

8 June 2010

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Chem-Bio News – Pandemic Influenza Edition #115

1. GENOMIC ANALYSIS OF PANDEMIC (H1N1) 2009 REVEALS ASSOCIATION OF INCREASING DISEASE SEVERITY WITH EMERGENCE OF NOVEL HEMAGGLUTININ MUTATIONS:

“Recently emerged HA mutants are: (1) detected in large proportion of virus isolates recovered from the postmortem samples; (2) documented in multiple independent reports around the world; (3) expanding within global viral population; (4) manifesting spatial and temporal patterns of association with increased mortality rate of hospitalized patients.”

2. INFLUENZA ANTIVIRAL DRUGS NOT HOARDED DURING RECENT H1N1 FLU SEASON, SAYS PRIME THERAPEUTICS:

“Despite concerns from public health officials, influenza antiviral drugs were not hoarded during the recent H1N1 flu season, according to a new analysis presented recently at the Academy of Managed Care Pharmacy's 22nd Annual Meeting in San Diego by Prime Therapeutics (Prime).....”

3. IDENTIFICATION OF SEASONAL VACCINE HEMAGGLUTININ SUBTYPE 1 (H1) EPITOPES IN MEXICAN ISOLATES OF THE NEW INFLUENZA A (H1N1) 2009 VIRUS:

“Our findings contribute to the estimation of the degree of epitope conservation among HI from vaccine virus strains as well as in the different viruses that circulate in the Mexican population.”

4. SIMULATING SCHOOL CLOSURE STRATEGIES TO MITIGATE AN INFLUENZA EPIDEMIC:

“In fact, relatively short school closures (ie, 2 weeks or less) may actually slightly increase the overall attack rate by returning susceptible students back into schools in the middle of the epidemic.”

5. PANDEMIC INFLUENZA A/H1N1 AND ORGAN DONATION:

“The donor also had received a complete course of antiviral treatment before donation. The recipients were transplanted at 2 different facilities and were managed differently. Neither recipient developed flu syndrome, and both had an uneventful outcome.”

6. SEVERE ALCOHOL HAND RUB OVERDOSE INDUCING COMA, WATCH AFTER H1N1 PANDEMIC:

“Unit-dose packaging or dispensing might decrease the risk of AHRs poisoning.”

7. GLOBAL MIGRATION DYNAMICS UNDERLIE EVOLUTION AND PERSISTENCE OF HUMAN INFLUENZA A (H3N2):

“The USA acts as the primary hub of temperate transmission and, together with China and Southeast Asia, forms the trunk of influenza's evolutionary tree.”

8. PRELIMINARY RESULTS: SURVEILLANCE FOR GUILLAIN-BARRÉ SYNDROME AFTER RECEIPT OF INFLUENZA A (H1N1) 2009 MONOVALENT VACCINE --- UNITED STATES, 2009—

2010: *“If end-of-surveillance analysis confirms this finding, this would correspond to 0.8 excess cases of GBS per 1 million vaccinations, similar to that found in seasonal influenza vaccines (2,3).”*

CB Daily Report

Chem-Bio News

GENOMIC ANALYSIS OF PANDEMIC (H1N1) 2009 REVEALS ASSOCIATION OF INCREASING DISEASE SEVERITY WITH EMERGENCE OF NOVEL HEMAGGLUTININ MUTATIONS

“We carried-out analysis of large volume of clinical, epidemiological and genomics data for assessment of evolution of the current pandemic in United States, Canada, United Kingdom, Australia and Japan based on official reports of public health agencies of corresponding countries. Analysis of reported sequences of virus strains isolated from postmortem samples indicates that 42.9% of individuals who died from laboratory-confirmed cases of the pandemic (H1N1) were infected with the hemagglutinin (HA) Q310H mutant virus. Overall, six of seven (86%) of virus isolates recovered from the necropsy samples have at least one mutation within the HA 301-316 or HA 219-240 regions. During the second wave of the pandemic (H1N1) 2009, there is an increased number of reported double mutant virus isolates with mutations within both of these HA regions. Mutations within HA 219-240 region at the position D239 (D239E/G/N) are reported with higher frequency. In addition, D239G mutants were detected more frequently in viruses isolated from patients with fatal outcomes and in isolates from lungs. Multiple viral isolates with the novel HA 301-316 mutations (I312V and P314S) have been documented. Statistically significant increase of detection of mutant viruses and H1N1-related death rates is documented in July-September reporting time periods. Our analysis seems to indicate that evolution of current pandemic is associated with notable changes in mortality rate among hospitalized patients and increasing number of reported cases of novel mutations of HA gene. Recently emerged HA mutants are: (1) detected in large proportion of virus isolates recovered from the postmortem samples; (2) documented in multiple independent reports around the world; (3) expanding within global viral population; (4) manifesting spatial and temporal patterns of association with increased mortality rate of hospitalized patients. Identification of candidate virus mutants with potential association to increasing disease severity should facilitate clinical and experimental testing of the validity of both "antigenic drift" and increase virulence hypotheses. The results of these follow-up experiments may have a significant impact on ultimate outcomes of current pandemic. Our analysis indicates the urgent need for international surveillance systems that track disease severity and individual patient influenza sequence data in a representative fashion.”

