Review Article

Review on Influenza Virus and its Prevention and Control

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Abstract

Influenza virus is one of the pandemic diseases that causes economic destruction and causes significant morbidity and mortality mainly in human as well in birds and swine. It is highly contagious disease that considered as emerging disease. According to the World Health Organization, every winter, tens of millions of people get the flu. Most are only ill and out of work for a week, yet the elderly are at a higher risk of death from the illness. Since many migratory birds can cross the boundary it is difficult to control its spread from one country to another. This influenza has ability to Antigenic Changes through Antigenic Drift and Antigenic Shift. Due to the high mutation rate of the virus, a particular influenza vaccine usually confers protection for no more than a few years. This paper attempt review general consideration of influenza virus and its prevention, especially in avian influenza virus free area.

INTRODUCTION

An emerging infectious disease (EID) is an infectious disease whose incidence has increased in the past 20 years and could increase in the near future. Emerging infections account for at least 12% of all human pathogens [1]. EIDs are caused by newly identified species or strains (e.g. Severe acute respiratory syndrome, HIV/AIDS) that may have evolved from a known infection (e.g. influenza) or spread to a new population (e.g. West Nile fever) or to an area undergoing ecologic transformation (e.g. Lyme disease). Influenza virus, the causative agent of the common flu, is a worldwide health problem with significant economic consequences [2].

Influenza viruses belong to the Orthomyxoviridae family. Although the extent to which birds are involved in the emergence and global spread of novel, pandemic human strains remains debated, even the most recent pandemic strain, H1N1, contains several segments that most likely originated in birds [3]. In some countries, seasonal influenza affects annually up to 40% of the population and 500 million people die from it worldwide every year [4]. These have been in circulation since 1997 and in addition to H5N1 avian influenza which cause severe infections in humans with lethality rates of up to 60%, recently a novel H7N9-subtyped virus has been causing epizootics in China with lethality rates around 20% [5]. Flu symptoms may begin suddenly and might be severe, including fever, dry cough, sore throat, headache, extreme tiredness, and body aches (http://www.mayoclinic.org). Several different approaches are currently available for diagnosis of influenza infections in humans such as viral isolation in cell culture, immunofluorescence assays, nucleic acid amplification tests, immunochromatography-based rapid diagnostic tests, etc. Newer diagnostic approaches are being developed to overcome the limitations associated with some of the conventional detection methods [6].

ETIOLOGY

Influenza viruses belong to the Orthomyxoviridae family and are classified into three distinct types: influenza A, B and C (Fathima, Sumana, et al., 2012) [7]. Pandemic influenza virus has its origins in avian influenza viruses [8], it is a single-stranded, helically shaped, RNA virus. Influenza A, B and C viruses are distinguished on the basis of their internal nucleoprotein and matrix proteins which are specific for each viral type (http://www.cdc.gov). These surface proteins are virulence factors contributing to the pathogenicity of the virus and in addition their antigenic uniqueness is used for classifying different strains of the virus into subtypes (http://www.cdc.gov/pdf/). There are 15 different H subtypes and 9 different N subtypes allowing for 135 potential different viral strains. Only 3 haemagglutinins (H1, H2, H3) and 2 neuraminidases (N1, N2) are found in influenza A viruses ordinarily infecting humans. These viruses are only distantly related to the human par influenza viruses, which are RNA viruses belonging to the Paramyxovirus family that are a common cause of respiratory infections in children such as croup [9], but can also cause a disease similar to influenza in adults [10]. The specific strains of influenza change frequently, necessitating parallel changes in the seasonal influenza vaccine. Since 1977, three types of influenza viruses had been in circulation in humans: influenzaA (H3N2), influenzaA (H1N1), and influenzaB. According to (Table 1) only type A influenza virus can cause a pandemic, because it is the
Table 1: Some characteristics of influenza A, B and C virus (http://www.infection.net.au).

<table>
<thead>
<tr>
<th></th>
<th>Influenza A</th>
<th>Influenza B</th>
<th>Influenza C</th>
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<tbody>
<tr>
<td>Genetics</td>
<td>8 RNA segments</td>
<td>8 RNA segments</td>
<td>7 RNA segments</td>
</tr>
<tr>
<td>Structure</td>
<td>10 viral proteins</td>
<td>11 viral proteins</td>
<td>9 viral proteins</td>
</tr>
<tr>
<td>Host range</td>
<td>Humans, swine, equine, avian, canine, marine mammals</td>
<td>Humans only</td>
<td>Humans, swine and canine</td>
</tr>
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<td>Clinical features</td>
<td>Can cause epidemics and pandemics with significant mortality in young persons</td>
<td>Severe disease seen usually in older adults or persons at high risk. No pandemics</td>
<td>Mild disease without pandemics</td>
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Influenza reaches peak prevalence in winter, and because the Northern and Southern Hemispheres have winter at different times of the year, there are actually two different flu seasons each year [14]. This is why the World Health Organization (assisted by the National Influenza Centers) makes recommendations for two different vaccine formulations every year; one for the Northern, and one for the Southern Hemisphere. Avian species, specifically shorebirds and waterfowl, are a reservoir of influenza.

