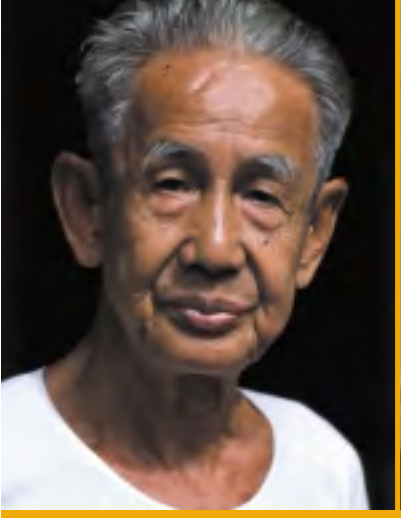



Influenza Asian Focus

Welcome to *Influenza – Asian Focus*, the official newsletter of the Asia-Pacific Advisory Committee on Influenza (APACI). The aims of the APACI are to understand the impact of influenza in Asia and to promote awareness of the disease among healthcare professionals in the region, with the intention of enhancing control measures and boosting pandemic preparedness in the region. *Influenza – Asian Focus* plans to keep you up to date on the work of the APACI and current issues in the field of influenza. It serves to provide expert opinions on a number of influenza-related topics and to provide answers to any questions you might have.

In each issue of *Influenza – Asian Focus*, the status of influenza in specific countries will be highlighted in order to give you further insight on the disease burden in Asia. You will be kept informed of new policies, consensus statements and recommendations for the prevention and treatment of influenza. Updates from the World Health Organization will be a regular feature, as we follow the ongoing work to improve influenza surveillance and prevention. Also featured are useful websites, details of upcoming meetings and informative articles on influenza-related subjects.

In this first issue, Professor John Tam, Chairman of the APACI, discusses how appropriate the influenza vaccine is in Asian populations. The new influenza control recommendations from the Advisory Committee on Immunisation Practice and the benefits of vaccinating healthy children are also reviewed. Our *World focus* section looks at current influenza data from across the globe and, finally, we revisit the 'Asian flu' epidemic of 1957 and discuss its devastating effect on the global population.

Contents

Advisory Committee Members

The role of the Asia-Pacific Advisory Committee on Influenza

Professor John Tam
John Siu-lun Tam is a Professor in the Department of Microbiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong. He is also Director of the Virology Laboratory at the Prince of Wales Hospital, the teaching hospital for the Medical Faculty of the Chinese University of Hong Kong in Shatin, Hong Kong.

Dr Lance Jennings
Lance Jennings is a Senior Clinical Lecturer at the Christchurch School of Medicine and Health Sciences, University of Otago, New Zealand. He is a member of two New Zealand Ministry of Health advisory groups and was instrumental in the establishment of the National Influenza Immunisation Strategy Group. He is Vice-Chairman of the Asian-Pacific Influenza Advisory Board, and has recently held WHO consultancies on influenza and measles.

Mission statement

To promote influenza awareness in the Asia-Pacific region, with the intention of improving prevention and control.

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 is a joint initiative of four pharmaceutical companies: Aventis Pasteur, Chiron, GlaxoSmithKline and Wyeth. Its members are highly regarded influenza and infectious disease experts from across the Asia-Pacific region.

The activities of the APACI are aligned with, and supplemental to, 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.
- To assist the development of country-specific public awareness programmes.
- To promote influenza awareness among healthcare professionals in the region.
- To provide educational resources to support influenza awareness activities.
- To assist the process of establishing or reviewing country-specific recommendations for influenza prevention and control.
- To facilitate the timely access to, and supply of, influenza vaccines.

Activities

Activities will include:

- promoting influenza awareness among healthcare professionals in the region:
  - identifying country-specific Key Opinion Leaders (KOLs)
  - a regular newsletter (*Influenza – Asian Focus*)
  - peer-reviewed publications (develop publication plan)
- 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.

