7 April 2009

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 #55

1. USE OF NORTHERN HEMISPHERE INFLUENZA VACCINES BY TRAVELERS TO THE SOUTHERN HEMISPHERE: *"Vaccines prepared for use in the northern hemisphere typically are administered to U.S. travelers to the southern hemisphere, even when the vaccine formulation is less than optimal, because influenza vaccines prepared for use in the southern hemisphere are not widely available in the United States."*

2. INTRADERMAL INFLUENZA VACCINATION OF HEALTHY ADULTS USING A NEW MICROINJECTION SYSTEM: A 3-YEAR RANDOMISED CONTROLLED SAFETY AND IMMUNOGENICITY TRIAL: *"An influenza vaccine with 9ug of haemagglutinin/strain given using an intradermal microinjection system showed comparable immunogenic and safety profiles to a licensed intramuscular vaccine, and presents a promising alternative to intramuscular vaccination for influenza for adults younger than 60 years. Trial registration: Clinicaltrials.gov NCT00703651."*

3. PANDEMIC PREPAREDNESS: TOWARD A UNIVERSAL INFLUENZA VACCINE: *"In the present article, we review approaches that aim to induce heterosubtypic immunity, that is, protection against challenge with influenza A viruses belonging to two or more subtypes."*

4. MALAYSIA TO TEST ABILITY TO CONTAIN INFLUENZA PANDEMIC: *"The health ministry, with support from World Health Organisation (WHO)'s Western Pacific Regional Office in Manila, is conducting a joint rapid containment exercise in Kuala Lumpur for two days, beginning today."*

5. INFLUENZA B MUTANT VIRUSES WITH TRUNCATED NS1 PROTEINS GROW EFFICIENTLY IN VERO CELLS AND ARE IMMUNOGENIC IN MICE: *"Therefore, these NS1-truncated mutants should prove useful as potential candidates for live-attenuated influenza virus vaccines."*

6. A CRITICAL ROLE FOR THE SPHINGOSINE ANALOG AAL-R IN DAMPENING THE CYTOKINE RESPONSE DURING INFLUENZA VIRUS INFECTION: *"These data indicate that sphingosine analogs display useful potential for controlling the immunopathology caused by influenza virus."*

CB Daily Report

Chem-Bio News

USE OF NORTHERN HEMISPHERE INFLUENZA VACCINES BY TRAVELERS TO THE SOUTHERN HEMISPHERE
Morbidity and Mortality Weekly Report
US Centers for Disease Control and Prevention
April 3, 2009

“The influenza season in temperate climates extends from October through March in the northern hemisphere and from April through September in the southern hemisphere (1--3). Recent studies indicate that influenza viruses can circulate throughout the year in the tropics and that influenza is the most frequently acquired vaccine-preventable disease among those traveling to tropical and subtropical countries (2--5). Influenza outbreaks have been reported among persons who travel from the northern hemisphere to the southern hemisphere and among persons from the northern hemisphere on group tours (4--7). To reduce the risk for influenza during travel, the Advisory Committee on Immunization Practices (ACIP) recommends that persons from the northern hemisphere who are recommended for annual vaccination or who want to avoid influenza illness but have not yet received the 2008--09 influenza vaccine should consider being vaccinated 1) before travel to the southern hemisphere during influenza season, 2) before travel to the tropics at any time of year, or 3) when traveling as part of a tour group that includes persons from areas where influenza circulates during April--September (e.g., the southern hemisphere) (8). Vaccine formulations for each hemisphere are updated yearly but might differ according to virus surveillance information from each hemisphere.

Vaccines prepared for use in the northern hemisphere typically are administered to U.S. travelers to the southern hemisphere, even when the vaccine formulation is less than optimal, because influenza vaccines prepared for use in the southern hemisphere are not widely available in the United States. However, this year the influenza virus strains represented in the 2008--09 northern hemisphere influenza vaccine currently available in the United States are identical to the strains represented in influenza vaccines intended for use in 2009 in the southern hemisphere (8,9).

