



# Respiratory Virus Report

fall 2007



## Avian Influenza Global Training Activities

**Dr. Gavin Smith describes recent avian influenza laboratory training workshops held in Nigeria and Vietnam**

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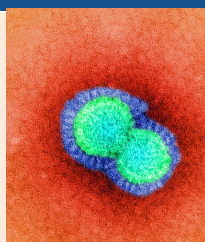
Report from the 2007 Annual General Meeting, election results, Surveillance Summit update, and a request for input from our members.

### isirv events:

**Viral Respiratory Disease Surveillance Summit**  
Malta  
21-24 May 2008

**FAO-OIE-WHO-isirv Joint International Meeting on Highly Pathogenic Avian Influenza at the Human-Animal Interface**  
Verona, Italy  
2008

*Options for the Control of Influenza VII 2010*



## Avian Influenza Virus Genomic and Bioinformatics Workshops

by Gavin JD Smith, PhD

Training of scientific and animal health workers in countries affected by highly pathogenic avian influenza (HPAI) is an important aspect of pandemic preparedness plans through the building of local capacity for virus detection and analysis. These workshops also provide contact between people from different countries, creating networks through which future assistance, if needed, may be sought.



Participants of the Abuja, Nigeria HPAI genetics training course. Courtesy of Chuong Huyn.

Recently, there have been two week-long training courses in Nigeria and Vietnam that have concentrated on training people in genetic analysis of HPAI sequence data. The success of these training courses has resulted from the collaboration of many different agencies and the organization of Chuong Huyn from the National Center for Biotechnology Information of the National Institutes of Health (NIH) of the United States.

The first course, held in Abuja, Nigeria in May 2007, was organized by the Nigerian Federal Ministries of Health and Science and Technology, the International Consortium of Anti-Virals (ICAV), the World Bank, and the World Health Organization (WHO). This meeting included participants from Cameroon, Ghana, Hong Kong, Nigeria, and the United States.

The second meeting was held in Hanoi, Vietnam in August 2007, and was organized by the Vietnam Ministry of Health, the United Nations agencies WHO and FAO, and the NIH and Centers for Disease Control and Prevention. A much larger affair, this workshop included faculty from Hong Kong, Switzerland, the United States, and Vietnam

with students attending from 12 countries throughout the Asia-Pacific region: Cambodia, Fiji, Indonesia, Korea, Laos, Malaysia, Mongolia, New Zealand, Papua New Guinea, Singapore, Thailand and, of course, Vietnam.

The courses included lectures on influenza biology and diagnostics, molecular virology and the H5N1 outbreaks, along with lectures and practical sessions on topics such as sequence alignment, mutation detection, and phylogenetic analysis, with the ultimate aim of the participants being able to characterize virus sequences for reporting to the relevant authorities.

**Training of scientific and animal health workers in countries affected by highly pathogenic avian influenza (HPAI) is an important aspect of pandemic preparedness plans through the building of local capacity for virus detection and analysis.**

Assessment of these courses by the participants indicates that they found them relevant, useful, and enjoyable. However, the most frequent request was that there should be regular workshops, that a committed effort is needed to train people to deal with HPAI in these affected countries. It is my sincerest hope that such efforts will continue.

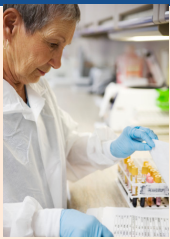
*Dr Smith is affiliated with the State Key Laboratory of Emerging Infectious Diseases, The University of Hong Kong.*



Participants of the Hanoi, Vietnam HPAI genetics training course. Courtesy of Chuong Huyn.



**Would you like to showcase viral respiratory disease activities in your region?** Drop us a line at [marge.tamas@intmedpress.com](mailto:marge.tamas@intmedpress.com).



