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World Flu Day 2024 with One Health Approach in Iran

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ABSTRACT

Introduction: The global impact and significance of influenza are profound, from the 1918 Spanish flu pandemic to recent seasonal and avian influenza outbreaks. The ongoing need for international collaboration to control and mitigate the effects of influenza remains crucial. World Flu Day, launched on November 1, 2018, at the Asian-Pacific Centenary Spanish 1918-flu Symposium in Shenzhen, China, aimed to raise public awareness, accelerate scientific research, advocate for the development of a universal influenza vaccine, and strengthen the global political efforts for influenza prevention and control. The main objective of the conference was to cover all aspects of influenza, including epidemiology, vaccination, cross-species outbreaks, and treatments. **Conference structure and highlights:** The structure of the conference included the history of the Pasteur Institute and its Influenza Department, pathogenesis, epidemiology, vaccination, and treatment of human and avian influenza. The key topics discussed were history of the Pasteur Institute's services, introducing the Influenza Department, pathogenesis and epidemiology of influenza infections in Iran and the region, influenza vaccines from past to present, current clinical status of influenza in humans, herbal remedies for influenza treatment, avian influenza and its risks to humans, and emerging influenza viruses and cross-species outbreaks. **Conclusion/impact:** The important lessons learned from past influenza outbreaks—including vaccination protocols, treatment strategies, cross-species outbreaks, and global collaborations—were acknowledged as critical for guiding current and future pandemic preparedness efforts under the One Health approach, contributing substantially to the global fight against influenza.

INTRODUCTION

The influenza virus belongs to the *Orthomyxoviridae* family, with three types: A, B, and C. Types A and B are considered the predominant causes of human and animal infections [1]. Among these, influenza A virus (IAV) causes the most severe respiratory illnesses, resulting in considerable morbidity and mortality [2].

Pandemics among humans, birds, and swine, caused by IAVs, occur sporadically and lead to significant economic burdens, including healthcare costs, lost productivity, and impacts on trade and travel. Vaccination is the primary strategy for preventing influenza; however, antigenic drift and shift, resulting from genetic mutations in the viral genome, can reduce vaccine efficacy [3, 4]. Antiviral drugs play a significant role in treating influenza, reducing the severity and duration of illness, and can also contribute to minimizing the spread of infection, particularly in outbreak settings. However, the potential for side effects and the emergence of antiviral resistance complicate treatment strategies [5].

World Flu Day was established on November 1, 2018, at the Asia-Pacific Centenary Symposium in Shenzhen, China, commemorating the 1918 Spanish flu pandemic. Its goals were to raise public awareness, accelerate scientific research, advocate for universal influenza vaccination, and strengthen global political commitment to influenza prevention and control. It aims to foster collaboration and the exchange of ideas among scientists from China, Japan, and other countries internationally. The outcomes of these discussions are expected to inform recommendations for influenza control, with a particular focus on the Asia-Pacific region, but also with global implications [6].

The 'One Health' approach recognizes the interconnected health of humans, animals, and the and

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environment calls for a coordinated strategy to address health challenges at this interface [7].

Cross-sectoral collaboration is essential under a One Health approach for addressing zoonotic diseases such as influenza. The development of new influenza vaccines and antiviral medications represents a crucial step towards more effective prevention and treatment [8].

Conference Overview

Date and Venue: November 1, 2024, at the Pasteur Institute of Iran.

Participants: Attendees included medical professionals, researchers, public health officials, students, and other healthcare workers.

Conference Proceedings

Opening Remarks

The opening remarks included a brief history of influenza epidemics in Iran over the past century and the role of the Pasteur Institute of Iran in responding to these outbreaks. The presentation also reviewed the history of the Pasteur Institute of Iran's establishment and its significant contributions to public health over its history. The Institute's current mission and key activities were also discussed. Speakers noted that the Institute's establishment in 1299 (Solar Hijri calendar) followed the Spanish flu pandemic, highlighting its founding purpose: to respond to that pandemic and control other infectious diseases affecting Iranian society.

Session Summaries

The sessions began with a brief overview of World Flu Day and the role of the Influenza and Respiratory Viruses Department in supporting the event's goals. Key highlights included:

- Designating November 1st as World Flu Day to commemorate the 100th anniversary of the 1918-1919 influenza pandemic.
- Increasing public awareness about influenza.
- Accelerating scientific innovation and basic research to address influenza challenges.
- Building strong global political will support influenza prevention and control.

Pathogenesis and epidemiology of influenza infections in Iran and the region

Discussions covered influenza virus morphology, classification, nomenclature, and antigenic changes, highlighting their role in epidemic and pandemic emergence. Influenza's significant impact on public health, economies, and social and political stability underscores the importance of global surveillance. The Global Influenza Surveillance and Response System (GISRS), since its formation in 1952, has been responsible for monitoring influenza viruses in collaboration with member countries. Finally, the distribution of influenza virus types and subtypes in Iran and neighboring countries was compared to the global distribution pattern.