A virus of different subtypes in nature with a few notable exceptions, influenza infections in these hosts are asymptomatic and are limited to the gastrointestinal and/or the respiratory tract. Influenza viruses infecting these hosts appear to be in evolutionary stasis compared with those infecting humans. High titers of influenza viruses are excreted from the gastrointestinal tract of infected birds, and viruses excreted into bodies of water can survive for several weeks [15].

There is a recurring supply of susceptible birds each season and up to 30% of juvenile birds are infected. Influenza A is a viral disease of global dimension, presenting with high morbidity and mortality in annual epidemics, and in pandemics which are of infrequent occurrence but which have very high attack rates [16]. The long-term epidemiologic success of influenza viruses is primarily due to antigenic variation that takes place in the two surface glycoproteins of the virus, the HA and NA. Antigenic variation renders an individual susceptible to new strains despite previous infection by influenza viruses or previous vaccination. Variation in influenza A and B viruses is caused by the accumulation of point mutations in the HA and NA genes (antigenic drift). During antigenic drift, a variety of mutations including substitutions, deletions, and insertions produce genetic variation in influenza viruses [15].

**TRANSMISSION**

The viruses spread to other susceptible avian species, such as...
turkeys, presumably through contamination of water in the farms along the flyways of migratory bird populations (http://eden.lsu.edu). Viruses that are pathogenic for shorebirds or waterfowl can be pathogenic for certain other avian species. For example, influenza A H5N1 viruses isolated from humans and chickens in Hong Kong in 1997 were highly pathogenic for chickens, and although they replicated to low titer in experimentally infected ducks, they did not cause disease signs in these birds [12]. The viruses isolated from ducks in the market were lethal for experimentally inoculated chickens. Alternatively, a previously avirulent influenza virus can acquire specific sequence changes, such as losing potential glycosylation sites or gaining multiple basic amino acid sequences in the connecting peptide of the HA, that confer virulence.

Influenza virus is transmitted among humans in three main ways: by direct contact with infected individuals, through contaminated objects (such as hairbrushes or towels—often called fomites) and by inhaling virus-laden aerosols. The contribution of each mode to overall transmission of influenza is not known according to Dr. Tomislav Meštrović, MD, PhD.

Influenza virus may be transmitted among humans in three ways: (1) by direct contact with infected individuals; (2) by contact with contaminated objects (called fomites, such as toys, doorknobs); and (3) by inhalation of virus-laden aerosols. The contribution of each mode to overall transmission of influenza is not known (http://www.virology.ws). The incidence of seasonal influenza typically increases in the late autumn and begins to decline in mid-spring. In the Northern hemisphere, this corresponds to November through March; in the Southern Hemisphere, this corresponds to April through September. In tropical countries, influenza occurs sporadically throughout the year, but more so in the rainy periods. Localized outbreaks of seasonal influenza also occur in inter-pandemic years, particularly when strains of virus penetrate communities with little or no preexisting immunity to the circulating virus. The reason for seasonality remains unclear. Because the primary mode of transmission is by large droplet aerosols, increased crowding in the colder months, the return to schools and university dormitories, and the start of military recruit courses have been suggested as contributing factors [17]. Fomites may serve as a secondary mode of transmission, and it has also been suggested that the higher intensity of sterilizing ultraviolet light in the summer months may serve to reduce the environmental burden of virus. Dry environments, such as those that prevail during the winter months, are also known to increase transmission for unknown reasons [18].

**RISK FACTOR**

Influenza is a very serious illness for anyone at high risk. Certain diseases that place people at high risk include: chronic lung disease such as asthma, COPD, bronchiectasis, or cystic fibrosis, heart disease, chronic kidney disease, diabetes or other chronic metabolic disorder, morbid obesity, severe anemia (including sickle cell anemia), diseases (HIV, AIDS) or treatments (steroids, chemotherapy) that suppress immunity, liver disorders, children and adolescents who are receiving long-term aspirin therapy (http://www.lung.org). In addition to that cold temperatures and low relative humidity are favorable to the spread of influenza virus. Although other factors likely contribute to the periodicity of influenza epidemics, it is clear that air temperature and RH could play an important role [19]. Mathematical modeling indicates that only a small seasonal forcing is required to produce oscillations in infection rate of high amplitude [20]. Further more risk factors that associated with host itself is also very important. For instance; skipping the shot, not washing your hands, not taking care of yourself, being pregnant, being a kid, being a senior, living in a retirement center [20].

