

23 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 #100

1. GASTROINTESTINAL ABSORPTION OF TAMIFLU IN CRITICALLY ILL PATIENTS

WITH H1N1: *"An increased dosage of Tamiflu (oseltamivir) for patients with critical illness is unlikely to be required in the treatment of pandemic (H1N1) influenza, contrary to current international guidelines, found a new study published in the Canadian Medical Association Journal (CMAJ)."*

2. WHO PICKS PANDEMIC STRAIN FOR NEXT SEASONAL FLU VACCINE:

"Given signs that the pandemic H1N1 virus will continue its dominance over other flu strains, the World Health Organization (WHO) today recommended adding the pandemic strain as the H1N1 component of the seasonal flu vaccine for the Northern Hemisphere's next flu season."

3. EUROPEAN REGULATOR RECOMMENDS FIFTH SWINE FLU VACCINE:

"The European Medicines Agency (EMA) on Friday recommended a swine flu pandemic vaccine produced by French pharmaceutical group Sanofi-Aventis for European use."

4. AMERICAN JOURNAL OF PATHOLOGY; OF SWINE, BIRDS AND MEN --

PANDEMIC H1N1 FLU: *"Chan et al conclude that "the pandemic [H1N1 virus] (but not the seasonal virus) infects conjunctival epithelium, suggest[ing] that the eye may be an important route for acquiring infection with [pandemic H1N1] as compared with seasonal influenza viruses."*

5. MOLECULAR CLONING OF THE FIRST HUMAN MONOCLONAL ANTIBODIES NEUTRALIZING WITH HIGH POTENCY SWINE-ORIGIN INFLUENZA A PANDEMIC VIRUS (S-OIV):

"This is the first report of molecular cloning of human monoclonal antibodies against the new pandemic swine-origin influenza virus."

6. COST-EFFECTIVENESS OF PHARMACEUTICAL-BASED PANDEMIC INFLUENZA MITIGATION STRATEGIES:

"At a willingness to pay of >A\$24,000 per life-year saved, more than half the simulations showed that a prepandemic vaccination program combined with antiviral treatment was cost-effective in Australia."

7. EVALUATION OF VACCINES FOR H5N1 INFLUENZA VIRUS IN FERRETS REVEALS THE POTENTIAL FOR PROTECTIVE SINGLE-SHOT IMMUNIZATION:

"Our data provide

the first indication that in the event of a future influenza pandemic, effective mass vaccination may be achievable with a low-dose 'single-shot' vaccine and provide not only increased survival but also significant reduction in disease severity."

CB Daily Report

Chem-Bio News

GASTROINTESTINAL ABSORPTION OF TAMIFLU IN CRITICALLY ILL PATIENTS WITH H1N1

Infection Control Today Magazine
February 16, 2010

"An increased dosage of Tamiflu (oseltamivir) for patients with critical illness is unlikely to be required in the treatment of pandemic (H1N1) influenza, contrary to current international guidelines, found a new study published in the Canadian Medical Association Journal (CMAJ).

World Health Organization (WHO) guidelines recommend that all critically ill patients should be treated with Tamiflu and if the patient was unresponsive to standard doses or critically ill, a higher dose should be considered."

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"Studying the absorption ability of Tamiflu in the critically ill became a priority with the large number of patients needing ICU and ventilation support," writes lead author Dr. Anand Kumar of the Health Sciences Centre at the University of Manitoba and coauthors. "Also, the number of obese patients suffering from H1N1 related critical illnesses were large which raised the question about whether the dose should be adjusted upwards with increased body weight."

The full article can be found at: <http://www.infectioncontrolday.com/hotnews/absorption-of-tamiflu.html>

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WHO PICKS PANDEMIC STRAIN FOR NEXT SEASONAL FLU VACCINE

By Lisa Schnirring
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
February 18, 2010

"Given signs that the pandemic H1N1 virus will continue its dominance over other flu strains, the World Health Organization (WHO) today recommended adding the pandemic strain as the H1N1 component of the seasonal flu vaccine for the Northern Hemisphere's next flu season.

The WHO also changed the other influenza A strain, replacing the Brisbane H3N2 component with a Perth H3N2 strain. The influenza B component remains the same Brisbane strain included in this year's seasonal flu vaccine."

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"Of the few H3N2 isolates the US Centers for Disease Control and Prevention (CDC) has analyzed over the past few months, most matched the Perth strain, not the Brisbane strain included in this season's vaccine.