Influenza infection: Clinical manifestation, vaccination, treatment and post-exposure prophylaxis

The session discussed influenza symptoms and groups at increased risk of severe illness, including adults aged 65 years and older, individuals with underlying chronic medical conditions, pregnant women, and children under 5 years of age. Influenza viruses primarily spread through respiratory droplets produced by coughing, sneezing, or talking. The session highlighted the optimal timing of influenza vaccination. For individuals requiring only one dose, vaccination in September or October is generally recommended, with the goal of vaccination by the end of October in the Northern Hemisphere. While vaccination is recommended for all pregnant women and adults aged 65 and older, the optimal timing may differ from the general recommendation due to concerns about waning immunity. These individuals should consult their healthcare provider to determine the best time to receive the influenza vaccine. Children requiring two doses of influenza vaccine should receive the first dose as soon as the vaccine becomes available, as the second dose must be administered at least four weeks later. The session also addressed vaccine efficacy and potential side effects. The discussion then turned to antiviral medications, such as oseltamivir, and their use in individuals with underlying medical conditions. Antiviral medications can reduce the severity and duration of influenza illness.

Herbal remedies against influenza

This session focused on herbal medicine for the treatment and prevention of influenza. Many modern pharmaceuticals are derived from or inspired by natural compounds. The effectiveness and safety of herbal medicines should be confirmed through high-quality clinical trials and standardization of purity and dosage. The World Health Organization (WHO) estimates that 80% of the population in some Asian and African countries currently use herbal medicines for some primary health care needs. This widespread use highlights the cultural significance of herbal medicine, but it's important to note that traditional use does not necessarily equate to proven efficacy or safety. The session then introduced pharmacognosy, a specialized field of pharmacy that studies medicinal plants and their bioactive compounds. The presentation then explored influenza from the perspective of Traditional Chinese Medicine (TCM), which classifies influenza-like illnesses into 'wind-cold' and 'wind-heat' syndromes, each with distinct characteristics and associated complications. The presentation highlighted two main categories of herbs used in TCM for influenza: expectorants and those believed to stimulate the immune

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system. Some of these herbal remedies are used in traditional medicine to manage influenza symptoms and complications, either as supportive care alongside conventional treatments or, in some cases, as alternatives. Finally, the presentation noted that, like other potential antiviral agents, these compounds are being investigated for their effects on virus-host interactions in *in vitro* and *in vivo* studies.

Avian influenza virus A (H5N1): A potential pandemic threat to human

This session focused on avian influenza A(H5N1) as a potential pandemic threat to humans. Humans can be infected with a number of avian influenza viruses including H5N1. Avian influenza virus strains are generally classified into two categories based on the severity of disease they cause in poultry: low pathogenic avian influenza (LPAI), which typically causes little or no clinical signs, and highly pathogenic avian influenza (HPAI), which can cause severe clinical signs and high mortality rates. A potential pandemic influenza strain could arise from reassortment between animal and human influenza viruses when they co-infect the same host cell. Iran's national program for preventing and controlling highly pathogenic avian influenza includes timely reporting and information sharing with poultry breeders and related industries, rapid diagnosis of suspect cases through a national diagnostic network, and quarantine measures. Finally, targeted vaccination of birds is one strategy to reduce mortality in poultry.

Influenza vaccine

This section reviewed the evolution of influenza vaccines. Since the 1930s, influenza vaccine development has evolved dramatically, from early inactivated vaccines to current recombinant and live-attenuated vaccines. Key advancements have focused on addressing the challenges posed by rapid viral mutation, aiming to balance safety with broad-spectrum efficacy against multiple influenza strains. Recent efforts have focused on overcoming the limitations of egg-based vaccine production and the challenges of strain-specific immunity, aiming to develop vaccines that offer improved efficacy across diverse populations. Modern influenza vaccines include inactivated, recombinant, and live-attenuated types, each with distinct benefits and limitations. These limitations highlight the ongoing challenges in achieving more broadly protective immunity and addressing the varying immune responses in different age groups and risk groups.

Avian influenza A(H5N1) in dairy cattle

The next presentation focused on the recent emergence of avian influenza A(H5N1) in dairy cattle. The recent detection of H5N1 avian influenza in United States dairy cattle raises critical biosecurity and zoonotic transmission concerns. Dairy cattle, not previously recognized as a major reservoir for H5N1, present unique containment challenges. This emergence has heightened awareness of cross-species transmission potential, prompting rapid government interventions. In response to H5N1 in cattle, federal and state authorities implemented strict biosecurity measures, including quarantine and enhanced surveillance. These actions aim to control potential outbreaks and safeguard both livestock and public health. This response underscores the importance of a One Health approach, with coordinated efforts between animal health, public health, and environmental agencies, to effectively manage zoonotic diseases.

