1 June 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 #114

1. GAME THEORY OF SOCIAL DISTANCING IN RESPONSE TO AN EPIDEMIC: *"In the absence of vaccination or other intervention measures, optimal social distancing never recovers more than 30% of the cost of infection. We also show how the window of opportunity for vaccine development lengthens as the efficiency of social distancing and detection improve."*

2. STUDY: US FLU STRAINS MAY HEAD SOUTH IN SPRING: *"The United States is a more important hub for the global circulation of seasonal flu strains than previously thought, a finding that may have practical public health implications for the best use of antivirals and vaccines, researchers reported today."*

3. ORIGINAL ANTIGENIC SIN AND PANDEMIC (H1N1) 2009: *"This observation raised the question about whether older persons were protected from infection with an influenza virus A (H1N1) strain acquired many years ago. Indeed, data from the Centers for Disease Control and Prevention showed that approximately two thirds of older persons have evidence of immunity to pandemic (H1N1) 2009 virus."*

4. REVERSIBLE CARDIAC DYSFUNCTION ASSOCIATED WITH PANDEMIC 2009 INFLUENZA A(H1N1): *"We conclude that potentially reversible cardiac dysfunction is a relatively common complication associated with hospitalized pandemic A(H1N1) influenza."*

5. HETEROSUBTYPIC NEUTRALIZING ANTIBODIES ARE PRODUCED BY INDIVIDUALS IMMUNIZED WITH A SEASONAL INFLUENZA VACCINE: *"These findings reveal that seasonal influenza vaccination can induce polyclonal heterosubtypic neutralizing antibodies that cross-react with the swine-origin pandemic H1N1 influenza virus and with the highly pathogenic H5N1 virus."*

6. UNSEASONAL TRANSMISSION OF H3N2 INFLUENZA A VIRUS DURING THE SWINE-ORIGIN H1N1 PANDEMIC: *"These results suggest that the unseasonal transmission of influenza A viruses may be more widespread than is usually supposed."*

CB Daily Report

Chem-Bio News

GAME THEORY OF SOCIAL DISTANCING IN RESPONSE TO AN EPIDEMIC
By Timothy C. Reluga
PLoS Computational Biology
May 27, 2010

"This paper formulates a differential-game to identify how individuals would best use social distancing and related self-protective behaviors during an epidemic. The epidemic is described by a simple, well-mixed ordinary differential equation model. We use the differential game to study potential value of social distancing as a mitigation measure by calculating the equilibrium behaviors under a variety of cost-functions. Numerical methods are used to calculate the total costs of an epidemic under equilibrium behaviors as a function of the time to mass vaccination, following epidemic identification. The key parameters in the analysis are the basic reproduction number and the baseline efficiency of social distancing. The results show that social distancing is most beneficial to individuals for basic reproduction numbers around 2. In the absence of vaccination or other intervention measures, optimal social distancing never recovers more than 30% of the cost of infection. We also show how the window of opportunity for vaccine development lengthens as the efficiency of social distancing and detection improve."

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"One of the easiest ways for people to lower their risk of infection during an epidemic is for them to reduce their rate of contact with infectious individuals. However, the value of such actions depends on how the epidemic progresses. Few analyses of behavior change to date have accounted for how changes in behavior change the epidemic wave. In this paper, I calculate the tradeoff between daily social distancing behavior and reductions in infection risk now and in the future. The subsequent analysis shows that, for the parameters and functional forms studied, social distancing is most useful for moderately transmissible diseases. Social distancing is particularly useful when it is inexpensive and can delay the epidemic until a vaccine becomes widely available. However, the benefits of social distancing are small for highly transmissible diseases when no vaccine is available."

The full article can be found at: http://www.ploscompbiol.org/article/info%3Adoi%2F10.1371%2Fjournal.pcbi.1000793;jsessionid=940F38A38F98F7875CFEA93F5C72E57F

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STUDY: US FLU STRAINS MAY HEAD SOUTH IN SPRING
By Lisa Schnirring
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
May 27, 2010

"The United States is a more important hub for the global circulation of seasonal flu strains

than previously thought, a finding that may have practical public health implications for the best use of antivirals and vaccines, researchers reported today.

