

9 February 2010

*This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.*

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## **Chem-Bio News – Pandemic Influenza Edition #98**

**1. SAFETY AND IMMUNOGENICITY OF A 2009 PANDEMIC INFLUENZA A H1N1 VACCINE WHEN ADMINISTERED ALONE OR SIMULTANEOUSLY WITH THE SEASONAL INFLUENZA VACCINE FOR THE 2009-10 INFLUENZA SEASON: A MULTICENTRE, RANDOMISED CONTROLLED TRIAL:** *"It can be safely co-administered with the 2009-10 seasonal influenza vaccine."*

**2. PHENOTYPIC CHARACTERISTICS OF NOVEL SWINE-ORIGIN INFLUENZA A/ CALIFORNIA/07/2009 (H1N1) VIRUS:** *"This finding suggests that this virus might be a good wild type parental prototype for live vaccine for potential use for controlling pandemic influenza."*

**3. INFLUENZA CIRCULATION AND THE BURDEN OF INVASIVE PNEUMOCOCCAL PNEUMONIA DURING A NON-PANDEMIC PERIOD IN THE UNITED STATES:** *"During recent seasonal influenza epidemics in the United States, a modest but potentially preventable fraction of invasive pneumococcal pneumonia was associated with influenza circulation."*

**4. VIRAL LOAD IN PATIENTS INFECTED WITH PANDEMIC H1N1 2009 INFLUENZA A VIRUS:** *"Among patients with pandemic H1N1 virus infection, peak viral load occurred on the day of onset of symptoms, and declined gradually afterwards, with no virus being detectable in respiratory specimens by RT-PCR 8 days and by culture 5 days after the onset of symptoms respectively, except in one patient."*

**5. TRANSMISSION OF PANDEMIC H1N1 INFLUENZA VIRUS AND IMPACT OF PRIOR EXPOSURE TO SEASONAL STRAINS OR INTERFERON TREATMENT:** *"In addition, the use of interferon as an antiviral prophylaxis may be an effective way to limit spread in at-risk populations."*

**6. GLOBAL TAMIFLU-RESISTANT H1N1 CASES REACH 225:** *"The World Health Organization (WHO) reported today that 225 cases of H1N1 flu with resistance to oseltamivir (Tamiflu) have been found worldwide, and resistant viruses have spread from person to person in several clusters but have not spilled into the community."*

# CB Daily Report

## Chem-Bio News

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### **SAFETY AND IMMUNOGENICITY OF A 2009 PANDEMIC INFLUENZA A H1N1 VACCINE WHEN ADMINISTERED ALONE OR SIMULTANEOUSLY WITH THE SEASONAL INFLUENZA VACCINE FOR THE 2009-10 INFLUENZA SEASON: A MULTICENTRE, RANDOMISED CONTROLLED TRIAL**

Medical Letter on the CDC & FDA

February 7, 2010

"With the ongoing 2009 pandemic of influenza A H1N1, development of pandemic influenza vaccines has generated much interest. We investigated the safety and immunogenicity of a whole-virion, inactivated, adjuvanted pandemic H1N1 vaccine in adult and elderly volunteers, given without or simultaneously with the 2009-10 seasonal trivalent influenza vaccine."

"This prospective, randomised study was undertaken in two centres in Hungary. 355 participants, including 203 adults (18-60 years) and 152 elderly people (>60 years), were assigned by stratified randomisation to either 0.5 mL of the pandemic vaccine (Fluval P, a monovalent vaccine with 6 µg haemagglutinin per 0.5 mL content and aluminium phosphate gel adjuvant; n=178) or 0.5 mL of the pandemic vaccine and 0.5 mL of the seasonal trivalent vaccine (Fluval AB, a trivalent inactivated whole-virion influenza vaccine; n=177). All vaccinations were done by specific study personnel, who did not take part in the assessment of safety or immunogenicity. Co-primary objectives were safety and immunogenicity by haemagglutinin inhibition testing. All analyses were done according to its pre-established analysis plan. This study is registered with ClinicalTrials.gov, number NCT01010893. Two participants receiving the pandemic vaccine only (group 1) and one receiving pandemic and seasonal vaccines (group 2) were lost to follow-up. In both groups developed antibody responses against the pandemic influenza A H1N1 virus (group 1: seroconversion for adults 74.3%, 95% CI 64.6-82.4 and for elderly people 61.3%, 49.1-72.4; group 2: 76.8%, 67.2-84.7 and 81.8%, 71.4-89.7, respectively). Single doses of 6 µg fulfilled European Union and US licensing criteria for interpandemic and pandemic influenza vaccines. Simultaneously, participants in group 2 developed the immune responses needed for licensing for all three seasonal strains in the seasonal vaccine for the 2009-10 season. All adverse events were rare, mild, and transient; the most frequent were pain at injection site (eight cases in group 1 vs 18 in group 2) and fatigue for 1-2 days after vaccination (three vs five cases). The present pandemic vaccine is safe and immunogenic in healthy adult and elderly patients, and needs low doses and only one injection to trigger immune responses to comply with licensing criteria."

