

Siena Summer School on Influenza

In this issue:

Wrap Up: Summary of the Siena	
Summer School on Influenza	2
Vaccines in the News	4
Meet the New isirv Board Members	5
In the Loop	B

Upcoming Events

isirv Antiviral Group Conference Influenza Antivirals: Efficacy and Resistance 8-10 November 2011 Rio de Janeiro, Brazil







By: Jackie Katz (Organizing Committee), John Wood (International Scientific Committee) and Emanuele Montomoli (Organizing Committee)

From 1-5 August, some of the leading influenza experts from around the world visited the beautiful city of Siena to lecture at the Summer School on Influenza. The Summer School was a new initiative, which was co-chaired by Emanuele Montomoli from the University of Siena and Lars Haaheim from the University of Bergen, Norway. They were ably assisted by excellent organising and international scientific committees and by the support of **isirv**. Sadly Lars was not able to be present at the Summer School due to his untimely death a couple of months before http://www.isirv.org/news/Lars-R-Haaheim-Obituary. Lars was an enthusiastic advocate of the Summer School and had personally invited many of the speakers. Tributes to Lars' scientific achievements and personal qualities were paid during the Summer School.

The Summer School was designed for those who were newly started on their influenza careers, be it in basic or applied research, government or private sector activities and it was attended by 35 students from Australia, Europe, India, South America and the USA. The students were provided with an excellent introduction to many aspects of influenza ranging from theoretical concepts to basic techniques used in research and surveillance. The scientific programme was organised into eight different themes: societal impact; global influenza surveillance and prevention; human and animal influenza; pathogenesis; immunology; vaccines; antivirals; and finally regulatory issues.

After a welcome and introduction on behalf of the University of Siena by Emanuele Montomoli and on behalf of **isirv** by Jackie Katz (CDC, USA), the programme got underway with a historical overview of influenza and its impact on communities by Chris Potter (University of Sheffield, UK), followed by a detailed examination of influenza surveillance from a national and global perspective by Lyn Finelli (CDC, USA). Examples from past and more recent events were used to explain some basic concepts of epidemic and pandemic influenza. Roberto Gasparini (University of Genoa, Italy) continued Dr Finelli's discussion of surveillance by focusing on prevention strategies by use of vaccines and antiviral drugs. The theme of prevention was then reinforced by Geert Leroux-Roels (University of Ghent, Belgium) as he described the various components of vaccination policy. Key messages were the use of vaccine to protect not only individuals but also communities, and the rather low vaccine coverage in most countries. The importance of virological surveillance in detecting new influenza strains was stressed by Olav Hungnes (Norwegian Institute of Public Health, Norway). Such new virus strains can be considered for use in vaccines, but also may provide a clearer insight into the molecular markers for virulence and drug resistance in human infections.

The students were given a thorough insight into the structure and replication strategies of the influenza virus by Sylvie Van der Werf (Institut Pasteur, France), which prepared the students for further discussion on human and animal influenza viruses and on virus pathogenesis. The vast range of influenza viruses circulating in birds and their interaction with other animal and human hosts was described by Giovanni Cattoli (Istituto Zooprofilattico Sperrimentale



delle Venezie, Italy). Dr Cattoli stressed the importance of coordinated surveillance and intervention strategies in animals and humans. The clinical importance of the influenza virus as an important respiratory agent in humans was stressed by Karl Nicholson (University of Leicester, UK). Although past pandemics have been attributed to viruses with their origins in animals, it is difficult to estimate the pandemic potential of H5N1 avian viruses. The devastating H1N1 pandemic of 1918-19 and the reconstruction of the H1N1 pandemic virus from preserved human tissue was described by Alan Hay (NIMR, UK). Studies of this virus and the H5N1 virus may lead to a greater understanding of virus pathogenicity. Hans Dieter Klenk (Philipps-Universitaet, Germany) further elaborated on virus pathogenicity by examining the role played by different virus proteins, particularly by the haemagglutinin (HA), NS1 and the polymerase complex. Dr Klenk concluded by saying that the pandemic potential of the H1N1 virus may not yet be exhausted.

