

Welcome to the 13th issue of *Influenza - Asian Focus*, the official newsletter of the Asia-Pacific Advisory Committee on Influenza (APACI). Since its establishment in 2002, the APACI has continued to highlight the impact of influenza in the Asia-Pacific region and offer guidance on disease control. *Influenza - Asian Focus* offers wide-ranging and in-depth coverage of important issues relating to influenza, and features articles on new recommendations and recent events relating to influenza and its surveillance, control and prevention.

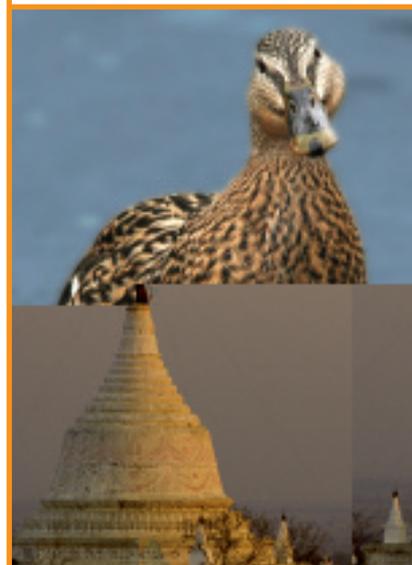
This new issue of *Influenza - Asian Focus* features highlights from the APACI Clinician Symposium in New Delhi, India, and from the Third European Influenza Conference in Vilamoura, Portugal. Held in October 2008, the APACI Clinician Symposium was organised in conjunction with the Influenza Foundation of India and included presentations from local experts. Following the meeting, the APACI issued recommendations on the use of the Northern versus Southern Hemisphere influenza vaccine formulation in tropical and subtropical areas. The consensus statement and related country-specific data are summarised on pages 6-7. In other APACI news, planning is ongoing for the regional burden of influenza study; a progress report in this issue summarises the results of a feasibility questionnaire that identified existing capabilities and resourcing needs in member countries. An interview with Shelley de la Vega on page 8 provides insight into the strategies successfully used in the Philippines to involve policymakers in efforts to prevent seasonal influenza. This issue also includes reviews of recent influenza outbreaks in the region.

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Prof Paul Chan

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The role of the Asia-Pacific Advisory Committee on Influenza

Mission statement

To promote influenza awareness in the Asia-Pacific region, with the intent to improve the prevention and control of influenza.

The Asia-Pacific Advisory Committee on Influenza (APACI) was established in early 2002 to address epidemiological issues relating to influenza and the impact of the disease in Asia. The APACI members are highly regarded influenza and infectious disease experts from across the Asia-Pacific region. The Committee is a joint initiative of five pharmaceutical companies: GlaxoSmithKline, Novartis Vaccines, Roche, Sanofi Pasteur and Solvay Biologicals.

The activities of the APACI are aligned with those of the World Health Organization (WHO). The APACI intends to work in cooperation with the WHO to complement its work on influenza surveillance and promote influenza awareness throughout Asia.

Objectives

- To identify and develop activities that complement the WHO Global Agenda on Influenza Surveillance and Control.
- To assist in the development of country-specific public awareness programmes on influenza.
- To promote influenza awareness among healthcare professionals in the region.
- To provide educational resources to support influenza awareness activities.
- To assist in the process of establishing or reviewing country-specific recommendations for influenza prevention and control.
- To advocate the timely access to, and supply of, influenza vaccines and antiviral medications.

Activities

Activities include:

- promoting influenza awareness to healthcare professionals in the region:
 - identifying country-specific key opinion leaders (KOLs)
 - publishing a regular newsletter (*Influenza – Asian Focus*)
 - producing peer-reviewed publications
- providing educational resources to support influenza awareness activities:
 - healthcare professional's resource package
 - case management guidelines
 - speaker's kit
 - continuing medical education programmes

- assisting the process of establishing or reviewing country-specific recommendations for influenza prevention and control:
 - to establish a list of existing recommendations
 - to evaluate international recommendations in the Asia-Pacific context
 - to facilitate development of consensus statements and information exchange
- assisting the development of country-specific public awareness programmes:
 - identifying country-specific requirements
 - developing a strategy to increase country-specific public awareness
 - media kit
 - media training for KOLs
- identifying and developing activities that complement the WHO Global Agenda on Influenza Surveillance and Control.

Meeting highlights

The 15th APACI meeting was held in New Delhi, India, on 4 and 5 October 2008 and was hosted by the Influenza Foundation of India (IFI). The APACI board meeting focussed on determining the next steps for implementing the regional influenza disease burden study, and on developing APACI recommendations for the use of the Northern versus Southern Hemisphere vaccine in tropical countries. The recommendations were drawn up after the examination of the current vaccine choice and timing in each member country, with board members agreeing that high-quality influenza surveillance was essential to guide these decisions. Constructive engagement with policymakers will be a goal for future APACI activities, and the success of the Philippines in this area was noted. On the second day of the meeting, local physicians attended a joint APACI and IFI Clinician Symposium, which featured a variety of regional and local topics followed by a panel discussion. Highlights of the Clinician Symposium are included in this newsletter.

