Postviral Complications
Bacterial Pneumonia

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KEYWORDS

• Influenza • Respiratory viruses • Bacterial pneumonia • Innate immunity • Interferons

KEY POINTS

- Pneumonia remains one of the leading causes of death in the United States and worldwide.
- Influenza and other respiratory viral infections often predispose individuals to a more severe clinical course with greater morbidity and mortality than bacterial pneumonia alone.
- Postviral bacterial pneumonia is mediated by complex interactions between viruses, normal nasopharyngeal bacterial flora, and the host immune system.
- Current management strategies are largely directed toward influenza vaccination and selection of appropriate antimicrobial agents.
- Novel diagnostic tests and therapies that address the complex pathogenesis of postviral bacterial pneumonias are needed to mitigate this potentially serious complication, particularly given the ongoing threat of influenza pandemics.

BACKGROUND

Introduction

As the so-called Spanish flu raged around the world during 1918 to 1919, the burden of morbidity and mortality resulted not only from influenza infection but also from subsequent bacterial pneumonia, accounting for more than 90% of the estimated 50 million deaths caused by the pandemic.[1–4] During the 1957 and 1968 influenza pandemics, secondary bacterial infection was associated with 50% to 70% of severe infections, with the decrease attributed to the advent of antibiotics.[5–7] Coinfection was noted in approximately 30% of those infected during the H1N1 pandemic in 2009, particularly in fatal cases.[8–11] Despite substantial advances in medicine and the availability of potent antibacterial and antiviral agents, influenza and pneumonia remain among the leading causes of death in the United States and worldwide.[12,13] The complex mechanisms underlying the pathogenesis of postviral bacterial pneumonia are incompletely understood, but involve a variety of host and microbial factors that allow secondary opportunistic bacterial infections to arise in virally infected individuals. This article reviews the current understanding of how virally infected hosts are more susceptible to bacterial pneumonia as well as the management of this important complication of viral infections.

Common Causal Organisms

Viral-bacterial coinfections are a commonly encountered clinical problem. Although the precise rates of secondary bacterial infections are difficult to quantify because of a lack of comprehensive reporting systems and the impracticality of obtaining microbiologic testing in all patients with respiratory infections, bacterial pneumonia

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is estimated to complicate from 0.5% to 6% of influenza infections, with higher rates among hospitalized patients in intensive care units and fatal cases. Influenza is one of many viral pathogens that have been associated with bacterial coinfections.[14] Human parainfluenza virus, adenovirus, human metapneumovirus, measles, respiratory syncytial virus (RSV), human rhinovirus, and coronavirus are also commonly associated with secondary bacterial pneumonia.[15–22] Of these viruses, influenza is arguably most important given its continuously evolving virulence factors and the sheer number of individuals infected on an annual basis. Given its public health importance, as well as the fact that influenza is the most extensively studied, bacterial pneumonia following influenza infections is the primary focus of this article.

Irrespective of the offending viral organism, causal agents of secondary bacterial pneumonia largely reflect colonizing nasopharyngeal flora. This finding has fueled the theory that viral infection causes impaired mucosal and ciliary clearance of these normally nonpathogenic bacteria, which enables particular bacteria to flourish and causes invasive infections. Epidemiologically, *Streptococcus pneumoniae* and *Staphylococcus aureus* (both methicillin-sensitive *S aureus* and methicillin-resistant *S aureus* [MRSA]) are most common, with *Streptococcus pyogenes* and *Haemophilus influenzae* less frequently isolated.[23–27] However, infections in humans are often polymicrobial, involving combinations of multiple viruses and/or bacteria. Common viral-bacterial coinfections are summarized in **Table 1**.

Clinical Presentation

The incidence of bacterial pneumonia mirrors the seasonal nature of viral infections, with increases during peak viral seasons.[19,28–31] Data from the 2009 H1N1 epidemic show that coinfection usually occurs within the first 6 days of influenza infection,[32,33] although it can develop up to 14 days after other viral infections. This delay likely represents the time needed for viral replication and the immunomodulatory effects of infection to occur.[34–36] Patients with secondary pneumonia tend to have a more severe, protracted course, with increased mortality compared with those without antecedent viral infection.[7,25,30,31,33,37–41] Although patients with comorbid conditions or at the extremes of age are at increased risk of complicated influenza infections, even previously

Table 1
Common viral-bacterial coinfections and their associated clinical infections in human hosts

Virus	Known Bacterial Coinfections	Associated Secondary Infections
Influenza	*S pneumoniae* *S aureus* *S pyogenes* *H influenzae* *Moraxella catarrhalis* *Neisseria meningitidis*	Pneumonia Otitis media Sinusitis Meningitis
Respiratory syncytial virus	*S pneumoniae*	Pneumonia Bronchitis/bronchiolitis
Adenovirus	*S pneumoniae* *H influenzae* *M catarrhalis*	Pneumonia
Coronavirus	*H influenzae*	Pneumonia
Human rhinovirus	*S pneumoniae* *H influenzae* *S aureus* *M catarrhalis*	Pneumonia Sinusitis Otitis media
Parainfluenza virus	*S pneumoniae* *M catarrhalis*	Pneumonia
Human metapneumovirus	*S pneumoniae*	Pneumonia Bronchitis
Measles virus	*S pneumoniae* *S aureus* *H influenzae*	Otitis media Pneumonia Tracheobronchitis