23 March 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 #104

1. RISK FOR TRANSMISSION OF PANDEMIC (H1N1) 2009 VIRUS BY BLOOD TRANSFUSION: *"These results suggest that the viremia with pandemic (H1N1) 2009 virus, if any, is very low and can be missed by current NAT or that the viremic period is too brief to identify viremia. Although the risk for transmission of pandemic influenza by transfusion seems to be low, further investigation is needed to elucidate this risk."*

2. PRELIMINARY ESTIMATES OF MORTALITY AND YEARS OF LIFE LOST ASSOCIATED WITH THE 2009 A/H1N1 PANDEMIC IN THE US AND COMPARISON WITH PAST INFLUENZA SEASONS: *"We conclude that the 2009 A/H1N1 pandemic virus had a substantial health burden in the US over the first few months of circulation in terms of years of life lost, justifying the efforts to protect the population with vaccination programs. Analysis of historic records from three other pandemics over the last century suggests that the emerging pandemic virus will continue to circulate and cause excess mortality in unusually young populations for the next few years."*

3. STRUCTURE AND RECEPTOR BINDING PROPERTIES OF A PANDEMIC H1N1 VIRUS HEMAGGLUTININ: *"Receptor binding properties of this protein reveals a strict preference for human-type receptors."*

4. A NOVEL ELECTROCHEMICAL DEVICE TO DIFFERENTIATE PANDEMIC (H1N1) 2009 FROM SEASONAL INFLUENZA. INFLUENZA AND OTHER RESPIRATORY VIRUSES: *"The ElectraSense ® Influenza A assay proved to be a useful assay to quickly and accurately differentiate pandemic (H1N1) 2009 influenza from seasonal influenza."*

5. PUBLIC HEALTH AND ECONOMIC IMPACT OF VACCINATION WITH 7-VALENT PNEUMOCOCCAL VACCINE (PCV7) IN THE CONTEXT OF THE ANNUAL INFLUENZA EPIDEMIC AND A SEVERE INFLUENZA PANDEMIC: *"Current infant vaccination practices may prevent >1 million pneumococcal-related deaths in a severe influenza pandemic, primarily due to herd protection."*

6. SWINE-ORIGIN PANDEMIC H1N1 INFLUENZA VIRUS-LIKE PARTICLES PRODUCED IN INSECT CELLS INDUCE HEMAGGLUTINATION INHIBITING

ANTIBODIES IN BALB/C MICE: *"Immunization induced high serum antibody titers against A/California/04/2009 as well as hemagglutination inhibiting antibodies."*

Chem-Demil News

1. UMATILLA CHEMICAL DEPOT - OFFICIALS CONFIRM UMATILLA CHEMICAL DEPOT WORKER EXPOSED TO MUSTARD AGENT: *"It's the first chemical weapon exposure at the depot since incineration began and only the second one in the history of the nation's chemical demilitarization program, said Army Chemical Materials Agency spokesman Greg Mahall."*

CB Daily Report

Chem-Bio News

RISK FOR TRANSMISSION OF PANDEMIC (H1N1) 2009 VIRUS BY BLOOD TRANSFUSION
By Matsumoto C, Sobata R, Uchida S, Hidaka T, Momose S, Hino S, et al.
Emerging Infectious Diseases
US Centers for Disease Control and Prevention
April, 201 [epub ahead of publication]

"To the Editor: Influenza A pandemic (H1N1) 2009 virus emerged in early 2009 in Mexico and has since spread worldwide. In Japan, the first outbreak of the novel influenza was reported in May 2009 (1) and became pandemic in November. Although no cases of transfusion-transmitted influenza have been published, evidence exists of brief viremia before onset of symptoms (2,3). The possibility of transmission of this virus through transfusion of donated blood is of concern. The Japanese Red Cross Blood Centers have intercepted blood products with accompanying postdonation information indicating possible pandemic (H1N1) 2009 infection and attempted to identify the viral genome in those products by using nucleic acid amplification technology (NAT).