Influenza burden of disease study: progress report

Planning is well under way for the APACI's regional burden of influenza disease study. Board members met at the last APACI meeting to discuss the results of a feasibility survey and determine the next steps for implementing the study.

The APACI study will follow the WHO protocol for the design and conduct of influenza disease burden studies and will record hospital-based cases of laboratory-confirmed, acute lower respiratory tract infections (LRTIs) over a 1-year period. An initial priority for the group was completing a feasibility survey to identify potential study sites in each country and to determine whether particular sites have the capacity to implement the WHO protocol.

Study sites have been identified for most APACI member areas: Australia, Hong Kong (two sites), India, Indonesia, Korea, Malaysia, the Philippines, Singapore, Taiwan and Vietnam. Most of the proposed sites are hospitals treating all age groups, while three sites treat only children (one Hong Kong site) or adults (the Australian and Korean sites). The number of acute LRTI cases admitted each year ranges from under 200 in Korea and the Philippines to over 3000 in Hong Kong and Vietnam; estimates for the number of patients able to be enrolled in 1 year range from 100 to over 500 at each site.

The responses to the feasibility survey showed that most sites use electronic or other easily retrievable records, which may allow retrospective data analysis. All countries except Australia and Vietnam routinely collect respiratory specimens from patients with

severe LRTIs, but only about half routinely test for influenza. None of the proposed sites currently use reverse transcriptase polymerase chain reaction (RT-PCR) to confirm influenza infection, but all except Vietnam have this capacity provided that funding is available.

Estimating the cost of participating in the study is challenging due to the varying requirements of each country and site. Both Hong Kong sites are able to participate without needing external funding, while preliminary estimates for the additional funding required per 100 patients range from US\$8700 in Malaysia to US\$15,000–20,000 in Australia, Korea and Taiwan. Malaysia and Vietnam may need additional resources to enable systematic data collection. The APACI will now identify potential partners for the study and apply for funding.

The WHO protocol, *A practical guide for designing and conducting influenza disease burden studies*, published in November 2008, is now available at: www.wpro.who.int/NR/rdonlyres/68608B77-891B-4B36-B21D-F49E526E0B28/0/GuideforDesigningandConductingInfluenzaStudies.pdf.



Dr Shelley de la Vega

Shelley de la Vega is Chairperson of the Committee on Aging and Degenerative Diseases for the National Institutes of Health at the University of the Philippines in Manila. Dr de la Vega is a founding member and the Secretary of the Philippine Foundation for Vaccination. In 2004, she served on a Department of Health expert panel on guidelines for influenza vaccination and was involved with the Asian International Influenza Pandemic Preparedness Planning Workshop in Beijing, China.



A/Prof Nguyen Thi Hong Hanh

Nguyen Thi Hong Hanh is Deputy Director of the National Institute of Hygiene and Epidemiology, Hanoi, Vietnam. She serves as the Vice-head of both the Vietnamese Committee for Rabies Control and Prevention and the Vietnamese National Influenza Surveillance Committee.

Obituary: Graeme Laver



Well-known Canberra scientist and influenza researcher Graeme Laver died in October 2008, aged 79. Dr Laver researched the influenza virus for more than 30 years and made several important discoveries in the development of influenza vaccines.

Dr Laver's first discovery, published in 1964, involved the use of detergents to disassemble the influenza virus and to isolate the two surface proteins,

haemagglutinin and neuraminidase. Breakthroughs made by Dr Laver enabled the development of subunit influenza vaccines, as well as that of neuraminidase inhibitors such as zanamivir and oseltamivir. Other research successes included tracing human influenza viral strains to sea birds during the 1970s, successfully crystallising and solving the structure of N2 neuraminidase, and contributing to the early research on antigenic drift.

Dr Laver was made a Fellow of the Royal Society in London in 1987, and was co-winner of the 1996 Australia Prize for science. He was on his way to the Third European Influenza Conference in Vilamoura, Portugal, when he died.

Highlights from the APACI Clinician Symposium in New Delhi

The APACI and the Influenza Foundation of India (IFI) held a joint Clinician Symposium on 5 October 2008 in New Delhi to reinforce the need for controlling seasonal influenza. Local presenters included IFI Chairman Anil Prasad, who discussed the contribution of influenza to lung and chronic diseases in India; Randeep Guleria from the All India Institute of Medical Sciences in New Delhi, who reviewed the local influenza disease burden; and Akhilash Chandra Mishra from the Indian National Institute of Virology, who reported on India's influenza surveillance network.