The full article can be found at: (G.V. Glinsky, et. al., "Genomic analysis of pandemic (H1N1) 2009 reveals association of increasing disease severity with emergence of novel hemagglutinin mutations". Cell Cycle, 2010;9(5):958-970). Link not available.

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INFLUENZA ANTIVIRAL DRUGS NOT HOARDED DURING RECENT H1N1 FLU SEASON, SAYS PRIME THERAPEUTICS

The Medical News
May 21, 2010

“Despite concerns from public health officials, influenza antiviral drugs were not hoarded during the recent H1N1 flu season, according to a new analysis presented recently at the Academy of Managed Care Pharmacy's 22nd Annual Meeting in San Diego by Prime Therapeutics (Prime), a thought leader in pharmacy benefit management.”

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“Researchers examined antiviral use among nine million members enrolled in commercial health plans across 11 states between September 2006 and December 2009 to determine the frequency of high-quantity and multiple-refill oseltamivir (a common influenza antiviral drug) claims among different geographic regions. While there was variability in antiviral use across geographic regions, use of antivirals during the H1N1 season was comparable to past flu seasons, and there was little indication of hoarding.”

The full article can be found at: <http://www.news-medical.net/news/20100521/Influenza-antiviral-drugs-not-hoarded-during-recent-H1N1-flu-season-says-Prime-Therapeutics.aspx>

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IDENTIFICATION OF SEASONAL VACCINE HEMAGGLUTININ SUBTYPE 1 (H1) EPITOPES IN MEXICAN ISOLATES OF THE NEW INFLUENZA A (H1N1) 2009 VIRUS

Medical Letter on the CDC & FDA

June 6, 2010

"Pre-existing immunity in individuals is a determinant condition for epidemic dynamics. During the current influenza A (H1N1) virus pandemic, cross-reactivity of seasonal vaccines from the last years and previous contact with seasonal influenza viruses was suggested as the cause of low severity and low incidence of the disease in persons aged 50-65 years and with history of seasonal influenza vaccination."

"We performed a detailed search and analysis of 74 previously reported H1 epitopes present in influenza A virus contained in seasonal vaccines applied in Mexico from 2004 to date and in sequences from Mexican isolates from 2003, as well as in the recent influenza A (H1N1) 2009, and calculated the epitope conservation among vaccine, seasonal and pandemic influenza A (H1N1) virus. H1 epitope sequence identity ranged from 61.53-100 %. Of the 74 epitopes previously reported, 31 (41.9%) were completely conserved among all sequences analyzed in this study, whereas 43 (58.1%) had changes in one or more amino acids. Our findings contribute to the estimation of the degree of epitope conservation among HI from vaccine virus strains as well as in the different viruses that circulate in the Mexican population."

The full article can be found at: (M. Rodriguezalvarez, et. al., "Identification of Seasonal Vaccine Hemagglutinin Subtype 1 (H1) Epitopes in Mexican Isolates of the New Influenza A (H1N1) 2009 Virus". Archives of Medical Research, 2009;40(8 Sp. Iss.):687-692). Link not available.

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SIMULATING SCHOOL CLOSURE STRATEGIES TO MITIGATE AN INFLUENZA EPIDEMIC

TB & Outbreaks Week

May 25, 2010

"There remains substantial debate over the impact of school closure as a mitigation strategy during an influenza pandemic. The ongoing 2009 H1N1 influenza pandemic has provided an unparalleled opportunity to test interventions with the most up-to-date simulations."

"To assist the Allegheny County Health Department during the 2009 H1N1 influenza pandemic, the University of Pittsburgh Models of Infectious Disease Agents Study group employed an agent-based computer simulation model (ABM) of Allegheny County, Pennsylvania, to explore the effects of various school closure strategies on mitigating influenza epidemics of different reproductive rates (R-0). Entire school system closures were not more effective than individual school closures. Any type of school closure may need to be maintained throughout most of the epidemic (ie, at least 8 weeks) to have any significant effect on the overall serologic attack rate. In fact, relatively short school closures (ie, 2 weeks or less) may actually slightly increase the overall attack rate by returning susceptible students back into schools in the middle of the epidemic. Varying the illness threshold at which school closures are triggered did not seem to have substantial impact on the effectiveness of school closures, suggesting that short delays in closing schools should not cause concern."

