Influenza Asian Focus

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Welcome to the eighth 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.

As the number of countries reporting avian influenza outbreaks and cases of human infection continues to increase, *Influenza – Asian Focus* reviews recent developments in the influenza A(H5N1) situation. This issue examines trends in the infection pattern in Indonesia – including a decreasing interval between reports of human cases and several family clusters suggestive of person-to-person transmission – and the measures Indonesia is taking to counteract this threat. We also draw attention to the question of oseltamivir resistance and its practical implications, and discuss the role of strategic pandemic planning exercises that aim to improve coordination and enhance preparedness at a regional level.

Also included in this issue are updates on influenza surveillance in Thailand and India, a report on the establishment of the Influenza Foundation, India, news from the APACI meeting held in New Delhi in February, and answers to some common questions about seasonal and pandemic influenza vaccination.

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Advisory Committee Members

Visit APACI's website at www.apaci-flu.org

The role of the Asia-Pacific Advisory Committee on Influenza

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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 (formerly Chiron Vaccines), Roche, Sanofi Pasteur and Solvay Pharmaceuticals.

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 programme
- 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 10th APACI meeting was held in New Delhi, India, in February 2006. Spanning two days, the meeting featured presentations from international guest speakers Jonathan Van Tam from the Health Protection Agency in the UK and Mark Simmerman from the WHO in Vietnam. Jonathan Van Tam led board members on a pandemic planning exercise that required them to review their country's capacity to react to the announcement of an influenza pandemic. Mark Simmerman reported on the first year results from Thailand's Influenza Project.

Lalit Kant and special guest attendee, Deepak Gadkari, discussed the newly founded Influenza Foundation, India and current surveillance data from that country, while Ai Ee Ling reported on a joint collaboration between Singapore and Indonesia to fight avian influenza. David Smith gave an off-the-cuff talk on the Australian Influenza Specialist Group and members from Thailand, the Philippines and Singapore presented their most recent influenza seasonality data. The meeting was followed by a well-attended press conference (see page 10).

Pandemic planning exercises

With the ever-present threat of an influenza pandemic currently heightened by the potential for the H5N1 avian strain to become easily transmissible between humans, pandemic planning is a high priority. This article reviews the role of planning exercises in ensuring an effective and coordinated response in the event of a pandemic.

A national pandemic preparedness plan that covers alerting, response and disaster management is an essential component of preparing for an influenza pandemic. Researchers from the London School of Hygiene and Tropical Medicine, UK, evaluated pandemic influenza preparedness in Europe and the Asia-Pacific region, comparing the completeness and quality of national preparedness plans against a WHO checklist. Europe was found to be moderately prepared for an influenza pandemic overall – mean scores for the completeness and quality of plans were 54% and 58%, respectively, but there was substantial variation between countries and a number of critically important gaps in preparedness were identified.[1] These gaps included, among others, weak co-ordination between human and animal surveillance and response systems; failure to detail how international cooperation will be achieved; lack of clarity regarding the roles and responsibilities of different levels of government; and deficiencies in planning for the provision of vaccines and antiviral drugs. A similar report assessing preparedness across the Asia-Pacific region will be available soon.

Testing the response

While analysis of national plans provides important insights into a country's pandemic preparedness, the true test is its ability to mount an effective response. In an effort to improve coordination and enhance preparedness, many countries and regions have undertaken pandemic planning exercises. These exercises pose hypothetical scenarios, such as the announcement of sustained human-to-human transmission, to test the response measures in place and expose potential deficiencies. Domestic exercises typically include representatives from the police, fire and emergency services in addition to healthcare providers and government officials. Participants in a tabletop exercise remain in their normal working environment and are required to respond in real time to updates from a central controller. These exercises test key aspects of the pandemic response: risk communication, isolation and quarantine procedures, mass prophylaxis and dispensing capabilities, control of population movements, and protection of staff.[2] Regional pandemic planning exercises may also highlight communication between the emergency operation centres in different countries, logistical issues in sharing vaccines and other supplies and, in particular, the need for effective central coordination.

Of key concern to vaccine suppliers is the identification of an appropriate trigger for the switch from routine vaccine production to maximum production in the face of a pandemic.

APACI members at the New Delhi meeting participated in a desktop exercise led by Jonathan Van Tam, who heads the Pandemic Influenza Office at the UK Health Protection Agency. This was an opportunity to assess pandemic preparedness from a regional perspective and identify areas for improvement. Consistent with the European analysis, which found a correlation between the pandemic plan completeness and per capita gross domestic product,[1] it was evident that countries with fewer resources will need assistance from more developed countries. This could include sharing vaccine and antiviral supplies and assisting with surveillance.

