International Symposium on Viral Respiratory Disease Surveillance

Seville, Spain will host the first isirv surveillance symposium continued on page 7

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Rhinoviruses are members of the Picornaviridae family; these viruses have a single-stranded RNA genome of a positive sense polarity, and are unenveloped with icosahedral symmetry. The Picornaviridae family is composed of 9 genera, including Enteroviruses (EVs), Hepatoviruses, Parechoviruses, and Rhinoviruses (RVs) which are known to infect humans. RVs and EVs are closely related, but they differ in several biological traits.

RVs only grow in the respiratory tract and they are acid-labile. EVs grow at multiple sites—the respiratory tract, gut, and systemically—and they are acid-stable. While it was previously thought that rhinoviruses grow better at 33 °C and enteroviruses better at 36 °C, it is now known that at least some RVs may grow equally well at either temperature.

Rhinoviruses were first grown in vitro in an attempt to identify agents responsible for the common cold. They grew best at slightly lower temperatures, at a pH of 7.0, with rolling of the culture in human diploid or HeLa cells. A number of serologically distinct rhinoviruses were first described in the 1950s and 1960s when numerous RVs were isolated and subsequently classified into 101 serotypes. Unlike the EVs, where serotyping became a relatively routine laboratory test, typing of RVs has not became a standard test due to the presence of multiple serotypes, the requirement for high-titred neutralizing antibodies, and the technical skill and time required to establish serotype.

A variety of phenotypic assays including serotyping, drug susceptibility, and use of cellular receptors have been used to distinguish or group RVs. More recently, phenotypic assays have been replaced by use of phylogenetic trees to group the RVs into 2 major species, Human rhinovirus A (HRV-A) and Human rhinovirus B (HRV-B). Genotyping based analysis of sequence data obtained from various subgenomic regions is now available for typing of wild type isolates.

RVs have been established as the most frequent cause of the common cold, accounting for > 50% of infections. Additionally, RVs have been associated with severe lower respiratory infections, asthma exacerbations, and otitis media. RVs have occasionally been associated with outbreaks at long-term care facilities. In 2003 an outbreak involving 67 staff and residents, including the deaths of 12 residents, was attributed to RV. The RV was typed by sequence analysis as RV 82. The role that HRV serotype may play with respect to clinical severity or with particular clinical syndromes remains unresolved; although based on the analogy to EVs, where different serotypes have known epidemiologic and clinical associations, similar associations might also be expected to occur for rhinoviruses.

Until recently the study of RVs had been limited to those viruses that could be successfully cultured. Culture is a relatively insensitive method for detection of RVs, as less than 1 TCID$_{50}$ may initiate a human infection. Direct detection by labelled antibodies has not been successful because multiple serotypes do not share a common antigen. The difficulty with direct detection of infected cells may also be due to the limited number of respiratory cells that are actually infected. However, with the advent of direct detection by molecular
detection by molecular sequence-based methods, a better understanding of the diversity, genetics, taxonomy, and prevalence of HRVs has followed.

One new insight has been the discovery of a much greater diversity of HRVs than has been recognized by analysis of cultured RVs by use of newer methods such as microarray,\(^3\) MassTag PCR,\(^4,5\) and HRV-specific PCR.\(^6,7\)

For example, microarray has been shown to be much more sensitive than culture for detection of RVs in respiratory tract infections.\(^3\) Sequence analysis has identified a new diverse group, including 5 that were highly divergent in sequence to known HRVs, but more similar to HRV-A than HRV-B; none of these highly divergent RVs could be grown in culture.

MassTag PCR is a method that uses degenerate primers directed at conserved 5’ noncoding sequences. Using this method, RVs were detected in 18 of 79 specimens previously tested for other viruses from cases with influenza-like illness.\(^3\) Further analysis of the capsid-coding region sequences showed that at least 8 of these clustered in a new group related to, but distinct from, HRV-A. In a subsequent report using the MassTag PCR method, 30 additional HRVs that were most closely related to the HRVs discovered by previous use of MassTag PCR technology were identified in respiratory specimens from Germany.\(^5\) It was not reported if culture of virus from clinical specimens was attempted.