India: influenza in lung and chronic diseases

India has performed influenza surveillance since 1972. An early study in New Delhi found that influenza virus was present in 13–18% of acute respiratory infection (ARI) and chronic bronchitis cases.¹ A longitudinal 5-year study in preschool children found that 47% of all illnesses were caused by respiratory viruses, of which 22% were influenza-type strains.² Ongoing epidemiological research continues to show that the influenza virus is a leading cause of ARI among children in India and that it can also exacerbate respiratory conditions. Anil Prasad and his colleagues at the Vallabhbai Patel Chest Institute found that in patients with asthma, respiratory viruses accounted for 62–78% of acute asthma exacerbations; 32% of those were influenza viruses. These findings warrant greater participation on the part of clinicians in ongoing surveillance and prevention measures.

Influenza disease burden in India

A variety of complications may arise from influenza infection, with high-risk groups including young children, the elderly and those with chronic conditions. In children, influenza can contribute to an increased incidence of acute otitis media, while elderly patients may encounter chest complications, and both groups are at increased risk of hospitalisation from infection.³ Influenza is also a major contributor to acute exacerbations of respiratory diseases, such as chronic obstructive pulmonary disease (COPD). Chronic respiratory diseases are the second largest killer and the leading cause of morbidity amongst non-

communicable diseases in India,⁴ due to factors such as cigarette smoking, industrial pollution and the use of biomass fuels for cooking. Influenza vaccination is highly effective in the prevention of influenza-related ARIs in patients with COPD, and should be recommended for all such patients.⁵

Influenza surveillance in India

India's influenza surveillance system was developed out of a need for the prevention and early detection of an influenza pandemic. By the 1980s, there were eight strategically located influenza monitoring centres, including a Pune site that gained WHO recognition as a national influenza centre. These facilities are involved in a surveillance programme, initiated in 2003, that monitors human influenza and ARI outbreaks in India. The isolates collected are sent to the USA to assist with decision-making on vaccine composition. Surveillance data show interesting seasonal and regional distributions of influenza isolates in India; northern cities such as New Delhi have

both a winter peak and a smaller rainy season peak, whereas Chennai and Kolkata experience a single peak during their respective rainy seasons.

Influenza disease patterns

Although influenza disease patterns vary between different tropical and subtropical locations, seasonality is less pronounced when compared with temperate locations. Subtropical countries, such as Hong Kong and Taiwan, show influenza activity predominantly in December, with occasional small spikes in the Northern Hemisphere summer.⁶ In tropical countries, influenza isolates are detected year-round and do not show pronounced peaks. A recent study has revealed that respiratory viral infections are also prevalent during periods of increased rainfall and humidity in the tropics.⁷

Various novel hypotheses have been proposed to explain the seasonal nature of influenza. A migratory concept where influenza swings between the hemispheres was suggested as early as 1987; recent theories include the inactivation of viruses by solar ultraviolet radiation

The Influenza Foundation of India

- The IFI formed in 2005 to increase awareness of seasonal and pandemic influenza in India.
- It aims to produce and distribute unbiased scientific information on influenza to medical and lay audiences.
- Its recent activities include clinical symposia, press events, published newsletters and continuing medical education courses.
- The IFI collaborates with groups such as APACI to further contribute to influenza prevention.





The APACI and IFI joint Clinician Symposium in New Delhi.

and a source-sink model for the evolution of influenza A viruses.^{8,9} Developing and expanding surveillance networks throughout the Asia-Pacific region will help to solve the many unanswered questions about influenza epidemiology.

Avian influenza: the Hong Kong experience

In 2008, H5N1 isolates were discovered in Indonesia, Egypt, Vietnam, China and Bangladesh. The majority of human cases occur in patients below the age of 40. In cases reported to the WHO, the fatality rate is lowest among children under 10 years, with 47% of cases resulting in death; the rate rises to 70–75% in patients aged between 10 and 40 years.¹⁰

Hong Kong experienced its first outbreak of human H5N1 in 1997. None of the 18 affected patients had any direct connection with poultry handling or a proximity to wet markets, and the mortality rate was 33%.¹¹ Several of the case reports noted the presence of reactive haemophagocytic syndrome, which until then had rarely been observed in influenza cases. Subsequent research supports the hypothesis that hypercytokinaemia contributes to the pathogenesis of H5N1 disease.¹² Persistent serum cytokine elevation could therefore function as a negative prognostic marker.

Influenza vaccines and antivirals

The efficacy rate for the currently used influenza vaccine is 70–90% in healthy adults aged under 60 years, falling to 30–50% in older adults. Nevertheless, seasonal vaccination reduces hospitalisations and all-cause mortality in the

elderly by up to 70%.¹³ Improved vaccine efficacy will be achieved with future developments such as incorporating antigens with broader protection and chimeric or DNA vaccine technologies. Recommendations for annual influenza vaccination typically include all older individuals, patients with chronic illnesses and the residents of long-term aged-care facilities. Recent recommendations include healthcare workers, children aged 6–23 months old, and pregnant women (see *Flu Review*, page 11).