"School closures alone may not be able to quell an epidemic but, when maintained for at least 8 weeks, could delay the epidemic peak for up to a week, providing additional time to implement a second more effective intervention such as vaccination."

The full article can be found at: (B.Y. Lee, et. al., "Simulating School Closure Strategies to Mitigate an Influenza Epidemic". Journal of Public Health Management and Practice, 2010;16(3):252-261). Link not available.

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PANDEMIC INFLUENZA A/H1N1 AND ORGAN DONATION

Obesity, Fitness & Wellness Week

May 22, 2010

"One of the concerns regarding the pandemic of novel influenza A/H1N1 virus is its potential to hamper transplant programs if the decision is made that organs from donors with influenza A/H1N1 should not be used. Evidence of transmissibility through organ transplantation is speculative at best."

"We report the outcome of 2 kidney transplant recipients who received kidneys from the same deceased donor, in whom the diagnosis of infection by the novel virus became available only after engraftment. The donor also had received a complete course of antiviral treatment before donation. The recipients were transplanted at 2 different facilities and were managed differently. Neither recipient developed flu syndrome, and both had an uneventful outcome."

The full article can be found at: (R. Lattes, et. al., "Pandemic influenza A/H1N1 and organ donation". *Transplant Infectious Disease*, 2010;12(2):169-172). Link not available.

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SEVERE ALCOHOL HAND RUB OVERDOSE INDUCING COMA, WATCH AFTER H1N1 PANDEMIC

Virus Weekly

May 25, 2010

"Alcoholic hand rubs (AHRs) have been proven effective in preventing nosocomial infections, and healthcare authorities include AHRs use among quality-of-care criteria. Since the onset of the influenza A (H1N1) pandemic, AHRs have gained considerable popularity among the general public."

"We report a case of intentional AHRs self-poisoning inducing rapid coma with hyperlactatemia, and a full recovery. The relevant literature was reviewed. To our knowledge, this is the third reported case of intentional AHRs poisoning. 3 patients presented with a picture of acute alcohol intoxication, of variable severity depending on the amount ingested and speed of ingestion. The blood alcohol level was 414 mg/dl and tests for other drugs were performed 30 min after admission. The blood lactate level increased briefly to 4.8 mmol/l, without renal or hepatic function disturbances. She regained consciousness after 6 h then achieved a full recovery allowing extubation and readmission to the psychiatric ward after 24 h. She reported gulping down the entire contents of the Aniosgel bottle. Whereas overdrinking in social settings (wine and liquor) leads to a gradual increase in blood alcohol levels, AHRs poisoning is usually characterized by a sudden massive alcohol load. The unusual nature of the alcohol source may lead to diagnostic wanderings. AHRs are currently available in bottles that facilitate the ingestion of large amounts."

"Unit-dose packaging or dispensing might decrease the risk of AHRs poisoning."

The full article can be found at: (M. Henry-Lagarrigue, et. al., "Severe alcohol hand rub overdose inducing coma, watch after H1N1 pandemic". *Neurocritical Care*, 2010;12(3):400-2). Link not available.

ANALYST NOTE: This problem was noted earlier in the CB Daily Pandemic Influenza Edition #80, dated 29 September 2009. In that edition, an article titled "Hand Gel Removed After Prisoners Make Hooch" noted the misuse of open access alcohol-based hand sanitizer dispensers by prisoners and vagrants in the UK.

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GLOBAL MIGRATION DYNAMICS UNDERLIE EVOLUTION AND PERSISTENCE OF HUMAN INFLUENZA A (H3N2)

“Abstract

The global migration patterns of influenza viruses have profound implications for the evolutionary and epidemiological dynamics of the disease. We developed a novel approach to reconstruct the genetic history of human influenza A (H3N2) collected worldwide over 1998 to 2009 and used it to infer the global network of influenza transmission. Consistent with previous models, we find that China and Southeast Asia lie at the center of this global network. However, we also find that strains of influenza circulate outside of Asia for multiple seasons, persisting through dynamic migration between northern and southern regions. The USA acts as the primary hub of temperate transmission and, together with China and Southeast Asia, forms the trunk of influenza's evolutionary tree. These findings suggest that antiviral use outside of China and Southeast Asia may lead to the evolution of long-term local and potentially global antiviral resistance. Our results might also aid the design of surveillance efforts and of vaccines better tailored to different geographic regions.”

