

5 January 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 #93**

1. GLYCANS ON INFLUENZA HEMAGGLUTININ AFFECT RECEPTOR BINDING AND IMMUNE

RESPONSE: *"Thus, removal of structurally nonessential glycans on viral surface glycoproteins may be a very effective and general approach for vaccine design against influenza and other human viruses."*

2. AN ASSESSMENT OF THE VALIDITY OF SOFA SCORE BASED TRIAGE IN H1N1 CRITICALLY

ILL PATIENTS DURING AN INFLUENZA PANDEMIC: *"SOFA [Sequential Organ Failure Assessment] score based triage could lead to withdrawal of life support in critically ill patients who could survive with an acceptably low length of stay in the intensive care unit."*

3. ABSOLUTE HUMIDITY AND THE SEASONAL ONSET OF INFLUENZA IN THE CONTINENTAL

US: *"The model results indicate that direct modulation of influenza transmissibility by absolute humidity alone is sufficient to produce this observed seasonality. These findings provide epidemiological support for the hypothesis that absolute humidity drives seasonal variations of influenza transmission in temperate regions."*

4. EFFICIENT SIMULATION OF THE SPATIAL TRANSMISSION DYNAMICS OF INFLUENZA:

"Here, we describe a significant improvement in the efficiency of an individual-based stochastic disease simulation framework that has been used for multiple previous studies."

5. IDENTIFICATION OF AMINO ACIDS IN HA AND PB2 CRITICAL FOR THE TRANSMISSION OF

H5N1 AVIAN INFLUENZA VIRUSES IN A MAMMALIAN HOST: *"We found that two viruses, A/duck/Guangxi/35/2001 (DKGX/35) and A/bar-headed goose/Qinghai/3/2005(BHGQH/05), were transmitted from inoculated animals to naïve contact animals. Our mutagenesis analysis revealed that the amino acid asparagine (Asn) at position 701 in the PB2 protein was a prerequisite for DKGX/35 transmission in guinea pigs. In addition, an amino acid change in the hemagglutinin (HA) protein (Thr160Ala), resulting in the loss of glycosylation at 158–160, was responsible for HA binding to sialylated glycans and was critical for H5N1 virus transmission in guinea pigs."*

6. STUDY: H1N1 NOT HIGHLY CONTAGIOUS IN HOUSEHOLDS: *"People living in the same household were less likely to catch H1N1 influenza from a sick family member than they would have been in past pandemics or during a normal flu season, a team from University College London and the Centers for Disease Control and Prevention report today in the New England Journal of Medicine."*

CB Daily Report

Chem-Bio News

GLYCANS ON INFLUENZA HEMAGGLUTININ AFFECT RECEPTOR BINDING AND IMMUNE RESPONSE

Health Risk Factor Week
December 22, 2009

"Viral transmission begins with a critical interaction between hemagglutinin (HA) glycoprotein, which is

on the viral coat of influenza, and sialic acid (SA) containing glycans, which are on the host cell surface."

"To elucidate the role of HA glycosylation in this important interaction, various defined HA glycoforms were prepared, and their binding affinity and specificity were studied by using a synthetic SA microarray. Truncation of the N-glycan structures on HA increased SA binding affinities while decreasing specificity toward disparate SA ligands. The contribution of each monosaccharide and sulfate group within SA ligand structures to HA binding energy was quantitatively dissected. It was found that the sulfate group adds nearly 100-fold (2.04 kcal/mol) in binding energy to fully glycosylated HA, and so does the biantennary glycan to the monoglycosylated HA glycoform. Antibodies raised against HA protein bearing only a single N-linked GlcNAc at each glycosylation site showed better binding affinity and neutralization activity against influenza subtypes than the fully glycosylated HAs elicited."

Thus, removal of structurally nonessential glycans on viral surface glycoproteins may be a very effective and general approach for vaccine design against influenza and other human viruses."

The full article can be found at: (C.C. Wang, et. al., "Glycans on influenza hemagglutinin affect receptor binding and immune response". Proceedings of the National Academy of Sciences of the United States of America, 2009;106(43):18137-18142). Link not available.

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AN ASSESSMENT OF THE VALIDITY OF SOFA SCORE BASED TRIAGE IN H1N1 CRITICALLY ILL PATIENTS DURING AN INFLUENZA PANDEMIC

Health & Medicine Week
December 21, 2009

"Sequential Organ Failure Assessment (SOFA) score based triage of influenza A H1N1 critically ill patients has been proposed for surge capacity management as a guide for clinical decision making. We conducted a retrospective records review and SOFA scoring of critically ill patients with influenza A H1N1 in a mixed medical-surgical intensive care unit in an urban hospital."

"Eight critically ill patients with influenza A H1N1 were admitted to the intensive care unit. Their mean (range) age was 39 (26-52) years with a length of stay of 11 (3-17) days. All patients met SOFA score based triage admission criteria with a modal SOFA score of five. Five patients required invasive ventilation for a mean (range) of 5 (4-11) days. Five patients would have been considered for withdrawal of treatment using SOFA scoring guidelines at 48 h. All patients survived."

"SOFA score based triage could lead to withdrawal of life support in critically ill patients who could survive with an acceptably low length of stay in the intensive care unit."

The full article can be found at: (Z. Khan, et. al., "An assessment of the validity of SOFA score based triage in H1N1 critically ill patients during an influenza pandemic". Anaesthesia, 2009;64(12):1283-1288). Link not available.

