Influenza Asian Focus

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Welcome to the 14th 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.

his issue of Influenza – Asian Focus features highlights from The Lancet Conference on Influenza in the Asia-Pacific and from the APACI's own Clinician Symposium in Kuala Lumpur, Malaysia, which combined presentations from Malaysian experts with updates on avian influenza, influenza disease patterns in the tropics and seasonal influenza. APACI board members met after the symposium to share their experiences of trialling initiatives to increase awareness of influenza; these national reports are summarised on pages 8-9. This issue also investigates strategies to increase the seasonal influenza vaccination rate among healthcare workers. Low vaccine coverage in this group persists in many countries - however, some Asian countries are achieving vaccine coverage rates far higher than the international average. Finally, we report on the influenza pandemic (H1N1) 2009 in the Asia-Pacific region and the APACI's response.

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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 countryspecific 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 APACI board met in Kuala Lumpur, Malaysia, on 14 March 2009 to participate in the latest APACI Clinician Symposium. Entitled Uncovering the impact of influenza, the workshop was attended by local doctors, including primary care physicians, paediatricians and infectious diseases specialists. Lance Jennings welcomed the prominent local speakers, Dato' Dr Haji Ramlee bin Haji Rahmat, Deputy Director General of the Malaysian Ministry of Health, and Professor Datuk Dr Mohd Sham Kasim, the Chairman of Malaysia's Influenza Advisory Group, Presentations were also given by APACI members Paul Chan, Paul Tambyah and Lance Jennings, and were followed by a lively panel discussion. Presentation highlights are reported on pages 6-7. The official APACI board meeting was held the following day and focused on recent influenza awareness initiatives in each country represented. A summary of the varied successes and challenges encountered in each country is presented on pages 8-9.

VACCINATING HEALTH WORKERS

Seasonal flu vaccination in HCWs

Seasonal influenza is highly contagious and annual influenza vaccination is widely recommended for healthcare workers (HCWs), who may transmit the virus to vulnerable patients. However, the vaccination rate among HCWs remains low in many countries and further efforts are needed to understand and overcome the barriers to vaccination.

'First do no harm'

Exposure to the influenza virus is common in HCWs during the course of their work and HCWs who continue working with mild or subclinical influenza infection may transmit the virus to their patients, many of whom are at high risk for influenza-related complications. Elderly and immunocompromised patients may have an inadequate response to the influenza vaccine, thus vaccination of close contacts is required for optimum protection.

Nosocomial influenza infection has been shown to prolong hospital stays and increase mortality in hospitalised patients, while low HCW vaccination rates have been linked to influenza outbreaks in hospitals.¹ Conversely, vaccination of HCWs significantly reduced mortality in elderly residents of long-term care hospitals and residential homes.²⁻⁴ Vaccinating HCWs also benefits the vaccinated individual, reduces absenteeism and is cost effective.^{5.6}

Influenza vaccine coverage in Asia

Annual vaccination for HCWs against seasonal influenza is recommended by many Asia-Pacific countries, including Hong Kong, Korea, Malaysia, Singapore, Taiwan, Thailand, Australia and New Zealand. The US Centers for Disease Control and Prevention (CDC) recommends vaccinating all HCWs, including doctors, nurses, emergency-response personnel, other workers in hospitals and out-patient settings, nursing home employees, and students; furthermore, the level of vaccination coverage in HCWs should be used as a quality indicator for patient safety.⁵

The influenza HCW vaccination rate in the Asia-Pacific region shows considerable variation between countries with available data. Vaccine coverage in Hong Kong is estimated to be 20–50%, but closer to 20% in public hospitals,⁷ whereas vaccination rates of 80–90% have been reported in Korea,⁸ Thailand⁷

Strategies to increase vaccine uptake^{6,12-13}

- Promotional material in high-traffic areas
- Informational handouts
- Conduct seminars with opportunistic vaccination
- Clinics in employee cafeterias
- Mobile units on wards
- Vaccine available at multiple times and locations
- Empower nurses to organise local clinics
- Pre-printed documentation
- Senior staff participation and endorsement
- Incentive prizes

and Taiwan.⁷ Singaporean studies reported rates of 39% (HCWs at two hospitals)⁹ and 77% (HCWs at 18 polyclinics and one hospital).¹⁰ In NZ, vaccine coverage is typically around 33% in HCWs, but reached 51% in one large district in 2008,⁷ while recent Australian studies have reported a vaccination rate of 28–38%.⁶ By comparison, the vaccination rate among HCWs in the USA during the 2005–2006 season was 44%.⁵

Overcoming barriers to vaccination

Several factors may account for the surprisingly low uptake of influenza vaccination in HCWs. These include lack of convenient access to the vaccine, together with the attitudes and beliefs of HCWs, including a perception that vaccination is unnecessary, concerns about adverse reactions, and doubts about efficacy.⁶¹¹ In a review of studies exploring self-reported reasons for rejecting or accepting influenza vaccination, all but two studies identified self-protection as the most important reason for vaccine acceptance.¹¹ As the vaccination rate varies between different occupational, ethnic and demographic subgroups of HCWs,⁵ the reasons for vaccine rejection may also vary.