During June–November 2009, blood samples were collected from plasma and erythrocyte products that had been processed from donations; postdonation information indicated diagnosis of pandemic (H1N1) 2009 infection soon after donation. Viral RNA was extracted from plasma samples and erythrocyte fractions by using a QIAamp Virus Biorobot MDx kit (QIAGEN, Valencia, CA, USA) and a High Pure Viral Nucleic Acid Large Volume kit (Roche Diagnostics, Indianapolis, IN, USA), respectively. RNA samples were subjected to real-time reverse transcription–PCR (RT-PCR) of hemagglutinin (HA) and matrix (M) genes of influenza A by using PRISM 7900 (Applied Biosystems, Foster City, CA, USA). The RT-PCR of HA was specific for pandemic (H1N1) 2009 virus, whereas the RT-PCR of M was designed to detect both pandemic (H1N1) 2009 and seasonal influenza A viruses. The sequences of probes and primers were synthesized according to the protocols developed by the Japanese National Institute of Infectious Diseases (4). Either 200 •L of a plasma sample or 100 •L of packed erythrocytes was used for each test, and the test was performed 2× for each gene in

each sample. Before the investigation using donated blood samples, the sensitivity of the NAT system was checked by spiking experiments. Viral particles of pandemic (H1N1) 2009 virus (A/California/04/2009 [H1N1]), donated by the National Institute of Infectious Diseases, were spiked into plasma and erythrocyte samples from healthy volunteers. Viral RNA was detected in the plasma samples spiked with viral particles corresponding to 300 genome equivalents/mL and in the packed erythrocyte samples spiked with viral particles corresponding to 3,000 genome equivalents/mL.

NAT was conducted by using 96 plasma and 67 erythrocyte samples obtained from 96 blood donors who had symptoms of influenza within 7 days postdonation. For 20 donors, pandemic (H1N1) 2009 was diagnosed within 1 day postdonation and, for another 20, within 2 days postdonation (Figure). Pandemic (H1N1) 2009 virus was not found in any of the samples tested, but it was consistently detected in the external positive control. These results suggest that the viremia with pandemic (H1N1) 2009 virus, if any, is very low and can be missed by current NAT or that the viremic period is too brief to identify viremia. Although the risk for transmission of pandemic influenza by transfusion seems to be low, further investigation is needed to elucidate this risk."

The full article can be found at: http://www.cdc.gov/eid/content/16/4/pdfs/09-1795.pdf

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PRELIMINARY ESTIMATES OF MORTALITY AND YEARS OF LIFE LOST ASSOCIATED WITH THE 2009 A/H1N1 PANDEMIC IN THE US AND COMPARISON WITH PAST INFLUENZA SEASONS

By Cecile Viboud, Mark Miller, Don Olson, Michael Osterholm et al.
PLoS Currents Influenza
March 22, 2010

"The on-going debate about the health burden of the 2009 influenza pandemic and discussions about the usefulness of vaccine recommendations has been hampered by an absence of directly comparable measures of mortality impact. Here we set out to generate an "apples-to-apples" metric to compare pandemic and epidemic mortality. We estimated the mortality burden of the pandemic in the US using a methodology similar to that used to generate excess mortality burden for inter-pandemic influenza seasons. We also took into account the particularly young age distribution of deaths in the 2009 H1N1 pandemic, using the metric "Years of Life Lost" instead of numbers of deaths. Estimates are based on the timely pneumonia and influenza mortality surveillance data from 122 US cities, and the age distribution of laboratory-confirmed pandemic deaths, which has a mean of 37 years. We estimated that between 7,500 and 44,100 deaths are attributable to the A/H1N1 pandemic virus in the US during May-December 2009, and that between 334,000 and 1,973,000 years of life were lost. The range of years of life lost estimates includes in its lower part the impact of a typical influenza epidemic dominated by the more virulent A/H3N2 subtype, and the impact of the 1968 pandemic in its upper bound. We conclude that the 2009 A/H1N1 pandemic virus had a substantial health burden in the US over the first few months of circulation in terms of years of life lost, justifying the efforts to protect the population with vaccination programs. Analysis of historic records from three other pandemics over the last

century suggests that the emerging pandemic virus will continue to circulate and cause excess mortality in unusually young populations for the next few years. Continuing surveillance for indicators of increased mortality is of key importance, as pandemics do not always cause the majority of associated deaths in the first season of circulation."

The full article can be found at: http://knol.google.com/k/cecile-viboud/preliminary-estimates-of-mortality-and/35hpbywfdwl4n/8?collectionId=28qm4w0q65e4w.1&position=1#

STRUCTURE AND RECEPTOR BINDING PROPERTIES OF A PANDEMIC H1N1 VIRUS HEMAGGLUTININ

By Hua Yang, Paul Carney and James Stevens
PLoS Currents Influenza
March 22, 2010

"The first influenza pandemic of the new century emerged in April 2009, when a new H1N1 influenza virus (H1N1pdm), found in patients in Mexico and the United States, spread rapidly across the world by human-to-human transmission, resulting in the World Health Organization declaring a global pandemic on June 11th 2009 [1]. The pandemic H1N1 virus (2009 H1N1) was unique in that it had a gene constellation from both North American and Eurasian swine lineages that had not been isolated previously in either swine or human populations [2]. Phylogenetic and antigenic analysis of the hemagglutinin (HA) gene revealed it to be distinct from seasonal human H1N1 viruses but more similar to the classical North American swine lineage.

