope (Prasad et al., 2020).

5. Conclusion

In conclusion, the relationship between influenza virus infection and otitis media is both clinically significant and well-documented. Influenza can lead to inflammation and dysfunction of the Eustachian tube, creating an environment that facilitates the development of middle ear infections, particularly in children. Understanding this connection emphasizes the importance of preventive measures such as influenza vaccination and early treatment of flu symptoms to reduce the risk of secondary complications like otitis media. Continued research into viral pathogenesis and immune response will further aid in managing and preventing these interconnected conditions.

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Conflict of Interest Disclosure

The authors declare no conflicts of interest relevant to the content of this review, No financial relationships, personal interests, or affiliations influenced the research design, analysis, interpretation, or reporting of the findings.

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