Physicians play a crucial role in encouraging vaccination uptake

Antiviral treatment remains an important adjunct to influenza control, though resistance can occur. Neuraminidase inhibitors, such as oseltamivir and zanamivir, offer up to 90% efficacy in preventing illness and are active against all strains of influenza, including H5N1.¹⁴ Antiviral agents should be used early to maximise benefit from treatment.

Strategies for seasonal influenza control

Effective intervention strategies for seasonal influenza are important precursors to pandemic influenza preparedness. The use of both pharmacological and non-pharmacological methods is vital in reducing the burden of seasonal influenza.

Physicians play an important role in encouraging the uptake of vaccines: numerous studies show that provider endorsement is one of the biggest influences on a patient's decision to receive vaccination.¹⁵ Other strategies for seasonal influenza control include increased respiratory hygiene and com-

munity strategies such as closing schools and avoiding public gatherings, while interventions such as hand washing and face masks also help to mitigate the effects of all types of influenza.

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Influenza vaccination in the tropics



Prof Li-Min Huang

Li-Min Huang is a Professor at the National Taiwan University in the Department of Paediatrics and the Graduate Institute of Preventive Medicine in the College of Public Health. He is also Chief of the Division of Paediatric Infectious Diseases at National Taiwan University Hospital. He is currently the chief editor of the *Journal of the Formosan Medical Association* and has served on the editorial board of the *Journal of Microbiology, Immunology and Infection*.



Prof Ilina Isahak

Ilina Isahak is Assistant Head of the Department of Diagnostic Laboratory Services at the Hospital University Kebangsaan in Kuala Lumpur, Malaysia. She is a member of several regional organisations and has been involved in the registration of new antiviral agents and vaccines in Malaysia.

The seasonality of influenza in tropical and subtropical regions remains poorly understood, leading to the underuse of seasonal influenza vaccination and uncertainty over whether to use the Northern or Southern Hemisphere vaccine formulation. Nationwide influenza surveillance is key to providing the high-quality data needed to guide vaccine selection and timing. At the last APACI meeting, members reported on the use of the Northern versus Southern Hemisphere vaccine formulations in their country, the timing of vaccination, and whether these decisions are based on surveillance data (Table 1). The ensuing discussions led to the development of an APACI consensus statement on the use of seasonal influenza vaccines in Asian and Pacific countries (see text box).

Table 1. Seasonal influenza vaccine use in selected APACI member countries

Country	Influenza vaccine		
	Recommended formulation	Selection based on surveillance data	Recommended timing
India	Northern	Yes	Any
Indonesia	Most current	No	Any
Philippines	Southern	Yes	Before June
Singapore	Most current	No	Any
Taiwan	Northern	Yes	October
Vietnam	Most current	No	August

India

Anil Prasad

India's sentinel surveillance network for influenza continues to expand. Based on surveillance data, the Northern Hemisphere vaccine formulation best matches the influenza strains prevalent in India, even in the south of the country, and the WHO-recommended vaccine formulation is generally a good match for the Indian strains. As the influenza virus circulates continuously in India, patients can be vaccinated at any time, subject to vaccine availability (the Northern Hemisphere formulation is usually available from September to the end of July the following year). However, virus circulation does show regional variation, with seasonal peaks occurring during the northern winter and the monsoon season. Increased surveillance may in future lead to regional targeting of the optimum vaccination period.

Indonesia

Cissy Kartasasmita

In Indonesia, the Southern Hemisphere vaccine is given between February and July; from September onwards, patients receive the Northern Hemisphere formulation. The choice of vaccine is based solely

on the most recent formulation available, as there are no data to indicate which formulation would provide the best match for circulating strains. Overall, more doses of the Northern Hemisphere formulation are administered (approximately 58% of total doses in 2006 and 2007). This is due, at least in part, to the high uptake of influenza vaccination among Hajj travellers.

Philippines

Shelley de la Vega

The Philippines switched from the Northern to the Southern Hemisphere influenza vaccine in 2004, based on epidemiological data from the Research Institute for Tropical Medicine (RITM). Released in 2003, this RITM data provided the first insight into the epidemiology of influenza in the Philippines; prior to this time, the Northern Hemisphere formulation was used as it was readily available. Surveillance data obtained since 2004 confirm that influenza isolates generally follow Southern Hemisphere trends. The main influenza peak occurs from June to August, consistent with the Southern Hemisphere winter pattern but, in the Philippines, this coincides with the monsoon period rather than the coldest months.