**Age**

The very young and the very old are at higher risk for upper respiratory tract infections and their associated complications (http://www.nytimes.com). Before the immune system matures, all infants are susceptible to upper respiratory infections, with a possible frequency of one cold every 1 - 2 months. The elderly have diminished cough and gag reflexes, and their immune systems are often weaker (http://www.nytimes.com).

**Pregnancy**

Pregnancy has frequently been reported in cases of hospital admission related to pdm (H1N1)09 into ICUs. Pregnancy conveys a 4-5 fold increased rate of serious illness and hospitalization with influenza. During previous influenza outbreaks, pregnancy has also been associated with increased mortality and morbidity; particularly if infection occurs during the third trimester (http://www.nytimes.com).

Also other factors can contribute to the spread of Al viruses including globalization and international trade (legally and illegally), marketing practices (live bird markets), farming practices and the presence of the viruses in wild birds [21]. Some of wild birds normally can carry avian influenza viruses in their respiratory or intestinal tracts and usually do not get sick as a reservoir host for this virus. Around the world, surveillance measures have been put in place to monitor occurrence and characteristics of AI viruses in wild birds. Generally, there are many uncertainties about the wild species involved, the migratory routes used and, above all, the possibility that some species could become permanent reservoirs of the H5N1 virus, with carriers showing no clinical sign [22].

**CLINICAL SIGNS OF THE INFLUENZA**

In the mild form, signs of illness may be expressed only as ruffled feathers, reduced egg production, or mild effects on the respiratory system [23]. In the severe form of the disease, the virus not only affects the respiratory tract, as in the mild form, but also invades multiple organs and tissues that can result in massive internal hemorrhaging. Some or all of the following clinical signs are evident in birds infected with a highly pathogenic strain of AI (including H5N1 strain): quietness and extreme depression; sudden drop in production of eggs, many of which are soft-shelled or shell-less; wattles and combs become swollen and congested; swelling of the skin under the eyes;
coughing, sneezing and nervous signs; diarrhea; hemorrhages on the hock; a few deaths may occur over several days, followed by rapid spread and a mortality rate that can then approach 100% within 48 hours (http://www.oie). Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis) [24]. Among children, otitis media, nausea, and vomiting also are commonly reported with influenza illness. Uncomplicated influenza illness typically resolves after 3-7 days for the majority of persons, although cough and malaise can persist for >2 weeks (https://www.cdc.gov).

In general, only about 50% of infected persons will develop the classic clinical “Classic” influenza disease is characterized by the abrupt onset of fever, myalgia, sore throat, nonproductive cough, and headache [25]. The fever is usually 101°-102°F, and accompanied by prostration (bedridden). The onset of feverish often so abrupt that the exact hour is recalled by the patient. Myalgias mainly affect the back muscles. Cough is believed to be a result of tracheal epithelial destruction [26].

Additional symptoms may include rhinorrhea (runny nose), headache, substernal chest burning and ocular symptoms (e.g., eye pain and sensitivity to light) [27]. Systemic symptoms and fever usually last from 2 to 3 days, rarely more than 5 days. They may be decreased by such medications as aspirin or acetaminophen. Aspirin should not be used for infants, children, or teenagers because they may be at risk for contracting Reye syndrome following an influenza infection. Recovery is usually rapid, but some patients may have lingering asthenia (lack of strength or energy) for several weeks [26].

**DIAGNOSIS**

Avian influenza (AI) may be suspected on the basis of clinical signs and events leading to the disease [27]. Laboratory tests are required to confirm the diagnosis (OIE Terrestrial Animal Health Codeand OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals). Respiratory virus testing should be considered in individuals presenting during influenza season with fever and influenza-like symptoms of myalgia, arthralgia, headache, and/or sore throat. Influenza testing is not needed for all patients with signs and symptoms of influenza to make antiviral treatment decisions. Nasal swabs, throat swabs, nasopharyngeal aspirates and sputum are the specimens usually submitted to the laboratory [26]. Virus can readily be isolated from these specimens by growing the virus in embryonated eggs or tissue culture (http://www.infection.net.au). Testing is appropriate for hospitalized inpatients, especially if a positive test would result in a change in clinical management. Nasopharyngeal swab specimens are the preferred specimen for the purpose of respiratory virus testing. This is valuable information for the physician as it greatly enhances the accuracy of their clinical diagnosis. Physicians in close communication with the microbiology laboratory and aware of the arrival of influenza season should be able to diagnose most influenza infections clinically. This should reduce unnecessary additional laboratory testing and inappropriate antimicrobial treatment [28].