## New Adenovirus Typing Strategy May Aid Clinicians and Epidemiologists

by Gregory C Gray, MD, MPH, FIDSA

While adenoviruses have been recognized as human pathogens since their discovery in the 1950s, understanding the epidemiology of the 51 major strains has been hampered by the tedious weeks of serological characterization work that is required, and which is available only at reference laboratories. Even so, it has been observed that such typing is potentially very useful. Adenovirus epidemics are often clonal and some strains are likely more virulent than others. Were a particularly virulent strain to be detected in a long-term care facility for the immunocompromised, public health authorities might wish to employ aggressive interventions to reduce transmission and morbidity. Immunocompromised patients, especially transplant patients, may suffer serial infections with adenoviruses and adenovirus typing can help clinicians determine whether a specific virus is a nosocomial-acquired strain, a community-acquired strain, a donor-associated strain, or represents the reactivation of a latent strain. Some adenovirus strains may be resistant to specific antivirals<sup>1</sup> and rapid typing could influence therapy decisions. Finally, adenoviruses have been associated with a number of chronic conditions including myocarditis, cardiomyopathy, mononucleosis-like syndromes, intussusception, sudden infant perinatal death, and obesity.<sup>2</sup> Adenovirus typing can help us better understand these associations.

Recently, several molecular DNA sequence-based typing strategies<sup>3-5</sup> have been proposed that could markedly reduce the strain typing time. These techniques rely upon hypervariable regions of the adenovirus hexon and fiber genes which are specific for the 51 recognized human strains. In collaboration with 22 US medical facilities, we adapted Lu and Erdman's procedure<sup>4</sup> in sequence typing 2237 clinical adenovirus specimens collected over a 25-month period during 2004 to 2006.<sup>6</sup> The molecular approach compared well to the classical serotyping approach and most specimens were DNA sequence typeable directly from either culture or swab specimens (DFA or PCR positive), reducing the adenovirus typing time from weeks to 2-3 days. Multivariable risk factor modeling for severe adenovirus disease revealed that age < 7 years (OR = 3.2; 95% CI = 1.4-7.4), chronic disease (OR = 3.6; 95% CI = 2.6-5.1), recent transplantation (OR = 2.7; 95% CI = 1.3-5.2), and infection with adenovirus 5 (OR

= 2.7; 95% CI = 1.5-4.7) or adenovirus 21 (OR = 7.6; 95% CI = 2.6-22.3) increased the risk of severe disease. This molecular typing strategy could greatly benefit patient care and the epidemiological study of adenoviruses.

**"Immunocompromised patients, especially transplant patients, may suffer serial infections with adenoviruses and adenovirus typing can help clinicians determine whether a specific virus is a nosocomial acquired strain, a community-acquired strain, a donor-associated strain, or represents the reactivation of a latent strain."**

*Dr. Gray is Director, Center for Emerging Infectious Diseases and Professor, Department of Epidemiology, at the University of Iowa College of Public Health.*

### References

1. Morfin F, Dupuis-Girod S, Mundweiler S, et al. In vitro susceptibility of adenovirus to antiviral drugs is species-dependent. *Antivir Ther.* 2005;10:225-229.
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4. Lu X, Erdman DD. Molecular typing of human adenoviruses by PCR and sequencing of a partial region of the hexon gene. *Arch Virol.* 2006;151:1587-1602.
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**Would you like to see a synopsis of your recent research in the isirv newsletter?** Drop us a line at [marge.tamas@intmedpress.com](mailto:marge.tamas@intmedpress.com).

# In the Loop



**Recent publications  
and news items of  
special interest to  
isirv members**



## **PATHOGENESIS**

### **PB1-F2 protein contributes to the pathogenicity of 1918 and H5N1 strains**

The PB1-F2 protein increases the virulence of highly pathogenic influenza A viruses, including the 1918 pandemic strain and recent H5N1 strains. Improved replication, enhanced inflammation, and elevated cytokines are implicated. Sources: McAuley JL, Horning F, Boyd KL, Smith AM, McKeon R, Bennink J, Yewdell J, McCullers JA. The 1918 PB1-F2 protein contributes to virulence and immunopathology of primary viral and secondary bacterial infections. *Cell Host Microbe*. 2007;2:240-249; Conenello GM, Zamarin D, Perrone LA, Tumpey T, Palese P. A single mutation in the PB1-F2 of H5N1 (HK/97) and 1918 influenza A viruses contributes to increased virulence. *PLoS Pathog*. 2007;3:1414-1421.

