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Short Communication

HOW TO PREPARE FOR AN AVIAN INFLUENZA H5N1 PANDEMIC OUTBREAK: LESSONS LEARNED FROM THE INFLUENZA H1N1 PANDEMIC OF 1918

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Abstract: In this paper, we highlight the significant challenges encountered during the influenza H1N1 pandemic of 1918. These lessons are being utilized to prepare for potential avian influenza H5N1 pandemic outbreaks, as this virus will impact both humans and food-serving animals. Preparation for this threat is crucial because H5N1 infections are already affecting the United States and many other countries.

Keywords: Avian influenza H5N1, Bird flu, Pandemic outbreak, Influenza A, Food security.

INTRODUCTION

The recent SARS-CoV-2 pandemic outbreak has ended, but the virus continues to circulate within the human population, infecting numerous people. The avian influenza virus H5N1 is currently attempting to mutate to infect humans and mammalian populations, including cows, pets, foxes, and whales. In the United States, the presence of this virus has been confirmed in pasteurized milk, and 71 people are currently being monitored for the virus. As of May 13, 2024, one person has been infected, despite May typically not being a peak month for influenza infections (1).

The author has analyzed literature on the influenza virus H1N1 1918 outbreak and cases of influenza H5N1. In this and future work, we aim to develop blueprints to tackle potential H5N1 outbreaks, as this virus poses a threat to human life and the food industry, including poultry, milk, and beef.

PANDEMIC INFLUENZA VIRUS H1N1 1918

The influenza virus H1N1 1918 outbreak revealed several essential traits, such as the virus's rapid spread throughout the human population in the United States and the United Kingdom. This is evidenced by literature available from scanned newspaper content online from the University of Utah Marriott Library and the BBC's audio documentaries. The infection's symptoms included fever, headache, body pains, and coughing with colored sputum, which led to pneumonia in fatal cases. Rarely, there was also diarrhea and brain inflammation.

In the United States, this virus came in three waves: July, September to November 1918, and February to March 1919. It caused a large number of fatalities among the afflicted population in a short period of time, with the fatality rate reaching 10% to 15% in certain situations. Many notable people became infected, including the King of Spain and prominent leaders from the United Kingdom and the United States. Measures used to prevent this virus included masking the mouth and nose, gargling, and oral disinfection. Public institutions and schools were closed. Pneumonia was often caused by subsequent bacterial infections. Most fatalities occurred in young people aged 26 to 40. Symptoms appeared several hours to a day after infection and lasted three days, which is why this illness is also known as three-day fever. In certain cases, symptoms could last up to six days. Infected persons were asked to stay at home and rest until symptoms subsided. The virus was brought to the United States and the United Kingdom by armed forces fighting in Europe during World War I, which was nearing its end. Vitamin D was recommended and used. Social distancing was employed to prevent infection from coughing and sneezing people (2-9).

In the USA, vaccination was used against secondary bacterial infections. These vaccines were made by growing bacteria and inactivating them through a heating process. This bacterial vaccination led to a

reduction in pneumonia cases, saving many lives, as no antibiotics were available at that time. The vaccine was administered both as a curative measure for early-stage infections and as a prophylactic measure for non-infected persons (10, 11, 12).

AVIAN INFLUENZA VIRUS H5N1

To date, the avian influenza virus H5N1 has caused around 700 infections and approximately 300 fatalities. From the literature, it is evident that this virus causes flu-like symptoms similar to those of influenza H1N1 1918. However, many reports indicate brain involvement in several cases. Publications have emphasized learning lessons from the 1918 pandemic outbreak (13, 14, 15). Today, better therapies are available for treating secondary bacterial infections, and various monitoring and diagnostic tools can quickly identify outbreaks of this virus. A narrow choice of antiviral therapies, such as neuraminidase and matrix inhibitors, is also available.

This virus spreads through migratory birds in wildlife, transmitting the virus to livestock, which serve as food and are in close contact with humans. Therefore, there are two important aspects of this virus: its impact on the human population and animals (Figure 1).

Transmission to pets, particularly cats, is another urgent area of attention. In the USA, several cats have suffered fatal infections with Clade 2.3.4.4b from infected cows. Similar feline infections have been reported in other countries like Poland and Korea. This raises concerns about the possibility of transmission from infected cats to their owners (16).

Another alarming issue is that house mice in the USA have been infected with H5N1 strains, potentially playing a significant role in spreading the virus to other species. Many wild species and pets, such as cats, feed on mice as a source of nutrition. Controlling and monitoring the mouse population is challenging,

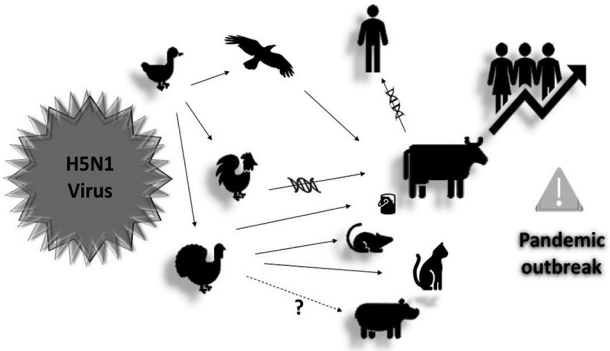

Figure 1. *Possible transmission routes of avian influenza virus H5N1 in USA*

and total elimination is not feasible, as it could lead to an imbalance in the ecosystem (17).