Reporting outcomes

While detailed examples of how to conduct a pandemic planning exercise are readily available,[2] the results of such exercises may be sensitive and are typically treated as confidential. There are of course exceptions, with a large-scale exercise broadcast live on television in Vietnam and public involvement included in a July drill in Singapore.[3,4] In addition, in June 2006, all members of the Asia Pacific Economic Cooperation forum (APEC) participated in a major desktop simulation exercise testing regional emergency responses and information sharing. An outcomes report from the exercise, which was coordinated by Australia and Singapore, will be released in November 2006, and should provide valuable information for countries across the region.

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Avian influenza case reports and trends

Professor Cissy Kartasasmita of the Dr Hasan Sadikin General Hospital in Bandung, Indonesia, discusses some recent disturbing trends in human avian influenza A(H5N1) infections in Indonesia and the evidence for possible person-to-person transmission.

Indonesia reported its first human case of avian influenza A(H5N1) in July 2005 and is currently second only to Vietnam for the number of confirmed human cases. From July 2005 to mid-February 2006, there were a total of 26 confirmed cases, 18 of which were fatal. At 69%, the case fatality rate is comparable with that of Thailand over the same period (14 of 22; 63%), but higher than that of Vietnam (42 of 93; 45%) and Turkey (4 of 20; 29%). In addition to these confirmed cases, there were 11 probable and 80 suspected cases, with case fatality rates of 45% and 29%, respectively. Most of these cases occurred in Jakarta and West Java (Figure 1).

Among the 26 confirmed cases of avian influenza, 62% were male and 58% were aged 15–34 years. Eight patients (31%) were children aged 1–14 years. Most patients were admitted to hospital more than 7 days after putative infection; all had fever and cough on admission, while dyspnoea (n = 21) and pneumonia (18) were also common.

In addition to the high case fatality rate, worrying features of H5N1 infection in Indonesia include the decreasing interval between human cases and the existence of several family clusters that might indicate person-to-person transmission. Indonesia's first avian influenza outbreak in poultry was reported in late January 2004, with 26 of 33 provinces affected as of January 2006. Over this 2-year period, poultry deaths decreased but spread over a wider area. Approximately 18 months passed between the official declaration of an outbreak in poultry and the first confirmed human death from avian influenza, but the second confirmed death occurred 2.5 months later, while from September 2005 to January 2006, there were 15 confirmed deaths over a 21-week period.

Case clusters

Five family clusters (each consisting of 2–4 people) of avian influenza have been detected since July 2005. The most recent of these occurred in West Java, a region in which there were 10 confirmed and 40 suspected cases between July 2005 and February 2006.

A 13-year-old girl who developed fever, cough and dyspnoea on 5 January was admitted to an Indramayu hospital on 12 January and died 2 days later. Her brother, aged 4 years, developed a fever and cough on 10 January and was hospitalised the following day after developing dyspnoea. Laboratory findings included: white blood cells 4300/mm^3, platelets 50,000/mm^3, haemoglobin 10 g/dl, haematocrit 29%, and erythrocyte sedimentation rate 25–50/mm^3; X-rays revealed pneumonia involving the right medial lobe. On 15 January, the child was transferred to the Dr Hasan Sadikin General Hospital in Bandung, where he died 2 days later. A polymerase chain reaction (PCR) test for avian influenza was positive. A third sibling, aged 15 years, developed fever on 11 January and was admitted to the same hospital the next day. She was discharged on 28 January and tested negative for avian influenza. The children's father was also hospitalised with respiratory symptoms on 18 January, but recovered and tested negative for the H5N1 avian influenza virus.

Investigations into the background of this cluster identified sudden deaths among neighbourhood chickens prior to the reported cases. Furthermore, 10 chickens kept by the family died in early January and all family members had close contact with the diseased chickens. However, in a cluster that occurred in Tangerang, 40 km west of Jakarta, there was no known contact with infected poultry, raising the possibility of person-to-person transmission of the virus. This cluster involved a 38-year-old father (the first confirmed Indonesian case of H5N1) who died on 12 July 2005 and whose two daughters aged 1 and 8 years also died of severe pneumonic illness.[1] H5N1 infection was subsequently confirmed in the 8-year-old. All environmental samples tested nega-

Figure 1. *Distribution of human H5N1 cases in Indonesia, July 2005 to February 2006.*

tive for the H5N1 virus, as did samples taken from individuals who had been in contact with the patients.[2]

