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Review Article

Influenza: under complications and management, mention needs to be made of secondary bacterial infection and its treatment

Mohammed Abdulmuttalib Abdul Bari*

Department of Pharmacology, Baghdad College of Medical Sciences, Baghdad, Iraq

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*Correspondence:

Dr. Mohammed Abdulmuttalib Abdul Bari,
Email: mohammed_abdulmutalib@yahoo.com

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ABSTRACT

This review explains the complications and the management of influenza, focusing on their secondary bacterial infections. It outlines the types of influenza viruses, transmission, and vaccination. It outlines the different secondary infections that may arise after an influenza infection; hence, one considers the bacterial, fungal, and viral infections. It emphasizes the need for timely diagnosis and proper management, which would involve the use of antibiotics, antifungal agents, or antiviral drugs depending on the infection. It further advises on prevention techniques, which involve vaccination and proper hygiene of hands to avert the incidence of secondary infection. From the discussion above, this document has identified a wide précised account of the complications and management approaches with influenza and its complicating secondary infections.

Keywords: Influenza, Secondary infections, Bacterial infections, Pneumonia, Antibiotic resistance, Vaccination, Antiviral medications, *Streptococcus pneumoniae*

INTRODUCTION

Influenza is a viral respiratory infection caused by the influenza virus, and it affects a large population around the world annually. In this light, influenza can be seen as an infectious disease because it transmits to other people very easily and quickly. The symptoms of the disease can be mild or very serious and adverse with serious complications such as pneumonia, bronchitis, and sinusitis. There are three types of the virus, which include A, B, and C. The A and B types of the influenza virus present the leading causes of seasonal influenza outbreaks and epidemics. Influenza C viruses also inspire only faint respiratory symptoms and have never been reported to cause an epidemic. Numbers range from 1 to 4 in this user text.¹

The flu viruses are typed according to their surface proteins: hemagglutinin (H) and neuraminidase (N). There are now 18 recognized H subtypes and 11 recognized N subtypes. Influenza A viruses are classified by analysing the differences in two proteins that exist on the surfaces of

the various viruses: hemagglutinin (H) and neuraminidase (N). The currently circulating and causing seasonal flu epidemics in humans are two subtypes of influenza A viruses: H1N1 and H3N2. All influenza B viruses fall into two lineages called the Victoria lineage and the Yamagata lineage. All of these could conceivably cause seasonal flu epidemics, and all influenza C viruses are decidedly uncommon, usually causing only mild symptoms of respiratory illness.

Influenza viruses may also be found in an infected person's respiratory secretions for example, in mucus and saliva and, occasionally, in the secretions from the nose. Infection can result from a person inhaling the viruses and may also occur when a person touches something that has the virus on it and then touches his or her mouth, nose, or possibly his or her eye. The virus is also able to stay infectious on a number of surfaces for a few hours. From here, the virus can be transmitted by coming into contact with the contaminated surfaces. An infected person can proceed to infect others for seven days even after the appearance of symptoms.²

Annual vaccination confers the most effective protection against flu. Vaccination is conducted annually to protect from such kinds of influenza viruses that seem most common throughout a particular flu season, as based on empirical findings. It diminishes the chances of getting infected with the virus of flu and lessens the intensity of the symptoms one has. Other prevention measures include cleaning hands as frequently as possible by washing them with soap and water, avoiding close contact with persons one suspects have an infection, keeping the mouth and nose covered with a tissue when sneezing or coughing, and staying home when unwell.³

Secondary infection is usually due to an initial viral illness, for example, influenza, which may bring very serious complications. These include bacterial, fungal, and other viral infections that can become serious as the illness prolongs. Of all the secondary infections, bacterial superinfections are the most frequent complications after the influenza infection. Other than pneumonia, other bacterial complications which influenza can lead to, include sinusitis, otitis media, and bronchitis. The fungal infections can also present themselves in the patients, particularly in those rendered immunocompromised. Also to include, the other two viruses are RSV and HMPV, causing a secondary infection because of the influenza.⁴