Organised campaigns have been shown to increase the vaccination rate in HCWs.^{12,13} Successful initiatives combine education - which should address misconceptions about influenza and vaccination as well as reinforce the duty of care to patients - with convenient access to vaccination, free of charge (see text box).⁶ Nevertheless, the limited success of these efforts in some countries has led to consideration of mandatory HCW vaccination. The CDC and Australian experts have recommended that HCWs who refuse influenza vaccination should sign a compulsory optout declaration form,5.6 and be transferred out of critical high-risk areas (e.g., intensive care units and cancer, transplant and neonatal wards).⁶ While controversial, these suggestions recognise the imperative for healthcare institutions to protect their most vulnerable patients.

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Dr Shelley de la Vega

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A/Prof Nguyen Thi Hong Hanh

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Evolution of pandemic (H1N1) 2009

The first cases of a novel influenza A(H1N1) strain of swine origin were detected in Mexico during mid-March 2009 and the WHO declared a pandemic on 11 June 2009. Transmission of the virus occurred with remarkable speed, taking under 6 weeks to spread to an extent which had usually taken over 6 months in previous pandemics.¹ As the pandemic is still evolving, the epidemiology, clinical characteristics and treatment recommendations outlined below may change over time.

Pandemic (H1N1) 2009 is a new subtype of influenza A(H1N1) that contains genes from the North American swine virus, North American avian virus, Eurasian swine virus, and human virus.² In contrast to avian influenza A(H5N1), pandemic (H1N1) 2009 is readily transmitted between humans, with substantially higher transmissibility than seasonal influenza.^{2,3} However, rapid transmission is not an indicator of disease severity.

Clinical course of infection

Pandemic (H1N1) 2009 causes similar symptoms to seasonal influenza (high fever, cough and sore throat), but diarrhoea and vomiting have been more commonly reported.^{2,4} In most cases, symptoms are mild and resolve without treatment, but severe and sometimes fatal pneumonia have been described in healthy young adults.⁵ In contrast to the typical pattern of seasonal influenza, morbidity has so far been lower in adults aged over 60 years, who may have crossprotection from prior exposure to a similar strain.⁵

As with seasonal influenza, certain groups seem to be at a higher risk of severe disease. The WHO analysed the clinical features of hospitalised cases from North America, Chile and Mexico.6 A hospitalisation rate of 2-6% of confirmed cases was initially reported, but current US estimates are below 1%.6 While the median age of all infected patients is 12-17 years (based on data from North America, Chile, Japan and the UK),7 the median age of hospitalised patients is somewhat older (15-42 years), and most deaths occur in patients aged 40 years or over.6 An early estimate of the case fatality rate was 0.4%.3

The main cause of hospitalisation is primary viral pneumonia due to direct viral invasion of lung tissue, which may progress rapidly to respiratory failure and

death.⁶ Many hospitalised patients have had underlying medical conditions that are also risk factors for complications of seasonal influenza.⁶ High-risk individuals and patients with severe clinical influenza-like illness should receive prompt treatment with a neuraminidase inhibitor, regardless of whether they are hospitalised.8

Pregnant women have a high risk of complications: of 34 confirmed or probable cases reported in the USA, 11 were hospitalised and 6 died.9 Prompt treatment with a neuraminidase inhibitor is recommended for pregnant women with suspected pandemic (H1N1) 2009 infection.10 Obesity, or its related morbidity, also appears to be a risk factor for very severe or fatal disease. Patients with a body mass index $> 30 \text{ kg/m}^2$ accounted for 30 of 50 fatal cases in California, and 11 of these 30 cases had no known risk factors for developing complications of influenza.6

Danger signs in patients with pandemic (H1N1) **2009 infection**¹⁰

- Shortness of breath during activity or resting
- Difficulty breathing
- Cyanosis
- Bloody or coloured sputum
- Chest pain
- Altered mental status
- High fever persisting beyond 3 davs
- Low blood pressure
- In children: rapid or difficult breathing, reduced alertness, difficulty waking up, or little desire to play

Widespread community transmission

Once sustained community transmission of the virus is established – as has already occurred in many countries - it is appropriate to move from a containment strategy to one of mitigation. At this stage, obtaining laboratory confirmation of every case is neither practical nor useful and reporting of individual confirmed cases to the WHO is no longer required.1 Monitoring remains important, but should focus on unusual events (such as clusters of severe or fatal cases, or unexplained clinical patterns associated with such cases) and changes in the pattern of transmission (e.g., a sudden increase in absenteeism or emergency department visits).1

As a consequence of the reduced reporting requirements, the total number of reported cases is greatly underestimated once community transmission becomes widespread. Nevertheless, it appears that the average age of cases may be increasing.7 Areas with high levels of pandemic virus activity have also reported a shift in severe hospitalised cases from healthy young people with primary viral pneumonia to older individuals with chronic medical conditions.6

By the start of July, the pandemic (H1N1) 2009 virus was circulating in most Asia-Pacific countries, coinciding with the Southern Hemisphere seasonal influenza epidemic. However, activity varied widely. Australia had reported over 10,000 confirmed cases as of 15 July and Thailand had approximately 8900 cases as of 2 August, compared with 2000-3000 cases in Japan, the Philippines and New Zealand, 1000-1500 in Singapore, Hong Kong and mainland China, and lower rates in other parts of the region.

