IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ON REPORTED ACTIVITIES OF INFLUENZA A VIRUS SUBTYPE H3N2

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Abstract: To provide vaccination against infection due to 2009 pandemic influenza A virus subtype H1N1 (A[H1N1]pdm09) to resource-constrained countries with otherwise very little access to the A(H1N1)pdm09 vaccine, the World Health Organization (WHO) coordinated distribution of donated vaccine to selected countries worldwide, including those in Africa. From February through November 2010, 32.2 million doses were delivered to 34 countries in Africa. Of the 19.2 million doses delivered to countries that reported their vaccination activities to WHO, 12.2 million doses (64%) were administered. Population coverage in these countries varied from 0.4% to 11%, with a median coverage of 4%. All countries targeted pregnant women (median proportion of all vaccine doses administered [mpv], 21% [range, 4%–72%]) and healthcare workers (mpv, 9% [range, 1%–73%]).

Keywords: influenza, human influenza influenza A virus, avian influenza, H5N1 subtype, sentinel surveillance, epidemiology, viruses, policy review

I. INTRODUCTION

Fourteen of 19 countries targeted persons with chronic conditions (mpv, 26% [range, 5%–66%]) and 10 of 19 countries vaccinated children (mpv, 54% [range, 17%–75%]). Most vaccine was distributed after peak A(H1N1)pdm09 transmission in the region. The frequency and severity of adverse events were consistent with those recorded after other inactivated influenza vaccines. Pandemic preparedness plans will need to include strategies to ensure more-rapid procedures to identify vaccine supplies and distribute and import vaccines to countries that may bear the brunt of a future pandemic. [1]

Influenza virus, with a global distribution, diverse animal host range and multiple virus subtypes, has caused several pandemics. To better prepare for the emergence of new subtypes and the possible threat of the next pandemic, the global status of animal influenza must be defined and documented. We created a global database of animal influenza events by searching scientific databases and the primary literature on animal influenza-related events up to and including 2016. The temporal, spatial and host distribution of animal

influenza and the diversity of influenza subtypes in different regions were analyzed. A total of 70,472 records and 4712 events of animal influenza throughout the world were identified. Events involving subtypes H5N2, H7N7 and H7N9 were relatively constant, with a slow upward trend during the past decade. Asia was the region with the most clusters of events. Poultry was the main host reported in Asia and Africa, and wild birds in Europe and North America. We found that wild birds carried a very rich array of virus subtypes, a warning for the possible generation of reassortment viruses with pandemic potential. Influenza virus subtype diversity - a risk for virus reassortment - was greatest in Asia, North America and Europe. Our database provides a comprehensive overview of the historical and current status of animal influenza events throughout the world. Influenza surveillance needs to be strengthened in some countries and regions to prevent the emergence of new subtypes. Importantly, improvement of the global influenza surveillance system and structures to enable sharing of surveillance data is very much needed to prepare for the next pandemic.[2]

The relative antiviral activities of four drugs against contemporary strains of influenza A and B viruses were determined in Madin-Darby canine kidney cell monolayers with a plaque inhibition assay. This assay proved to be a reliable, rapid method of determining 50% inhibitory concentrations that correlated well with clinically achievable drug levels and the results of clinical trials. Contemporary strains of influenza A viruses (subtypes H1N1, H3N2, HSW1N1) required amantadine hydrochloride and rimantadine hydrochloride 50% inhibitory concentrations in the range of 0.2 to 0.4 microgram/ml, whereas 50% inhibitory concentrations ranged from approximately 50 to 100 micrograms/ml against influenza B viruses. Ribavirin was approximately 10-fold less active than amantadine hydrochloride against influenza A viruses, and the ribavirin 50% inhibitory concentrations against both influenza A and B viruses ranged from 2.6 to 6.8 micrograms/ml. Inosiplex had no antiviral activity in this test system.[3]

This report summarises information collected for the surveillance of influenza virus infection in England and Wales from October 1995 to June 1996 (weeks 40/95 to 25/96). Total respiratory disease' activity, as reported by the Birmingham Research Unit of the Royal College of General Practitioners, rose to peaks in weeks 48/95, 51/95, and 01/96. The first peak coincided with a peak in "influenza and flu-like illness'. The subsequent peaks were accounted for by an increase in reports of acute bronchitis, including bronchiolitis, and may have been associated with the annual rise in infections with respiratory syncytial virus. Influenza A virus was responsible for most infections, with moderate activity occurring in the early part of the winter, peaking in December (week 48/95). Influenza A subtype H3N2 predominated until week 07/96, after which subtype H1N1 accounted for most infections. Influenza activity was first seen in central and northern England, followed by the south of England, Wales, and Scotland. Circulating influenza viruses were antigenically similar to the components of the 1995/96 vaccine. International surveillance during 1995/96 has led to a different H3N2 component being included in the influenza vaccine recommended for 1996/97.[4]