Two presentations on virus immunology followed; first a description of basic influenza immunology and then the immune responses to influenza vaccines. Jackie Katz (CDC, USA) described both the innate and adaptive immune responses, which work in harmony to first control and slow early infection and then to clear infection and allow recovery. Dr Katz remarked that the B cell mediated immune responses to both natural infection and vaccination in children were much more virus strain specific than those in adults and that immunosenescence in the elderly was a challenge for effective vaccination. The use of adjuvants to augment immune responses to vaccines was described by Rino Rappuoli (Novartis Vaccines and Diagnostics, Italy). There have been rapid advances in both development of new adjuvants and also in understanding their mode of action.

Influenza vaccines were a major topic at the Summer School and there were several presentations on different aspects of vaccines. The first of these was a critical assessment of the global response to pandemic influenza by David Fedson (Sergy Haut, France), indicating that pandemic H1N1 vaccine deployment was well below what was needed and that there was insufficient use of adjuvanted vaccines. The development of newer inactivated vaccines particularly those based on mammalian cell culture was described by Otfried Kistner (Baxter Innovation, Austria) and the use of live attenuated influenza vaccines (LAIV) was described by John Treanor (University of Rochester, USA). The main advantage of LAIV over inactivated vaccines is through stimulation of both mucosal and T cell mediated immunity and they are particularly advantageous in children. Strategies to enhance the effectiveness of LAIV in adults and the elderly are needed. Alan Shaw (VaxInnate Corporation, USA) gave a glimpse into the future of influenza vaccines when he described VaxInnate's approaches to HA-based, M2e-based and live virus vaccines by fusing the influenza antigens with Toll-like Receptors.

Antiviral drugs occupy a key role in strategies to control influenza infections. Alan Hay (NIMR, UK) described the drugs targeting the influenza proteins M2 and NA. Of particular concern is the emergence of drug resistant viruses, which may limit their future use. Dr Hay stressed the importance of basic studies into virus structure, which may lead to new drugs. An alternative view was expressed by David Fedson (Serge Haut, France) who urged further studies into host interaction with the virus in order to understand cell-signalling pathways. Such studies may lead to development of new classes of antiviral drugs.

Of particular interest to the students was a critical examination by Angus Nicoll (ECDC, Sweden) of the European response to the recent H1N1 pandemic. In planning for the future, health authorities should allow for responses, which are suitable for various grades of pandemic severity.

As is usual at scientific meetings, regulatory issues were the last topic examined at the Summer School. John Wood (formerly NIBSC, UK) gave a historical and personal insight into the EU regulatory environment which was followed by a critical examination of the correlates of protective immunity by Rebecca Cox (University of Bergen, Norway). As newer types of vaccines emerge, it is vital that there is a better understanding of immune correlates of protection against influenza, so as to facilitate vaccine development and licensure, particularly for vaccines based on newer technologies. Finally Bettie Voordouw (Medicines Evaluation Board, The Netherlands) considered some of the regulatory challenges in vaccine development and evaluation. A key consideration is the benefit-risk analysis that could be different for different human populations and for different epidemic situations.

The students attending the Summer School appreciated the opportunity to learn more about influenza and to network with both young and "seasoned" influenza scientists. All agreed that Siena was a fantastic location and welcomed the two evening social events which showcased the city and its surrounds. **isirv** was pleased to support this teaching initiative and we thank in particular, Francesca Marzari for organizing and also Mario Cruz Panzica for writing the full report of the Summer school. The good news is that a second Summer School will be held in 2012 so if you are interested, then make a note of 16-20 July 2012 in your diary.





Vaccines in the News

Ensuring Flu Vaccine Reserves in England

According to England's Department of Health, it holds 400,000 doses of the trivalent influenza vaccine for the 2011-2012 flu season in an emergency reserve. This reserve will be utilised in the event that the expected supplies of the seasonal vaccine, available through conventional supply chains, are exhausted. If manufacturer's supplies are depleted, the reserve will be released in 2 waves, in order to ensure that the reserve supply does not run out. In the event that the reserve vaccines are issued, priority will be given to the elderly, pregnant women and persons in high risk groups (described by the Green Book and the CMO's letter from 25 May 2011).