PANDEMIC (H1N1) 2009

Vaccination against pandemic (H1N1) 2009

Although seasonal influenza vaccination is unlikely to protect against the pandemic (H1N1) 2009 virus, it may prevent morbidity from dual infection with both viruses. In addition, clinicians will be better able to confidently diagnose and treat pandemic (H1N1) 2009 infection if patients are immunised against seasonal influenza. Recognising these factors, the New Zealand Ministry of Health made seasonal influenza vaccine freely available to all individuals from mid-July for the current influenza season. Several companies are developing vaccines against the pandemic (H1N1) 2009 virus. Vaccine supplies will initially be limited. Both the Strategic Advisory Group of Experts on Immunization (SAGE) and the US CDC's Advisory Committee on Immunization Practices (ACIP) recommend immunising healthcare workers and pregnant women as a priority, but their recommendations differ somewhat for other populations. ^{11,12} SAGE recommends considering stepwise vaccination of individuals aged > 6months with chronic medical conditions (including morbid obesity), healthy adults aged > 15 years and < 49 years, healthy children (to reduce transmission), healthy adults aged > 49 and < 65 years, and healthy adults aged > 65 years,¹¹ while ACIP proposes targeting household contacts of infants aged < 6 months, young people aged 6 months to 24 years, and adults aged < 65 years with underlying risk conditions.¹²

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APACI position statement on pandemic (H1N1) 2009 in South-East Asia

- Pandemic (H1N1) 2009 highlights the importance of ongoing pandemic preparedness. Annual seasonal influenza control can contribute to a pandemic response by ensuring resources and infrastructure are in place to deal with a pandemic.
- The seasonality of influenza in South-East Asia is different from that of temperate regions. Consistent surveillance is essential to monitor the emergence of the pandemic and co-circulation of pandemic (H1N1) 2009 with pre-existing strains.
- Antiviral medications should be used in accordance with each country's national influenza pandemic preparedness plan.
- Vaccine production capacity is limited in the South-East Asian region. Strategies to secure the supply of vaccine should be actioned promptly. In addition, many countries in South-East Asia do not have an existing structure to deliver seasonal influenza vaccine. These countries should plan in advance to allow timely delivery of the new vaccine to at-risk groups once it is available.

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Indonesian Influenza Foundation celebrates first year

On Saturday, 30 May 2009, the Indonesian Influenza Foundation (IIF) held a mini-symposium on seasonal and swine influenza in Jakarta to commemorate the group's first anniversary.

Three invited speakers were moderated by Dr Sardikin Giriputo, Director of Sulianti Saroso Infectious Diseases Hospital in Jakarta. The first speaker was Professor Tjandra Yoga Aditama, the Director General for Disease Control and Environmental Health, Ministry of Health. He spoke on *The Global Picture and Indonesia*, focusing on the new influenza pandemic (H1N1) 2009 and the preparedness of the Indonesian Ministry of Health to face pandemic influenza. Dr Iris Rengganis, an Immunologist from the University of Indonesia, then presented a paper on seasonal influenza awareness. The final speaker was Dr Surachmi Setyaningsih from the Department of Animal Disease and Veterinary Health at the Institut Pertanian Bogor (Bogor Agricultural University). Her topic was swine influenza viruses.

More than 60 participants from Jakarta, Bogor and Bandung attended the seminar. The programme was well received and stimulated discussion between the audience and speakers, particularly regarding the prevention of seasonal and swine influenza and the role of seasonal influenza vaccination against the new A(H1N1) virus. The participants agreed to meet regularly to discuss progress in the prevention of influenza.



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.

Highlights of the APACI Clinician Symposium

The latest APACI Clinician Symposium, Uncovering the impact of influenza, featured insightful presentations on the Malavsian influenza situation from Dato' Dr Haji Ramlee bin Haji Rahmat, Deputy Director General of the Ministry of Health (MOH) and Professor Datuk Dr Mohd Sham Kasim, who chairs the Influenza Advisory Group in Malaysia, Additional presenters included Paul Chan (an update on avian influenza), Paul Tambyah (influenza disease patterns in the tropics) and Lance Jennings (prevention and treatment of seasonal influenza).

Influenza in Malaysia

Dr Ramlee explained that Malaysia has a sentinel surveillance scheme for influenza-like illness (ILI) that began in 2004 and now includes 216 sites. The influenza virus is present year-round in Malaysia, with 3-6 strains typically circulating simultaneously. Influenza is not viewed as a public health problem, but outbreaks do occur in boarding schools and other crowded places. Seasonal influenza vaccination is only available privately and is not subsidised. However, the MOH provides the seasonal influenza vaccine to approximately 185,000 front-line healthcare workers each year, and advises vaccination for pilgrims, particularly those aged 60 or over.

Dr Ramlee outlined Malaysia's comprehensive National Influenza Pandemic Preparedness Plan (NIPPP), which incorporates strategies for the organisational, public health, medical, laboratory, risk communication and social responses to a pandemic and is underpinned by a strong political and funding commitment. The MOH has designated 21 hospitals to manage severe or complicated cases. The NIPPP includes yearly pandemic simulation exercises in each state as well as exercises at national and international level, including a March 2009 tabletop exercise involving the MOH and the United States Pacific Command (USPACOM). Malaysia is actively strengthening its laboratory capacity and has approved a pre-pandemic vaccine. It is also making strong progress towards achieving its target for stockpiling antiviral agents.