Singapore

Paul Tambyah

In Singapore, influenza peaks that correspond with the Northern and Southern Hemisphere winters occur against a background of year-round virus circulation. Although Singapore has a sentinel surveillance system for acute respiratory illness, the combination of continual influenza virus activity and very high international visitor numbers make it impractical to choose between the Northern and Southern Hemisphere formulations. Instead, annual vaccination using the most current formulation (Northern or Southern Hemisphere) is recommended for high-risk groups.

Taiwan

Li-Min Huang

Influenza activity in Taiwan shows a definite peak in winter (December–February), with a second peak occurring during summer in some years. A national influenza vaccination programme offers free vaccination to target groups beginning on 1 October each year. Taiwan uses the Northern Hemisphere vaccine formulation, but has relatively high strain mismatch rates because influenza strains often originate from this area.¹ To circumvent this problem, Taiwan may in future incorporate locally prevalent strains into the seasonal influenza vaccine when these strains differ from the WHO recommendations. Local vaccine production could be possible in the next 5 years as production facilities are completed.

Vietnam

Nguyen Thi Thu Yen

Vietnam has a recently established influenza surveillance network comprising four regional public health institutes and 15 sentinel sites. Data from the first 2 years of surveillance (2006–2007) show year-round influenza virus circulation but distinct peaks are observed for the major influenza subtypes. Due to considerable climatic variation, influenza peaks occur 1 month earlier in the north of the country, which has a defined winter season, compared with the more

tropical southern region. Further data are needed before any recommendation on using the Northern or Southern Hemisphere formulation can be made. At present, both formulations are used, depending on availability, and immunisation in August is recommended.

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APACI consensus statement: recommendation on the use of seasonal influenza vaccines in Asian and Pacific countries

Influenza is a serious disease that is an important cause of morbidity and mortality worldwide, including tropical and subtropical countries. Seasonal vaccination provides the best protection against influenza. It is safe and is the most effective measure to reduce the burden of disease. However, it is under-utilised in many countries in the Asian and Pacific regions, especially in tropical and subtropical zones.

APACI supports the WHO's initiatives to increase seasonal influenza vaccine usage and strongly encourages countries:

- to recognise that high-quality influenza surveillance data are essential for assisting the implementation of influenza vaccine policy
- to introduce nationwide surveillance, especially in countries which cross tropical, subtropical and temperate climate zones
- to use existing and future seasonality data to determine the most appropriate time of the year for annual vaccination.

APACI also supports the WHO advice to use the most current seasonal influenza vaccine composition.



Dr Lalit Kant

Lalit Kant is Senior Deputy Director-General of the Indian Council of Medical Research, New Delhi, India, and heads the Division of Epidemiology and Communicable Diseases. Dr Kant has facilitated the set-up of a multi-site, epidemiological and virological influenza surveillance network in India.



Prof Cissy Kartasasmita

Cissy Kartasasmita is President Director of the Dr Hasan Sadikin General Hospital in Bandung, Indonesia. She participated in the Indonesian Ministry of Health's Health Technology Assessment on Influenza in Adults and Children in 2003 and is a member of the Immunization Working Group of the Indonesian Society of Pediatricians.

Update from the Indonesian Influenza Foundation

The Indonesian Influenza Foundation (IIF) held a mini-symposium entitled '*New commitment on influenza control in Indonesia*' in Jakarta on 26 October 2008. The symposium featured presentations by APACI members Lance Jennings, providing an update on influenza in the Asia-Pacific region, and Cissy Kartasasmita, reporting on influenza in children, while Samsuridjal Djauzi, the head of Allergy and Clinical Immunology at the University of Indonesia, discussed influenza in the elderly. During a question-and-answer session, important questions were raised concerning the best choice of influenza vaccine

for Indonesia: Northern Hemisphere, Southern Hemisphere, or both? (For related information and the APACI's recommendations on influenza vaccination in tropical countries, see above article.) Other issues discussed during the question-and-answer session included the efficacy of seasonal influenza vaccination, the potential for seasonal vaccination to provide cross protection against H5N1 infection, the threshold for declaring an influenza outbreak, the role of rapid antigen tests and non-prescription medicines, and how to increase community awareness of the need for seasonal influenza vaccination.

Members' corner: interview with Shelley de la Vega

Dr Shelley de la Vega, APACI representative for the Philippines, speaks to *Influenza – Asian Focus* about strategies for approaching policymakers and stakeholders about influenza vaccination, and her experience with formulating recommendations and guidelines on improving vaccine availability and administration.

1. What steps has the Philippines Department of Health (DOH) taken to address the influenza disease burden?

The DOH was instrumental in organising a Technical Working Group for Influenza (TWGI). Over the years, the DOH has helped to gather various stakeholders who were involved in the formulation of our country's influenza vaccination guidelines, as well as an interpandemic preparedness plan.