Two family clusters were reported among 10 Vietnamese patients diagnosed with H5N1 during December 2003 and January 2004.[3] While the available information was compatible with direct infection via poultry, person-to-person transmission could not be excluded. Probable person-to-person transmission also occurred in a family cluster in Thailand.[4] The index patient, an 11-year-old girl who lived with her aunt, died on 8 September 2004, 6 days after the onset of fever. The household chickens had died over a period of several weeks, with the last deaths on 29 or 30 August. The patient's mother, who lived in another province, cared for her daughter in hospital on 7–8 September and first noted fever on 11 September. She developed pneumonia and died 9 days later. The aunt also provided bedside care for the child on 7 September and developed symptoms 9 days later, but recovered. Both women tested positive for the H5N1 virus by PCR. This family cluster provides strong evidence for person-to-person transmission, as the mother had no known exposure to poultry, but did have prolonged, unprotected exposure to her sick daughter. The evidence to date suggests that limited person-to-person transmission of the H5N1 virus does occur, but such cases are rare and have not resulted in infection beyond people in very close contact with a sick individual.[5]

Prevention and control strategies

The size and diversity of Indonesia's population present a challenge for controlling avian influenza. Key management strategies, to be implemented in conjunction with influenza pandemic preparedness, include reducing the number of H5N1-infected wild fowl, poultry and other animals, minimising virus transmission from animals to humans, and managing patients with avian influenza. Indonesia's *National Strategic Plan for Avian Influenza Control and Pandemic Influenza Preparedness 2006–2008*, emphasises protection of high-risk groups, human and animal epidemiological surveillance, communication and education programmes, and redesigning systems in the poultry industry.

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Update – Indonesia*

In May 2006, another family cluster of cases was reported in Kubu Simbelang village, north Sumatra. This cluster, the largest reported to date in any country, involved an initial case and seven subsequent laboratory-confirmed cases, all of which involved members of an extended family who experienced close contact with their sick relatives. Seven of eight patients died.

In late June, Indonesia hosted a 3-day consultation with international avian influenza experts to address both the widespread presence of the virus in poultry across Indonesia and the significant number of human cases. As of 23 August 2006, there had been 60 confirmed cases of human infection with the H5N1 avian influenza virus in Indonesia, of which 46 cases were fatal, bringing the case fatality rate to 77%.

*For further information, visit the WHO disease outbreak news website at www.who.int/csr/don/en/.

Indonesia Department of Health strategy for controlling avian influenza

- Disseminate information and guidance on avian influenza
- Perform active surveillance
- Establish an avian influenza taskforce
- Appoint and equip 44 referral hospitals to treat avian influenza cases
- Strengthen laboratory capacity
- Supply oseltamivir to referral hospitals, provincial and district health offices, and create a central stockpile
- Perform PCR and serological testing for avian influenza cases
- Provide protective equipment for staff at referral hospitals
- Provide insurance for health personnel at high risk of exposure
- Promote national, regional and international cooperation.

Antiviral resistance in influenza viruses

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M2 ion channel inhibitors have been used for many years to treat influenza A outbreaks, but antiviral resistance now limits the efficacy of this class and neuraminidase inhibitors have become the treatment of choice.[1,2] Evidence of widespread resistance to M2 inhibitors raises the question of whether the same pattern will emerge with neuraminidase inhibitors, which could have potentially dramatic implications for pandemic planning.[3,4] Key issues include the incidence of resistance and whether resistant viruses are transmissible and pathogenic.[4,5]

Emergence of oseltamivir resistance

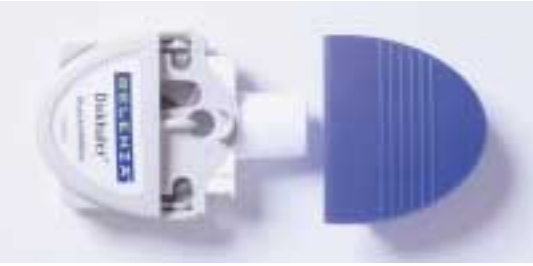
Although several mutations conferring resistance to neuraminidase inhibitors have been identified, resistance is very uncommon compared with M2 inhibitors. Surveillance conducted by the Neuraminidase Inhibitor Susceptibility Network (NISN), a group of experts dedicated to monitoring the emergence of neuraminidase resistance, found only one resistant A(H1N1) variant among 622 community isolates collected during the first 3 years after oseltamivir was introduced.[4] A similar investigation was conducted in Japan, where approximately 6 million courses of oseltamivir were administered to 5% of the population during the 2003–2004 influenza season.[6] Oseltamivir resistance was detected in 0.4% of 1180 A(H3N2) community isolates tested, with low-level transmission of resistant strains considered more likely than spontaneous emergence of resistance.