PCR methods designed for the specific detection of HRVs have revealed the existence of additional variants, including some not closely related to those described by microarray or MassTag PCR methods. PCR primers directed to the 5’ noncoding HRV region designed specifically for detecting and typing of HRV by sequencing of this region have been demonstrated to successfully serotype cultured HRVs.\(^6\) This PCR assay could also be used for direct detection and sequencing of HRVs from original clinical specimens. In one study, 103 of 108 HRVs detected by PCR were typed. Fifty-four of them did not match known serotypes, and 9 strains representing 17 HRVs formed a new distinct genetic group provisionally named HRV-C. Independently, PCR primers reacting with the 5’ noncoding region were developed for HRV detection and typing at the California Department of Public Health–Viral and Rickettsial Disease Laboratory.\(^7\) The type resulting from sequencing the 5’ region compared to that determined by the sequence of the VP4 and VP2 regions\(^8\) agreed for 70 of 71 isolates. The same primers used in direct testing of clinical specimens identified 24 HRVs, including five which belonged to the previously described novel HRV-C genotype. No virus could be cultured from any of the HRV-C specimens described in these two reports.

Use of nucleic acid detection for detection of HRVs in children and their family members\(^9,10\) were recently reported. As suspected, PCR was far more sensitive than culture, allowing for a more comprehensive analysis of HRV prevalence, persistence, and association with symptoms. The prevalence of RV infection was higher in ill compared with healthy asymptomatic subjects (37% vs 22%). Quantitatively, there was no difference in the number of copies of RV RNA between those with or without symptoms, and PCR was able to detect RV for up to 100 days.

In summary, our knowledge on the diversity, prevalence, genetics, and taxonomy of RVs has expanded greatly in recent years. RV infections account for a broad spectrum of clinical illness, and are associated with asymptomatic infection and the common cold, but may also play a role in more severe clinical illness. Use of multiplex detection systems will be important in providing additional information about the prevalence and importance of coinfection with other viral and bacterial pathogens. The potential to identify serotype or genotype by nucleic acid detection methods is exciting, and may help elucidate the association with recently described variant HRVs and particular clinical syndromes or severity of infections. Better knowledge of the role of particular serotypes or genotypes in clinical disease could have important implications for understanding clinical outcomes, prevention strategies with potential vaccines, development of antiviral agents, and the value of typing itself.
Multiplex detection systems will provide information about the prevalence and importance of rhinovirus coinfection with other viral and bacterial pathogens.

Dr Schnurr is Chief, Viral Isolation Section, at the Viral and Rickettsial Disease Laboratory, Division of Communicable Disease Control of the California Department of Public Health in Richmond, California, USA

References


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<th>Molecular diagnosis of ARI from 7 countries by using MassTag PCR and VP4/2 sequencing†</th>
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†ARI, acute respiratory illness; HRV, human rhinovirus; HEV, human enterovirus. †With previous HRV diagnosis.

**Distribution of rhinovirus clades by MassTag PCR in selected countries.**

Recent publications and news items of special interest to isirv members

by Gregory C Gray, MD, MPH, FIDSA
gregory-gray@uiowa.edu

ANTIVIRALS
More case reports describing the use of cidofovir-ribavirin combination therapy against an adenovirus strain.

CLINICAL MEDICINE
Key changes in the United States influenza management guidelines include annual seasonal vaccination of all schoolchildren and prioritized use of neuraminidase inhibitors in severely ill patients. Hospitalized patients may have less morbidity and mortality even if treated > 48 hours after onset of symptoms.

EMERGING INFECTIOUS DISEASES
Influenza A (H9N2) is transmissible in ferrets: could it be the next pandemic strain?

According to the authors, “HealthMap is a freely accessible, automated real-time system that monitors, organizes, integrates, filters, visualizes, and disseminates online information about emerging diseases.”

PANDEMIC PLANNING
Why antibiotics and bacterial vaccines should be part of pandemic stockpiles.

United States Health and Human Services (HHS) report shows wide variations between states in their progress toward building an influenza antiviral stockpile.

VACCINES
New clinical trial data are available for several novel influenza vaccines and administration routes.


**VIROLOGY**

Exposure to the 1918 pandemic strain conferred lifelong immunity among survivors.


The discovery of neuraminidase inhibitor resistance in H1N1 strains isolated from untreated patients will require vigilant surveillance.


Avian influenza gene segments have been found in a novel swine influenza strain.


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

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**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.

**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
- Organize 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
New Cells for New Vaccines III: From Lab Bench to Clinical Trials  
28 September-01 October 2008  
Wilmington, Delaware, USA

A key aspect of the success and viability of a vaccine development project is the choice of an appropriate cell substrate. The past fifty years have seen a dramatic increase in the types of cells available for vaccine production. Nevertheless, there remains a need for new and innovative approaches to extend the range of vaccines available for the protection of human and animal health.

Recent developments involving cells of insect and plant origin are attracting considerable scientific interest. Presentations at the last two New Cells for New Vaccines workshops included development of influenza vaccines in plants, clinical trials of an HPV vaccine produced with the baculovirus expression vector systems in insect cells and antibody expression in microalgae.