### **Severity of RSV bronchiolitis determined by the virus, not the immune response**

Severe disease and death in infants with lower respiratory tract infections from respiratory syncytial and influenza viruses correlated with the presence of viral antigen and apoptosis, not lymphocyte-derived cytokines as previously suspected. Source: Welliver TP, Garofalo RP, Hosakote Y, Hintz KH, Avendano L, Sanchez K, Veloso L, Jafri H, Chavez-Bueno S, Ogra PL, McKinney L, Reed JL, Welliver RC Sr. Severe human lower respiratory tract illness caused by respiratory syncytial virus and influenza virus is characterized by the absence of pulmonary cytotoxic lymphocyte responses. *J Infect Dis*. 2007;195:1126-1136.

## **TRANSMISSION**

### **Environmental conditions matter in the spread of influenza**

Transmission of influenza virus between guinea pigs was enhanced at low relative humidity and low temperatures. A hot, humid environment appears to be the least favorable for spread. Source: Lowen AC, Mubareka S, Steel J, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. *PLOS Pathog*. 2007;3:1470-1476.

## **TREATMENT AND PREVENTION**

### **Monoclonal antibodies can treat or prevent H5N1**

Monoclonal antibodies were derived from humans who survived infection with H5N1 influenza viruses. Mice were protected from disease and death by prophylactic administration or treatment up to 72 hours after infection. Source: Simmons CP, Bernasconi NL, Suguitan AL Jr, Mills K, Ward JM, Chau NVV, Hien TT, Sallusto F, Ha DQ, Farra J, de Jong MD, Lanzavecchia A, Subbarao K. Prophylactic and therapeutic efficacy of human monoclonal antibodies against H5N1 influenza. *PLOS Pathog*. 2007;4:928-936.

## **CLINICAL MEDICINE**

### **New viruses associated with asthma**

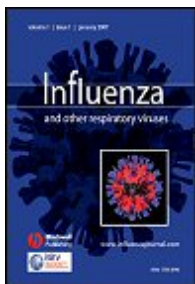
A probe of the link between asthma exacerbations and respiratory viruses revealed unexpected diversity in isolates from asthma patients. A large array of human coronaviruses and rhinoviruses including several new serotypes were found. Source: Kistler A, Avila PC, Rouskin S, Wang D, Ward T, Yagi S, Schnurr D, Ganem D, DeRisi JL, Boushey HA. Pan-viral screening of respiratory tract infections in adults with and without asthma reveals unexpected human coronavirus and human rhinovirus diversity. *J Infect Dis*. 2007;196:817-825.

## VETERINARY MEDICINE

### Comprehensive guide to avian influenza to be published in 2008

Avian Influenza, edited by David Swayne, includes disease control strategies for both wild and domesticated birds. This publication is sponsored by the American Association of Avian Pathologists (AAAP), a nonprofit professional organization that supports research and education in avian health. All sales royalties from this book go to the AAAP.

See the last page of this newsletter for more details.



### Influenza and Other Respiratory Viruses

The first 4 issues of volume 1 of the official isirv journal are now available online. All content is downloadable in PDF format, and may be accessed at <http://www.blackwell-synergy.com/loi/IRV>. Potential authors will be pleased to learn that online submission and early publication have recently been added by Blackwell Publishing.



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## Options VI by the Numbers

### Total Delegates **1601**

North America	794
Europe	416
Asia	235
South America	50
Oceania	41
Eurasia	32
Middle East	17
Africa	16

### Total Abstracts **618**

Oral	112
Poster	506

## Options VI Update

Major international conferences such as the Options meeting require years of behind the scenes development. To that end, site selection for the *Options for the Control of Influenza VII* conference is underway. Enthusiasm for hosting the conference was evident in the bid responses received from Brasília (Brazil), Hong Kong, and Cape Town (South Africa).

