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Global Pandemic Strain of Swine-Origin Influenza A (H1N1) Virus

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Abstract: Swine Influenza is a respiratory disease of pig caused by Type A influenza viruses. H1N1 is an Influenza A virus. Influenza viruses are able to infect humans, swine, and avian species, and swine have long been considered a potential source of new influenza viruses that can infect humans. Swine has been believed to play a vital role in interspecies transmission of influenza viruses. Influenza A causes moderate to severe illness and affects all age groups. The WHO declared the H1N1 pandemic on June 11, 2009, after more than 70 countries reported 30000 cases of H1N1 infection. In 2015 the instances of Swine Flu substantially increased to five year highs with over 10000 cases reported and 774 deaths in India. The CDC recommends real time PCR as the method of choice for diagnosing H1N1. Prevention of swine influenza has three components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans. If a person becomes sick with swine flu, antiviral drugs can make the illness milder and make the patient feel better faster. Antiviral drugs are most effective if they are started within the first 48 hours after the clinical signs begin. CDC recommends the use of Oseltamivir (Tamiflu) or Zanamivir (Relenza) for the treatment. In this review, a brief overview on swine flu is presented highlighting the characteristics of the causative virus, the disease and its advances made in its diagnosis, control and Treatment to be adapted in the wake of an outbreak.

Keywords: H1N1 Influenza, Epidemiology, Diagnosis, RT-PCR, Treatment

INTRODUCTION

Influenza ("flu") is a contagious disease that spreads around the World every winter, usually between October and May. Viruses are the cause of several deadly diseases such as yellow fever, dengue, hepatitis or seasonal Influenza. The etiologic agent of the latter, the Influenza virus, can cause mild to severe illnesses depending on the Influenza type and strain [1]. A pandemic occurs when a new viral strain appears, against which the human population has no immunity, resulting in epidemics worldwide with high mortality and morbidity [2]. The influenza A virus has been responsible for three global pandemics in the last century: the Spanish Flu in 1918, Asian Flu in 1957 and the Hong Kong Flu in 1968 [3]. The outbreak of the novel A H1N1 virus (swine flu) was declared a global pandemic by the World Health Organization (WHO) from 11 June 2009 until 10 August 2010 [3]. As of January 10, 2010, more than 208 countries have reported the laboratory confirmed cases of the novel influenza H1N1 2009 strains, including at least 13,554 deaths [4].

EPIDEMIOLOGY

Swine flu is an infection caused by a virus. It's named for a virus that pigs can get. People do not normally get swine flu, but human infections can and do happen [5]. The new virus shares some characteristics of a pandemic strain, e.g. it can be transmitted from

humans to humans, causes disease, people are not or only partially immune to the virus from previous infections and exposure results in productive infection [6]. The novel H1N1 strain which is responsible for the current outbreak of swine origin influenza was first recognized at the border between Mexico and United States in April 2009 and during a short span of two months became the first pandemic of the 21st century [7]. Prior to this the same triple reassorted virus has been isolated in swine as early as 1998 with sporadic infections in humans as well [8, 9]. The pandemic influenza A H1N1 2009 virus (A/2009/H1N1) finally arrived, causing the first pandemic influenza of the new millennium, which has affected over 214 countries and caused over 18,449 deaths [10]. It is estimated that the influenza pandemic that started with the 1918 Spanish flu killed 20 to 50 million people worldwide, followed by epidemics of Asian flu in 1957, Hong Kong flu in 1968 and Russian flu in 1977, each with random severe attacks on human populations [2]. As of January 10, 2010 more than 208 countries have reported the laboratory confirmed cases of the novel influenza H1N1 2009 strains, including at least 13,554 deaths [4].