**Serological tests**

As all influenza A viruses have antigenically similar nucleoprotein and matrix antigens, these are preferred targets of influenza [29]. Some of serological methods such as gel immunodiffusion tests can be used to detect antibodies to these antigens [29]. Concentrated virus preparations containing either or both type of antigens are used in such tests. Not all species of birds develop demonstrable precipitating antibodies. Enzyme-linked immunosorbent assays have been used to detect antibodies to influenza A type-specific antigens in either species-dependent (indirect) or species-independent (competitive) test formats. Hemagglutination inhibition tests have also been employed in routine diagnostic serology, but it is possible that this technique may miss some particular infections because the hemagglutinin is subtype specific [27].

**CONTROL AND PREVENTION**

People who do not regularly come into contact with birds are not at high risk for contracting avian influenza. It is extremely important to have early detection and warning systems and prevention measures in place as part of an effective strategy for AI. This needs to be coupled with similar efforts placed on preparing for a potential outbreak.Round the world, surveillance measures have been put in place to detect the presence of infection in poultry according to OIE standards for the surveillance of avian influenza (OIE Terrestrial Animal Health Code). Additionally, surveillance programmes monitor the occurrence, prevalence and characterization of AI viruses found in wild birds. Wild bird surveillance considers different migratory flyways and particularly at mingling points for migrating birds from different continents [30].

**The best prevention is to avoid sources of exposure**

It is essential for poultry producers to maintain biosecurity practices to prevent introduction of the virus in their flock (bien). People who work with poultry or who respond to avian influenza outbreaks are advised to follow recommended biosecurity and infection control practices; these include use of appropriate personal protective equipment and careful attention to hand hygiene. Additionally, CDC recommends that people responding to poultry outbreaks should get seasonal influenza vaccination every year, preferably at least two weeks before engaging in an outbreak response. Seasonal influenza vaccination will not prevent infection with avian influenza A viruses, but can reduce the risk of co-infection with human and avian influenza A viruses (https://www.cdc.gov) in addition to that immunoprophylaxis with vaccine. Inactivated (i.e., killed virus) influenza vaccine and live, attenuated influenza vaccine are available for use in the United States (see Recommendations for Using Inactivated and Live, Attenuated Influenza Vaccine). Vaccinating persons at high risk for complications and their contacts each year before seasonal increases in influenza virus circulation is the most effective means of reducing the effect of influenza [31]. Vaccinating residents and healthcare personnel (HCP) is the only truly effective strategy for influenza control.
Although vaccination may not be 100% preventative, studies have shown that an effective vaccine program reduces influenza-related complications and deaths, and can also lower HCP absenteeism (http://www.cdc.gov). Well-defined influenza policies and procedures to be reviewed with the infection prevention committee prior to the influenza season. A designated “Influenza Vaccination Week.” Choose one week where influenza vaccination is featured to vaccinate as many residents and HCP as possible. The CDC currently recommends that vaccination programs begin as soon as the flu vaccine is available at the facility, even as early as August, and continue through the end of April of the following year.

Education for all residents, visitors, and HCP concerning the importance of vaccination, recognizing symptoms of infection, facility policies regarding work restrictions when ill, visitor restrictions, appropriate respiratory precautions, and hygiene cough etiquette are very important to control it. A campaign should encourage employees to vaccinate their family members and visitors to be vaccinated.

Healthcare Personnel Vaccination Develop and distribute written information that describes the benefits of influenza vaccination and the possible side effects of the vaccine. Strongly encourage influenza vaccination for all HCP including administrative personnel. Vaccinate new employees or request proof of vaccination prior to their start date. Resident Vaccination Vaccinate current residents during the designated seasonal influenza vaccination week. Vaccinate new admissions at any time between August and April, if not already vaccinated. Consider having residents or the resident’s advocate (e.g., a family member, friend, or ombudsman) sign a “Consent to be Vaccinated” form. Assess immunization history and ensure that updated pneumococcal vaccination standing orders are in place for residents ≥ 65 years [32].

Generally for future avian influenza threats, the WHO suggests a 3 phase, 5 part plan [33]. Phase 1: Pre-pandemic; Reduce opportunities for human infection and Strengthen the early warning system. Phase 2: Emergence of a pandemic virus; Contain or delay spread at the source. Phase 3: Pandemic declared and spreading internationally, Reduce morbidity, mortality, and social disruption and Conduct research to guide response measures.

REFERENCES