Health-care providers should ask patients about upcoming travel plans, inform them regarding the risk for influenza during travel, and be aware that vaccination of travelers with the currently available northern hemisphere influenza vaccine will provide the most recently updated vaccine formulation for the southern hemisphere.

The expiration dates in the prescribing information indicate that certain lots of northern hemisphere influenza vaccines in the United States can be used as late as June 30, 2009. If possible, influenza vaccine should be administered to travelers a minimum of 2 weeks before departure, but can be administered up to the date of travel. No information is available regarding the benefits of revaccinating persons before summer travel who already were vaccinated during the preceding fall (8). In addition, before their trip, persons should learn

about health risks in the destination country (information available at http://www.cdc.gov/travel). Members of the public, especially those at higher risk for influenza complications, should consult with their health-care practitioner to discuss the risk for influenza and other travel-related diseases before embarking on travel (4,8)."

The full article can be found at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5812a4.htm

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INTRADERMAL INFLUENZA VACCINATION OF HEALTHY ADULTS USING A NEW MICROINJECTION SYSTEM: A 3-YEAR RANDOMISED CONTROLLED SAFETY AND IMMUNOGENICITY TRIAL

By Jiri Beran, Arvydas Ambrozaitis, Alvydas Laiskonis, Narseta Mickuviene, Patrick Bacart, Yvan Calozet , Etienne Demanet, Stephane Heijmans, Paul Van Belle l, Francoise Weber, and Camille Salamand
BioMed Central
April 2, 2009

"Background

Intradermal vaccination provides direct and potentially more efficient access to the immune system via specialised dendritic cells and draining lymphatic vessels. We investigated the immunogenicity and safety during 3 successive years of different dosages of a trivalent, inactivated, split-virion vaccine against seasonal influenza given intradermally using a microinjection system compared with an intramuscular control vaccine."

"Methods

In a randomised, partially blinded, controlled study, healthy volunteers (1150 aged 18 to 57 years at enrolment) received three annual vaccinations of intradermal or intramuscular vaccine. In Year 1, subjects were randomised to one of three groups: 3ug or 6ug haemagglutinin/strain/dose of inactivated influenza vaccine intradermally, or a licensed inactivated influenza vaccine intramuscularly containing 15ug/strain/dose. In Year 2 subjects were randomised again to one of two groups: 9ug/strain/dose intradermally or 15ug intramuscularly. In Year 3 subjects were randomised a third time to one of two groups: 9ug intradermally or 15ug intramuscularly. Randomisation lists in Year 1 were stratified for site. Randomisation lists in Years 2 and 3 were stratified for site and by vaccine received in previous years to ensure the inclusion of a comparable number of subjects in a vaccine group at each centre each year. Immunogenicity was assessed 21 days after each vaccination. Safety was assessed throughout the study."

"Results

In Years 2 and 3, 9ug intradermal was comparably immunogenic to 15ug intramuscular for all strains, and both vaccines met European requirements for annual licensing of influenza vaccines. The 3ug and 6ug intradermal formulations were less immunogenic than

intramuscular 15ug. Safety of the intradermal and intramuscular vaccinations was comparable in each year of the study. Injection site erythema and swelling was more common with the intradermal route."

"Conclusions

An influenza vaccine with 9ug of haemagglutinin/strain given using an intradermal microinjection system showed comparable immunogenic and safety profiles to a licensed intramuscular vaccine, and presents a promising alternative to intramuscular vaccination for influenza for adults younger than 60 years. Trial registration: Clinicaltrials.gov NCT00703651."

The full article can be found at: http://www.biomedcentral.com/content/pdf/1741-7015-7-13.pdf

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PANDEMIC PREPAREDNESS: TOWARD A UNIVERSAL INFLUENZA VACCINE
By Kenny Roose, Walter Fiers and Xavier Saelens
Drug News & Perspectives
April 2009