Secondary infections following influenza can be categorized into further, secondary bacterial infections post-influenza may also be classified depending on the causative bacteria of the disease, the site of occurrence, and on the severity of infection. The former may be categorized based on causative bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Infections can be classified depending on their infection site, such as pneumonia, sinusitis, and otitis media. Their symptoms may show variable intensity; it can range from benign to very serious. They may present with the symptoms of fever, cough, dyspnea, chest discomfort, and generalized fatigue.⁵

Order of other infections after flu

Secondary infections following flu illness may develop very quickly, with severe symptoms and potentially life-threatening complications. If not treated, bacterial pneumonia may result in severe complications like sepsis and respiratory failure. The other potential secondary infections are an acute respiratory distress syndrome - ARDS, septic shock, and multiple organ failure. Commonly, secondary infections are associated with a number of factors. Common influencing factors in the presence of secondary infections are age, state of health, type of bacterium responsible for the infection, and comorbid conditions.⁶

Rate of infection due to influenza

Complicating illnesses after influenza vary in frequency depending on the population under study and the severity

of the flu season. In fact, one of these studies published in the journal of infectious diseases had estimated that as many as 30% of deaths during the 2009 H1N1 influenza pandemic were related to complications caused by secondary bacterial infections. In the same study, about 20% of the influenza infection patients admitted showed a development of secondary bacterial pneumonia. Due to the existence of certain vulnerable demographic groups such as the elderly, children, and people with underlying health issues.⁷

EPIDEMIOLOGICAL SURVEY OF THE PREVALENCE OF POST-INFLUENZA SECONDARY DISEASES

Incidence and distribution of secondary infections following influenza may also vary upon the particular type of infection under consideration and demographic group being studied. Bacterial infections are the most common type of secondary infection that follows influenza and are particularly prone to develop in the aged and in patients with prevalent conditions. According to the CDC, the most important bacterial cause of pneumonia that develops after influenza is *Streptococcus pneumoniae*. Other organisms which may cause pneumonia following an influenza infection include *Staphylococcus aureus*, *Haemophilus influenzae*, and *Klebsiella pneumoniae*. People with compromised immune states- those that have HIV/AIDS or cancer- can easily become victim to fungal disease. The incidence of secondary infections after influenza might also be influenced by the intensity of the influenza outbreak; indeed, higher rates of secondary infections have been reported during pandemic years.⁸

Treatment of the secondary infection ensuing from influenza is actually based on the type of infection, the severity of infection, and the health status of the patient. Usually, such infections are treated with a course of antibiotics, antifungal agents, or antiviral agents. The section below will further discuss in detail various options of secondary infections that come forward post influenza.⁹

Bacterial diseases are the common type of secondary infection that happens after influenza, and antibiotics have been commonly prescribed to treat such bacterial diseases. The strain of bacteria causing the infection, along with the age, medical history, and any hypersensitivity a patient has, determines the kind of antibiotic that will be prescribed. The most prescribed antibiotics against bacterial infections are from classes such as macrolides, penicillin, cephalosporins, and fluoroquinolones.¹⁰

Antifungal medications

It is when a person's immune response is suppressed and can be controlled only through the administration of antifungal agents. The antifungal therapy administered varies according to the species that caused infection and the severity of the infection as well. The commonly used antifungal agents in this case are azoles, polyenes, and

echinocandins. Most severe forms of fungal infection will require hospitalization and thus the antifungal agents should be administered intravenously.¹⁰

Antiviral drugs

Antiviral medications would be given to treat secondary infections from other viruses, such as RSV and HMPV. Antiviral medications work best if started early in the course of an infection. The correct kind of antiviral would depend on which kind of a virus was causing the infection. Antiviral medications most commonly used include oseltamivir, zanamivir, and ribavirin.¹¹

Palliative care

The above symptom relief along with the pharmacological management assists in the effective reduction of symptoms as well as risks of future infection. The interventions also comprise of rest periods, adequate intake of fluids as well as control of body fever and discomfort. In conditions of very severe state, where the patient's health state has worsened considerably, the patient is hospitalized for further treatment comprising of ventilator support in respiratory failure leading to inability to function properly.¹²