Whereas oseltamivir resistance is rare in adults, the reported incidence in children was 4% in the registration studies for the drug. The higher incidence of resistance in children may reflect increased viral replication rates due to lack of prior immunity and the greater viral burden seen in children.[7] There have been reports of higher rates of resistance, reaching 18% in one small study in Japan.[5] The higher rate seen in the Japanese study may be related to the different dosage regimen used in Japan compared with the rest of the world. The dosing schedule used outside of Japan is such that smaller children receive a higher dose relative to their weight than older children, which compensates for the higher rate of drug clearance in younger children. This means that younger children in Japan receive lower drug exposures than their counterparts in other countries. In addition, Japanese children are often dosed only until their fever resolves; this generally occurs at around day 3, whereas viral shedding may continue beyond this time. Consequently, children treated in this manner may experience ongoing viral replication in the presence of declining drug levels.

Antiviral resistance in influenza A(H5N1)

Stockpiling of oseltamivir is an important component of pandemic preparedness plans, yet there are limited data for oseltamivir in human A(H5N1) infection. Two reports from Vietnam described the isolation of oseltamivir-resistant virus from patients infected with A(H5N1).[7,8] The first report concerned a teenager who recovered from an infection with partial resistance to oseltamivir.[8] The patient had received prophylactic oseltamivir at a dosage of 75 mg once daily, followed by the recommended therapeutic regimen of 75 mg twice daily for 5 days. In the second report, two patients died after developing resistance during treatment with oseltamivir 75 mg twice daily; one of the deaths occurred despite early treatment initiation.[7] While sub-optimal dosing may facilitate the emergence of oseltamivir resistance, further data are required to establish the benefit of higher doses or longer treatment duration.[4]

A histidine-to-tyrosine substitution at neuraminidase position 274 (His274Tyr) was identified in the three cases described above.[7,8] Neuraminidase mutations tend to be associated with reduced pathogenicity in animal models, although transmission of resistant



variants was documented in ferrets.[5] Zanamivir retains activity against oseltamivir-resistant viruses harbouring the His274Tyr mutation in preclinical studies, but inhaled delivery may be problematic in patients with pneumonia.[6]

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Strategies for the use of neuraminidase inhibitors in avian influenza infection

In May 2006, the WHO published guidelines for the pharmacological management of humans infected with influenza A(H5N1).[9] The following recommendations apply to the current pre-pandemic situation when neuraminidase inhibitors are available.

Recommendations for patients with confirmed or strongly suspected A(H5N1) infection

- Clinicians should administer oseltamivir (strong recommendation).
- Zanamivir may be used as an alternative to oseltamivir (weak recommendation), but the quality of evidence is lower.
- Clinicians should not administer M2 inhibitors alone as a first-line treatment (strong recommendation).
- A combination of a neuraminidase inhibitor and an M2 inhibitor may be used if the H5N1 virus is known or likely to be susceptible according to local surveillance data (weak recommendation), but only in the context of prospective data collection.

Recommendations for chemoprophylaxis

- *In high-risk exposure groups**, including pregnant women, oseltamivir should be administered prophylactically, continuing for 7–10 days after the last exposure (strong recommendation); zanamivir can be used as an alternative (strong recommendation).
- *In moderate-risk exposure groups**, including pregnant women, oseltamivir may be administered prophylactically, continuing for 7–10 days after the last exposure (weak recommendation); zanamivir might be used as an alternative (weak recommendation).
- *In low-risk exposure groups**, neuraminidase inhibitors should probably not be administered prophylactically (weak recommendation). Pregnant women in the low-risk group should not receive prophylactic oseltamivir or zanamivir (strong recommendation). M2 inhibitors should not be administered prophylactically (strong recommendation).

*For definitions of high-, moderate- and low-risk groups, see the brief guidelines summary available at: www.who.int/csr/disease/avian_influenza/guidelines/pharmamanagement/en/index.html.

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Influenza in Thailand: surveillance, disease burden and cost

Dr Mark Simmerman, recently seconded from the US Centers for Disease Control and Prevention (CDC) in Thailand to the WHO in Hanoi, Vietnam, describes the initial findings of a prospective study documenting the burden of influenza in Thailand.

Influenza vaccine, although effective, is under-utilised in Thailand, with less than 1% of the population vaccinated annually.[1] With global concern over an imminent influenza pandemic, there exists a need for high-quality surveillance and vaccination programmes to improve preparedness. Thailand is the first country in South-East Asia to make a systematic effort to describe the population incidence of influenza in outpatients with influenza-like illness (ILI) and hospitalised pneumonia patients using active surveillance systems and comprehensive laboratory testing.

A unique collaboration between Thailand's Ministry of Public Health (MOPH) and the US CDC International Emerging Infections Program has made possible an ongoing prospective study to document the burden of influenza in Thailand; results from the first year have now been published.[2] Based in the Sa Kaeo province, the study collected laboratory-confirmed, population-based data on influenza cases with the aim of documenting the burden of the disease, determining the direct and indirect costs of influenza and estimating the national burden and costs associated with influenza in Thailand. The study also investigated the field performance of rapid influenza tests and their potential role in surveillance programmes.