Dr Sham provided information on Malaysia's Influenza Advisory Group, which aims to promote influenza awareness as a means to improving influenza prevention and control. Its objectives include raising awareness among health professionals and the public, providing educational resources, working with the MOH to develop recommendations for influenza prevention and control, and supporting influenza pandemic preparedness. Various short- and longterm activities are planned, including identification of specific target groups, contributing to the influenza studies needed to generate local data, raising awareness of the group, and developing influenza guidelines.

Avian influenza update

Paul Chan provided a brief update of recent human avian influenza A(H5N1) data and insights from the Hong Kong experience. The geographical distribution of cases from 2003 to 2009 shows two main clusters, one in South-East Asia and, beginning in 2006, a second in the Middle East. Indonesia and Vietnam have the highest cumulative number of confirmed cases, but the majority of cases in 2009 have occurred in Egypt, which now has the third highest total. Cumulative WHO data show that approximately 90% of cases have occurred in individuals aged below 40 years, with an overall case fatality rate (CFR) of approximately 60%. However, there is a clear interaction between age and survival: the CFR exceeds 70% in the 10-19, 20-29 and 30-39 age groups, but is below 50% in children aged 0-9 years. Up-to-date statistics and maps are available from the WHO Regional Office for the Western Pacific website: www.wpro.who.int.

Professor Chan addressed misconceptions pertaining to avian influenza infection: it is not simply a severe version of seasonal influenza, a result of naïve immunity, or a manifestation of avian virus in an unadapted host. Investigation of cases from the 1997 outbreak in Hong Kong provided insight into the clinical and pathological course of A(H5N1), which differs in several ways from that of the usual human subtypes, H1-3. Viral replication triggers the induction of large quantities of pro-inflammatory cytokines, which can lead to the development of reactive haemophagocytic syndrome, leading to multiple organ failure.^{1,2}

Influenza disease patterns

Paul Tambyah reviewed influenza disease patterns in the tropics and their clinical implications. In contrast to the well-defined seasonality observed in temperate countries, influenza seasonality in tropical and subtropical regions remains poorly understood. However, the morbidity and excess mortality attributable to influenza in Asia is increasingly well documented. In particular, influenza is an important cause of hospitalisation in young children^{3,4} and of mortality in the elderly,⁵ with rates exceeding those reported in temperate countries.3,5

The influenza virus circulates year-round in the tropics. Seasonality is complex, varying between

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regions and from year to year; peaks are often observed during the rainy season, may occur more than once a year, and typically have a longer duration than in temperate regions.⁶ A Singaporean study showed a strong correspondence between peaks in influenza A isolates and peaks in all-cause deaths, underlying pneumonia and influenza deaths, and underlying circulatory and respiratory deaths.⁵ Similarly, a Hong Kong study showed a temporal association between influenza activity and hospitalisation for both acute respiratory disease and pneumonia or infection.⁷

Another factor to consider is that continuous transmission in tropical regions creates a persistent influenza reservoir that promotes viral evolution.⁸ Together with the complex seasonality of influenza, this may generate confusion over the optimum vaccine formulation and timing of administration in tropical and subtropical regions, or even whether to vaccinate at all. However, tropical cities may be among the first affected in a pandemic and have higher mortality.⁹ In these regions it is best to administer the most current available vaccine when the patient attends the clinic.

Seasonal influenza prevention and treatment

Lance Jennings reviewed strategies for preventing and treating seasonal influenza. He emphasised that physicians have a vital role in preventing and treating influenza and it is increasingly important for them to be familiar with epidemiology and surveillance data. Although non-pharmacological interventions such as personal hygiene are beneficial, annual vaccination is the best way to prevent seasonal influenza and its associated morbidity. Furthermore, increased seasonal vaccination uptake will aid pandemic preparedness. Influenza vaccination rates vary widely in the Asia-Pacific region, with Korea and Japan having the highest rates. Challenges for influenza vaccination include the antigenic variation of the virus, the limited immunogenicity of vaccines, and the fact that vaccines provide strain-specific protection of limited duration. An adjuvanted subunit vaccine containing MF59 enhances antibody responses in the elderly, who generally do not respond as well as younger adults. Live attenuated influenza vaccines, which are administered by nasal spray and are effective in children and adults aged from 2 to 49 years, may offer some cross-protection against drift variants. Current directions in vaccine research include intradermal vaccination, incorporating antigens that induce broader protection (e.g., matrix proteins), development of new adjuvants such as liposomes and immunostimulatory complexes, and the use of new technologies such as chimeric and DNA vaccines.