Meeting highlights

The APACI inaugural meeting was held in Hong Kong in January 2002. The Committee focused on how to meet the objectives raised, and members from Hong Kong, Australia, Indonesia, Malaysia, New Zealand, the Philippines and Thailand presented data on influenza in their respective countries.

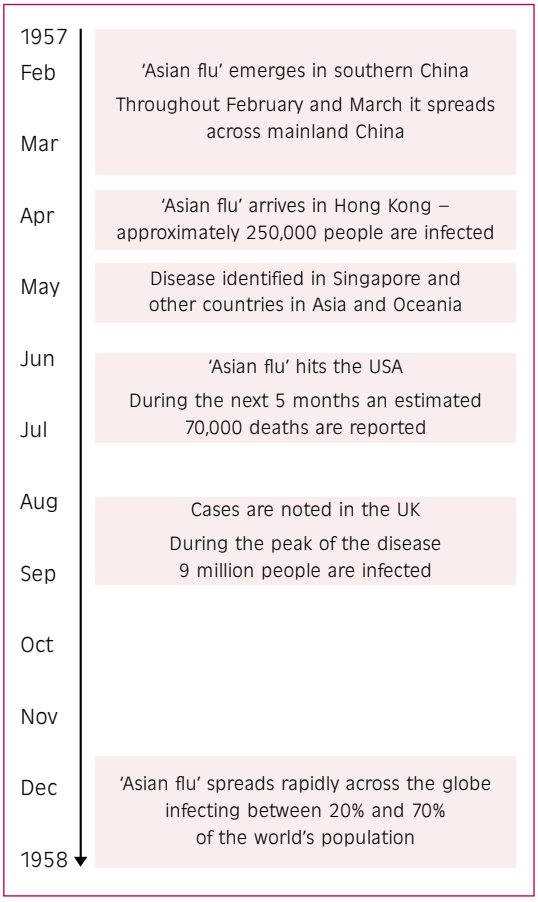
The 2nd APACI meeting was held in Bangkok in June 2002. Dr Klaus Stohr of the WHO Influenza Programme discussed recent developments of the WHO global agenda on influenza and its possible impact in Asia. Influenza data from Singapore, Taiwan, Korea and China were presented, and country-specific consensus statements on antiviral usage were discussed.

The 3rd APACI meeting is due to take place in Kuala Lumpur, Malaysia, from 29 to 30 October 2002.

The history of 'Asian flu'

In 1957, a new strain of influenza A virus made an appearance that was to cause one of the world's most severe influenza pandemics (a worldwide epidemic).

The pandemic, which was later dubbed the 'Asian flu', was first located in February 1957 in southern China, somewhere between Kutsing and Kweiyang. It was the second pandemic to sweep the world, the first being the 1918 'Spanish flu'.



Timeline of the 1957 'Asian flu' outbreak.

All age groups were susceptible to infection during the pandemic; however, those most severely affected were school children, young adults and pregnant women. Mortality rates increased dramatically in people aged ≥65 years, and excess mortality was reported in people with underlying medical conditions, such as cardiopulmonary disease. Despite this, around 40% of deaths occurred in healthy individuals aged <65 years. Although mortality was high, infection was much less severe than the 1918 'Spanish flu' pandemic when 20–40 million deaths occurred worldwide. The number of 'Asian flu'-related deaths worldwide ranged from 1:2000 to 1:10,000 infections. Although the pandemic of 1957 probably infected more people than the outbreak in 1918, the availability of antibiotics to treat secondary infections, which are the most common cause of death, may have resulted in a much lower mortality rate.

Genetic reassortment

Epidemic influenza occurs most frequently with outbreaks due to influenza A subtype viruses. The viruses are subtyped based on two proteins found on the virus' surface. These proteins are haemagglutinin (H) and neuraminidase (N). Influenza A viruses are able to undergo antigenic change using two different methods: antigenic drift and antigenic shift.

Antigenic drift is a process in which a new strain of influenza virus is produced by the occurrence of small mutations in the viral genes. These changes can occur continually over time, resulting in the gradual accumulation of new epitopes on the H and N proteins of the influenza A virus. Each new mutated influenza virus displaces the one before it and is not recognised by the individual's immune system. Therefore, if a person has developed antibodies against a particular strain of influenza, when the newer strain emerges the antibodies no longer recognise the virus and influenza infection recurs.