New Cells for New Vaccines III will be of interest to scientists in the biotechnology and pharmaceutical industry involved in vaccine development and production, as well as academics, regulatory and public health authorities, and medical and veterinary experts.

More information about this workshop is available on the isirv Web site, www.isirv.org.

International Symposium on Viral Respiratory Disease Surveillance  
Seville, Spain  
25-27 March 2009

by John Watson  
john.watson@hpa.org.uk

Join your peers and global respiratory disease scientists in the quest to forge consensus and foster collaboration on the preferred methodologies, performance characteristics, and outcomes for viral respiratory disease surveillance at the isirv International Symposium on Viral Respiratory Disease Surveillance. Following keynote presentations and status reports from global researchers and scientists in viral respiratory disease surveillance, panel discussions and interactive question and answer sessions will be held.

The isirv International Symposium on Viral Respiratory Disease Surveillance will discuss various forms of unilateral and multilateral collaboration and assistance, with the goal of bringing developing countries closer to the international surveillance networks. The meeting will emphasize practical implementation of surveillance methods consistent with national and/or regional resources.

Register for the Symposium online at: https://isirv.org/events/surveillance-register.cfm. Registration fees before 31 December 2008 for isirv members are only €350. A limited number of scholarships are available. (Proof of financial hardship required. Apply before 31 December 2008.)

For further details, visit https://isirv.org/events/surveillance-intro.cfm or call +1 404 233 6446.

Dr Watson serves as Chair for the isirv International Symposium on Viral Respiratory Disease Surveillance, and Deputy Chair, isirv. He is also Director, Respiratory Diseases Department, at the Health Protection Agency Centre for Infections, UK.
The isirv board has identified virus transmission as a critical issue in respiratory disease, and has approved a draft proposal for a new meeting on this topic. A logical follow-on to the Surveillance Symposium, this meeting will weigh the evidence supporting various tools and strategies for community mitigation, including nonpharmaceutical interventions, vaccines, and antiviral agents for viral respiratory disease. It will emphasize addressing practical challenges associated with community mitigation actions called for in pandemic response plans to viral respiratory disease outbreaks. Audience participation and panel discussions will be prominent features of the Symposium. Jonathan Van-Tam, MBE, DM, FFPH, FRIPH, Professor of Health Protection at the University of Nottingham, UK, has graciously agreed to chair this new meeting. Further details about the meeting objectives are available at www.isirv.org. Inquiries regarding participation in or support of this Symposium may be directed to Lynne Pryor at lynne.pryor@meetintegress.com.

Options for the Control of Influenza VII
3-7 September 2010
Hong Kong

Launched in 1985, Options for the Control of Influenza has grown into the largest international conference exclusively devoted to influenza, covering every imaginable topic from basic science to health care policy.

Whatever your domain of expertise – science, human medicine, animal medicine, public health policy, industry or media – Options for the Control of Influenza VII will provide comprehensive scientific guidance for all disciplines involved in influenza prevention, control and treatment, including seasonal and pandemic planning.

Save the date! Don’t miss this triennial event, mark your calendar and check the isirv Web site for updated information as it becomes available.

Other events of interest
Tell Us How We’re Doing!

The Fall 2008 issue marks a full year of publication of Respiratory Virus Report. We’d like to get your opinion about the newsletter. Your response to this survey will help us customize the Report to better serve you. All survey responses received by 31 October 2008 will be entered in a drawing for a book, courtesy of Blackwell Publishing.

What one thing would you add or change in Respiratory Virus Report?

________________________________________________________________________

________________________________________________________________________

Please provide your name and mailing address to be entered in the drawing.

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Please circle the number that best expresses your impressions of the isirv newsletter, then fax the completed survey to +1 404 506 9393, attention Marge Tamas. If you prefer, you may scan and e-mail the survey to marge.tamas@intmedpress.com.

5 = strongly agree, 4 = somewhat agree, 3 = neutral, 2 = somewhat disagree, 1 = strongly disagree.

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Community Acquired Pneumonia: Strategies for Management

Dr Antoni Torres, Hospital Clínic de Barcelona, Spain
Dr Rosario Menéndez, Hospital Clínic de Barcelona, Spain


Community Acquired Pneumonia: Strategies for Management is the first book to cover in-depth the management of pneumonia acquired outside of hospitals or extended-care facilities, which is a most common respiratory infection.