Antiviral agents can prevent and treat influenza and have demonstrated a meaningful clinical benefit in non-trial settings, but resistance is sometimes an issue. An oseltamivir-resistant A(H1N1) strain containing a histidine to tyrosine substitution at amino acid 274 emerged spontaneously and has spread internationally, but this is not driven by antiviral use.¹⁰ The US Centers for Disease Control and Prevention (CDC) recommends using either oseltamivir or zanamivir if treatment is indicated and recent local surveillance data indicate that circulating viruses are likely to be A(H3N2) or influenza B. Otherwise, zanamivir should be used; if this is not possible, oseltamivir plus an adamantane (preferably rimantadine) is recommended.¹¹ Implementing these recommendations requires the physician to be familiar with local surveillance and epidemiological data. Dr Jennings suggested asking patients four questions to guide decisions on antiviral use:

1. Has the person been exposed to influenza?

- Local influenza activity
- Travel
- Contact with proven influenza

2. Do you think they have influenza?

- Positive point-of-care (POC) test during influenza season: > 90% chance of influenza
 Strong clinical suspicion during influenza
- season: 60-80% chance of influenza

3. Will the patient benefit significantly from antiviral treatment?

- Early in illness
- Highly symptomatic
- High risk of severe or complicated influenza
- Likely to pass influenza to a high-risk contact

4. Is it likely to be seasonal A(H1N1)?

- Need to know local activity and resistance patterns
- Not an issue if POC test shows influenza B

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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.

INFLUENZA - ASIAN FOCUS

National reports: raising influenza awareness

APACI Board Members discuss current influenza awareness initiatives in their respective countries.

Hong Kong (Paul Chan)

Although Hong Kong has no dedicated society to promote influenza awareness, Malik Peiris leads an active governmentfunded research group. Paul Chan is represented on the scientific committee that collaborates with government officials to maintain up-to-date influenza guidelines, which are distributed to doctors annually before the start of the influenza vaccination programme. Awareness activities have included media interviews, giving talks on seasonal and pandemic influenza to a range of groups. and participating in television programmes to promote influenza vaccination and clarify related issues of public interest. As a result of increased awareness, the Hong Kong government now subsidises influenza vaccination in children; the elderly, high-risk groups and healthcare workers also receive free vaccination. Paul Chan identified public awareness of influenza and the relatively low vaccine uptake among healthcare workers as being areas where more work was needed.

India (Anil Prasad)

Awareness of influenza in India is low and the government does not view respiratory diseases, including influenza, as a priority. The Influenza Foundation of India (IFI) is actively working to increase awareness by improving knowledge of influenza and its epidemiology in India, producing and disseminating unbiased information on influenza to the medical community and the public, increasing awareness of the links between seasonal influenza vaccination and pandemic preparedness, and coordinating influenza news and activities between private practitioners and the government.

The IFI's initial activities have been directed towards the medical fraternity. Activities in 2008 included organising influenza seminars. workshops. continuing medical education (CME) meetings and press conferences in various locations, with topics including epidemiology, prevention and the importance of vaccinating healthcare workers during an avian influenza outbreak. The IFI also produces educational and scientific materials such as newsletters, pamphlets and posters, including a twice-yearly newsletter. To accomplish its goals, the IFI works with governmental and scientific bodies, as well as co-sponsoring activities with pharmaceutical companies. Submissions on influenza control guidelines have been made to the government and the Indian Council for Medical Research. Future priorities for the IFI include promoting increased use of seasonal vaccination in children, the elderly and other at-risk groups; increasing awareness of influenza control in rural populations, and working towards the establishment of vaccine manufacturing units in India.

Indonesia (Cissy Kartasasmita)

The Indonesian Influenza Foundation (IIF) was inaugurated in May 2008 and its membership now includes over 100 primary care physicians and specialists in paediatrics, geriatrics, internal medicine, pulmonology and allergy-immunology. Cissy Kartasasmita is the Foundation's Chairperson.

The IIF is involved in a range of activities to promote influenza awareness, including participation in seminars, advisory group membership, the development of guidelines for influenza vaccination in adolescents, research and pandemic planning exercises. The IIF participated in a number of symposia during 2008, including the Asian Congress of Pediatric Infectious Diseases (ACPID) meeting in Surabaya. Activities planned for the coming year include advocacy for the general public and medical communities, participation in symposia, media advocacy and small aroup discussions.

Cissy Kartasasmita noted that influenza A(H5N1) is the main focus for influenza awareness and guidelines in Indonesia. However, there has been an increase in requests for the seasonal influenza vaccine for Hajj and Umrah pilgrims and the use of the seasonal influenza vaccine in private practice continues to grow, despite anti-vaccination groups claiming that the vaccine is forbidden to Muslims. See page 5 for details of the IIF's first anniversary celebration.

Malaysia (Ilina Isahak)

Malaysia's Influenza Advisory Group was formed in 2007. It includes clinicians, epidemiologists, virologists and representatives from the Ministries of Health and Education, as well as from multinational companies. The group's activities include epidemiological surveillance and research, in addition to promoting influenza awareness.

Awareness initiatives to date have included CME programmes for hospital doctors, public symposia targeted to specific groups (including kindergartens, primary school teachers and farm managers), and public education through media conferences and newspaper articles. The availability of local data is important for raising awareness, and the advisory group is involved in studying the effectiveness of influenza vaccination in different groups: healthy working adults, Hajj pilgrims, dental healthcare workers and students, residents of aged care facilities, and children living in welfare homes. The Influenza Advisory Group also participates in guideline development and updates.