Active surveillance

The study capitalised on the active, population-based surveillance system established by the Thailand MOPH and US CDC collaboration. This system employs dedicated surveillance officers at all hospitals in designated provinces to actively monitor outpatient clinics and admission logs for patients with ILI and admission diagnoses consistent with pneumonia. In its first year, the study enrolled 1092 outpatients who met the WHO case definition for ILI (fever > 38˚C and a cough or sore throat) and 762 inpatients with pneumonia who had received a chest X-ray. Outpatients were given a QuickVue® rapid test (Quidel Corporation, USA) to confirm the presence of influenza. All patients had nasopharyngeal swabs taken for reverse transcriptase polymerase chain reaction (RT-PCR) testing and cell culture. Acute and convalescent sera collection for serological testing was completed in approximately 70% of the hospitalised pneumonia cases.

Population incidence

Of the 1092 outpatients, 23% tested positive for influenza, translating to an annual incidence of 1420 cases per 100,000 population. Most of those who tested positive (84%) were under the age of 15 years. The rate of hospitalisation for influenza-related pneumonia was high in infants and children under the age of 5 years, low in older children and adults through to middle age, and rose steeply with increasing age in those aged 60 years and above. The annual incidence of hospitalisations for influenza-related pneumonia was estimated at 18–111 per 100,000 population.

The incidence of influenza demonstrated a marked seasonal distribution, with a very low incidence in January and February rising to a peak in the months of June, July and August, before falling again. Based on this information, vaccination programmes during March and April – anticipating the rise in influenza cases from June to August – may be of particular benefit.

Results of rapid influenza testing

Rapid influenza testing in this study was slightly more sensitive (77% versus 73%), but slightly less specific (86% versus 96%), than indicated by the manufacturer. When compared to the gold standard diagnostic test, cell culture, the rapid test had a positive predictive value of 82%. This was related to season, with the positive rapid test more likely to be confirmed by a gold standard test during periods of high prevalence.

Direct and indirect costs

The cost per outpatient visit for influenza ranged between US$3.65 and US$14.25. Remarkably, 73% of patients were prescribed an antibiotic despite the availability of a positive rapid test result for influenza. The average number of days of work lost was 4.46 for sick adults and 3.28 for parents caring for sick children, amounting to a total of 3,121,562 lost work days and 1,701,450 lost school days over a 1-year period. The average cost per hospital admission for patients with influenza-related pneumonia was US$138. On average, 6.6 days of work were lost. The total burden of influenza in Thailand in 2003–2004 was estimated at between US$23.4 and US$62.9 million (Figure 1).

Future research

Currently, data from the second year of the study are being analysed to compare findings on seasonality and disease burden. Another potential extension of this study may be to compare the disease burden in large cities with the mostly rural Sa Kaeo province. In addition, the study results would provide a useful benchmark for future investigation of the impact of influenza vaccination programmes on children in the Sa Kaeo province.

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Figure 1. *Burden of influenza in Thailand, 2003–2004.*

Influenza surveillance in India

Dr Deepak Gadkari (National Institute of Virology, Pune, India), was a guest speaker at the APACI meeting in New Delhi and provided this update on India's influenza surveillance scheme.

A multi-site human influenza surveillance programme was established in 2005 to address the paucity of information on influenza activity in India. Linked to the WHO Global Surveillance Network, the programme involves five regional centres in New Delhi, Dibrugarh, Kolkata, Chennai and Pune, where the National Institute of Virology also functions as the referral centre responsible for quality control and international collaboration.

Overcoming obstacles

Surveillance commenced in September 2004, although laboratory testing did not start until February–March 2005 due to funding delays. During the year ending September 2005, over 1500 specimens were collected from patients meeting the influenza case definition (predominantly hospital outpatients). A total of 84 influenza strains were isolated throughout the year, except during the month of May, which was particularly hot.

The number of virus isolates and the distribution of strains differed between regions (Figure 1). Influenza A(H3N2) dominated in New Delhi and Chennai, whereas A(H1N1) and influenza type B were more common in Pune and Dibrugarh. The lack of virus isolates from Kolkata was partly attributable to the project starting late, but there were also specimen-handling problems (see below). In southern India, influenza viruses were isolated throughout the year, whereas in the west of the country, isolation increased following the rainy season.

The influenza isolation rate was relatively low (6% of influenza-like-illness [ILI] samples tested). Contributing factors were the initial difficulties experienced in Dibrugarh and Kolkata, both of which lacked cell culture facilities and encountered problems with transporting specimens to New Delhi and Pune for testing. Laboratory facilities have recently been established in Dibrugarh and the second year of surveillance is expected to provide more reliable results.