Antigenic shift causes a more dramatic change in the virus and results in a new influenza A subtype, created when two different strains of influenza A virus are combined within a dually infected host. Using sequencing techniques, investigators have been able to determine that 'Asian flu' occurred as a result of the genetic mixing of avian and human influenza A strains. Influenza A is present in many animals, including birds, horses, seals, whales, pigs, ferrets and some other mammals. The influenza virus is believed to have an avian origin and wild birds, in particular waterfowl, act as a large reservoir for all subtypes of influenza A. Although birds shed large quantities of influenza A virus, they do not usually become unwell. However, in other animals influenza A often results in sickness and death.

The 'Asian flu' influenza A virus was believed to have emerged in pigs found on farms in southern China. Pigs are an ideal host for facilitating the occurrence of antigenic shift as they have low barriers to infection and can be infected simultaneously with both human and avian influenza A strains. Studies have shown that the genetic reassortment of eight influenza A genes can occur in pigs, leading to both small and large variations in the virus H and N proteins.

Professor 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 has served on the editorial boards of the *Journal of AIDS Prevention* and the *Journal of Microbiology, Immunology, and Infection*.

Dr Ling Ai Ee

Ling Ai Ee is Director of the Virology Section, Department of Pathology at the Singapore General Hospital, and a Senior Consultant. She is responsible for the National Influenza Centre and the National HIV Reference Laboratory in Singapore.

Asian influenza A virus is shed in the faeces of waterfowl and released into the environment. In places where pigs and waterfowl live in close contact, it is possible for influenza virus to be deposited in pigs' drinking water. Once ingested by the pig, the avian influenza A virus combines with the human influenza A virus, which the pig has contracted through regular handling by humans. An antigenically new influenza A virus develops in the pig, which may suffer the same symptoms as humans – runny nose, fever and cough. Once the pig sneezes, the new strain of influenza is released. If that strain is infectious to humans and is able to be transmitted easily from person to person, then it has the potential to cause a pandemic.

The new virus

'Asian flu' was believed to have originated from a circulating human H1N1 influenza A strain first reported in Vladivostok, Russia, which underwent genetic reassortment with an avian H2N2 influenza A strain, possibly from ducks. The resulting influenza subtype was known as influenza A (H2N2). It contained H from the avian strain and other genes from the human strain. As a result, the genes within the virus allowed it to replicate easily in humans. The H was new to humans and there was no immunity in the population. The new virus was named A/Asian/57(H2N2) or A/Singapore/57 (H2N2) since Singapore was the first country in which the virus was identified after leaving China.

When a new strain of virus appears, it often displaces the previous existing strain and becomes predominant. In 1957, the type A (H2N2) virus completely replaced the type A (H1N1) virus, which had circulated since the pandemic of 1918. The H1N1 strain subsequently disappeared from the human population.

Why China?

Mainland China holds an optimum geographical position for influenza A outbreaks, allowing the disease to spread to both the East and West. Primarily, Chinese outbreaks spread to Russia and Europe before travelling across to the American continent. The climate of China also contributes to the production of new influenza A viruses. There is a wide variation in climate from the north to the south of China, so that during a single year, human infection by influenza is likely somewhere in the country. Influenza A virus antigenic shift is prevalent in China due to the close proximity of humans, pigs and domestic ducks. The crowded living conditions on farms in rural China also contribute considerably to influenza outbreaks and interspecies influenza transmission. In many villages, pigs are an integral part of rural life and often share the same living quarters as their owners; also, ducks are raised in huge numbers in mainland China (a current estimate stands at 612 million).