2. What was your role within the DOH TWGI and what are some of the key achievements of the group?

As a clinical epidemiologist, I am involved in reviewing available scientific data, proposing areas for additional research and drafting the influenza guidelines. As a geriatrician, I advocate for the vaccination of the elderly.

3. What strategies have you found to be effective in raising public awareness of the need for vaccination?

A tri-media approach, which targets different media platforms, is effective in raising public awareness of the need for vaccination. The timing of media campaigns is key; these activities should be held before the two influenza seasons and when the new vaccine formulation is available. The messages should be brought to various regions throughout the country.

4. As a geriatrician, what initiatives have you seen that have successfully increased influenza vaccination rates among elderly people living in the community?

It is important to incorporate the concept of 'Wellness and Preventive Geriatrics' in the training of medical students, residents in internal medicine,

and fellows in geriatrics. We want our physicians to be aware that vaccination is one of the most effective primary prevention strategies for the elderly. This puts the value of vaccination into a proper context and allows physicians to become more powerful advocates of vaccination in doctor-to-patient counselling. It is also important to find ways to subsidise the cost of vaccination. Discussions with policymakers, local government officials and also non-governmental organisations have been helpful in this regard.

5. What strategies have proven effective in promoting the importance of influenza vaccination and other preventative health measures to various stakeholders?

The first and most important step is to identify the various stakeholders. The stakeholders should be made aware of how they can benefit by having their patients vaccinated. Both plenary and roundtable discussions are effective methods of communicating these health messages. While the discussions should cover seasonal influenza, pandemic preparedness should also be discussed. Key stakeholders include patients; their caregivers; midwives; nurses and doctors in professional medical organisations for specialties such as paediatrics, obstetrics, general medicine and geriatrics. Apart from infectious disease specialists, other physicians such as cardiologists, pulmonologists and endocrinologists should also be involved. Other stakeholders include local government officials, the Philippine Health Insurance Corporation, and national health insurance officials who approve and allocate the budget for vaccination. Vaccine manufacturers are important partners in advocacy.



Highlights from the Third European Influenza Conference

The European Scientific Working Group on Influenza (ESWI) held the Third European Influenza Conference on 14–17 September 2008 in Vilamoura, Portugal, focusing on the latest developments in influenza prevention, control and treatment. A significant feature of the meeting was the tailor-made ‘Science in Practice’ programme, which ran parallel to the scientific programme and sought to involve stakeholders such as government representatives and healthcare opinion leaders in the discussion on the impact of influenza. The APACI was represented at the conference with its own exhibition stand, and presented a clinical poster on the seasonality of influenza in the Asia-Pacific region.¹ APACI members Lance Jennings and Paul Chan were in attendance and share some highlights from the conference below. For more information, visit www.eswiconference.org.

Plagues and people: planning for pandemics

Roy Anderson from the Imperial College of London opened the conference with the keynote lecture. His presentation gave an overarching view of the different objectives of the various stakeholders in pandemic planning. While scientists look for the ideal solution, focusing on drug and vaccine efficacy, policymakers must contend with budget constraints, drug stockpiling and the pharmacoeconomics involved. He also stressed that given the rapid evolutionary path of viruses, government pandemic plans need sufficient detail and implementation in order to be able to counter the next major pandemic – likely to be a global event due to the mobility of the human population today.

Evaluating vaccine effectiveness

Day 2 of the conference featured a panel discussion that debated vaccine efficacy in the elderly population. Lone Simonsen from George Washington University in the USA highlighted a disparity between observational studies that consistently report that vaccination reduces the risk of all-cause winter deaths by 50%, and the assessment from excess mortality studies that less than 10% of all winter deaths are attributable to influenza.² Kristin Nichol from the Minneapolis VA Medical Center (also in the USA) acknowledged the need to minimise bias and confounding in observational studies, but pointed out that the actual number of influenza-related deaths is under-reported as patients die from a diverse range of complications.³

Seasonal vaccination of healthcare workers

During the ‘Science in Practice’ programme, a number of speakers participated in a panel discussion session regarding the seasonal vaccination of healthcare workers. The participants pointed out that, while many countries now recommend the inoculation of healthcare workers, uptake is generally low (less than 25% in Europe and the UK).⁴ While there are many contributors to low uptake of influenza vaccination, including budget constraints and policy differences, there is still no consensus on the best method of improving uptake. The panel discussed at length the merits of compulsory or conditional vaccination strategies for healthcare workers in high-risk environments such as retirement homes.