The tangible results of influenza awareness activities include the introduction of free influenza vaccination for healthcare workers as well as vaccination for Hajj pilgrims. Ongoing needs include encouraging paediatricians to vaccinate children against influenza and targeting travel agents for the Umrah pilgrimage, which may be performed at any time during the year.

New Zealand (Lance Jennings)

New Zealand's National Influenza Strategy Group (NISG) was formed in 1999; Lance Jennings is a founding member of the group and its national spokesperson. The NISG may be viewed as a unique partnership of planners, providers, industry, general practitioners and practice nurses and the indigenous Maori people. The group's focus is on developing resources, such as the influenza kit, and on raising awareness through television and radio advertising. The annual influenza campaign for promoting awareness and vaccination commences in March each year. Another role of the NISC is to provide seed funding for local and regional influenza working groups. It also evaluates promotional materials and contributes recommendations to the immunisation handbook produced by the Ministry of Health.

Lance Jennings noted that New Zealand needs to increase influenza vaccine coverage of at-risk persons in all age groups. Although vaccine coverage is approximately 65% in individuals aged over 65 years, the estimated coverage in risk groups from 6 months to 64 years is only 35% and uptake is similarly low in healthcare workers, with some regional variation. Immunisation of children is also needed, but recommending influenza vaccination in young children is problematic due to the anti-vaccination lobby.

Singapore (Paul Tambyah)

Singapore does not have an influenza foundation, but the Society for Infectious Diseases is an active group with a broad membership that includes infectious disease specialists, microbiologists and primary care physicians. In addition, an Influenza Public Health Network has been established to focus on public health research and modelling. Singapore is a small country and does not need a new influenza society or foundation; however, an interest group could be formed within the Society for Infectious Diseases.

Raising awareness of influenza in Singapore is challenging and vaccination rates are low. Distribution of the APACI newsletter, talks and research have been used to promote influenza awareness. The Ministry of Health updated its influenza vaccine recommendations in 2008; the recommendations have been broadened to include vaccination of highrisk individuals, all children aged 6-36 months (and their contacts), and Hajj travellers. The guidelines are sent to healthcare professionals in a letter, but are not publicly available on the Ministry of Health website and compliance with the recommendations is poor. The influenza vaccine is not subsidised, although the cost is not particularly high.

Paul Tambyah pointed out that Singapore is a consumer-driven and highly internetdependent society. The APACI and its sponsors could assist in raising awareness by proactive 'social marketing', including updating the APACI website, and by supporting the Singapore Influenza Public Health Network. Strengthening the link between APACI and the Society for Infectious Diseases could also be beneficial.

Taiwan (Li-Min Huang)

Influenza awareness is high in Taiwan. The government and the Taiwanese Centers for Disease Control and Prevention (CDC) actively promote influenza awareness to the public and to professional groups, and strongly encourage influenza vaccination. The government has produced an educational video that is played on buses and in cinemas to raise awareness of influenza and the importance of vaccination. Taiwan also has an Influenza Advisory Committee, formed in 2005, which is involved in influenza virus surveillance, making recommendations for immunisation, pandemic influenza preparedness, and education and training programmes. It also aims to foster connections between the media, healthcare providers, professionals and the public.

The heightened awareness of influenza in Taiwan has had measurable impacts:

- expansion of age groups eligible for free influenza vaccination
- measured by vaccine coverage and budgets for vaccine funds
- media announcements of influenza prevention measures and the vaccination programme
- measured by the number of news reports
- disclosure of serious influenza cases to the public via the media.

In 2009, influenza vaccine coverage will be expanded to include all children aged 6 months to 10 years in addition to the groups already covered. The vaccination rate is 50–60% in both the elderly and in children, while vaccine coverage in healthcare workers is close to 90%, which may be attributed to Taiwan's experience with severe acute respiratory syndrome (SARS), according to Li-Min Huang. One area that does need improvement is the ability of clinicians to correctly diagnose influenza, he said.

NATIONAL INITIATIVES

Thailand (Prasert Thongcharoen)

The Influenza Foundation, Thailand (IFT) was formed in 2004 and has its own website, www.ift2004.org (in Thai, with some English content). In 2008, its activities included presentations at domestic scientific seminars and on national television, organising lectures for the general public, and distributing free brochures and posters on seasonal and avian influenza. The health ministry launched a national influenza vaccination programme in June 2008, with an initial focus on the elderly and those with chronic diseases.

The IFT collaborated with Thailand's Bureau of Emerging Infectious Diseases and the US CDC's International Emerging Infections Program to organise workshops on the diagnosis, treatment and prevention of pandemic influenza in healthcare workers. The participants, some of whom travelled from Laos. included physicians, nurses, the Surveillance Rapid Response Team, laboratory scientists and administrative officers. Strategies for raising pandemic awareness include holding workshops for village health volunteers, a door-knocking campaign to communicate risk, handwashing and hygiene campaigns, and communication via a range of mass media. The stepwise expansion of seasonal influenza vaccination is viewed as a step towards establishing a local capacity to manufacture a pandemic influenza vaccine.