The nature of pandemics

Pandemics are the result of antigenic shifts and nearly always occur when a new influenza A virus emerges and a new H and/or N protein is acquired. They are associated with severe illness and significant mortality on a global scale. The occurrence of a pandemic can be broken down into a number of phases.*

- Phase 0 – there are three levels: i) no indication of new virus; ii) appearance of new virus; and iii) human infection confirmed.
- Phase 1 – confirmation of onset of the pandemic.
- Phase 2 – regional and multi-regional epidemics.
- Phase 3 – end of the first wave of the pandemic.
- Phase 4 – second wave of the pandemic.
- Phase 5 – end of the pandemic.

The phases of a pandemic do not occur simultaneously throughout the world, and it can take up to 2 years for the pandemic to be finished completely.

* These are the phases of a WHO pandemic alert.

Vaccine production

Production of vaccine for 'Asian flu' began in May 1957, some 3 months after the strain emerged. Vaccine was available by August 1957, although the supply was limited. In 1948, the World Health Organization (WHO) had set up an influenza surveillance network to track the global activity of influenza. Fortunately, this allowed the Asian virus to be tracked as it spread across the globe as laboratory procedures were in place to identify the virus. In 1957, Dr Maurice Hilleman – a pioneer in the field of vaccine production – detected the 'Asian flu' outbreak while it was still in Hong Kong. Having procured throat swabs from infected people in Hong Kong, Dr Hilleman was able to isolate the influenza A strain in time for 40 million doses of influenza vaccine to be produced. Vaccine manufacturers were provided with samples of the newly isolated virus, which were passed through chicken embryos in order not to cause further disease. In excess of 150,000 chicken eggs were used every day for vaccine production in the USA, thus providing a solution to the 'Asian flu' pandemic.

The next pandemic

The rate at which 'Asian flu' spread was alarming, as was the rate at which the 1968 'Hong Kong flu' pandemic spread. It is almost certain that the next pandemic which arises will spread even faster – the relaxation of trade and tourism restrictions, particularly in China, has allowed people to travel more freely. This, along with a general increase in air passenger services, will undoubtedly facilitate the spread of virus to other countries. There is now greater surveillance in China, with 12 influenza surveillance sites currently established. As a result, influenza isolates can be rapidly identified; for example, in the past 2 years, the WHO collaboration centre has received and identified more than 300 influenza viruses from China.

Further reading

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Update on the ACIP's recommendations

Highlights from the Advisory Committee on Immunisation Practice (ACIP)'s recommendations on the use of influenza vaccine, with special reference to healthy children.

Recommendations for using an influenza vaccine

Target groups for vaccination

- Those at risk for complications.

These include people aged ≥65 years, residents of nursing homes and other chronic care facilities, those with chronic disorders of the pulmonary or cardiovascular systems including asthma, those with chronic metabolic diseases who have needed regular medical follow-up or hospitalisation during the preceding year, children and adolescents receiving long-term aspirin therapy and women who will be in their second and third trimester during the influenza season.

- People aged 50–64 years.
- Individuals who can transmit influenza to others at high risk.

Timing of annual vaccination

The optimal time for influenza vaccination in the northern hemisphere is during October and November. However, due to the current delay in vaccine distribution the ACIP recommends that people at high risk for serious complications should be vaccinated during September. In October, vaccination of those at high risk for influenza, healthcare workers and children aged ≤9 years should also be carried out. Vaccination of other groups should begin in November and continue in December, and then for as long as the vaccine is available (Figure 1).

Simultaneous administration of other vaccines

As adult target groups for influenza and pneumococcal vaccination overlap, it is recommended that healthcare providers give serious consideration to administering both vaccines simultaneously. Children at high risk for influenza-related complications, including those aged 6–23 months, can receive influenza vaccine at the same time as other routine vaccinations.

Timing of annual vaccination and dosage

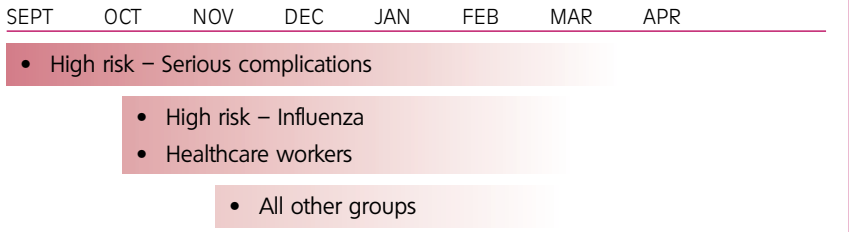

Figure 1. Optimal timing of annual influenza vaccination for the northern hemisphere.