Over the past few years, other researchers have tagged China and Southeast Asia as tropical regions where seasonal flu strains originate. When a research group from the University of Michigan and Florida State University used mathematical modeling techniques incorporating gene sequence analysis to test the hypothesis, they found that the more temperate United States region also makes important contributions to the migration of seasonal flu, which they found often travels to South America at the end of the flu season.

The authors based their study on genetic analysis of influenza A H3N2 viruses collected from around the world between 1998 and 2009, which allowed them to identify relationships between the viruses. The modeling method allowed them to account for evolutionary processes and migration rates. Their findings appear in today's issue of Public Library of Science (PLoS) Pathogens."

The full article can be found at: http://www.cidrap.umn.edu/cidrap/content/influenza/general/news/may2710strains.html

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ORIGINAL ANTIGENIC SIN AND PANDEMIC (H1N1) 2009
By Amesh A. Adalja and D.A. Henderson
Emerging Infectious Diseases
June 2010

"To the Editor: While pandemic (H1N1) 2009 was in its earliest stages, age distribution data indicated surprisingly few cases among persons >65 years of age. The initial assumption was that few persons >65 years of age had yet to be exposed. However, as more data became available from Mexico, Australia, and the United States, the age distribution pattern persisted (1).

This observation raised the question about whether older persons were protected from infection with an influenza virus A (H1N1) strain acquired many years ago. Indeed, data from the Centers for Disease Control and Prevention showed that approximately two thirds of older persons have evidence of immunity to pandemic (H1N1) 2009 virus. In 1960, Thomas Francis proposed the hypothesis of original antigenic sin, a phenomenon whereby a person who as a child was first exposed to a specific influenza virus A would, throughout life, mount an immune response to the virus of childhood, even when exposed to other antigenically dissimilar influenza viruses. In effect, the original antibody response generated by the immune system against a specific influenza viral strain was hypothesized to have colored all future responses to influenza (2).

Serologic responses of humans and other mammals have supported this theory. A new hemagglutinin (HA) subtype emerged in 1918 that was responsible for the pandemic that year. Through 1956, the strain evolved, accumulating mutations. In an era before influenza viruses were subtyped was performed, the original 1918 influenza virus A (H1N1) was

dubbed a swine strain, whereas the virus of the 1930s was known as influenza A. However, the amount of drift accrued by 1947 was enough to render the seasonal vaccine of the time ineffective, and the new drifted virus strain was named A´. Throughout the period, the virus continued to be the subtype H1N1, as it is now designated."

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"One recent study is at variance with the others. It showed that monoclonal antibodies generated through vaccination were highly specific to the current vaccine strain rather than to influenza strains that had circulated in the past (10).

At the advent of the 2009 pandemic, fears of a severe pandemic were rampant. However, any prior immunity that was present in the population would dampen the impact of the virus. Early reports confirmed that the virus was less common in groups of older adults. Vaccine recommendations for certain age groups were developed according to that pattern of illness.

Because influenza virus A (H1N1) circulated continually after 1918 until 1957, most persons born before 1957 had been infected primarily with subtype H1N1. According to the theory of original antigenic sin, these persons may have partial protection from severe disease from infection with the new influenza virus A (H1N1), i.e., pandemic (H1N1) 2009. Supporting this hypothesis is the paucity of infections in Mexico from persons now in their 50s and 60s and few reports in the United States or Australia of cases in this age group (1). This fact should inform policy decisions and merits further immunologic consideration. Influenza surge planning is premised on a high incidence of illness among elderly persons, but if the current pattern of illness continues, healthcare facilities also should prepare to treat younger persons who may constitute the bulk of cases. Additionally, studies of persons born during 1957–1968 should be conducted to quantify antibody levels to pandemic (H1N1) 2009 virus, focusing on the degree of preexisting immunity that may have existed and was boosted by prior encounters with subtype H1N1 viruses."

The full article can be found at: http://www.cdc.gov/eid/content/16/6/1028.htm

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REVERSIBLE CARDIAC DYSFUNCTION ASSOCIATED WITH PANDEMIC 2009 INFLUENZA A(H1N1)
Medical Letter on the CDC & FDA
May 30, 2010

"Historical influenza A epidemics have carried elevated rates of cardiovascular disease, including transient cardiac dysfunction. Whether such an association holds for the novel influenza A strain, pandemic 2009 influenza A(H1N1) [A(H1N1)], remains unknown."