Review Article on the Effectiveness of Vaccines

In a study published in Lancet Infectious Diseases, Dr Michael Osterholm and colleagues found that influenza vaccine prevented influenza illness in approximately 59% of adults, in 8 out of 12 flu seasons examined. The study urged that new and better influenza vaccines be produced, but also conceded that current influenza vaccines offer the best available protection against flu at this time and concluded that people should continue to get vaccinated. The Centers for Disease Control and Prevention and its Advisory Committee on Immunization Practices share similar views regarding influenza vaccines, and have published information on their website on influenza vaccine effectiveness at http://www.cdc.gov/flu/about/qa/vaccineeffect. htm. The citation for this study is included in the "In the Loop" section of this newsletter

Since 2008, cases of human enterovirus 68 (HEV68), a respiratory virus, have been on the rise in Japan, the Phillipines, the United States and the Netherlands. Source: CDC Morbidity and Mortality Weekly

According to the CDC, people should get the seasonal flu vaccine before December to ensure that protective antibodies are in place before the flu becomes highly active. Source: CDC Key Facts About Seasonal Flu Vaccine



Meet the New isirv Board Members

Elections at the Annual General Meeting conducted during the ESWI conference were very successful and the board extends its gratitude to all of the members that voted! **isirv** welcomes the following new board members!



Rebecca Cox, PhD

Rebecca Cox is Professor of Medical Virology and Head of the Influenza Centre at the University of Bergen, Norway. Rebecca Cox completed her Ph.D. in 1995 at the London Hospital Medical College, University of London, UK with Professor John Oxford on the immune response to Influenza vaccines in man. She then had post doc. positions at Guys Hospital, UK and at the University of Bergen under Professor Lars Haaheim. In 2000 she was appointed lecturer in Medical Virology, University of Bergen continued from 2001 as a Research Scientist. In 2008 she was appointed head of the Influenza Centre with a current staff of 7 and from 2009 Professor in Medical Virology. Her research has focused on preclinical and clinical research into seasonal and pandemic influenza vaccines and is currently funded by the European Union, Norwegian Research Council and the Department of Health. The main areas of research are preclinical research and development of novel adjuvants and influenza vaccines, clinical trials of new influenza vaccines from phase I to IV with focus on detailed characterisation of the immune response. Rebecca has over 50 peer-reviewed publications in journals or book chapters Rebecca is a member of The Norwegian Influenza Pandemic committee, which provides advice to the Ministry of Health and Care Services. She has served as an expert reviewer for investigator-initiated trials for the European Union and for influenza vaccines to the vaccine industry. She has been invited to the World Health Organization meetings on pandemic vaccines and Broad Spectrum and Long-lasting Immune Responses and served as an advisor to the European Medicines Agency on Scientific Aspects of Serological assays.



Lyn Finelli, DrPH, MS

Lyn Finelli, DrPH, MS graduated from the Bryn Mawr Hospital School of Nursing in 1978, and received her BSN in 1981, and Master of Science in Pediatric Primary Care in 1983 from Columbia University. From 1984 to 1990, she taught pediatrics and public health at Columbia University. She received her doctorate in infectious disease epidemiology from Columbia University, School of Public Health in 1990. Dr. Finelli began working with CDC in 1990, where she held the positions of epidemiologist and acting State Epidemiologist in New Jersey. Dr. Finelli moved to Atlanta, Georgia in 1997 to work as an epidemiologist in the Division of Sexually Transmitted Diseases, in 2001 joined the Division of Viral Hepatitis as Chief of the Surveillance Team, and is now the Chief of Surveillance and Outbreak Response, Influenza Division, National Center for Immunization and Respiratory Diseases. In the Influenza Division, Dr. Finelli is responsible for leading a team of 35 scientists in conduct of influenza surveillance and special research studies. The Team is responsible for national surveillance for influenza,



fall 2011

Meet the New isirv Board Members

and a wide array of research activities conducted within current surveillance platforms and in clinical agencies. The Team is currently conducting two cross-cutting studies of community acquired pneumonia and medically attended acute respiratory infection, in addition to a new clinical trial to determine the effectiveness of empiric antiviral treatment in the prevention of complications of severe acute respiratory infection. Dr. Finelli directed the epidemiology response for CDC during the H1N1 influenza pandemic, leading a team of more than 200 scientists in response to the 2009 H1N1 pandemic. The Team assisted in identifying the first two cases of pandemic influenza in the United States through routine surveillance and described the epidemiology and epidemiologic parameters used to develop national recommendations for vaccine prioritization, antiviral prophylaxis and treatment, and community mitigation. Her research interests include influenza-bacterial co-infection, influenza complications including influenza-related pneumonia, and zoonotic influenza. Dr. Finelli is co-author of more than 100 published abstracts.