Ten months after the first viruses were isolated, the virus is still antigenically homogeneous [3]. However, as the HA continues to circulate in the human population, its HA antigenic sites will continue to be targeted by antibody-mediated selection pressure. Therefore it is important from a public health perspective to structurally characterize the hemagglutinin so that the research community has a template with which to visualize any changes affecting antigenicity or virulence that may emerge as this virus evolves. To this end, we have cloned, expressed and solved the structure of a pandemic H1 hemagglutinin by x-ray crystallography. The structure was used to analyze amino acid substitutions in the HA that have raised some concern during the last 11 months of global surveillance activities. The same protein was analyzed by glycan microarray and compared to seasonal and other pandemic variants. Results reveal a strict human-like receptor specificity."

"Conclusions

Although a number of mutations have been reported in circulating pandemic H1N1 viruses, they have not affected virus antigenicity and pathogenicity. The use of the Darwin09 structure to analyze the interactions of these HAs with virus receptors highlights the importance of having structural information to aid such analysis. The expression system used here also provides an important route for the safe production of these pandemic proteins on a large scale. Availability of recombinant protein enables its use for downstream applications such as glycan microarray analysis, as described here, reagents for diagnostic kit development or as antigens for antibody production. If this methodology were not available, HA production from the virus would have been difficult at the start of the

pandemic, due to stringent biosafety requirements. Rapid determination and dissemination of the pandemic H1N1 hemagglutinin 3-D structure and characterization of its receptor specificity should enable the medical and public health research community to develop improved intervention approaches to control and prevent influenza morbidity and mortality as this virus becomes endemic in human populations."

The full article can be found at: http://knol.google.com/k/hua-yang/structure-and-receptor-binding/250q41vwql45q/3?collectionId=28qm4w0q65e4w.1&position=2#

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A NOVEL ELECTROCHEMICAL DEVICE TO DIFFERENTIATE PANDEMIC (H1N1) 2009 FROM SEASONAL INFLUENZA. INFLUENZA AND OTHER RESPIRATORY VIRUSES
Health Risk Factor Week
March 23, 2010

"One of the challenges of the recent pandemic (H1N1) 2009 influenza outbreak was to differentiate the virus from seasonal influenza when confronting clinical cases. The determination of the virus has implications on treatment choice, and obvious epidemiologic significance."

"We set out to apply a novel electrochemical device to samples derived from clinical cases of pandemic (H1N1) 2009 influenza to examine the ability of the device to differentiate these samples from cases of seasonal influenza. An IRB approved protocol allowed for the use of original nasal wash samples from 24 confirmed human cases pandemic (H1N1) 2009 influenza. Clinical samples from cases of seasonal influenza (Influenza A/H1N1, A/H3N2, and B) were included as controls. Nucleic acids were extracted and samples examined by the ElectraSense ® Influenza A assay (CombiMatrix, Inc). Samples were also examined by RT-PCR or Luminex assays as a comparator. The ElectraSense ® Influenza A assay correctly identified 23 of 24 samples of laboratory-confirmed pandemic (H1N1) 2009 Influenza. The assay correctly identified all samples of influenza A/H1N1 and A/H3N2, and differentiated these from pandemic (H1N1) 2009 Influenza in all cases."

"The ElectraSense ® Influenza A assay proved to be a useful assay to quickly and accurately differentiate pandemic (H1N1) 2009 influenza from seasonal influenza."

The full article can be found at: (T.M. Straight, et. al., "A novel electrochemical device to differentiate pandemic (H1N1) 2009 from seasonal influenza. Influenza and Other Respiratory Viruses", 2010;4(2):73-79). Link not available.

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PUBLIC HEALTH AND ECONOMIC IMPACT OF VACCINATION WITH 7-VALENT PNEUMOCOCCAL VACCINE (PCV7) IN THE CONTEXT OF THE ANNUAL INFLUENZA EPIDEMIC AND A SEVERE INFLUENZA PANDEMIC

Preventive Medicine Week
March 28, 2010

"Influenza pandemic outbreaks occurred in the US in 1918, 1957, and 1968. Historical evidence suggests that the majority of influenza-related deaths during the 1918 US pandemic were attributable to bacterial pneumococcal infections."