"It can be safely co-administered with the 2009-10 seasonal influenza vaccine. Funding Omninvest, Hungary."

The full article can be found at: (Z. Vajo, et. al., "Safety and immunogenicity of a 2009 pandemic influenza A H1N1 vaccine when administered alone or simultaneously with the

seasonal influenza vaccine for the 2009-10 influenza season: a multicentre, randomised controlled trial". Lancet, UNKNOWN DATE;375(9708):49-55). Link not available.

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## **PHENOTYPIC CHARACTERISTICS OF NOVEL SWINE-ORIGIN INFLUENZA A/ CALIFORNIA/07/2009 (H1N1) VIRUS**

Biotech Week

February 3, 2010

"The 2009 novel A(H1N1) virus appears to be of swine origin. This strain causing the current outbreaks is a new virus that has not been seen previously either in humans or animals."

"We have previously reported that viruses causing pandemics or large outbreaks were able to grow at a temperature above the normal physiological range (temperature resistance, non-ts phenotype), were found to be inhibitor resistant and restricted in replication at suboptimal temperature (sensitivity to grow at low temperature, non-ca phenotype). In this study, we performed phenotypic analysis of novel A(H1N1) virus to evaluate its pandemic potential and its suitability for use in developing a live attenuated influenza vaccine. The goal of this study is to identify phenotypic properties of novel A(H1N1) influenza virus. A/California/07/2009 (H1N1) swine-origin influenza virus was studied in comparison with some influenza A viruses isolated in different years with respect to their ability to grow at non-permissive temperatures. We also analyzed its sensitivity to gamma-inhibitors of animal sera and its ability to agglutinate chicken, human and guinea pig erythrocytes. Swine-origin A/California/07/2009 (H1N1) virus was found to be non-ts and inhibitor resistant and was not able to grow at 25 degrees C (non-ca). We did not find any difference in the ability of the hemagglutinin of A/California/07/2009 (H1N1) virus to bind to erythrocytes of different origin. The novel swine-origin A(H1N1) virus displays a phenotype typical of the past pandemic and epidemic viruses."

"This finding suggests that this virus might be a good wild type parental prototype for live vaccine for potential use for controlling pandemic influenza."

The full article can be found at: (I. Kiseleva, et. al., "Phenotypic characteristics of novel swine-origin influenza A/California/07/2009 (H1N1) virus". Influenza and Other Respiratory Viruses, UNKNOWN DATE;4(1):1-5). Link not available.

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## **INFLUENZA CIRCULATION AND THE BURDEN OF INVASIVE PNEUMOCOCCAL PNEUMONIA DURING A NON-PANDEMIC PERIOD IN THE UNITED STATES**

Biotech Week

February 10, 2010

"Animal models and data from influenza pandemics suggest that influenza infection

predisposes individuals to pneumococcal pneumonia. Influenza may contribute to high winter rates of pneumococcal pneumonia during non-pandemic periods, but the magnitude of this effect is unknown."

"With use of United States surveillance data during 1995-2006, we estimated the association between influenza circulation and invasive pneumococcal pneumonia rates. Weekly invasive pneumococcal pneumonia incidence, defined by isolation of pneumococci from normally sterile sites in persons with clinical or radiographic pneumonia, was estimated from active population-based surveillance in 3 regions of the United States. We used influenza virus data collected by World Health Organization collaborating laboratories in the same 3 regions in seasonally adjusted negative binomial regression models to estimate the influenza-associated fraction of pneumococcal pneumonia. During similar to 185 million person-years of surveillance, we observed 21,239 episodes of invasive pneumococcal pneumonia; 485,691 specimens were tested for influenza. Influenza circulation was associated with 11%-14% of pneumococcal pneumonia during periods of influenza circulation and 5%-6% overall. In 2 of 3 regions, the association was strongest when influenza circulation data were lagged by 1 week."