Modelling the use of antivirals in a pandemic

Among the comprehensive range of poster presentations was some novel research into the use of antivirals during a pandemic situation. Merler *et al.* used mathematical modelling to investigate the antiviral interventions required to minimise the impact of an influenza pandemic at a national level. The authors calculated that a combination of antiviral treatment for all infected individuals and antiviral prophylaxis for younger individuals (2–25 years old) would reduce the cumulative attack rate and minimise the number of antiviral courses used during a pandemic situation. The results also highlighted that even a 48-hour delay in both antiviral treatment and prophylaxis would lead to a 50% decrease

in antiviral efficacy.⁵ Therefore, in addition to stockpiling antiviral courses, greater effort should be put into organising antiviral distribution and speeding up the detection of an influenza pandemic.

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Severe influenza cluster in Singapore: incident report

Roland Jureen, MD, of the Department of Laboratory Medicine at Alexandra Hospital, Singapore, reports on a cluster of atypical respiratory tract infections that led to the implementation of the hospital's influenza pandemic plan in April 2008.

Several young men were admitted to Alexandra Hospital, a 380-bed acute care facility, with fever and respiratory symptoms on 22 April 2008. All were migrant workers living in three dormitories at different locations. The majority had signs of haziness, opacities or consolidation on chest X-ray. By late afternoon, the cluster of patients numbered six and the attending doctor contacted the infection control team. A rapid investigation confirmed that four patients had been admitted to an isolation ward with negative pressure rooms and airborne transmission precautions, but two were in a general ward. In addition, four similar cases had been admitted to the isolation ward and a high-dependency unit during the previous days.

All cases were transferred to the isolation ward and both the hospital pandemic taskforce and the Ministry of Health were alerted. By the next morning,

the total number of cases had risen to 14. Controlled access to the general ward was instituted and staff were required to wear full protective gear. Laboratory investigations were urgently performed, including multiplex polymerase chain reaction (PCR) analysis of nasal and throat swabs (in collaboration with the National Public Health Laboratory), urinalysis and blood cultures.

Laboratory results, available within 8 hours, showed influenza A in five cases and influenza B in seven, while two patients had *Haemophilus influenzae* or *Streptococcus pneumoniae* only. *S. pneumoniae* was also identified in one influenza A case and three influenza B cases, including all but one of the patients admitted to intensive care or high dependency units. Tests for severe acute respiratory syndrome (SARS), H5N1 and *Legionella* were negative and the precautionary measures were stepped down. The influenza A isolates were subsequently shown to be similar to circulating seasonal strains. This cluster of mixed influenza with bacterial superinfection highlights the importance of prompt influenza testing in clusters of severe respiratory illness.

Childhood influenza outbreak in Hong Kong

APACI board member Paul Chan from the Chinese University of Hong Kong reports on an outbreak of severe influenza in children that led to the temporary closure of schools in March 2008.

Seasonal influenza activity in Hong Kong increased in early February 2008 and peaked in mid-to-late March, with the timing and level of activity being consistent with previous years. During the peak period, about half of the circulating strains were influenza B, one-third were A(H1N1) and the remainder were A(H3N2), which had been the predominant subtype during the previous few years. In early March, influenza was suspected in several children with severe and/or fatal illnesses, and outbreaks were reported in kindergartens and schools. As a precautionary measure, all primary schools and preschool facilities were closed prior to Easter in order to interrupt the transmission of influenza in the community.

Thorough investigations were conducted for the fatal cases. Influenza A(H1N1) was isolated from a 7-year-old boy who died with pathological features of acute necrotising encephalopathy. Influenza with encephalopathy

is associated with an overall mortality rate of 15–30% and is an important cause of mortality and morbidity in children, especially in Japan where 100–500 cases occur every year.¹ A 3-year-old girl had influenza A(H3N2) isolated. Her death probably resulted from acute cardiac arrhythmia produced by an anatomical variation in her coronary artery and predisposing genetic polymorphisms; influenza-related stress was a possible precipitating factor.

This unfortunate incident serves as a reminder of the potential seriousness of influenza: while most infections in children are mild and self-limiting, severe and even fatal cases can occur. In November 2008, the Hong Kong Government began subsidising influenza vaccination for children aged 6 months to 5 years. The use of vaccination to prevent influenza in children should be encouraged.

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Flu review

Ginsberg J, Mohebbi MH, Patel RS et al. Detecting influenza epidemics using search engine query data. *Nature* 2008; 457: 1012–14.

Scientists at Google Inc. have developed a model to accurately estimate weekly influenza activity levels using search engine query data. Their linear model estimates the percentage of visits to physicians for influenza-like illness (ILI) by combining historical data from US Centers for Disease Control and Prevention (CDC) influenza surveillance with ILI-related search queries such as 'general influenza symptoms', 'influenza complications' and 'term for influenza'. The automated process was applied to data from nine public health regions in the USA, and combined to generate a final linear model of ILI activity. In the US 2007/2008 influenza season, the model was consistently able to estimate the current percentage of visits to physicians for ILI cases 1–2 weeks ahead of the US CDC's own ILI surveillance network. By harnessing the collective intelligence of millions of web search users, the authors affirmed that this model could prove to be an important and timely influenza monitoring system in the USA, and perhaps eventually worldwide. For more information, visit: www.google.org/flutrends.