VIROLOGY

The types of influenza virus found in pigs are known as swine influenza generally called swine flu or swine-origin influenza virus (S-OIV) [11]. Swine Influenza is a respiratory disease of pig caused by Type

Influenza viruses that cause regular outbreaks in pigs [12]. Influenza virus belongs to the genus Orthomyxovirus in the family Orthomyxoviridae which consists of influenza A, B and C viruses and has an envelope, single-stranded, negatively sensed RNA, eight separate segments and pleomorphic appearance

with an average diameter of 120nm [13]. The virus was found to be an H1N1 virus that was genetically and antigenically unrelated to human seasonal influenza viruses and genetically related to viruses circulating in swine [6].

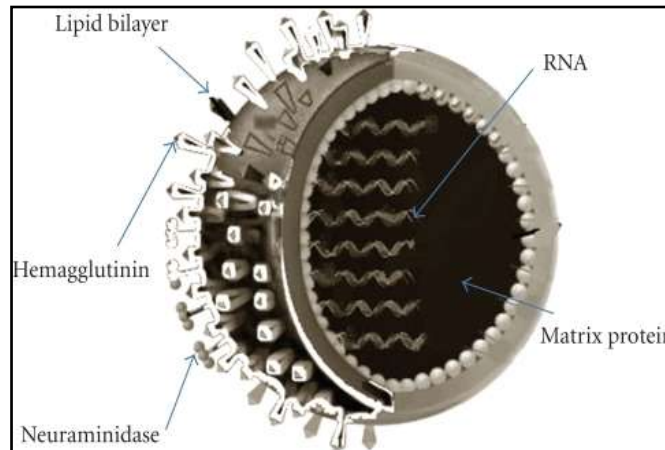


Fig-1: The pandemic H1N1 flu virus [14]

TRANSMISSION

People who work with poultry and swine, especially those with intense exposures, are at increased risk of zoonotic infection with influenza virus endemic in these animals, and constitute a population of human hosts in which zoonosis and reassortment can co-occur [15]. The transmission is by droplet infection and fomites. Pigs are thought to have an important role in

inter-species transmission of influenza, because they have receptors to both avian and human influenza virus strains. Consequently, they have been considered a possible “mixing vessel” in which genetic material can be exchanged, with the potential to result in novel progeny viruses to which humans are immunologically naive and highly susceptible [16].

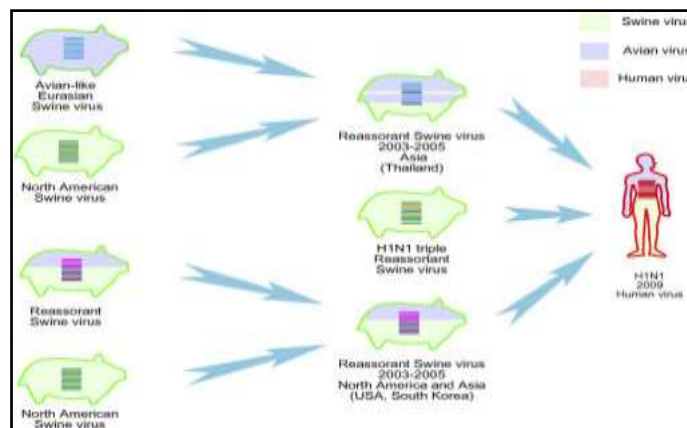


Fig-2: The Transmission of Influenza A Viruses [17]

The virus has crossed the species barrier to humans, exhibits sustained human-to-human transmission and appears to retain the potential to transmit back to swine. Thus continued reassortment with swine viruses is a cause for concern. H1N1, H1N2, H3N2 subtype swine influenza viruses have occasionally infected humans before, but such zoonotic transmission events did not lead to sustained human-to-human transmission. Its transmission among humans appears to be higher than that observed with seasonal influenza [6].

Swine flu (H1N1) is a rapidly spreading influenza A virus transmitted between humans through coughing or sneezing or via contaminated hands or surfaces [18].