Prophylaxis

The second importance of influenza vaccination is to prevent the acquisition of secondary infections upon contraction of the primary infection which is in this case influenza. The intervention here is vaccination against influenza as well as other vaccine-preventable diseases. This also encompasses interventions such as regular washing of hands and the use of alcohol-based hand sanitizers, which mostly prevent transmission. For those with an impaired immune system, such as patients with HIV or those on chemotherapy, it may be wise to receive

prophylactic treatments with antivirals or antibacterial drugs to prevent secondary infections.¹³

Management of secondary infections that develop after influenza depends on the specific type and severity of the infection; often, antibiotics, antifungal agents, and antiviral medications are applied along with supportive treatment. The most important is to prevent the development of secondary infections: this can be done by the use of vaccines and the observance of proper hand hygiene.¹⁴ Of course, all of the bacteria that are described in this chart are each potentially capable of presenting a serious infection. The differences in which do present the greatest risk start to relate to other factors such as the individual's immune system and the severity of the infection along with the bacterium's antibiotic-resistant properties.¹⁵ However, *Streptococcus pneumoniae* is still a highly dangerous bacterium capable of causing various infections: from pneumonia and meningitis to sepsis. It also played a key role in morbidity and mortality among small children, older adults, and those whose immune system was compromised worldwide.¹⁶ The Table 1 indicates that one of the complications related to influenza can be secondary infections attributed to *Streptococcus pneumoniae*. This bacterium has been known to have resistance to most antibiotics including the traditionally used drug of choice, penicillin. In recent times, antibiotic-resistant strains of *S. pneumoniae* have increased rapidly at an astonishing rate, thereby compounding the challenges that go along with its treatment and control. Essential to the decrease in both spread and burden of infections with *S. pneumoniae* are prevention strategies that include vaccination and judicious use of antibiotics. It is of utmost importance to point out and insist on immediate medical intervention upon suspicion of being infected, and it is by strict compliance with the recommended treatment protocol that complications can be avoided and the risk for acquired antibiotic resistance minimized.¹⁷

Table 1: Represent the bacteria involved in the secondary infections and common antibiotics treatments with mechanism of action.

Bacteria involved	Common antibiotic treatments	Mechanism of action
<i>Streptococcus pneumoniae</i>	Penicillin, Amoxicillin, Ceftriaxone	Inhibits bacterial cell wall synthesis
<i>Haemophilus influenzae</i>	Amoxicillin, Augmentin, Cefuroxime	Inhibits bacterial cell wall synthesis
<i>Staphylococcus aureus</i>	Methicillin, Vancomycin, Linezolid	Inhibits bacterial cell wall synthesis, inhibits protein synthesis
Group A <i>Streptococcus</i>	Penicillin, Clindamycin, Cephalexin	Inhibits bacterial cell wall synthesis, inhibits protein synthesis
<i>Klebsiellapneumoniae</i>	Ciprofloxacin, Meropenem, Gentamicin	Inhibits DNA synthesis, inhibits cell wall synthesis, inhibits protein synthesis

Treatment of *Streptococcus pneumoniae* infections will depend on the specific type of infection, the severity of the infection given the age and general health of the patient, and the resistance characteristics of the antibiotic in the

bacterium. The following is an all-encompassing guideline of the treatment of *S. pneumoniae* infections.¹⁸ Pneumonia is a common pathological condition characterized by inflammation of the lungs. Moderate and severe diseases

should be treated with oral antibiotics, including but not limited to amoxicillin, doxycycline, and the macrolides: azithromycin. If the disease is severe, then management may need hospital care and intravenous injections of ceftriaxone, cefotaxime, or fluoroquinolones. Meningitis is usually an infection of the meninges, which is the protective covering of the brain and the spinal cord. Normally, treatment is done by hospitalization and the use of intravenous antibiotic with either ceftriaxone, cefotaxime. Another adjunctive therapy that can be offered is dexamethasone to decrease brain inflammation.¹⁹