Influenza virus infection is a major public health problem that leads to significant morbidity and mortality. The emergence of resistance to the currently available anti-influenza agents has necessitated the development of new drugs with novel targets. Studying known ethno-medicinal plants is a promising approach for the discovery of new antiviral compounds. *Alchemilla mollis* is used in traditional medicine in Europe for different indications, including minimizing the symptoms of a sore throat. In this study, we found that *A. mollis* extract has anti-influenza activity, and investigated the mechanism underlying its inhibition of influenza virus replication. Plaque assays demonstrated that treatment of cells with *A. mollis* extract prior to infection did not inhibit influenza virus infection. However, plaque formation was markedly reduced when infected cells were overlaid with an agarose gel containing *A. mollis* extract. In addition, exposure of the virus to *A. mollis* extract prior to infection and treatment of cells during virus infection significantly suppressed plaque formation. Influenza virus-induced hemagglutination of chicken red blood cells was inhibited by *A. mollis* extract treatment. The inhibitory effect was observed against influenza A virus subtypes H1N1, H3N2, and H5N2. These findings suggest that *A. mollis* extract has virucidal or neutralizing activity against influenza virus particles. Furthermore, inhibitory effect of zanamivir synergistically increased after combination with *A. mollis* extract. Our results suggest that *A. mollis* extract has the potential to be developed as an anti-influenza agent.[5]

A system of reverse genetics was used to generate influenza A/H1N1 viruses harbouring neuraminidase (NA) mutations previously associated with resistance to NA inhibitors in various viral subtypes. The His274Tyr and Glu119Gln mutants were rescued whereas the Arg292Lys and Glu119→Gly, Val, Ala or Asp mutants could not be generated. In NA inhibition assays, the His274Tyr mutant was resistant to oseltamivir (430-fold over wild-type) and BCX-1812 (50-fold) but was sensitive to zanamivir. A similar trend was seen when the mutant was evaluated by plaque reduction assay (PRA). The Glu119Gln mutant expressed a low level of resistance to oseltamivir (ninefold) and zanamivir (fourfold) in NA inhibition assay but was only marginally resistant to oseltamivir (fourfold) in PRA. The replication capacity of both mutants, in particular that of the His274Tyr virus, was impaired when compared with the wild-type virus in vitro.[6]

The emergence of a novel strain of influenza virus A (H1N1) in April 2009 focused attention on influenza surveillance capabilities worldwide. In consultations before the 2009 outbreak of influenza subtype H1N1, the World Health Organization had concluded that the world was unprepared to respond to an influenza pandemic, due in part to inadequate global surveillance and response capacity. We describe a sentinel surveillance system that could enhance the quality of influenza epidemiologic and laboratory data and strengthen a country's capacity for seasonal, novel, and pandemic influenza detection and prevention. Such a system would 1) provide data for a better understanding of the epidemiology and extent of seasonal influenza, 2) provide a platform for the study of other acute febrile respiratory illnesses, 3) provide virus isolates for the development of vaccines, 4) inform local pandemic planning and vaccine policy, 5) monitor influenza epidemics and pandemics, and 6) provide infrastructure for an early warning system for outbreaks of new virus subtypes.[7]

Influenza activity in the United States began to increase in mid-November, remained elevated through February 21, 2015, and is expected to continue for several more weeks. To date, influenza A (H3N2) viruses have predominated overall. As has been observed in previous seasons during which influenza A (H3N2) viruses predominated, adults aged ≥65 years have been most severely affected. The cumulative laboratory-confirmed influenza-associated hospitalization rate among adults aged ≥65 years is the highest recorded since this type of surveillance began in 2005. This age group also accounts for the majority of deaths attributed to pneumonia and influenza. The majority of circulating influenza A (H3N2) viruses are different from the influenza A (H3N2) component of the 2014–15 Northern Hemisphere seasonal vaccines, and the predominance of these antigenically and genetically drifted viruses has resulted in reduced vaccine effectiveness (1). This report summarizes U.S. influenza activity* since September 28, 2014, and updates the previous summary (2). Influenza activity in the United States began to increase in early November 2017 and rose sharply from December through February 3, 2018; elevated influenza activity is expected to continue for several more weeks. Influenza A viruses have been most commonly identified, with influenza A(H3N2) viruses predominating, but influenza A(H1N1)pdm09 and influenza B viruses were also reported. This report summarizes U.S. influenza activity* during October 1, 2017–February 3, 2018,† and updates the previous summary (*1*). [8]