Lynda Browning, Vice President, Conference and Travel Services of MediTech Media Conferencing, the Options VII secretariat, has recently completed a tour of convention facilities and hotels in Hong Kong, and will visit Cape Town in December. Dates for her visit to Brasília are still being finalized.

Ms Browning anticipates completion of all bid site visits by December 2007, at which time she will apprise the **isirv** board of her findings and recommendations for their consideration in a formal vote during the first quarter of 2008. Ms Browning previously played a key role in recommending Toronto for the *Options VI* conference, the largest *Options* conference to date

## Options for the Control of Influenza VI Conference Summary

by Jacqueline Katz, Theresa Turski, and Ann Moen



In June 2007, Toronto, Ontario, Canada was the site of the Options for the Control of Influenza VI Conference, an international scientific forum exclusively devoted to influenza. Since its inception in 1985, the Options meetings, held every 3 to 4 years, have continued to grow in scope and size. Options VI was

the largest in the series to date, with 1600 delegates from over 66 countries in attendance. While half of the delegates came from North America, just over 40% were from Europe and Asia, with the remaining delegates coming from South America, Oceania, the Middle East, and Africa. This record attendance reflects the expanded interest in influenza, in part due to the continuing circulation of highly pathogenic avian influenza viruses, and ongoing pandemic preparedness efforts. Dr David Heymann, Assistant Director-General of the World Health Organization, Communicable Diseases, opened the conference. His keynote address focused on the International Health Regulations, newly revised to ensure that any international public health concerns are rapidly detected and managed in today's highly mobile and interconnected world. The welcome reception on Sunday evening was held in the main ballroom of the historic Fairmont Royal York Hotel. Guests were greeted with welcome addresses from Canadian health officials and dined on epicurean delights prepared by the Fairmont's world-renowned chefs.

The scientific program included 30 invited international experts in public health and basic research who presented their state-of-the-art knowledge on influenza. The morning translational sessions, a new feature at Options VI, were designed to provide meeting participants with a broad understanding of concepts and issues in public health, the latest advances in basic or clinical research, and their application for the control and prevention of influenza. Topics included communicating science to the

public, molecular targets for antiviral drugs, immunity and pandemic vaccines, effective use of mathematical models in influenza research and pandemic preparedness, and clinical and pathologic findings and treatment options for human H5N1 virus infections. Translational sessions were followed by plenary sessions, showcasing recent advances in epidemiology or basic research in a specific field of interest. Plenary session topics included discussions on the international challenges for pandemic preparedness and

**"The core of the meeting's information was delivered through over 600 abstracts submitted to 14 workshop categories, presented in either oral or poster form, that encompassed every aspect of influenza surveillance, epidemiology, and research."**

response in both developed and developing nations, virus structure, replication and receptor binding, the control of influenza in animals, and interactions of the virus and the host including the molecular basis of virulence and transmissibility. Translational and plenary session presentations can be viewed until June 2008 at <http://www.controlinfluenza.com>.

The core of the meeting's information was delivered through over 600 abstracts submitted to 14 workshop categories, presented in either oral or poster form, that





encompassed every aspect of influenza surveillance, epidemiology, and research. Afternoon workshops ran in parallel with public health and basic/applied science tracks. Public health track topics included disease surveillance, developments in diagnostics and serological techniques, clinical vaccine evaluation, antivirals and resistance, and clinical guidance and policies. Two new public health track topics covered in the expanded Options VI workshop sessions were included to reflect the ongoing outbreak and pre-pandemic responses to avian influenza worldwide, and growing interest in the use of mathematical modeling to predict virus evolution and spread or to guide control efforts. Basic/applied science track topics included structure/function and receptor binding, replication and assembly, animal influenza ecology, genetic and antigenic evolution, innate and adaptive immunity, virus-host interactions and pathogenesis, and preclinical vaccines and other intervention strategies. The Options VI proceedings publication will be available in January 2008. Complementing the information provided by invited speakers and abstract presenters in the Options VI scientific program were the daily morning satellite symposia sponsored by industry and presenting the latest information on control measures for seasonal and pandemic influenza.