"We report an index case of transient cardiac dysfunction associated with A(H1N1) infection. Next, we reviewed 123 sequential cases of patients hospitalized with pandemic A(H1N1) at a single academic medical center in the United States from April 1, 2009, through October 31,

2009. We identified that 4.9% (6/123) of patients had either new or worsened left ventricular dysfunction. These cases ranged in age from 23 to 51 years, and all had preexisting medical conditions. ICU level care was required in 83% (5/6) of the cases. Sixty-seven percent (4/6) of the cases had follow-up echocardiograms, and left ventricular function improved in all four."

"We conclude that potentially reversible cardiac dysfunction is a relatively common complication associated with hospitalized pandemic A(H1N1) influenza."

The full article can be found at: (S.S. Martin, et. al., "Reversible cardiac dysfunction associated with pandemic 2009 influenza A(H1N1)". Chest, 2010;137(5):1195-7). Link not available.

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HETEROSUBTYPIC NEUTRALIZING ANTIBODIES ARE PRODUCED BY INDIVIDUALS IMMUNIZED WITH A SEASONAL INFLUENZA VACCINE
Genomics & Genetics Weekly
May 28, 2010

"The target of neutralizing antibodies that protect against influenza virus infection is the viral protein HA. Genetic and antigenic variation in HA has been used to classify influenza viruses into subtypes (H1-H16)."

"The neutralizing antibody response to influenza virus is thought to be specific for a few antigenically related isolates within a given subtype. However, while heterosubtypic antibodies capable of neutralizing multiple influenza virus subtypes have been recently isolated from phage display libraries, it is not known whether such antibodies are produced in the course of an immune response to influenza virus infection or vaccine. Here we report that, following vaccination with seasonal influenza vaccine containing H1 and H3 influenza virus subtypes, some individuals produce antibodies that cross-react with H5 HA. By immortalizing IgG-expressing B cells from 4 individuals, we isolated 20 heterosubtypic mAbs that bound and neutralized viruses belonging to several HA subtypes (H1, H2, H5, H6, and H9), including the pandemic A/California/07/09 H1N1 isolate. The mAbs used different VH genes and carried a high frequency of somatic mutations. With the exception of a mAb that bound to the HA globular head, all heterosubtypic mAbs bound to acid-sensitive epitopes in the HA stem region. Four mAbs were evaluated in vivo and protected mice from challenge with influenza viruses representative of different subtypes."

"These findings reveal that seasonal influenza vaccination can induce polyclonal heterosubtypic neutralizing antibodies that cross-react with the swine-origin pandemic H1N1 influenza virus and with the highly pathogenic H5N1 virus."

The full article can be found at: (D. Corti, et. al., "Heterosubtypic neutralizing antibodies are produced by individuals immunized with a seasonal influenza vaccine". Journal of Clinical Investigation, 2010;120(5):1663-73). Link not available.

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UNSEASONAL TRANSMISSION OF H3N2 INFLUENZA A VIRUS DURING THE SWINE-ORIGIN H1N1 PANDEMIC
Medical Letter on the CDC & FDA
May 30, 2010

"The initial wave of swine-origin influenza A virus (pandemic H1N1/09) in the United States during the spring and summer of 2009 also resulted in an increased vigilance and sampling of seasonal influenza viruses (H1N1 and H3N2), even though they are normally characterized by very low incidence outside of the winter months. To explore the nature of virus evolution during this influenza 'off-season,' we conducted a phylogenetic analysis of H1N1 and H3N2 sequences sampled during April to June 2009 in New York State."

"Our analysis revealed that multiple lineages of both viruses were introduced and cocirculated during this time, as is typical of influenza virus during the winter. Strikingly, however, we also found strong evidence for the presence of a large transmission chain of H3N2 viruses centered on the south-east of New York State and which continued until at least 1 June 2009."

"These results suggest that the unseasonal transmission of influenza A viruses may be more widespread than is usually supposed."

The full article can be found at: (E. Ghedin, et. al., "Unseasonal transmission of H3N2 influenza A virus during the swine-origin H1N1 pandemic". Journal of Virology, 2010;84 (11):5715-8). Link not available.

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