Community Acquired Pneumonia: Strategies for Management presents an in-depth review of the important new advances in therapeutics, including drug resistance of the three major classes of antibiotics used for its treatment: beta-lactams, macrolides and quinolones. Guideline recommendations are highlighted and a balanced analysis is presented to help physicians comply with the requirement for the highest standard of care. In addition, the authors provide an insight into the 10% of patients that do not respond to antibiotics and could benefit from adjunctive therapies, some still under review.

This volume will be welcomed by pulmonologists and all clinicians involved in managing community-acquired pneumonia.
isirv Membership Application

First Name | Last Name
--- | ---

Current Position | Academic Title
--- | ---

Institution Name

Institution Type:  
- [ ] Academic  
- [ ] Industry  
- [ ] Public Health  
- [ ] Governmental

Industry | Department
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Address 2

City | State | Postal Code
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Country

Phone | Fax
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E-mail Address

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

- [ ] Animal health/disease
- [ ] Human health/disease
- [ ] Zoonoses/ecology
- [ ] Pandemic preparedness
- [ ] Policy for control and prevention
- [ ] Cost benefit and health economics
- [ ] Diagnostics, epidemiology, and surveillance
- [ ] Vaccines
- [ ] Immunology
- [ ] Antivirals
- [ ] Viral structure & replication
- [ ] Other?

Which virus(es) are your main interest?

The Society’s members will elect the officers of isirv.

If proposed, would you accept nomination for election? [ ]

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

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. 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
17 Sunnyfield, Mill Hill
London NW7 4RD, UK

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.
Antiviral Therapy for Influenza

A Case-based Approach for Optimal Management

Tuesday, October 28, 2008
6:00 AM-6:30 AM Breakfast
6:30 AM-8:30 AM Scientific Program

Chair
Frederick G. Hayden, MD
University of Virginia School of Medicine
Charlottesville, Virginia, USA

Faculty
Anthony Fiore, MD, MPH, CAPT, USPHS
Centers for Disease Control and Prevention
Atlanta, Georgia, USA

David S.C. Hui, MBBS, MD, FRACP, FRCP, FCCP, FHKCP, FHKAM
The Chinese University of Hong Kong
Prince of Wales Hospital
Shatin, Hong Kong SAR, China

Renaissance Washington DC Hotel
Grand Ballroom
999 9th Street NW
Washington, DC 20001
USA

Activity Overview
An increase in pediatric deaths, emergence of influenza strains resistant to current antiviral treatments, and ongoing reports of human cases of highly pathogenic avian influenza have heightened awareness that influenza is not always a mild, self-limiting disease. These developments have renewed interest in better diagnostic tests and treatments for influenza infection. Further, there is great interest among CDC and WHO officials in improving clinical outcomes in patients with severe influenza illness.

Join us for this industry supported CME symposium while attending the 2008 ICAAC/IDSA Joint Meeting

CME Accreditation and Designation Statements
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Institute for Medical and Nursing Education (IMNE) and International Medical Press (IMP). IMNE is accredited by the ACCME to provide continuing medical education for physicians.

IMNE designates this educational activity for a maximum of 2.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Commercial Support Acknowledgments
This activity is supported by an educational grant from BioCryst Pharmaceuticals, Inc.

Americans with Disabilities Act Compliance
IMNE and IMP fully comply with the legal requirements of the Americans with Disabilities Act and the rules and regulations thereof. If any participant in this educational activity is in need of accommodations, please contact Katie Fidanza at 1 404 443 1511 or katie.fidanza@intmedpress.com by October 21, 2008.

Registration
Registration for this program is available at HTTPS://SECURE.INTMEDPRESS.COM/FLU2008

Registration is not required, though it is recommended.
Preregistration ensures priority admission to the activity if total registration exceeds room capacity.
No fee is required for this activity.

Intended Audience
Infectious disease physicians, researchers, scientists, and other healthcare providers with an interest in infectious diseases

Learning Objectives
At the conclusion of this activity, the participant should be able to:
• Cite the rationale for this year’s CDC recommendations for influenza management
• Describe current best practices in influenza diagnosis and treatment
• Discuss treatment options for severe influenza, including human cases of highly pathogenic (H5N1) avian influenza, in the context of increased resistance to current antiviral agents
• Review the status of current research aimed at developing new influenza antiviral agents
• Summarize the current status of global pandemic planning efforts

Learning Format
This symposium will feature lectures with audiovisual enhancements, case studies, and an Audience Response System that will be used throughout the activity to increase program interactivity. At the conclusion of the symposium, a panel discussion led by the faculty will address questions from the audience.

Jointly sponsored by the Institute for Medical and Nursing Education and International Medical Press.

Supported by an educational grant from BioCryst Pharmaceuticals, Inc.