Key outcomes

One Health calls for an integrated approach to optimize the health of humans, animals, and the environment. According to the Iran Food and Drug Administration (IFDA), Iran's influenza vaccine supply is met through a combination of domestic production and imports. Over 1.8 million doses of imported vaccines (from Dutch and French manufacturers) have been procured. The following influenza vaccines are currently available in Iran: Vaxigrip (egg-based, France), Influvac (egg-based, Netherlands), and Fluguard recombinant vaccine (Iran).

While influenza vaccines for the 2024-2025 season are primarily quadrivalent, designed to protect against two influenza A viruses and two influenza B viruses (one from each of the B/Victoria and B/Yamagata lineages), the WHO has recommended the removal of the B/Yamagata component for future formulations, transitioning to trivalent vaccines containing only two influenza A viruses and one influenza B/Victoria lineage virus. Influenza vaccine recommendations vary by age and individual health status. Different vaccine formulations are licensed for specific age groups, and certain vaccines may be contraindicated or not recommended for individuals with certain underlying conditions or allergies.

For adults and children under 65 years of age, vaccine options include inactivated influenza vaccines, recombinant influenza vaccine, and live attenuated influenza vaccine. In general, there is no preferential recommendation for one of these vaccine types over another in this age group, in the absence of contraindications.

For adults aged 65 years and older, there are three influenza vaccines that are preferentially recommended over standard-dose unadjuvanted influenza vaccines. These include Fluzone High-Dose Quadrivalent influenza vaccine, Flublok Quadrivalent recombinant influenza vaccine, and Fluad Quadrivalent adjuvanted influenza vaccine. While influenza vaccines are overwhelmingly safe and effective, there is a very small potential risk of Guillain-Barré Syndrome (GBS), a rare neurological disorder, following vaccination [9]. However, the benefits of influenza vaccination in

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preventing serious illness, hospitalization, and death far outweigh this very small risk.

Future Directions

Establishing a clear epidemic threshold – the level of influenza activity that signals an outbreak – is crucial for A key limitation is that a proportion of influenza cases may go unreported within the healthcare system. While underreporting is a common challenge in healthcare systems globally, improvements in public health coverage in Iran are expected to lead to better recording of influenza cases over time [11].

Global Impacts

According to the WHO, influenza remains one of the world's greatest public health challenges, responsible for an estimated 290,000 to 650,000 deaths annually. Globalization, urbanization, and increased human mobility are expected to accelerate the spread of future influenza pandemics. Furthermore, individuals infected with influenza are at increased risk of other serious health complications, such as heart attacks, strokes, and severe pneumonia.

The WHO's Global Influenza Strategy for 2019-2030 aims to strengthen national influenza programs, focusing on three key goals:

- Reducing the burden of seasonal influenza.
- Minimizing the risk of zoonotic influenza transmission.
- Mitigating the impact of a future influenza pandemic.

In addition, the WHO calls for the development and implementation of improved tools to prevent, detect, control, and treat influenza, such as more effective vaccines and antiviral drugs [10].

Implications

The WHO has provided essential supplies to enhance the influenza response capacity of the National Influenza Center and National Collaborating Laboratory in Iran. This support aims to improve influenza surveillance, diagnosis, and treatment, and to ensure equitable access to vaccines and antiviral medications for the Iranian population.

Conclusion

The World Flu Day 2024 conference, held at the Pasteur Institute of Iran, brought together experts to discuss the latest advancements and challenges in influenza prevention, control, and treatment, with a particular emphasis on the One Health approach. Key discussions focused on the ongoing threat of avian influenza, particularly the emergence of H5N1 in dairy cattle, and the need for enhanced surveillance and biosecurity measures. The conference also highlighted the evolution of influenza vaccines, the importance of timely vaccination, and the ongoing efforts to develop more broadly protective vaccines. The role of antiviral medications in treatment and prophylaxis was also emphasized. The conference underscored the critical importance of a One Health approach, recognizing the interconnectedness of human, animal, and environmental health, in effectively addressing the multifaceted challenges posed by influenza. Moving forward, continued collaboration between researchers, public health officials, veterinarians, and policymakers, both in Iran and globally, is essential to strengthen influenza surveillance, improve vaccine efficacy, and mitigate the impact of future outbreaks and pandemics. Further research into universal vaccines is also crucial. By embracing a One Health approach and fostering international collaboration, we can work towards a future with reduced influenza burden and improved global health security.

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CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interests associated with this manuscript.

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