Vietnam (Nguyen Thi Hong Hanh)

Vietnam has a national influenza surveillance scheme coordinated by the influenza laboratory at the National Institute of Hygiene and Epidemiology, which is designated as the WHO National Influenza Centre and also has responsibility for disease prevention and research consultancy. Awareness activities over the past year included organising symposia on the risks and prevention of influenza, and promotion of influenza awareness through the media. Governmental activities have focused on pandemic preparedness.

Goals for the next 12 months include the establishment of an influenza foundation to promote awareness and understanding, and organising more symposia for policymakers. Public health funding is very limited, making it difficult to implement an influenza control strategy. The influenza vaccine is currently funded only for infants. A greater focus on vaccinating healthcare workers is needed.



Prof Woo-Joo Kim Woo-Joo Kim is a Professor in the Division of Infectious Diseases in the Department of Internal Medicine at Guro Hospital, the College of Medicine at Korea University in Seoul, Korea.



Prof Malik Peiris

Malik Peiris is Chair Professor of Microbiology at The University of Hong Kong and Chief of Virology at the Oueen Mary Hospital, Hong Kong SAR, China. His recent research interests have focused on the ecology, evolution, clinical aspects and pathogenesis of avian and human influenza. He was elected a Fellow of the Royal Society of London in 2006.



Dr Yuelong Shu Yuelong Shu is

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Response to the H1N1 pandemic in the Philippines reviewed the DOH Guidelines for the Transport of

Contributed by: Shelley de la Vega, MD, MSc, University of the Philippines Manila-National Institutes of Health,

INFLUENZA – ASIAN FOCUS

Upon receiving news of a triple reassortment A(H1N1) virus, members of the medical community in the Philippines started to prepare for a possible pandemic. Although the country had been spared from the SARS and bird flu epidemics, this time there was a sense of foreboding about the A(H1N1). Perhaps it is because Filipinos and Mexicans share a common history of sea winds leading Spanish fleets to our shores, a shared language, or a similarity in culture, notwithstanding the common flight path of air travellers to and from the Americas and the Philippines. For many Filipinos, the first concern was whether they could safely eat their favourite national dish, "adobo," made from pork and chicken, and the roast pig "lechón" that is commonly served at feasts and parties. Pig growers, butchers and merchants felt a sudden dip in the market demand for this staple. Fortunately, remittances from overseas foreign workers helped sustain many families by enabling them to purchase the more expensive beef and poultry products. Many people began philosophising about the warnings against eating pork in various religions practiced in the country.

On 4 May 2009, The Medical City (TMC) and the Philippine Department of Health (DOH) hosted a joint forum, "OPLAN: Sagip Bayan", aimed at educating the medical community on the threat of the A(H1N1) virus and discussing the government's strategy to prevent an outbreak. At that time, there were no reported cases of A(H1N1) in the country. The issue of a looming global shortage of flu vaccines (seasonal and pandemic) was raised by this author, and an appeal for local vaccine production was forwarded. In mid-May, members of the Technical Working Group on Influenza (who prepared a consensus statement on dealing with such an occurrence in 2006) met and

Persons Likely to be Positive for A(H1N1) and Guidelines for Hotels and Similar Establishments.

Prior to the WHO declaration of the pandemic, a forum on Pandemic Preparedness for Nursing Homes was called. This was spearheaded by the UP Manila-National Institutes of Health Committee on Aging and hosted by the Religious of the Virgin Mary, a congregation that runs several nursing homes. The forum was well-attended by nursing home and community-based elderly care administrators, healthcare workers, and volunteers. The importance of hand hygiene, infection control policies, seasonal flu vaccination and the iudicious use of antivirals were discussed. Dr Ly-Suy of the DOH clarified misconceptions about A(H1N1) and discussed the DOH Pandemic Plan.

Hospital emergency rooms were soon flooded by requests for A(H1N1) swab tests. On 25 June, the DOH issued an updated guideline on the management of patients suspected to have influenza A(H1N1), to keep the influx of people at health and medical centres at a manageable level and enable healthcare providers to focus on providing care and treatment to patients with an increased risk of developing complications and death.

As of early July, more than 2,688 cases of A(H1N1) had been recorded in the country, with a 95% recovery rate. Since 9 July, the DOH has stopped daily updates on the cases of A(H1N1) in the country and instead focused its resources on mitigating the spread of the disease. On 18 August, the DOH announced that a vaccine against A(H1N1) would be made available to Filipinos by October. In July, during the National Academy of Science and Technology Annual Scientific Meeting, two respected Filipino scientists presented data on local influenza vaccine development.

The supply of imported seasonal flu vaccine has dwindled since July, and many Filipinos at risk of influenza-related complications remain unvaccinated.

Flu review

Lee N, Chan PKS, Hui DSC et al. Viral loads and duration of viral shedding in adult patients hospitalized with influenza. J Infect Dis 2009: 200: 492-500.

This prospective observational study characterised the viral load and factors influencing viral clearance in all 147 adults admitted with influenza A(H3N2) infection to the Prince of Wales Hospital in Hong Kong over a 1-year period. Nasal and throat swabs were collected daily for 1 week after symptom onset and the viral RNA concentration was determined using real-time reverse-transcriptase polymerase chain

reaction. Prolonged viral shedding was documented. Major comorbidities and systemic corticosteroid use were associated with slower viral clearance, whereas oseltamivir enhanced viral clearance if started within 4 days of symptom onset. Viral RNA was detected at 1 week after symptom onset in 26% of oseltamivirtreated patients versus 57% of untreated patients; viral clearance was more likely when oseltamivir was initiated on days 1-2 (odds ratio, 0.10), compared to days 3-4 (odds ratio, 0.30). The authors concluded that 'Patients hospitalised with severe influenza have more active and prolonged viral replication. Weakened host defences slow viral clearance, whereas antivirals started within the first 4 days of illness enhance viral clearance.'