Sinus

For those with mild cases, the best modality is close monitoring of the patient's condition with supportive care including saline nasal spray and decongestants. In more severe or chronic cases of infection, physicians may suggest the use of oral antibiotics, including amoxicillin-clavulanate and doxycycline.²⁰

Otitis media is an infection of the middle ear

Monitoring and administering key interventions in cases like pain relief and fever management through acetaminophen or ibuprofen. In cases that are severe in nature or chronic, medications such as amoxicillin-clavulanate or cefuroxime can be advised.¹⁹ Infections with *Streptococcus pneumoniae* can affect all age groups, but the disease burden falls into certain high-risk age groupings more than others. The people at an increased risk of pneumococcal infections are children below 2 and adults over 65 years. The people whose immune system is damaged, such as those with illnesses like HIV/AIDS, cancer disease, and on organ transplant procedures, constitute a group of persons at high risk. Other groups at high risk include people with other chronic underlying diseases that mainly involve cardiovascular conditions, pulmonary diseases, and diabetes mellitus.²⁰

Furthermore, individuals who smoke tobacco or are passively exposed to tobacco smoke are also at an increased risk for pneumococcal infection. The reason behind the higher chances is that smoking negatively affects lung function and impairs the immune system's response, thus making the body susceptible to bacterial infections.²¹ Vaccine is one of the important preventive measures against pneumococcal infections. The CDC recommends routine pneumococcal vaccination for all children under 2 years, persons above 65 years, and those with certain medical conditions. Vaccination is known to substantially reduce the risk of pneumococcal infection and further complications associated with them, in particular, in people who are at higher risk.²²

Treatment that targets symptom reduction

Antibiotics are the mainstay in treating bacterial infections that can be secondary to influenza. Some of the commonly used treatments employed in infections due to

Streptococcus pneumoniae and *Haemophilus influenzae* type b include penicillin, amoxicillin, and aminopenicillins. Commonly used agents in *Staphylococcus aureus* infections include methicillin, clindamycin, and vancomycin. Group A *Streptococcus* is another causative agent for which penicillin, amoxicillin, and aminopenicillin are often prescribed.²³ Antiviral drugs such as oseltamivir (Tamiflu) and zanamivir (Relenza) have been helpful in therapy by reducing the intensity and time duration of flu; they are optimally effective when treatment begins within 48 hours of the onset of symptoms.²⁴

Vaccination is definitely the mainstay of bacterial infections. Immunization in the early stages of life is thus the best way to prevent these causes of human disease. Vaccines for *staphylococcus aureus* and group A streptococcus will be available soon. Viral infections include influenza, in which antibiotics do not apply. The rest of the antibiotics can only work against bacterial infections that have resulted from an influenza attack. It goes without saying that unnecessary use of the class of drugs needs to be avoided as this can only lead to antibiotic resistance.²⁵ Vaccination is still the best way of preventing influenza and related complications. Vaccination against influenza is recommended yearly for everybody of six months and older. This recommendation is particularly needed for high-risk groups, which include the very young, the very elderly, pregnant women, and persons with medical conditions.^{26,27} In addition to vaccination and antiviral medications, many adjunct measures are available which can effectively slow the spread of influenza and decrease the likelihood of severe outcomes. These preventive measures include routine hand hygiene, avoiding close contact with people who show signs of being ill, properly covering coughs and sneezes, staying home when not feeling well, and staying healthy through sufficient rest, nutrition and exercise.²⁸ In summary Influenza is a highly contagious respiratory infection that is caused by the influenza virus. The infection can be severe and affects people of all ages, sometimes leading to death. This disease can produce symptoms, leading to mild or less destructive severity. Most people recover from this disease without complications; however, those with underlying health complications or weak immune systems may experience severe and sometimes fatal complications.²⁹

The most common complication attributed to influenza is the onset of secondary bacterial infections. The infections can present as the immune response of the host organism is depressed by the influenza virus, which then provides room for bacterial invasion of the host organism. One of the most common bacteria involved in secondary infections to influenza infection is *Streptococcus pneumoniae*. Common repercussions include pneumonia, sinusitis, otitis media, and meningitis. Clinical presentation of these infections is variable and depends on the nature and severity of the infection. In younger children, the elderly, and

immunocompromised individuals, the conditions can range from being benign to life-threatening.³⁰⁻³³