The rural population of India was not represented in the surveillance network, with the exception of one centre on the rural outskirts of New Delhi. Investigators at the regional centre in Pune used a large pilgrimage as an opportunity to collect ILI samples from rural patients. Each year, nearly 1 million devotees make the pilgrimage to Pandharpur in Maharashtra. The Pune team isolated nine viruses from 42 ILI samples, for a 21% isolation rate.

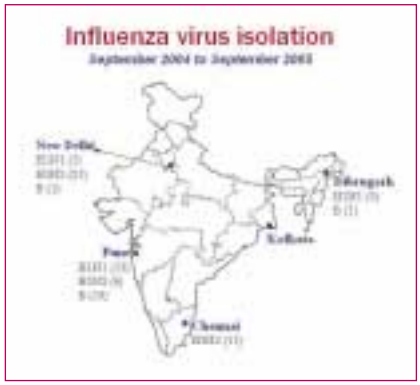


Figure 1. *Influenza strains isolated in India, September 2004 to September 2005.*

Prior to the scheme's establishment, only the National Institute of Virology in Pune collected ILI samples for virus isolation. The first results from the enhanced surveillance network show that Pune is not representative of the country as a whole and suggest that the scheme will make an important contribution to understanding the pattern of influenza infection in India.

The Influenza Foundation, India: establishment and activities

Dr Lalit Kant reports on the establishment of the Influenza Foundation, India.

India is waking up to the influenza threat. Coming a year after the initiation of a multi-site epidemiological and virological influenza surveillance scheme, the launch of the Influenza Foundation, India (IFI) in October 2005 represents a further welcome advance. Encouraged by the success of Influenza Foundations in other countries, notably Thailand, a group of public health specialists, clinicians, and virologists met to determine the structure and activities of the IFI. The mission of the IFI is to provide leadership in influenza, increase awareness of the disease and promote research.

A 1-day scientific seminar hosted by the Indian Council of Medical Research, with support from Sanofi Pasteur, was held to celebrate the IFI launch. Approximately 50 experts from across India participated, with presentations from Dr Jean-Claude Manuguerra of the French Institut Pasteur, together with experts from the fields of virology, paediatrics, and pandemic preparedness and public health.

The IFI's second meeting, at which a business plan was formulated, coincided with the APACI meeting in New Delhi. IFI President, Professor AK Prasad, and Secretary General, Dr Lalit Dar, coordinated the meeting. APACI Chair Lance Jennings invited IFI office bearers to attend the APACI meeting as observers to facilitate interaction between members of the two groups.

Q&A: seasonal and pandemic influenza vaccination

Professor 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.

Dr Yuelong Shu

Yuelong Shu is Director of the China National Influenza Center, National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention in Beijing, China.

The recent spread of H5N1 viruses among avian populations has raised concerns about a potential human pandemic. In this section, the APACI clarifies the differences between seasonal and pandemic influenza with a focus on vaccination, the most effective way to prevent illness.

What is seasonal influenza?

Seasonal influenza is a disease caused by subtypes of influenza virus that circulate among humans on an annual basis. Local outbreaks follow predictable patterns. Influenza peaks usually occur in winter in temperate climates. In tropical countries, peak prevalence tends to coincide with the rainy season.[1]

What is pandemic influenza?

Pandemic influenza occurs as a result of the emergence of a major new strain of influenza virus for which the general population has little or no immunity. Compared with seasonal influenza, it covers a wider geographical area, affects a large proportion of the population and can cause more severe illness or death. Three pandemics have been recorded in the 20th century, the last one being in 1968. Human cases of avian influenza in Asia are not part of an influenza pandemic.

Are there vaccines available against seasonal influenza?

Yes. Vaccination protects against the three strains identified by the World Health Organization as the ones most likely to circulate during the current influenza season.[2] In healthy adults, vaccination is 70–90% effective in terms of reducing influenza morbidity.[3] It also reduces healthcare costs and productivity losses associated with the illness. However, a seasonal influenza vaccine will not protect against a pandemic virus.

Are there vaccines available against pandemic influenza?

There is currently no vaccine to protect humans against pandemic influenza. However, efforts are underway to develop a vaccine to protect humans against a pandemic virus that might emerge from a highly pathogenic variation of the H5N1 subtype of avian influenza. (See Flu review, page 11).

How quickly can a vaccine be developed in the event of a pandemic?