Pigs and humans have shared influenza A viruses (IAV) since at least 1918, and many interspecies transmission events have been documented since that time. However, despite this interplay, relatively little is known regarding IAV circulating in swine around the world compared with the avian and human knowledge base. This gap in knowledge impedes our understanding of how viruses adapted to swine or man impacts the ecology and evolution of IAV as a whole and the true impact of swine IAV on human health. The pandemic H1N1 that emerged in 2009 underscored the need for greater surveillance and sharing of data on IAV in swine. In this paper, we review the current state of IAV in swine around the world, highlight the collaboration between international organizations and a network of laboratories engaged in human and animal IAV surveillance and research, and emphasize the need to increase information in high-priority regions. The need for global integration and rapid sharing of data and resources to fight IAV in swine and other animal species is apparent, but this effort requires grassroots support from governments, practicing veterinarians and the swine industry and, ultimately, requires significant increases in funding and infrastructure.[9]

Influenza virus continues to emerge and re-emerge, posing new threats for humans. Here we tested various Korean medicinal plant extracts for potential antiviral activity against influenza viruses. Among them, an extract of *Agrimonia pilosa* was shown to be highly effective against all three subtypes of human influenza viruses including H1N1 and H3N2 influenza A subtypes and influenza B virus. The EC_{50} value against influenza A virus, as tested by the plaque reduction assay on MDCK cells, was 14–23 μg/ml. The extract also exhibited a virucidal effect at a concentration of 160–570 ng/ml against influenza A and B viruses when the viruses were treated with the extract prior to plaque assay. In addition, when tested in

embryonated chicken eggs the extract exhibited a strong inhibitory effect *in ovo* on the H9N2 avian influenza virus at a concentration of 280 ng/ml. Quantitative RT-PCR analysis data showed that the extract, to some degree, suppressed viral RNA synthesis in MDCK cells. HI and inhibition of neuraminidase were observed only at high concentrations of the extract. And yet, the extract's antiviral activity required direct contact between it and the virus, suggesting that its antiviral action is mediated by the viral membrane, but does not involve the two major surface antigens, HA and NA, of the virus. The broad-spectrum antiviral activity of *Agrimonia pilosa* extract on various subtypes of influenza viruses merits further investigation as it may provide a means of managing avian influenza infections in poultry farms and potential avian-human transmission.[10]

814 (99.8%) of these were 2009 pandemic influenza A (H1N1) viruses, 18 (0.1%) were seasonal influenza A (H1), and 35 (0.1%) were influenza A (H3) viruses. Since 1 September, 252 of the 256 pandemic influenza A (H1N1) virus isolates tested for resistance to neuraminidase [sialidase] inhibitors were susceptible to oseltamivir, bringing the total number of such resistant isolates to 14 since April 2009. All the 256 tested isolates were sensitive to zanamivir. One influenza A (H3N2) virus isolate and 152 pandemic influenza A (H1N1) virus isolates were resistant to amantadine and rimantadine. State-specific influenza activity surveillance revealed that by mid-October, nearly all states reported geographically widespread influenza activity. The weekly percentage of outpatient visits for influenza-like illness (ILI) increased from 3.5% in the week ending 5 September to 7.7% in the week ending 31 October. In addition, influenza-associated hospitalization rates continued to trend upward in all age groups. 672 deaths associated with laboratory-confirmed influenza virus infections were reported. 85 paediatric deaths were identified, including 73 with the 2009 pandemic influenza A (H1N1) and 12 with influenza A of undetermined subtype. Continuous monitoring of the changes in geographical spread, type and severity of the 2009 pandemic influenza A (H1N1) is suggested. 867 (68%) were subtyped. 32 483 (99.8%) specimens positive for influenza A, 32 123 respiratory specimens tested were positive for influenza viruses (30%). Of the 48 585 of the 163 This report summarizes the influenza activity in the USA from 30 August 2009, defined as the beginning of the 2009-10 influenza season, through 31 October 2009. Data showed that 48[11]

Lonicera japonica Thunb, rich in chlorogenic acid (CHA), is used for viral upper respiratory tract infection treatment caused by influenza virus, parainfluenza virus, and respiratory syncytial virus, ect in China. It was reported that CHA reduced serum hepatitis B virus level and death rate of influenza virus-infected mice. However, the underlying mechanisms of CHA against the influenza A virus have not been fully elucidated. Here, the antiviral effects and potential mechanisms of CHA against influenza A virus were investigated. CHA revealed inhibitory against A/PuertoRico/8/1934(H1N1) (EC_{50} = 44.87 μM), A/Beijing/32/92(H3N2) (EC_{50} = 62.33 μM), and oseltamivir-resistant strains. Time-course analysis showed CHA inhibited influenza virus during the late stage of infectious cycle. Indirect immunofluorescence assay indicated CHA down-regulated the NP protein expression. The inhibition of neuraminidase activity confirmed CHA blocked release of newly formed virus particles from infected cells. Intravenous injection of 100 mg/kg/d CHA

possessed effective antiviral activity in mice, conferring 60% and 50% protection from death against H1N1 and H3N2, reducing virus titres and alleviating inflammation in the lungs effectively. These results demonstrate that CHA acts as a neuraminidase blocker to inhibit influenza A virus both in cellular and animal models. Thus, CHA has potential utility in the treatment of the influenza virus infection.[12]

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