Early identification and timely management of influenza and its complication will avoid further complications and improve the outcome. Oseltamivir and other antiviral drugs decrease the severity and duration of symptoms of influenza and may avoid complication. However, they are most effective when initiated within the first 48 hours after the onset of symptoms.³⁴ If influenza leads to bacterial infection, proper antibiotics are to be taken to make sure that the infection is properly managed. The kind of antibiotic used, however, would definitely vary with type and gravity of infection, as well as with the sensitivity of the bacteria to different types of antibiotics. Antibiotic applications are to be undertaken with careful administration to prevent the rise of antibiotic-resistant bacteria.³⁵

Supportive care is necessary while treating influenza, as well as its complications, including antivirals and antibiotics. This sort of support may include rest, hydration, analgesics, and temperature control.³⁶ It is important to emphasize prevention of influenza and its related outcomes. Influenza immunization annually is recommended to start at 6 months of age and especially for those at high risk of complications including younger children, older persons, and with health problems. Immunization can reduce the risks of influenza from occurring and causing other complications, including secondary bacterial infections.³⁷ This also includes several diseases and complications that are regarded as a result of influenza, such as the formation of secondary bacterial infections. Perhaps one of the most common bacteria among these that causes severe and sometimes even fatal infections is *Streptococcus pneumoniae* following influenza. Early diagnosis and treatment for influenza and its complications, cautious utilization of antiviral drugs and antibiotics, and a lot more are followed to prevent complications and lower the rate of morbidity.

Of prime importance is vaccination, which is done yearly, especially in susceptible groups. They also stand high chances of developing other bacterial infections in their bodies after having recovered from the influenza. Examples of such categories include patients with long-term medical conditions like diabetes, heart diseases, and chronic respiratory problems and those whose immune systems have been weakened due to cancer therapies, HIV/AIDS, and other debilitating diseases.³⁸ Additionally, it can result in a depressed immune system both in early stages of life and in advanced stages of life, leaving an individual prone to secondary infections. Antibiotics should be used only in cases of suspected or proven bacterial infection. Inappropriate or overuse and misuse of antibiotics is one of the more serious problems which leads to resistance to antibiotics. In this way, there is an additional burden on the judicious use of antibiotic medications.³⁹

Use of antibiotics should be the *prima facie* decision of medical attendants after diagnostic studies and clinical judgment. This is, in all clinically related evidences, an undeniable fact of the poor efficacy of antibiotics against the influenza virus or the common cold. In most cases, completing the course of antibiotic treatment is advised, as drug resistance and other complications may develop if not done so, even when symptoms are explicitly evident. Those at higher risk of developing secondary infections after such illness include those with a compromised immune system, young children, and the elderly. Specifically, antibiotics should be used accordingly and where the prescription is supported by appropriate diagnostic studies and clinical judgment. Indeed, the full course of treatment should be followed in order to prevent this resistance risk and to prevent the development of complications.⁴⁰

CONCLUSION

Influenza is a viral respiratory infection that may be complicated by grave conditions. The most frequent and serious complications associated with influenza are secondary bacterial infections like pneumonia, sinusitis, and otitis media, usually caused by pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Such secondary infections will be effectively managed with timely diagnosis and correct use of antibiotics, antifungal, or antiviral agents, depending on the causative agent. Preventive measures, such as annual vaccination against influenza, good hygiene, and washing of hands, will reduce the risk not only of primary influenza infection but also of complication development. Besides, the judicious use of antibiotics is necessary against the background of very significant antibiotic resistance-an actual global health problem.

Awareness of influenza, its complications, and further research into it would vastly aid in the management strategies, especially within the supposed vulnerable groups like the young children, elderly, and those individuals with immunocompromised conditions. Prevention combined with the effective management of secondary infections can go a long way in reducing the overall impact of influenza.

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