Zaman K, Roy E, Arifeen SE et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* 2008; 359: 1555–64.

Findings from a Bangladeshi study show maternal influenza immunisation significantly reduces the risk of proven influenza illness and febrile respiratory illnesses in mothers and young infants. The authors assigned 340 mothers to receive either inactivated influenza vaccine or the 23-valent pneumococcal polysaccharide vaccine as a control. Using weekly interviews, clinical tests and antigen testing, the authors estimated the incidence of respiratory illness and vaccine effectiveness in mothers and infants. There were fewer cases of laboratory-confirmed influenza in those infants whose mothers received influenza vaccination than in those in the control group, with an estimated vaccine efficacy of 63%. The rate of respiratory illness with fever in mothers and infants was reduced by 36% and 29%, respectively. The study gave valuable descriptive data on the natural history of influenza in a tropical setting, and suggests further study is needed to evaluate the effectiveness of the antenatal immunisation strategy for the prevention of seasonal influenza.



Clinical A/Prof David Smith

David Smith is Clinical Director of the Division of Microbiology and Infectious Diseases at the Western Australian Centre for Pathology and Medical Research. He is also Clinical Associate Professor in the Department of Microbiology at the University of Western Australia, and Director of the Arbovirus Research and Surveillance Group.

Avian influenza updates

Cumulative cases of A(H5N1) in 2008

A total of 42 confirmed human cases of influenza A(H5N1) were reported to the WHO during 2008, representing a substantial fall compared to the number of cases in 2006 (115 cases) and 2007 (88). Indonesia accounted for the majority of 2008 reports (22 cases), followed by Egypt (8), Vietnam (6), China (4) and an isolated case in Bangladesh. There were 31 deaths among the confirmed cases, giving a fatality rate of 74%. Aggregate data for the period 2003–2008 show a total of 393 cases, with a 63% fatality rate.

Reference

World Health Organization. Cumulative number of confirmed human cases of avian influenza A(H5N1) reported to WHO, 19 January 2009. Available at: www.who.int/csr/disease/avian_influenza. Accessed 21 January 2009.

Capacity building in Asia

Despite decreases in the number of confirmed human A(H5N1) cases, continued outbreaks of avian influenza leave no room for complacency. The Philippines has remained free of avian influenza, but

has a number of areas located on migratory bird paths. In December 2008, a regional avian influenza diagnostic laboratory was opened in Zamboanga City, which has been designated a priority area due to bird migration and its proximity to countries with confirmed avian influenza cases.¹ The centre is the third such facility in the Philippines.

In Indonesia, the largest hospital in Bali, Sanglah Hospital, has opened a dedicated ward for the treatment of patients infected with influenza A(H5N1) as part of the island's strategy for countering avian influenza.² The 27-bed ward has a sophisticated air filtration system and was designed in accordance with WHO standards. Staff will wear protective equipment when treating patients, who may include those with other communicable diseases such as severe acute respiratory syndrome and rabies. Bali experienced avian influenza outbreaks in 2004 and 2007, with the last reported case of infected poultry identified in March 2008.

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Upcoming meetings

International

Influenza Vaccines for the World - IVW 2009

Cannes, France

www.meetingsmanagement.com/ivw_2009/index.htm

27–30 April 2009

American Thoracic Society (ATS) 2009 International Conference

San Diego, California

www.thoracic.org

15–20 May 2009

19th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)

Helsinki, Finland

www.akm.ch/eccmid2009

16–19 May 2009

27th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID)

Brussels, Belgium

www.kenes.com/espид

9–13 June 2009

6th World Congress of the World Society for Pediatric Infectious Diseases (WSPID)

Buenos Aires, Argentina

www.kenes.com/wspid/

18–22 November 2009

Regional

7th International Symposium on Antimicrobial Agents and Resistance - ISAAR 2009

Bangkok, Thailand

www.isaar.org

18–20 March 2009

Australasian Society for Infectious Diseases (ASID) Annual Scientific Conference

Hunter Valley, Australia

www.asid.net.au

25–28 March 2009

Darwin 2009 - The Thoracic Society of Australia and New Zealand (TSANZ) and The Australian and New Zealand Society of Respiratory Science (ANZSRS) Annual Scientific Meetings

Darwin, Australia

www.thoracic.org.au/asm2009.html

3–8 April 2009

Next APACI meeting

The next meeting will be held in Kuala Lumpur, Malaysia, on 14–15 March 2009.

In the next issue ...

- Highlights from the APACI Clinician Symposium, Malaysia
- Highlights from the 3rd International Conference on Influenza Vaccines for the World
- Focus on influenza vaccination in healthcare workers.

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