Several publications indicate that individuals infected with H5N1 strains are often under 40 years of age, another similarity with the H1N1 pandemic outbreak (18, 19, 20). It is crucial to educate young people to break the infection cycle.

In this research work, we present new ideas to combat future avian influenza pandemic outbreaks. Our opinion is that this virus spreads very rapidly, as evidenced by its impact on poultry, leading to limited preventive options, particularly culling infected birds. The virus has now been found in many cows in the USA, and pasteurized milk has been found to be contaminated with it.

FOOD SECURITY

An important question arises regarding food safety: should contaminated milk, even if pasteurized, be consumed? The answer is no. If the milk is heavily contaminated, it should not be used for human or animal consumption, as pasteurization may not inactivate all pathogens. Additionally, killed viruses may still contain virulent parts that can cause complications. This example highlights the issue of food security.

We suggest that countries worldwide store milk and beef from infection-free cows in various forms, such as powder and frozen meat. Similarly, poultry products like eggs and meat from infection-free birds should be stored as frozen meat and egg powder to be used during a pandemic outbreak.

There is a need to define standards for contamination levels that can be treated with disinfectants like chlorine and hydrogen peroxide for meat. For milk and eggs, standards for pasteurization must be defined while ensuring that workers handling these products remain infection-free. Today, we have molecular tools to establish these standards. For instance, real-time Polymerase Chain Reaction (PCR) can be used to determine the Cycle Threshold (Ct) value of infected samples (21). If the Ct value exceeds 30, the food can be disinfected or pasteurized and deemed safe for human and animal consumption.

Similarly, antigen-detecting immunological tests and advanced nanotechnological tests can be utilized. Users must be instructed to cook food thoroughly before consumption. There is an urgent need for experimental research in this area.

Reducing the lifespan of poultry birds could also minimize infection risk, while their meat can be frozen for human consumption. Governments must invest heavily in creating new storage capacities, similar to those for oil and food grains.

PREVENTION

Developing avian influenza-resistant poultry birds and cows is crucial. Inexpensive therapeutic molecules should be developed for use in animal populations to reduce or eliminate these infections economically. Plant-derived molecules with antiviral properties show promise and can be synthesized to enhance efficacy and lower production costs. Research in this field must be accelerated. Boosting the immune system of animals is another important strategy. These immune-boosting molecules could also serve as preventive measures for human populations in endemic areas of influenza virus H5N1, as well as for travelers to these regions.

Genekam Biotechnology AG has developed an inexpensive molecule called Genekampowermolecule, which has shown effectiveness against SARS-CoV-2. Testing its efficacy against H5N1 in humans could provide a preventive and therapeutic option.

While vaccination development is crucial for controlling influenza viruses, our current understanding of bird and mammal physiology is insufficient for developing perfect vaccines. More research is needed in this area to avoid developing vaccines with questionable efficacy, as seen in the case of SARS-CoV-2 (22).

Improving short- and long-term preventive measures is urgent, as the 1918 pandemic showed that this virus spreads rapidly. It's crucial to determine whether H5N1 will affect young populations as it did in 1918. Additionally, understanding the role of SARS-CoV-2 in an H5N1 pandemic outbreak is essential for preparing effective prevention strategies against mixed infections, which can be highly fatal.

The roles of other avian influenza virus strains, such as H9N2 and H7N9, during human infections should also be investigated.

Each country should prepare with molecular testing kits stored in advance. My laboratory has developed a double-check real-time PCR test that provides broader coverage of circulating strains and is easy to use. Quality assurance of such tests is essential to avoid issues seen with questionable tests during the SARS-CoV-2 pandemic. Training for healthcare professionals, including medical, dental, and veterinary students, is crucial for identifying different pathological conditions during potential pandemic outbreaks and understanding the various blood profiles associated with these conditions, as observed during the SARS-CoV-2 outbreak (23).

This work serves as a global call to prepare for potential avian influenza pandemic outbreaks.

CONCLUSION

Here we have shown the lessons learned from pandemic outbreak H1N1 1918 and the steps needed to improve for potential H5N1 pandemic outbreak. We are working to write the full versions of this publication about the preparation of the influenza virus H5N1 pandemic outbreak.

Abbreviations

BBC - British Broadcasting Corporation
Ct - Cycle Threshold
PCR - Polymerase Chain Reaction
SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2
USA - United States of America

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Note: Artificial intelligence was not utilized as a tool in this study.

Sažetak

KAKO SE PRIPREMITI ZA PANDEMIJU PTIČJEG GRIPA H5N1: POUKE IZ PANDEMIJE INFLUENCE H1N1 IZ 1918

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U ovom radu ističemo značajne izazove s kojima smo se susreli tokom pandemije influence H1N1 1918. godine. Ove lekcije koristimo kako bismo se pripremili za potencijalna izbijanja pandemije ptičjeg gripa H5N1, s obzirom na to da ovaj virus može uticati kako na ljude tako i na životinje koje služe kao hrana. Priprema za ovu pretnju je od ključnog značaja jer su H5N1 infekcije već prisutne u Sjedinjenim Američkim Državama i mnogim drugim zemljama.

Ključne reči: Ptičja influenca H5N1, ptičji grip, izbijanje pandemije, influenca A, sigurnost hrane.

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