“Author Summary

Infections by the influenza A virus show highly seasonal patterns in temperate regions. Winter is flu season. Over the course of the autumn and winter, a small number of initial infections grow to encompass a significant proportion of the population. At the end of the winter, infection disappears. It has been suggested that the strains founding each temperate flu season originate from China and Southeast Asia, where influenza A is less seasonal. We test this hypothesis through analysis of genetic sequences from viruses sampled throughout the world between 1998 and 2009. We find that although China and Southeast Asia play the largest role in the migration network, temperate regions, particularly the USA, also make important contributions. Not all temperate strains of influenza die out with the end of the winter season. Instead many strains emigrate to more favorable climates. Thus, we find patterns of influenza transmission to be highly dynamic. Because of emigration out of temperate regions, mutations harbored by temperate strains of influenza A can spread to the global virus population. This means that regional public health decisions regarding influenza may have global impacts.”

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000918;jsessionid=73A38EA363316C0C314638897993C662.ambra01>
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PRELIMINARY RESULTS: SURVEILLANCE FOR GUILLAIN-BARRÉ SYNDROME AFTER RECEIPT OF INFLUENZA A (H1N1) 2009 MONOVALENT VACCINE

Morbidity and Mortality Weekly Report (MMWR)
US Centers for Disease Control and Prevention
June 02, 2010

“Guillain-Barré syndrome (GBS) is an uncommon peripheral neuropathy causing paralysis and in severe cases respiratory failure and death. GBS often follows an antecedent gastrointestinal or upper respiratory illness but, in rare cases, can follow vaccination. In 1976, vaccination against a novel swine-origin influenza A (H1N1) virus was associated with a statistically significant increased risk for GBS in the 42 days after vaccination (approximately 10 excess cases per 1 million vaccinations), a consideration in halting the vaccination program in the context of limited influenza virus transmission (1). To monitor influenza A (H1N1) 2009 monovalent vaccine safety, several federal surveillance systems, including CDC's Emerging Infections Program (EIP), are being used. In October 2009, EIP began active surveillance to assess the risk for GBS after 2009 H1N1 vaccination. Preliminary results from an analysis in EIP comparing GBS patients hospitalized through March 31, 2010, who did and did not receive 2009 H1N1 vaccination showed an estimated age-adjusted rate ratio of 1.77 (GBS incidence of 1.92 per 100,000 person-years among vaccinated persons and 1.21 per 100,000 person-years among unvaccinated persons). If end-of-surveillance analysis confirms this finding, this would correspond to 0.8 excess cases of GBS per 1 million vaccinations, similar to that found in seasonal

influenza vaccines (2,3). No other federal system to date has detected a statistically significant association between GBS and 2009 H1N1 vaccination. Surveillance and further analyses are ongoing. The 2009 H1N1 vaccine safety profile is similar to that for seasonal influenza vaccines, which have an excellent safety record. Vaccination remains the most effective method to prevent serious illness and death from 2009 H1N1 influenza infection; illness from the 2009 H1N1 influenza virus has been associated with a hospitalization rate of 222 per 1 million and a death rate of 9.7 per 1 million population.”

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“Editorial Note

This preliminary analysis showed an elevated, statistically significant association between 2009 H1N1 vaccination and GBS. If confirmed, the excess risk for GBS associated with 2009 H1N1 vaccine of 0.8 cases per 1 million vaccinations would be comparable to the excess described previously for some trivalent seasonal influenza vaccine formulations (approximately one excess case per 1 million vaccinations) (2,3), and much smaller than the risk for GBS observed during the 1976 swine influenza vaccine campaign (approximately 10 excess cases per 1 million vaccinations) (1). Notably, the high proportion of antecedent illnesses associated with GBS (e.g., gastrointestinal illness or respiratory infection) suggests that a number of the GBS illnesses observed after vaccination might be attributable to other antecedent illness; historically, 40%--70% of GBS patients report experiencing an antecedent infectious illness (7). Also, data demonstrating an association between GBS and the 1976 swine flu vaccines described a clustering of cases during the second and third weeks following vaccination (1). Similarly, a single study of seasonal influenza vaccine and GBS risk using combined data from 1992--93 and 1993--94 seasonal influenza vaccine formulations showed GBS cases peaked at 2 weeks following vaccination (2), whereas the EIP data did not demonstrate this same clustering effect for the 2009 H1N1 vaccine.”

The full article can be found at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm59e0602a1.htm>
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