"During recent seasonal influenza epidemics in the United States, a modest but potentially preventable fraction of invasive pneumococcal pneumonia was associated with influenza circulation."

The full article can be found at: (N.D. Walter, et. al., "Influenza Circulation and the Burden of Invasive Pneumococcal Pneumonia during a Non-pandemic Period in the United States". *Clinical Infectious Diseases*, 2010; 50(2): 175-183). Link not available.

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## **VIRAL LOAD IN PATIENTS INFECTED WITH PANDEMIC H1N1 2009 INFLUENZA A VIRUS**

Drug Week

February 5, 2010

"The aim of this study was to determine the viral load in different body sites," scientists in Hong Kong, People's Republic of China report."

"Viral loads of pandemic H1N1 virus in respiratory specimens, stool, urine, and serum were determined by quantitative reverse transcriptase-polymerase chain reaction (RT-PCR). Respiratory specimens from patients with seasonal influenza were used as historical controls. Initial pre-treatment viral load were compared between these two groups. Serial respiratory specimens from patients with pandemic H1N1 virus infection were obtained for analysis of viral dynamics. Twenty-two pandemic H1N1 cases and 44 seasonal influenza historical controls were included. The mean initial viral load before oseltamivir therapy was  $1.84 \times 10^8$  copies/ml for pandemic H1N1 virus compared with  $3.28 \times 10^8$  copies/ml in seasonal influenza historical controls ( $P=0.085$ ). Among patients with pandemic H1N1 virus infection, peak viral load occurred on the day of onset of symptoms, and declined gradually afterwards, with no virus being detectable in respiratory specimens by RT-PCR 8 days and

by culture 5 days after the onset of symptoms respectively, except in one patient. Pandemic H1N1 virus was detected in stool and in urine from 4/9 and 1/14 patients, respectively. Viral culture was also positive from the stool sample with the highest viral load. Younger age was associated with prolonged shedding in the respiratory tract and higher viral load in the stool."

The full article can be found at: (K.K.W. To, et. al., "Viral Load in Patients Infected With Pandemic H1N1 2009 Influenza A Virus". Journal of Medical Virology, UNKNOWN DATE; 82 (1): 1-7). Link not available.

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## **TRANSMISSION OF PANDEMIC H1N1 INFLUENZA VIRUS AND IMPACT OF PRIOR EXPOSURE TO SEASONAL STRAINS OR INTERFERON TREATMENT**

Drug Week

February 12, 2010

"Novel swine-origin influenza viruses of the H1N1 subtype were first detected in humans in April 2009. As of 12 August 2009, 180,000 cases had been reported globally," researchers in the United States report.

Despite the fact that they are of the same antigenic subtype as seasonal influenza viruses circulating in humans since 1977, these viruses continue to spread and have caused the first influenza pandemic since 1968. Here we show that a pandemic H1N1 strain replicates in and transmits among guinea pigs with similar efficiency to that of a seasonal H3N2 influenza virus. This transmission was, however, partially disrupted when guinea pigs had preexisting immunity to recent human isolates of either the H1N1 or H3N2 subtype and was fully blocked through daily intranasal administration of interferon to either inoculated or exposed animals. Our results suggest that partial immunity resulting from prior exposure to conventional human strains may blunt the impact of pandemic H1N1 viruses in the human population."

"In addition, the use of interferon as an antiviral prophylaxis may be an effective way to limit spread in at-risk populations."

The full article can be found at: (J. Steel, et. al., "Transmission of Pandemic H1N1 Influenza Virus and Impact of Prior Exposure to Seasonal Strains or Interferon Treatment". Journal of Virology, 2010; 84(1): 21-26). Link not available.

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## **GLOBAL TAMIFLU-RESISTANT H1N1 CASES REACH 225**

CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)  
February 05, 2010

"The World Health Organization (WHO) reported today that 225 cases of H1N1 flu with

resistance to oseltamivir (Tamiflu) have been found worldwide, and resistant viruses have spread from person to person in several clusters but have not spilled into the community.

Many of the resistant cases involved people with severely weakened immunity, reinforcing the importance of monitoring for the problem in such patients, the WHO said in today's issue of its Weekly Epidemiological Record.

The 225 cases come from 20 countries and include 65 cases in the Americas, 77 in Europe, 1 in Africa, and 82 in the Western Pacific region, the agency said. All the isolates had the H275Y mutation that confers resistance to oseltamivir but not to the other neuraminidase inhibitor in general use, zanamivir (Relenza)."

The full article can be found at: <http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/feb0510resist-jw.html>

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