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ABSOLUTE HUMIDITY AND THE SEASONAL ONSET OF INFLUENZA IN THE CONTINENTAL US

By Jeffrey Shaman, Virginia Pitzer, Cecile Viboud, Marc Lipsitch, and Bryan Grenfell
PLoS Influenza
December 18, 2009

"Much of the observed wintertime increase of mortality in temperate regions is attributed to seasonal influenza. A recent re-analysis of laboratory experiments indicates that absolute humidity strongly modulates the airborne survival and transmission of the influenza virus. Here we extend these findings to the human population level, showing that the onset of increased wintertime influenza-related

mortality in the United States is associated with anomalously low absolute humidity levels during the prior weeks. We then use an epidemiological model, in which observed absolute humidity conditions temper influenza transmission rates, to successfully simulate the seasonal cycle of observed influenza-related mortality. The model results indicate that direct modulation of influenza transmissibility by absolute humidity alone is sufficient to produce this observed seasonality. These findings provide epidemiological support for the hypothesis that absolute humidity drives seasonal variations of influenza transmission in temperate regions.”

The full article can be found at: <http://knol.google.com/k/absolute-humidity-and-the-seasonal-onset-of-influenza-in-the-continental-us?collectionId=28qm4w0q65e4w.1&position=3>

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EFFICIENT SIMULATION OF THE SPATIAL TRANSMISSION DYNAMICS OF INFLUENZA

By Meng-Tsung Tsai, Tsurng-Chen Chern, Jen-Hsiang Chuang, Chih-Wen Hsueh et al.

PloS Influenza

January 04, 2010

“Early data from the 2009 H1N1 pandemic (H1N1pdm) suggest that previous studies over-estimated the within-country rate of spatial spread of pandemic influenza. As large spatially-resolved data sets are constructed, the need for efficient simulation code with which to investigate the spatial patterns of the pandemic becomes clear. Here, we describe a significant improvement in the efficiency of an individual-based stochastic disease simulation framework that has been used for multiple previous studies. We quantify the efficiency of the revised algorithm and present an alternative parameterization of the model in terms of the basic reproductive number. We apply the model to the population of Taiwan and demonstrate how the location of the initial seed can influence spatial incidence profiles and the overall spread of the epidemic. Differences in incidence are driven by the relative connectivity of alternate seed locations.”

The full article can be found at: <http://knol.google.com/k/meng-tsung-tsai/efficient-simulation-of-the-spatial/3d7dm4m68r6wb/1?collectionId=28qm4w0q65e4w.1&position=1>

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IDENTIFICATION OF AMINO ACIDS IN HA AND PB2 CRITICAL FOR THE TRANSMISSION OF H5N1 AVIAN INFLUENZA VIRUSES IN A MAMMALIAN HOST

By Yuwei Gao, Ying Zhang, Kyoko Shinya, Guohua Deng, Yongping Jiang, Zejun Li, Yuntao Guan, Guobin Tian, Yanbing Li, Jianzhong Shi, Liling Liu, Xianying Zeng, Zhigao Bu, Xianzhu Xia, Yoshihiro Kawaoka, Hualan Chen

PloS Pathogens

December 24, 2009

“Since 2003, H5N1 influenza viruses have caused over 400 known cases of human infection with a mortality rate greater than 60%. Most of these cases resulted from direct contact with virus-contaminated poultry or poultry products. Although only limited human-to-human transmission has been reported to date, it is feared that efficient human-to-human transmission of H5N1 viruses has the potential to cause a pandemic of disastrous proportions. The genetic basis for H5N1 viral transmission among humans is largely unknown. In this study, we used guinea pigs as a mammalian model to study the transmission of six different H5N1 avian influenza viruses. We found that two viruses, A/duck/Guangxi/35/2001 (DKGX/35) and A/bar-headed goose/Qinghai/3/2005(BHGQH/05), were transmitted from inoculated animals to naïve contact animals. Our mutagenesis analysis revealed that the amino acid asparagine (Asn) at position 701 in the PB2 protein was a prerequisite for DKGX/35 transmission in guinea pigs. In addition, an amino acid change in the hemagglutinin (HA) protein (Thr160Ala), resulting in the loss of glycosylation at 158–160, was responsible for HA binding to sialylated glycans and was critical for H5N1 virus transmission in guinea pigs. These amino acid changes in PB2 and HA could serve as important molecular markers for assessing the pandemic potential of H5N1 field isolates.”

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000709;jsessionid=67F66F7203736B7912405D775D51091F>
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STUDY: H1N1 NOT HIGHLY CONTAGIOUS IN HOUSEHOLDS

By Maryn McKenna

CIDRAP News - Center for Infectious Disease Research & Policy (University of Minnesota)

December 30, 2009

“People living in the same household were less likely to catch H1N1 influenza from a sick family member than they would have been in past pandemics or during a normal flu season, a team from University College London and the Centers for Disease Control and Prevention report today in the New England Journal of Medicine.

Drawing on a database of information gathered about patients with lab-confirmed H1N1 during the pandemic’s early stages, the researchers found the new flu was not very contagious. There were secondary infections in 27% of 216 households and 13% of 600 household residents, compared to secondary attack rates that rose to 20% in the 1957 and 1968 pandemics and up to 40% in some flu seasons. Children and teenagers were twice as susceptible as adults.

The database was assembled from reports filed by state health departments in April and May 2009, while the CDC was still requesting case counts. The reports were written up for any patients whose flu infections were lab-confirmed either as H1N1 flu, or as neither of the H1 and H3 strains that circulated in the 2008-09 flu season.”

The full article can be found at:

<http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/dec3009household.html>

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