The ACIP encourages influenza vaccination of healthy children – what are the implications?

The ACIP is encouraging influenza vaccination of healthy children aged 6–23 months. A full recommendation for annual vaccination of this age group is expected in the coming 1–3 years. For some time, the ACIP has recommended vaccination of children aged ≥6 months who have high-risk medical conditions, and this population group continues to be a strong candidate for annual vaccination.

Vaccination is being encouraged by the ACIP.

There is much evidence to support the rationale for vaccinating healthy children in younger age groups. Studies have shown that young children have a higher rate of hospital admissions than older children during the influenza season, due to their lack of immunity and previous exposure to influenza viruses; these increased hospitalisation rates are comparable to those seen in other high-risk groups.

Influenza is considered a common disease in young children and is associated with increased morbidity. It has been reported that children aged <5 years, without high-risk conditions, have a hospitalisation rate of 100:100,000.[1] During epidemics, over 20% of paediatric admissions to hospital are for influenza-related illnesses.[2]

Several studies have confirmed that inactive influenza A vaccine can be safely and effectively used for prophylaxis in healthy children aged 6–23 months.

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Professor Park Seung-Chul

Park Seung-Chul is a Member of the Asian-Pacific Advisory Committee on Influenza, President of The Korean Society of Vaccinology, and Fellow of The Korean Academy of Science and Technology. Professor Park is also Director of the Institute of Emerging Infectious Disease at the College of Medicine, Korea University, and Chairman of the Advisory Committee for Influenza, National Institute of Health, Korea.

Questions & Answers

Influenza in individuals with asthma

Q. Are asthmatic patients at greater risk from influenza?

A. Influenza can pose a serious threat to those with asthma and cause a significant increase in morbidity. As a result, individuals with asthma have been classified as being in an influenza 'high-risk group'. Infection with influenza increases susceptibility to bronchoconstriction, exacerbates asthma and possibly causes a prolonged decline in lung function. In children with asthma, influenza has been found to be a common cause of hospitalisation. Some studies have shown that asthma attacks in eight out of 10 children and four out of 10 adults are triggered by viral infections such as influenza.

Q. Should patients with asthma be vaccinated against influenza?

A. There has been a great deal of controversy surrounding this question, as the influenza vaccine is thought to be associated with asthma exacerbation in some individuals. This is believed to be one of the reasons why less than 10% of patients with asthma currently receive the influenza vaccine. A recent study by the American Lung Association found inactivated influenza vaccine to be safe when administered to adults and children with asthma.[1]

Vaccination is now recommended in many countries for people with asthma aged ≥6 months

In the study, records were kept of daily peak expiratory rates, use of bronchodilator medication and asthmatic symptoms. The frequency of exacerbation of asthma following vaccination was found to be similar in groups of patients who received influenza vaccine and placebo, respectively. Influenza vaccination is now recommended in many countries for people with asthma aged ≥6 months. It is particularly recommended for individuals with severe asthma, i.e. those who suffer frequent asthma attacks and experience regular hospital admissions. Vaccination is also recommended for pregnant women with asthma, after the first trimester of pregnancy.

Q. Is the influenza vaccine beneficial for those with asthma?

A. Immunisation has been found to be 70–90% effective in preventing influenza in a healthy population when the strains included in the vaccine match those in general circulation. Some studies suggest that morbidity in asthmatic patients can be reduced by administration of influenza vaccine.[1]

Among asthmatic children aged 2–6 years and 7–14 years, vaccine efficacy of up to 54% and 78%, respectively, has been reported.[2] Given the adverse effects of influenza in patients with asthma and the efficacy of influenza vaccine, healthcare providers are being urged to advise their asthmatic patients to be immunised.