CLINICAL FEATURES & SYMPTOMS

The incubation period for influenza is usually 2 days, but can vary from 1 to 4 days. The severity of influenza illness depends on the prior immunologic experience with antigenically related virus variants. In

general, only about 50% of infected persons will develop the classic clinical symptoms of influenza [36]. The typical symptoms of swine flu are a sudden fever of at least 38 °C and sudden cough with at least one other symptom of chills, lethargy, dehydration, headache, sorethroat, coryza, diarrhoea, vomiting, abdominal pain,

myalgia or arthralgia. Gastro intestinal symptoms (vomiting and diarrhoea) have also been reported more often with H1N1 than with seasonal flu [3, 19]. Such reassortment has created novel and important human pathogens, which vary in virulence and human transmissibility [20].

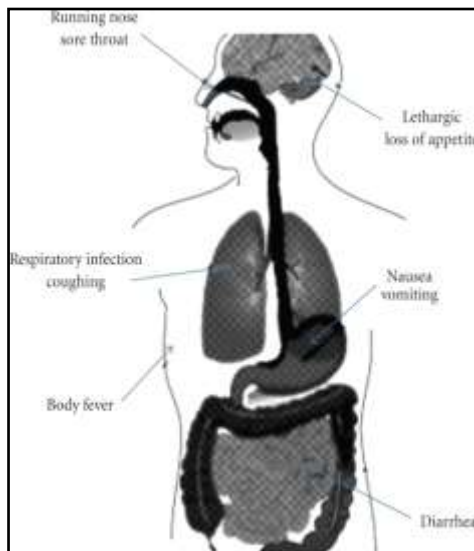


Fig-3: Symptoms of Swine flu due to novel H1N1 viral attack [14]

DIAGNOSIS

A diagnosis of confirmed swine flu requires laboratory testing of a respiratory sample (a simple nose and throat swab). Tests used to detect influenza virus infections in humans can include RT-PCR, virus isolation and assays to detect influenza virus antigens [21-23]. Many recent swine influenza cases were diagnosed by genetic methods, particularly RT-PCR [24].

Confirmation of Pandemic influenza A (H1N1) infection is through:

- Real time RT PCR or
- Isolation of the virus in culture or
- Four-fold rise in virus specific neutralizing antibodies.

Routine diagnostic tests used to detect human influenza viruses, including commercial rapid test kits, do not necessarily detect zoonotic viruses [21, 22, 25]. One indication that a novel, possibly zoonotic influenza, virus might be present is the detection of influenza A virus, but not the hemagglutinins in seasonal human influenza viruses [21].

The diagnosis of influenza A H1N1 swine flu was performed by RT-PCR testing of nasopharyngeal-swab specimens collected on admission to hospital, according to published guidelines from U.S. Centers of Disease Control and Prevention (CDC protocol of real-time RTPCR for influenza A (H1N1) [26, 27].

REAL-TIME RT-PCR

The CDC has developed a real-time RT-PCR assay to detect seasonal influenza A, B, H1, H3, and avian H5 serotypes. This assay has been approved by the Food and Drug Administration (FDA) and was distributed in December 2008 through U.S. Public Health laboratories and the WHO's Global Influenza Surveillance Network. The CDC Real time RTPCR (rRTPCR) Protocol for Detection and Characterization of Swine Influenza includes a panel of oligonucleotide primers and dual labeled hydrolysis (Taqman®) probes to be used in real-time RT-PCR assays for the in vitro qualitative detection and characterization of swine influenza viruses in respiratory specimens and viral cultures. The InfA primer and probe set is designed for universal detection of type A influenza viruses. The swInfA primer and probe set is designed to specifically detect all swine influenza A viruses. The swH1 primer and probe set is designed to specifically detect swine H1 influenza. This assay is utilized for testing influenza A positive respiratory specimens (unsubtypable) taken from suspect swine influenza A infected patients [28, 29].

PREVENTION

Prevention of swine influenza has three components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans [30]. Obviously, the most effective way to prevent any infectious disease pandemic is to invest in the improvement of social conditions. Tuberculosis is an excellent example. Data currently provided by the Global Influenza Surveillance Network are insufficient; they are not population based and therefore do not

provide reliable data on disease severity, nor on case fatality [31]. Prevention and control measures for swine influenza are based on our understanding of seasonal human influenza and consideration of potential modes of transmission [32].