Emanuele Montomoli, PhD

Emanuele Montomoli was born on 26 September 1968 in Siena, Italy. He graduated in 1988 from the Technical School in Siena as an expert industrial chemist. He graduated in 1997 in Human Biology discussing a thesis entitled "Optimisation of the use of MDCK cell cultures (Madin Darby canine kidney) for the epidemiological control of influenza". In 2002 he graduated discussing his thesis entitled "Purification of haemagglutinin of the type B influenza virus through isoelectric focalisation". In 1994 he was awarded a position assistant at the Hygiene Institute of the University of Siena. On 2 July 2002 he participated in a competition in the Procedure of Comparative Evaluation for a single posting as Associated University Professor, at the University of Turin, for the scientific sector MED/42 (General and Applied Hygiene). On 28 October 2002 he was appointed by the Faculty of Medicine and Surgery of the University of Siena.

During his studies he conducted research on epidemiological and microbiological field, particularly during the influenza season when he carries out the epidemiological and virological surveillance of the respiratory viruses circulating in Italy. Since 1994, he has carried out seroepidemiological research in order to evaluate the immune state of the population toward influenza viruses. Since 1995 he has mostly overseen clinical trials of influenza vaccines, in order to evaluate their immunogenicity and reactogenicity. Since 2002 he is the Head of Molecular Epidemiology Research Division at the University of Siena. He is the author of more than thirty articles with a total Impact Factor of 142, as well as numerous abstracts and letters, published in Italian and international scientific journals. In 2011 he was in the Organized Committee of the "Summer School on Influenza" in Italy. He is member of **isirv** Scientific Society since 2005.





Dr. Alan Hay

Dr. Alan Hay studied Biochemistry at the University of Aberdeen, where he first became involved in the study of viruses during his PhD research. Following two years of post-doctoral research at Duke University, North Carolina, he became a member of MRC scientific staff at the National Institute for Medical research (NIMR) in London, till his retirement in 2009. His research interests have been principally concerned with various aspects of the biochemistry of influenza viruses and their replication, in particular: the mechanisms of transcription and replication of the virus genome; the antiviral action of the anti-influenza drug amantadine and the proton channel function of the target M2 protein; and the molecular bases of resistance to antiviral drugs against the M2 and NA proteins.

As Director of the WHO Collaborating Centre for Reference and Research on Influenza at NIMR from 1993, his interests also encompassed the epidemiology and evolution of human and animal influenza viruses, in particular in relation to current changes in human viruses and the compositions of influenza vaccines, and the emergence of novel human viruses with the potential to cause a pandemic.

Alan Hampson, ex-officio as Editor-in-Chief of the Journal



Influenza Antivirals: Efficacy and Resistance 8 -10 November 2011 Rio de Janeiro (Copacabana Beach), Brazil

Specific topics to be covered in the programme include: the available anti-influenza drugs and their use in different situations and settings; the emergence and molecular basis of resistance; surveillance and detection of resistant phenotypes and resistance mutations, especially in relation to drug use; associated studies of potential local and community spread; animal studies of virus fitness and the potential clinical/epidemiological significance of resistant mutants; new antiviral approaches and drug combinations.

Visit **isirv.org** for complete details.

Options VIII Update

isirv is pleased to announce that **Options for the Control of Influenza VIII** will be held in Cape Town, South Africa 5-10 September 2013.

The **Options for the Control of Influenza VIII** website is now active!

Please go to **http://www.controlinfluenza.com** to take a look.