Some of the information highlights provided by the meeting included the prevalence of influenza antiviral drug-resistant viruses in different countries, the evaluation of new vaccine methodologies including novel adjuvants, particularly for pandemic vaccines, the expansion of global surveillance and pandemic preparedness efforts,

advances in understanding of receptor binding of human and avian influenza viruses and their role in influenza virulence and transmissibility, and the role of the PB1-F2 protein, discovered by Jonathan Yewdell and colleagues in 2001, in influenza virus pathogenesis.

While the focus of *Options VI* was the science of influenza, conference participants were able to enjoy a variety of social and cultural offerings courtesy of their Canadian hosts. Monday and Tuesday evening cocktail sessions offered a casual forum to highlight approximately 500 posters which covered the 14 workshop topics. On Wednesday afternoon, midway through the conference, participants sojourned to the natural and awesome beauty of Niagara Falls, where they enjoyed the magnificence of the waterfalls and surrounding municipal area. A Canadian barbecue was the theme for the final social event, providing attendees the opportunity to wind down after the intense week of in-depth scientific sessions as they feasted on seared meats and a myriad of tempting side dishes. These social activities, juxtaposed against the comprehensive Options VI scientific program, provided a balanced and enriching experience for meeting participants.

**isirv** is now the official "home" of the *Options for the Control of Influenza* conference, and will play a major role in the development of the *Options VII* conference scheduled for 2010.

*Drs Katz, Turski, and Moen are affiliated with the Influenza Division, National Center for Immunization and Respiratory Diseases, Coordinating Center for Infectious Diseases Centers for Disease Control and Prevention, Atlanta, Georgia, USA*



## Conference Activities Update

**isirv** board members John Wood and John Watson, deputy chair, met with delegates of the WHO, Food and Agriculture Organization of the UN (FAO), World Organization for Animal Health (OIE), and the Istituto Zooprofilattico Sperimentale delle Venezie (IZSVe) on 30 October 2007 to discuss the development of a joint international scientific meeting on highly pathogenic avian influenza at the human-animal interface. Following a productive discussion amongst all participants, it was agreed that evaluation of key questions at the human-animal interface, and the identification of knowledge gaps, would be of great value in setting future research goals as well as having immediate value for global public health.

In addition, the content and timing of the viral respiratory disease surveillance summit previously announced at Options VI was discussed. This meeting will examine the integration of epidemiologic and virologic surveillance systems in influenza and other human viral respiratory diseases. Proposals for practical, stepwise implementation of surveillance systems will be a highlight of the meeting. Special attention will be given to surveillance techniques for regions of the world with severe resource constraints. Current plans are to hold the first summit 21-24 May 2008 in Malta. Further details about these meetings will be published on the **isirv** website and in a future issue of this newsletter.

## 2007 Annual General Meeting Report:

The first Annual General Meeting (AGM) of **isirv** was held 19 June 2007 at 1230 h at the Metro Toronto Convention Center. Highlights of this meeting included reports by various interim board members. Dr Geoffrey Schild, interim chair, described the history and objectives of **isirv**.

Dr John Wood, interim secretary, summarized governance issues, including **isirv**'s charitable registration in the UK and expansion of the board. Dr John Watson presented the treasurer's report. Prof Lars Haaheim described current and future features of the **isirv** website. Dr Alan Hampson, editor-in-chief of the **isirv** journal *Influenza and Other Respiratory Viruses*, discussed the challenges of creating a new scientific journal.

After these reports were accepted, the new board was elected. A slate of 16 volunteers was adopted, with terms of service ranging from 1-3 years. The journal editor-in-chief was appointed an ex officio member of the board. A list of the new board members is available at [http://www.isirv.org/about/founding\\_members.cfm](http://www.isirv.org/about/founding_members.cfm).