"The possible emergence of a new influenza pandemic is considered a major threat for human health worldwide. Pandemics start by the introduction or reintroduction and spread in the human population of an influenza virus subtype against which almost nobody has protective immunity. Currently used influenza vaccines provide good protection only against antigenically matching influenza strains. However, neither the timing nor the subtype of the next pandemic virus is known. Therefore, different approaches are being pursued in anticipation of this pandemic threat. In the present article, we review approaches that aim to induce heterosubtypic immunity, that is, protection against challenge with influenza A viruses belonging to two or more subtypes. Experimental and epidemiological studies indicate that natural infection can provide some heterosubtypic immunity, possibly involving cellular immune responses directed against matrix and/or nucleoprotein as well as humoral responses against neuraminidase. Other approaches have focused on the use of conserved epitopes of the viral proteins, including matrix protein 2 ectodomain (M2e) and nucleoprotein (NP). Proof-of-concept of protection by these novel vaccines has been obtained in animal models, and promising results from several clinical trials have recently been reported. Demonstrating the efficacy of these new vaccines against a potential pandemic influenza endowed with human transmissibility remains a major challenge."

The full article can be found at: http://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=3&p_RefId=4365&p_IsPs=Y

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MALAYSIA TO TEST ABILITY TO CONTAIN INFLUENZA PANDEMIC
Yahoo! News Malaysia
April 7, 2009

“The health ministry, with support from World Health Organisation (WHO)'s Western Pacific Regional Office in Manila, is conducting a joint rapid containment exercise in Kuala Lumpur for two days, beginning today.

Health director-general Tan Sri Dr Mohd Ismail Merican said the exercise, 'Panstop III 2009', would focus on Malaysia's ability to respond swiftly to the early signs of an influenza pandemic.”

The full article can be found at: http://malaysia.news.yahoo.com/bnm/20090406/tts-health-panstop-993ba14.html

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INFLUENZA B MUTANT VIRUSES WITH TRUNCATED NS1 PROTEINS GROW EFFICIENTLY IN VERO CELLS AND ARE IMMUNOGENIC IN MICE
Drug Week
April 10, 2009

"The influenza B virus NS1-truncated mutants were impaired in their ability to counteract interferon (IFN) production, induce antiviral pro-inflammatory cytokines early after infection and show attenuated or restricted growth in IFN-competent hosts. In Vero cells, all of the mutant viruses replicated to high titres comparable to the wild-type influenza B virus. Mice that received a single, intranasal immunization of the NS1-truncated mutants elicited an antibody response and protection against wild-type virus challenge.”

"Therefore, these NS1-truncated mutants should prove useful as potential candidates for live-attenuated influenza virus vaccines."

The full article can be found at: (N. Wressnigg, et. al., “Influenza B mutant viruses with truncated NS1 proteins grow efficiently in Vero cells and are immunogenic in mice”. Journal of General Virology, 2009;90(Part 2):366-374). Link not available.

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A CRITICAL ROLE FOR THE SPHINGOSINE ANALOG AAL-R IN DAMPENING THE CYTOKINE RESPONSE DURING INFLUENZA VIRUS INFECTION
Virus Weekly
April 7, 2009

“Pulmonary tissue damage resulting from influenza virus infection is caused by both the cytolytic activity of the virus and the host immune response. Immune-mediated injury

results from T cell-mediated destruction of virus-infected cells and by release of cytokines and chemokines that attract polymorphonuclear leukocytes (PML) and macrophages to the infected site."

"The cytokines/chemokines potentiate dendritic cell (DC) activation and T cell expansion, which further enhances local damage. Here we report that immune modulation by local administration to the respiratory tract of sphingosine analog AAL-R significantly dampens the release of cytokines and chemokines while maintaining protective neutralizing antibody and cytotoxic T cell responses. As a result there was a marked reduction of infiltrating PML and macrophages into the lung and resultant pulmonary tissue injury. DC maturation was suppressed, which limited proliferation of specific antiviral T cells in the lung and draining lymph nodes. Further, AAL-R was effective in controlling CD8(+) T cell accumulation in the lungs even when given 4 days after initiation of influenza virus infection."

"These data indicate that sphingosine analogs display useful potential for controlling the immunopathology caused by influenza virus."

The full article can be found at: (D. Marsolais, et. al., "A critical role for the sphingosine analog AAL-R in dampening the cytokine response during influenza virus infection". Proceedings of the National Academy of Sciences of the United States of America, 2009;106 (5):1560-1565). Link not available.

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