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FLU REVIEW / H1N1 PANDEMIC

Flu review

Falsey AR, Treanor JJ, Tornieporth N, Capellan J, Gorse GJ. **Randomized, double-blind** controlled phase 3 trial comparing the immunogenicity of high-dose and standard-dose influenza vaccine in adults 65 years of age and older. J Infect Dis 2009; 200: 172-80.

Older adults may have a reduced response to influenza vaccination. This large US trial investigated the immunogenicity of a high-dose (HD) trivalent, inactivated influenza vaccine compared with a licensed standard-dose (SD) vaccine in 3837 adults aged 65 years or over. Patients were randomised 2:1 to receive HD or SD vaccine, which contained 60 μ g and 15 µg of haemagglutinin per strain, respectively.

Seroconversion rates and mean haemagglutinin inhibition titres were significantly higher in HD versus SD vaccine recipients at 28 days post-vaccination (Table 1). The HD vaccine was associated with an increase in mild-to-moderate local reactions, but not with clinically relevant adverse events.

Table 1. Mean post-vaccination haemagglutinin

Influenza strain	Standard dose	High dose
H1N1	67	116
H3N2	333	609
В	52	69

2009 update Pandemic (H1N1)

Pandemic (H1N1) 2009 news replaces our usual avian influenza A(H5N1) updates in this issue. During the first 6 months of 2009 only 41 avian influenza cases were reported (in China, Egypt and Vietnam), 12 of which were fatal.¹ The total number of confirmed avian influenza cases reported to the WHO from 2003 to 31 August 2009 was 440; this total included 262 deaths, giving a case fatality rate (CFR) of 60%.¹ By comparison, over 209,000 confirmed cases of pandemic (H1N1) 2009 were reported to 23 August 2009, with at least 2185 deaths (Table 2).² The CFR cannot be reliably estimated from these figures as the total number of cases is known to be an underestimate. However, the CFR was estimated to be only 0.005% in New Zealand, based on surveillance data, but the researchers noted that the health impact could be far more severe in developing countries ³

Severity in Asia-Pacific countries

As of 23 August 2009, approximately 17,200 laboratory-confirmed cases of pandemic (H1N1) 2009 had been reported from countries in the WHO South-East Asia region.⁴ Among Asia-Pacific countries, the highest number of fatal cases has been reported in Australia (154 deaths),⁵ Thailand (114),⁴ Malaysia (69),⁶ and India (63).4

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Table 2. Cumulative total of laboratory-confirmed pandemic (H1N1) 2009 cases to 23 August 2009

WHO region	Cases	Deaths
Africa (AFRO)	3843	11
Americas (AMRO)	110,113	1876
Eastern Mediterranean (EMRO)	3128	10
Europe (EURO)	Over 42,557	At least 85
SE Asia (SEARO)	15,771	139
Western Pacific (WPRO)	34,026	64
Total	Over 209,438	At least 2185



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Paul Tambyah is A/Prof and Head of the Division of Infectious Diseases at the National University of Singapore. He is an editorial consultant to the Singapore Medical Journal and serves as Vice Chair of the Chapter of Infectious Disease Physicians in Singapore.



Prof Anil K Prasad

Prof Prasad established the first Dept. of **Respiratory Virology at** the V Patel Chest Institute, where he served as President and Head of Dept. He is currently Chairman of the Influenza Foundation of India (IFI) and is a member of many national and international academic societies.



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Upcoming meetings

International

47th Annual Meeting of the Infectious Diseases Society of Americ Philadelphia, USA www.idsociety.org/Content.aspx?id=12006	a 29 October–1 November 2009
6th World Congress of the World Society for Pediatric Infectious E Buenos Aires, Argentina www.kenes.com/wspid	Diseases (WSPID) 18-22 November 2009
55th AARC International Respiratory Congress San Antonio, Texas www.aarc.org/education/meetings/congress_09	5-8 December 2009
XII International Symposium on Respiratory Viral Infections Taipei, Taiwan www.themacraegroup.com/2010-symposia/xii-international-symposium-c	11-14 March 2010 on-respiratory-viral-infections
World Vaccine Congress 2010 Washington DC, USA www.terrapinn.com/2010/wvcdc	19-22 April 2010
European Respiratory Society Annual Congress Barcelona, Spain www.erscongress2010.org	18-22 September 2010
Regional Australasian Society for Infectious Diseases (ASID) Annual Scient Conference 2010	ific
Darwin, Australia www.asid.net.au/meetings/index.asp	26-29 May 2010
Options for the Control of Influenza VII Hong Kong SAR, China www.controlinfluenza.com	3-7 September 2010

In the next issue ...

- Update on pandemic (H1N1) 2009
- Members' corner: highlights of recent activities in member countries

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