In a technical report released with its recommendation today, the WHO said circulation of the seasonal H1N1 strain this season has been markedly lower than previous years, but the few isolates received were related to the Brisbane strain covered by this season's vaccine.

Fukuda said even if the seasonal H1N1 continues to circulate, WHO experts don't think it will pose a major public health threat. The seasonal H1N1 virus had become widely resistant to oseltamivir (Tamiflu). The pandemic H1N1 virus has been generally susceptible to the drug, though a few resistant cases have been detected, mostly in those who received prophylaxis or treatment.

Influenza B viruses from two major lineages, Victoria and Yamagata, have been circulating, but the WHO said the Victoria lineage has been predominant since September. The B/Brisbane/60/2008 strain recommended for both hemispheres' seasonal flu vaccines is a member of the Victoria lineage.

The WHO recommends the following for next season's vaccine:

- * For the H1N1 component, a strain similar to A/California/7/2009, replacing A/Brisbane/59/2007
- * For the H3N2 component, a strain similar to A/Perth/16/2009, replacing A/Brisbane/10/2007
- * For the B component, a strain similar to B/Brisbane/60/2008-like virus"

The full article can be found at: <http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/feb1810strains-br.html>

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EUROPEAN REGULATOR RECOMMENDS FIFTH SWINE FLU VACCINE

Agence France-Presse on Google News
February 19, 2010

"The European Medicines Agency (EMA) on Friday recommended a swine flu pandemic vaccine produced by French pharmaceutical group Sanofi-Aventis for European use.

"The European Medicines Agency's Committee for Medicinal Products for Human Use has

recommended the granting of a conditional marketing authorisation for Humenza from Sanofi Pasteur," the EMEA said in a brief statement."

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"The other four swine flu vaccines are Arepanrix and Pandemrix, both produced by British drugmaker GlaxoSmithKline, Focetria from Swiss peer Novartis, and Celvapan which is made by US firm Baxter.

Celvapan, Focetria and Pandemrix have all won approval for use from the European Commission. However, Arepanrix has not yet been cleared for European usage."

The full article can be found at: <http://www.google.com/hostednews/afp/article/ALeqM5gEPbcfQKVK9QF8-4B1qDRAoHc6Fw>

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AMERICAN JOURNAL OF PATHOLOGY; OF SWINE, BIRDS AND MEN -- PANDEMIC H1N1 FLU

NewsRx Health

February 21, 2010

"Current research suggests that pandemic H1N1 influenza of swine origin has distinct means of transmission from the seasonal flu, yet does not result in the pathogenic severity of avian flu viruses. The related report by Chan et al, "Tropism and Innate Host Responses of the 2009 Pandemic H1N1 Influenza Virus in ex Vivo and in Vitro Cultures of Human Conjunctiva and Respiratory Tract," appears published online ahead of print in the April 2010 issue of The American Journal of Pathology."

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"Unlike seasonal flu, which only infects cells located in the nose and the throat, pandemic H1N1 can replicate efficiently in cells deeper in the lung, similar to the more pathogenic H5N1 'bird flu'. Researchers led by Drs. Michael C.W. Chan and Joseph S.Malik Peiris at Queen Mary Hospital, Hong Kong SAR, China compared the cell infection pattern and immune responses of pandemic H1N1 to seasonal flu as well as to highly pathogenic avian influenza strains. They found that in contrast to seasonal flu, pandemic H1N1 and highly pathogenic avian flu could infect the conjunctiva, a membrane that lines the eyelids and covers the white part of the eye, suggesting an additional route of transmission as well as differences in receptor binding profile. However, pandemic H1N1 did not differ from seasonal flu either in replication in nose, throat, and lung cells or in induction of an inflammatory immune response, which is dysregulated in high pathogenic avian flu infections. Taken together, these results are consistent with epidemiological data that suggest that while pandemic H1N1 has subtle differences in transmissibility and pathogenesis from seasonal flu, it does not induce as severe disease as bird flu viruses.

Chan et al conclude that "the pandemic [H1N1 virus] (but not the seasonal virus) infects

conjunctival epithelium, suggest[ing] that the eye may be an important route for acquiring infection with [pandemic H1N1] as compared with seasonal influenza viruses. Furthermore, this observation implies important differences in receptor preference and tissue tropism between the pandemic H1N1 and seasonal influenza viruses, which may have relevance in pathogenesis. ... [However,] the 2009 pandemic H1N1 influenza virus is comparable with seasonal influenza in inducing host innate responses and does not have the intrinsic properties of cytokine dysregulation possessed by [the highly pathogenic avian influenza] virus or the 1918 pandemic H1N1 influenza virus." "While generally mild in the majority of cases, the pandemic H1N1 virus is not just another seasonal flu virus and has subtle peculiarities of its own". Future studies using host-gene expression profiling of virus infected respiratory cells using microarrays are in progress to further investigate the pathogenesis of this virus."