VACCINATION

Influenza transmission depends on multiple factors, including swine age, immunity, vaccination status and the presence of maternal antibodies. Vaccination is commonly used as a control measure for influenza in swine farms [33]. The goal of immunization with the influenza vaccine is to generate antibodies to HA, because HA-specific antibodies neutralize the virus and provide protection against infection by circulating influenza virus. In contrast, the neuraminidase (NA) antigen of influenza is the target for the NA-inhibitor antivirals Oseltamivir and zanamivir, which played a vital role in managing 2009 H1N1 infections, preventing morbidity and mortality [34]. Antiviral drugs effective against H1N1 virus include Oseltamivir and Zanamivir and with good supportive care [35].

Antiviral agents for influenza are an adjunct to vaccine and are not a substitute for vaccine. Vaccination remains the principal means for preventing influenza related morbidity and mortality [36]. Presently government of India recommends Tamiflu as a drug of choice which is available at all government health bodies. Human influenza A is susceptible to both Oseltamivir and zanamivir, two antiviral medications approved for the prevention and treatment of influenza in the United States [37].

TREATMENT

If a person becomes sick with swine flu, antiviral drugs can make the illness milder and make the patient feel better faster. The U.S. Centers for Disease Control and Prevention recommends the use of Oseltamivir (Tamiflu) or zanamivir (Relenza) for the treatment and/or prevention of infection with swine influenza viruses; However, the majority of people infected with the virus make a full recovery without requiring medical attention or antiviral drugs [38]. The virus isolated in the 2009 outbreak has been found resistant to Amantadine and Rimantadine [39]. Treatment with Oseltamivir was associated with a reduction in days of fever, length of hospital stay, use of mechanical ventilation and mortality. Treatment was more effective if it was begun within the first 48 h after the onset of symptoms, but it was also useful if begun later. A safe and effective vaccine to prevent disease from this new influenza strain was available in developed countries soon after the pandemic began; thus, the rate of adverse effects was comparable to that of seasonal influenza vaccines [40].

Supportive Therapy

Supportive care for uncomplicated influenza in humans includes fluids and rest. Additional adjunct and

supportive treatments for more severe cases vary and can include various drugs, including antibiotics to treat or prevent secondary bacterial pneumonia, and mechanical ventilation [41].

DISCUSSION

Influenza viruses are able to infect humans, swine, and avian species, and swine have long been considered a potential source of new influenza viruses that can infect humans. Swine has been believed to play a vital role in interspecies transmission of influenza viruses, since it harbors receptors to both avian and human influenza virus strains. Pigs have been considered as a possible "mixing vessel" in which genetic material can be exchanged, with the potential to result in novel progeny viruses to which humans are immunological naive and highly susceptible. Sporadic cases of swine influenza in human, combined with seroepidemiological studies demonstrate increased risk of swine influenza in occupationally exposed workers, highlighting the crucial role that swine may play in the development of new strains of influenza viruses. H1N1 is an Influenza A virus. Influenza A viruses causes recurrent outbreaks at the local or global scale, with potentially severe consequences for human health and the global economy. Persons who work with swine should be considered for sentinel influenza surveillance, and may be an important group to include in pandemic planning. Determination of infection with influenza virus is required, testing with r RTPCR or virus isolation should be performed.

CONCLUSION

Swine flu refers to swine influenza or the viral infection caused by any of the several types of swine influenza virus. Only people who used to have direct contact with pigs were observed to get swine flu in the past. But, H1N1 virus is a new swine flu virus and it contains the genetic material of swine, bird and human influenza virus. Swine Flu is caused by influenza viruses, and is spread mainly by coughing, sneezing, and close contact. Flu can make some people much sicker than others. These people include young children, older, pregnant women and immunocompromised patients. Prevention and control measures for swine influenza are based on our understanding of seasonal human influenza and consideration of potential modes of transmission. As a result, the use of control strategies, especially vaccination, is critical for the control of influenza virus infections among domestic animals, to reduce their potential as sources for outbreaks among humans.

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