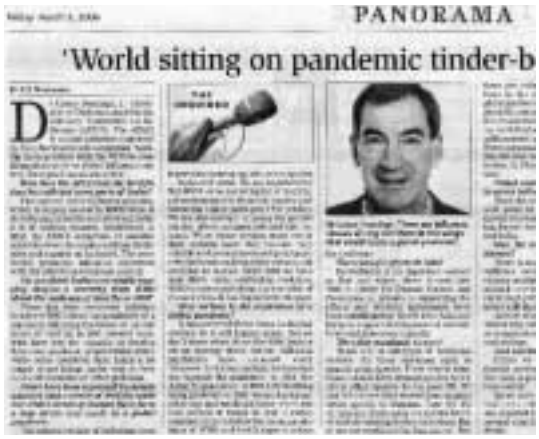
An influenza vaccine would probably not be available in the initial stages of population infection. Once the virus is identified, it could take several months before a vaccine is made available for use. At present, only 15 countries are listed as influenza vaccine manufacturers.[4] Meanwhile, engaging in preparedness activities for an influenza pandemic can help minimise social disruption, prevent health systems from being overwhelmed and, ultimately, save lives.

References

1. Beckett CG, Kosasih H, Ma'roef C *et al.* Influenza surveillance in Indonesia: 1999–2003. *Clin Infect Dis* 2004; 39: 443–9.
2. World Health Organization. Recommendations for influenza vaccines. Available at: www.who.int/csr/disease/influenza/vaccinerecommendations/en/. Accessed: 12 July 2006.
3. World Health Organization. Influenza. Fact Sheet no. 211. Revised March 2003 Available at: www.who.int/mediacentre/factsheets/fs211/en/. Accessed: 12 July 2006.
4. World Health Organization. Influenza vaccine manufacturers. Available at: www.who.int/csr/disease/influenza/manulist/en/index.html. Accessed: 12 July 2006.

Press conference, New Delhi

The 2-day APACI meeting held in New Delhi, February 2006, was followed by a press conference that drew dozens of journalists from national and regional publications. Lance Jennings spoke on the history of APACI and how the group helps its members promote influenza prevention and control in their own countries, particularly in light of the pandemic threat. Lalit Dar, Secretary General of the Influenza Foundation, India, was also present to address journalists on this newly formed group, which aims to improve influenza awareness and control in India. The ensuing coverage featured in print, television and electronic media.


PANORAMA

'World sitting on pandemic tinder-b

Flu review

This issue summaries of two recent studies testing experimental A (H5N1) vaccines.

Treanor JJ, Campbell JD, Zangwill KM, Rowe T, Wolff M. Safety and immunogenicity of an inactivated subvirion influenza A (H5N1) vaccine. *N Engl J Med* 2006; 354: 1343–51.

An experimental A(H5N1) avian influenza vaccine manufactured by Sanofi Pasteur was shown to induce immune responses in healthy adults. However, only about half of volunteers treated with the highest vaccine dose reached the pre-specified immunogenicity threshold, and the authors noted that supply of such a high-dose vaccine would be problematic. This multicentre, double-blind, two-stage US study involved 451 healthy adults who were randomised to receive two intramuscular doses of the vaccine (7.5, 15, 45 or 90 μg) or placebo, with a booster shot of the same dose or placebo 1 month later. At the highest dose level, 54% of patients developed an antibody titre of 1:40 or greater – typically thought of as seroprotective – compared with only 22% of the 15 μg group. The vaccine was generally well tolerated.

Bresson JL, Perronne C, Launay O *et al.* Safety and immunogenicity of an inactivated split-virion influenza A/Vietnam/1194/2004 (H5N1) vaccine: phase I randomised trial. *Lancet* 2006; 367: 1657–64.

A second A(H5N1) candidate vaccine developed by Sanofi Pasteur was immunogenic and well tolerated in a French phase I trial. The European and US studies were conducted independently, precluding direct comparison of the results. In the French study, 300 volunteers were randomised in an open-label manner to receive inactivated split influenza A/Vietnam/1194/2004 (H5N1) vaccine at a dose of 7.5, 15 or 30 μg, each given with or without aluminium hydroxide adjuvant. A booster shot was administered on day 21. The adjuvanted 30-μg formulation generated the highest immune response (67% seroconversion rate after two doses), with 'encouraging' responses at lower doses.

Clinical Associate Professor 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.

Influenza updates

Epidemiology of A(H5N1) cases

A WHO analysis of laboratory confirmed cases of avian influenza A(H5N1) infection identified a total of 203 cases in nine countries over the period from 1 December 2003 to 30 April 2006. The highest number of cases came from Vietnam (n = 91), followed by Indonesia (32), Thailand (22) and China (18), with three peaks that occurred in the northern hemisphere winter and spring. The overall case fatality rate was 56%, rising to 73% in those aged 10–19 years. The median age of confirmed cases was 20 years, with 90% of cases occurring in people aged < 40 years. However, interpreting these data is difficult as most cases occurred in countries with a young population and there is a complex relationship between age and risk of exposure. Time-sequence observations identified no change in the pattern of illness over the period studied.