Link not available.

The original article can be found at: <http://ajp.amjpathol.org/cgi/content/abstract/ajpath.2010.091087v1>

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MOLECULAR CLONING OF THE FIRST HUMAN MONOCLONAL ANTIBODIES NEUTRALIZING WITH HIGH POTENCY SWINE-ORIGIN INFLUENZA A PANDEMIC VIRUS (S-OIV)

Health Risk Factor Week
February 23, 2010

"The pandemic caused by the new H1N1 swine-origin influenza virus (S-OIV) strain is a worldwide health emergency and alternative therapeutic and prophylactic options are greatly needed. Two human monoclonal antibody Fab fragments (HMab) neutralizing the novel H1N1 influenza strain at very low concentrations were cloned from a patient who had a broad-range anti-H1N1 serum neutralizing activity."

"The two HMabs neutralized S-OIV with an IC50 of 2.8 and 4 microg/mL. The genes coding for the neutralizing HMabs could be used for generating full human monoclonal IgGs that can be safely administered with the potentiality of representing a novel drug to be used in the prophylaxis and the treatment of this human infection."

"This is the first report of molecular cloning of human monoclonal antibodies against the new pandemic swine-origin influenza virus."

The full article can be found at: (R. Burioni, et. al., "Molecular cloning of the first human monoclonal antibodies neutralizing with high potency swine-origin influenza A pandemic virus (S-OIV)". *The New Microbiologica*, 2009;32(4):319-24). Link not available.

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COST-EFFECTIVENESS OF PHARMACEUTICAL-BASED PANDEMIC INFLUENZA MITIGATION STRATEGIES

By Anthony T. Newall, James G. Wood, Noemie Oudin, and C. Raina MacIntyre
Emerging Infectious Diseases
February 2010

"We used a hybrid transmission and economic model to evaluate the relative merits of stockpiling antiviral drugs and vaccine for pandemic influenza mitigation. In the absence of any intervention, our base-case assumptions generated a population clinical attack rate of 31.1%. For at least some parameter values, population pre-pandemic vaccination strategies were effective at containing an outbreak of pandemic influenza until the arrival of a matched vaccine. Because of the uncertain nature of many parameters, we used a probabilistic approach to determine the most cost-effective strategies. At a willingness to pay of >A \$24,000 per life-year saved, more than half the simulations showed that a pre-pandemic vaccination program combined with antiviral treatment was cost-effective in Australia."

The full article can be found at: <http://www.cdc.gov/eid/content/16/2/224.htm>

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EVALUATION OF VACCINES FOR H5N1 INFLUENZA VIRUS IN FERRETS REVEALS THE POTENTIAL FOR PROTECTIVE SINGLE-SHOT IMMUNIZATION

Health Risk Factor Week
February 16, 2010

"Clinical trials of such vaccines indicate that two injections of preparations containing adjuvant will be required to induce protective immunity. However, this is a working assumption based on classical serological measures only. Examined here are the dose of viral hemagglutinin (HA) and the number of inoculations required for two different H5N1 vaccines to achieve protection in ferrets after lethal H5N1 challenge. Ferrets inoculated twice with 30 microg of A/Vietnam/1194/2004 HA vaccine with AIPO4, or with doses as low as 3.8 microg of HA with Iscomatrix adjuvant, were completely protected against death and disease after H5N1 challenge, and the protection lasted at least 15 months. Cross-clade protection was also observed with both vaccines. Significantly, complete protection against death could be achieved with only a single inoculation of H5N1 vaccine containing as little as 15 microg of HA with AIPO4 or 3.8 microg of HA with Iscomatrix adjuvant. Ferrets vaccinated with the single-injection Iscomatrix vaccines showed fewer clinical manifestations of infection than those given AIPO4 vaccines and remained highly active."

"Our data provide the first indication that in the event of a future influenza pandemic, effective mass vaccination may be achievable with a low-dose 'single-shot' vaccine and provide not only increased survival but also significant reduction in disease severity."

The full article can be found at: (D. Middleton, et. al., "Evaluation of vaccines for H5N1 influenza virus in ferrets reveals the potential for protective single-shot immunization". *Journal of Virology*, 2009;83(15):7770-8). Link not available.

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