Options for the Control of Influenza VIII will be held in beautiful Cape Town, South Africa 5-10 September 2013. The Conference Chairs are as follows:

Marc Mendelson Conference Chairman

John Watson Organizing Committee Deputy Chair

Neil Cameron Organizing Committee Co-Deputy Chair

Wolfgang Preiser Scientific Committee Deputy Chair

Stacey Schultz-Cherry

Scientific Committee Co-Deputy Chair

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

Osterholm MT, Kelley NS, Sommer A, et al. Efficacy and effectiveness of influenza vaccines: A systematic review and meta-analysis. *Lancet Infect Dis*. [Published online ahead of print, 26 October 2011].

Kelly H, Valenciano M. Estimating the effect of influenza vaccines. *Lancet Infect Dis*. [Published online ahead of print, 26 October 2011].

Griffin MR, Monto AS, Belongia EA, et al. Effectiveness of non-adjuvanted pandemic influenza A vaccines for preventing pandemic influenza acute respiratory illness visits in 4 U.S. communities. *PLoS One*. 2011;6(8):e23085.

Cattoli G, Fusaro A, Monne I, et al. Evidence for differing evolutionary dynamics of A/H5N1 viruses among countries applying or not applying avian influenza vaccination in poultry. *Vaccine*. [Published online ahead of print, 12 October 2011].

Perera RA, Riley S, Ma SK, et al. Seroconversion to pandemic (H1N1) 2009 virus and cross-reactive immunity to other swine influenza viruses. *Emerg Infect Dis*. 2011;17(10):1897-1899.

Doshi S, Kamimoto L, Finelli L, et al. Description of antiviral treatment among adults hospitalized with influenza before and during the 2009 pandemic: United States, 2005-2009. *J Infect Dis*. [Published online ahead of print, 19 October 2011].

Hui KP, Lee SM, Cheung CY, et al. H5N1 influenza virus-induced mediators upregulate RIG-I uninfected cells by paracrine effects contributing to amplified cytokine cascades. *J Infect Dis*. [Published online ahead of print, 19 October 2011].

Flaherty P, Natsoulis G, Muralidharan O, et al. Ultrasensitive detection of rare mutations using next-generation targeted resequencing. *Nucleic Acids Res.* [Published online ahead of print, 19 October 2011].

Tremblay D, Allard V, Doyon JF, et al. Emergence of a new swine H3N2 and pandemic (H1N1) 2009 influenza A virus reassortant in two Canadian animal populations, mink and swine. *J Clin Microbiol*. [Published online ahead of print, 19 October 2011].

isirv Solicits Member Input

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Do you have suggestions for recent articles that you believe your colleagues should not miss? **isirv** is asking members to submit recommendations for recently published articles of particular interest and relevance to the **isirv** membership to the **isirv** Editorial Board for publication in an upcoming issue of Respiratory Virus Report. Please submit references for articles (and optional headshot) to chris.carter@meditechmedia.com. The Editorial Board welcomes all suggestions and ideas for continuing to improve and publish a newsletter that serves as a valuable means of communication and service for the **isirv** membership.

isirv Membership Application

First Name	Last Name
Current Position	Academic Title
Institution Name	
Institution Type: 🗆 Academic 🗀 Industry 🗖 Public Health 🛛	Governmental
Industry	Department
Address 1	
Address 2	
City	State Postal Code
Country	
Phone	Fax
E-mail Address Please indicate your five main areas of interest (rate fror Animal health/disease Joonoses/ecology Pandemic preparedness Policy for control and prevention Cost benefit and health economics Which virus(es) are your main interest?	n '1' to '5', with 5 as the highest score): Diagnostics, epidemiology, and surveillance Vaccines Immunology Antivirals Viral structure & replication Other?
The Society's members will elect the officers of isirv If proposed, would you accept nomination for electior Please give any general suggestions you have on priori	• ? ties for isirv activities for the first 1-2 years:
Membership fees of €100 may be paid by cheque or bank tra Edgware, London, HA8 7RY. Sort code 20 29 41. Account #30. confirmation will be mailed to the address provided on the n If using a cheque please print and mail a copy of this form to	nsfer to the isirv account: Barclays Bank, Edgware Branch, 126 Station Road, 7 876 20. To register for isirv and pay online: visit www. isirv .org. Payment nembership form. gether with payment to:

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Make the cheque payable to **isirv** and write the member's name legibly on the cheque. The amount of the cheque must match the annual membership fee.