## About isirv

**isirv** is a scientific professional society to promote the prevention, detection, treatment, and control of influenza and other respiratory virus diseases. It will:

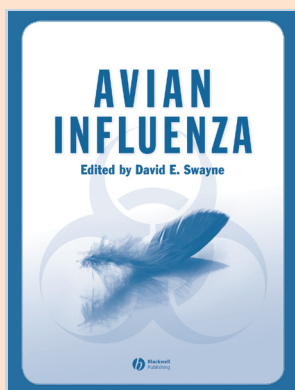
- Provide a forum for the exchange of information and for international collaboration
- Advocate for research and effective public health measures
- Promote relevant scientific and clinical training and education
- Organise scientific meetings and workshops on key topics and develop international consensus
- Support and develop partnerships with international bodies such as the WHO and other agencies

## Voices of isirv

The **isirv** board would like to broaden the society's reach to be of greatest interest to current and potential **isirv** members, and is keenly interested in your ideas for future events and newsletter articles. Is there a topic you'd like to write about for the newsletter? Do you have an idea for a meeting or satellite symposium? What are the most pressing issues in viral respiratory disease? Please send your thoughts to [marge.tamas@intmedpress.com](mailto:marge.tamas@intmedpress.com).



# AVIAN INFLUENZA ANNOUNCEMENT



## Avian Influenza

Edited By: David Swayne

Publication Date: February 2008

Avian Influenza has grown from a limited animal health issue to an international health concern with potential impacts on agriculture, veterinary medicine and public health. In the last decade, outbreaks have increased as have the research efforts to better understand, manage, and treat this disease.

Avian Influenza brings together chapters written by leading animal health researchers and veterinarians with significant experience working with this disease. Providing a summary and synthesis of important data and research on this virus, its impact on both wild and domesticated birds, and approaches to controlling the spread of the disease, Avian Influenza will be an invaluable resource for all veterinarians dealing with this virus.

### Special Features:

- *Avian Influenza* is the first comprehensive resource on this increasingly important disease.
- Provides a summarization of peer-reviewed and empirical data on avian influenza viruses, the infection and diseases they cause.
- Discusses strategies used in control of the disease.

### About the Editor:

**David E. Swayne**, DVM, PhD, DACVP, DACPV, is Laboratory Director at the Southeast Poultry Research Laboratory, a branch of U.S. Department of Agriculture's Agricultural Research Service, in Athens, Georgia.

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**Please indicate your five main areas of interest (rate from '1' to '5', with 5 as the highest score)**

<input type="checkbox"/> Animal health/disease	<input type="checkbox"/> Diagnostics, epidemiology, and surveillance
<input type="checkbox"/> Human health/disease	<input type="checkbox"/> Vaccines
<input type="checkbox"/> Zoonoses/ecology	<input type="checkbox"/> Immunology
<input type="checkbox"/> Pandemic preparedness	<input type="checkbox"/> Antivirals
<input type="checkbox"/> Policy for control and prevention	<input type="checkbox"/> Viral structure & replication
<input type="checkbox"/> Cost benefit and health economics	<input type="checkbox"/> Other? <input type="text"/>

**Which virus(es) are your main interest?**

<input type="text"/>
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**The Society's members will elect the officers of isirv.**

If proposed, would you accept to be nominated for election?

Please give any general suggestions you have on priorities for **isirv** activities for the first 1-2 years

<input type="text"/>
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Membership fees of €100 may be paid by cheque or bank transfer to the **isirv** account: Barclays Bank, Edgware Branch, 126 Station Road, Edgware, London, HA8 7RY. Sort code 20 29 41. Account #307 876 20. To register for **isirv** and pay online: visit [www.isirv.org](http://www.isirv.org). Payment confirmation will be mailed to the address provided on the membership form.

If using a cheque please print and mail a copy of this form together with payment to:

**Dr Geoffrey C Schild**  
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