Reference

World Health Organization. Epidemiology of WHO-confirmed human cases of avian influenza A(H5N1) infection. *Wkly Epidemiol Rec* 2006; 81: 249–57.

WHO, China set up centre to fight influenza

The WHO and China recently launched a centre to fight influenza and other emerging infectious diseases in the Guangdong province. The WHO Collaborating Centre will investigate pilot projects to enhance epidemiological and virological surveillance and will initiate programmes aimed at improving the integration of current surveillance systems. The Centre will also help carry out research in areas such as the animal origins of severe acute respiratory syndrome (SARS), the human–animal interface in influenza transmission, and estimating the disease burden of influenza and other infections.

Reference

WHO Regional Office for the Western Pacific. China and WHO collaborate to fight emerging infectious diseases. Available at: www.wpro.who.int/media_centre/press_releases/pr_12062006.htm. Accessed: 15 June 2006.

First influenza journal debuts

The first international journal focusing on influenza will be launched this October. In its inaugural issue, *Influenza and Other Respiratory Viruses* will feature the development of influenza vaccines, how viruses are evolving and the scale of the global problem, amongst other topics. It will be published six times a year on behalf of the International Society for Influenza and other Respiratory Diseases (ISIRV) by Blackwell Publishing Ltd.

Reference

Blackwell Publishing. WHO expert to edit first international influenza title as pandemic fears grow. Available at: www.blackwellpublishing.com/press/press.asp. Accessed: 15 June 2006.

Professor Prasert Thongcharoen

Prasert Thongcharoen is a Professor Emeritus of Virology at Mahidol University, at the Faculty of Medicine, Siriraj Hospital. He currently serves as President of the Thai Clinical Chemistry Association and is a member of numerous other professional organisations, including the Asia-Pacific Society of Medical Virology.

Dr Luningning Villa

Luningning Villa is National Program Manager for the Emerging Infections Control Program and Medical Specialist IV at the National Center for Disease Prevention and Control at the Department of Health (DOH) in the Philippines. She is also a member of the DOH Task Force for Avian and Pandemic Influenza Prevention and Control.

Professor Jen-Ren Wang

Jen-Ren Wang is Professor in the Department of Medical Technology, College of Medicine, National Cheng Kung University Medical Center (NCKUMC), Taiwan. She is also Principal Investigator for the Department of Health's Taiwan Center for Disease Control Virology Contract Laboratory and the National Health Research Institutes Tainan Virology Laboratory for Diagnosis and Research, NCKUMC.

Upcoming meetings

International

World Vaccine Congress
Lyon, France — 9–11 October 2006
www.terrapinn.com/2006/wvcl_fr/Custom_7693.stm

44th Annual Meeting of the Infectious Diseases Society of America (IDSA)
Toronto, Canada — 12–15 October 2006
www.idsociety.org

2nd International Conference on Influenza Vaccines for the World (IVW)
Vienna, Austria — 18–20 October 2006
jherriot@meetingsmgmt.u-net.com

European Directorate for the Quality of Medicines (EDQM) Scientific Symposium: Requirements for Production and Control of Avian Influenza Vaccines
Strasbourg, France — 19–20 October 2006
www.pheur.org/site/page_597.php

1st International Congress of Central Asia Infectious Diseases (ICCAID)
Bishkek, Kyrgyzstan — 30 October–2 November 2006
www.iccaid.org

3rd Scientific Meeting of the Australian Virology Group
Phillip Island, Australia — 9–12 December 2006
www.avg.org.au

American Association for Respiratory Care (AARC): 52nd International Respiratory Congress
Las Vegas, USA — 11–14 December 2006
www.aarc.org/

Regional

7th Asia-Pacific Congress of Medical Virology (APCMV): Viral Infections in the Developing World
New Delhi, India — 13–15 November 2006
www.apcmv2006.com

11th Congress of the Asian Pacific Society of Respirology (APSR)
Kyoto, Japan — 19–22 November 2006
www.apsr2006.org

Joint International Tropical Medicine Meeting (JITMM) 2006 and 6th Asia-Pacific Travel Health Conference (APTHC)
Bangkok, Thailand — 29 November–1 December 2006
www.tm.mahidol.ac.th.

10th Western Pacific Congress on Chemotherapy and Infectious Diseases (WPCCID)
Fukuoka, Japan — 3–6 December 2006
www.congre.co.jp/10wpccid/

In the next issue ...

- Avian influenza preparedness cooperation between Singapore and Indonesia
- Update on regional pandemic plans
- Pandemic response modelling
- Recommendations for paediatric influenza vaccination

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