"The 2009 novel influenza A (H1N1) outbreak highlights the importance of interventions that may mitigate the impact of a pandemic. A decision-analytic model was constructed to evaluate the impact of 7-valent pneumococcal conjugate vaccine (PCV7) on pneumococcal disease incidence and mortality during a typical influenza season (13/100) and a severe influenza pandemic (30/100). Outcomes were compared for current PCV7 vaccination practices vs. no vaccination. The model was estimated using published sources and includes indirect (herd) protection of non-vaccinated persons. The model predicts that PCV7 vaccination in the US is cost saving for a normal influenza season, reducing pneumococcal-related costs by $1.6 billion. In a severe influenza pandemic, vaccination would save $7.3 billion in costs and prevent 512,000 cases of IPD, 719,000 cases of pneumonia, 62,000 IPD deaths, and 47,000 pneumonia deaths; 84% of deaths are prevented due to indirect (herd) protection in the unvaccinated. PCV7 vaccination is highly effective and cost saving in both normal and severe pandemic influenza seasons."

"Current infant vaccination practices may prevent >1 million pneumococcal-related deaths in a severe influenza pandemic, primarily due to herd protection."

The full article can be found at: (J.L.Rubin, et. al., "Public health and economic impact of vaccination with 7-valent pneumococcal vaccine (PCV7) in the context of the annual influenza epidemic and a severe influenza pandemic". BMC Infectious Diseases, 2010;10 ():14). Link not available.

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SWINE-ORIGIN PANDEMIC H1N1 INFLUENZA VIRUS-LIKE PARTICLES PRODUCED IN INSECT CELLS INDUCE HEMAGGLUTINATION INHIBITING ANTIBODIES IN BALB/C MICE
Health Risk Factor Week
March 23, 2010

"Recent outbreaks of influenza A highlight the importance of rapid and sufficient supply for pandemic and inter-pandemic vaccines. Classical manufacturing methods for influenza vaccines fail to satisfy this demand."

"Alternatively, cell culture-based production systems and virus-like particle (VLP)-based technologies have been established. We developed swine-origin pandemic H1N1 influenza VLPs consisting of hemagglutinin (A/California/04/2009) and matrix protein. Hemagglutinin and matrix protein were co-expressed in insect cells by the baculovirus expression system. VLPs were harvested from infection supernatants, purified and used for intraperitoneal immunization of BALB/c mice. Immunization induced high serum antibody titers against A/

California/04/2009 as well as hemagglutination inhibiting antibodies. Additionally, we compared VLP production in two different insect cell lines, Sf9 and BTI-TN5B1-4 (High Five)."

The full article can be found at: (F. Krammer, et. al., “Swine-origin pandemic H1N1 influenza virus-like particles produced in insect cells induce hemagglutination inhibiting antibodies in BALB/c mice”. Biotechnology Journal, 2010;5(1):17-23). Link not available.

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Chem-Demil News

UMATILLA CHEMICAL DEPOT - OFFICIALS CONFIRM UMATILLA CHEMICAL DEPOT WORKER EXPOSED TO MUSTARD AGENT
By Annette Cary
The TriCity Herald
March 23, 2010

“It's the first chemical weapon exposure at the depot since incineration began and only the second one in the history of the nation's chemical demilitarization program, said Army Chemical Materials Agency spokesman Greg Mahall.

Two workers were in an airlock as they were leaving a portion of the incineration plant about 4 p.m. Wednesday when an alarm sounded, indicating low levels of mustard agent.

They had their protective clothing and other clothing removed and were decontaminated. But one worker developed first a red spot and then a 1-inch diameter blister on his skin.

The U.S. Army Chemical Materials Agency believes that a drop of mustard agent may have seeped through protective clothing, which includes cotton coveralls, apron, gloves and boots.

The incineration plant was not processing mustard agent last week while the depot awaits approval to proceed with its trial burn. But some of the chemical agent was incinerated during the shakedown period in preparation for the trial burn.

The worker had been calibrating a scale used when mustard agent is drained from containers. Large weights were placed on a conveyor system and sent into an area of the plant where one-ton containers of mustard had previously been punctured and then drained with a wand that suctions out the agent during the shakedown.

The working theory for the incident investigation is that the wand was contaminated and may have dripped mustard agent onto the weights, which one of the workers then was exposed to, Mahall said.”

The full article can be found at: http://www.tri-cityherald.com/2010/03/23/949366/officials-confirm-umatilla-chemical.html#ixzz0izfe9Zk5

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