Q. How often should asthmatic patients be vaccinated?

A. Individuals with asthma should be vaccinated against influenza annually. Influenza viruses mutate frequently so strains used in the vaccine composition are changed on a yearly basis. It is essential that vaccination be repeated each year so it can produce an immune-specific response as well as eliciting a booster response to related virus strains that the individual has been exposed to before. As it takes approximately 14 days for the vaccination to provide maximum protection, it is recommended that individuals receive the vaccine well before the onset of the peak influenza season.

Q. Are there any other precautions that should be taken?

A. Although asthma, in the absence of obstructive lung disease, has not been identified as a risk factor for invasive pneumococcal disease, pneumonia can occur as a complication of influenza. The target groups for influenza and pneumococcal vaccination overlap considerably and for this reason healthcare providers have been encouraged to vaccinate asthmatic patients against pneumococcal disease. Both pneumococcal and influenza vaccines can be administered simultaneously at different sites without increasing the risk of side-effects. However, the influenza vaccine must be administered each year, whereas the pneumococcal vaccine is administered only once.

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2. Bridges C, Fukuda K, Uyeki T *et al.* Prevention and control of influenza. Recommendations of the Advisory Committee on Immunisation Practices (ACIP). *MMWR* 2002; 51: 1–31.

The rationale for influenza vaccine in Asia

Influenza – Asian Focus speaks to Professor John Tam, Chairman of the Asia-Pacific Advisory Committee on Influenza (APACI), and Director of Virology, The Prince of Wales Hospital, Hong Kong.

In Asia, medical professionals are not really aware of the impact of influenza. This can also be said of the general population, where there is a lower level of understanding of the seriousness of the disease compared with the USA and Europe. An increase in influenza awareness in the general and medical community must occur before influenza vaccine can be properly introduced in Asia.

The impact of influenza in each individual country in Asia must be taken into consideration and there needs to be an increase in the collection of country-specific influenza data so that morbidity and mortality figures can be determined. The effect of influenza on various groups, such as school children and the elderly, also has to be understood. The economic impact of influenza in each country must also be calculated and cost-benefit analyses should be undertaken to identify the influenza disease burden across Asia.

Influenza is not perceived as an important illness in Asia, because it is not thought to cause many deaths

The effects of immunising against influenza can be seen in Japan where, until recently, children were routinely vaccinated. Vaccination appeared to have a significant effect on the prevention of mortality in older people. However, following public concern and media pressure over the safety of vaccines, routine vaccination of Japanese children was stopped. As a result, mortality in older people is increasing and the Japanese health authorities are beginning to realise how important it is to vaccinate against influenza. In Korea, high population density increases the risks of influenza mortality and morbidity. Consequently, Korean government health authorities have put in place wide-ranging health measures to control influenza and routinely administer influenza vaccine. In Taiwan, influenza vaccination is also on the increase following the recent promotion of immunisation.

China is considered to be the most important country in Asia for influenza surveillance, as it is the source of many influenza pandemics. In vaccine strains identified by the World Health Organization (WHO), over 70% originate in China. As a result, the WHO – with the aid of the Chinese medical authorities – has made an extensive effort to raise awareness of the disease among the Chinese population. The Chinese authorities are trying to understand the impact of influenza, and several surveillance centres have been created to follow the activity of the disease. Consequently, vaccination against influenza in older people has begun in some cities in China.

Although China is an epicentre for influenza activity, the use of vaccine is not very high

The most important rationale for the use of influenza vaccine is to reduce morbidity and control mortality, particularly in high-risk groups. Asian countries are slowly recognising the need to vaccinate against influenza. The occurrence of respiratory viral infections in Asia is poorly defined and more studies need to be conducted to gain a true understanding of country-specific community influenza rates. Economic imperatives in Asia should allow employers to appreciate the benefits of vaccinating their employees, as it leads to less time taken off work due to illness. A gradual increase in the use of influenza vaccine in Asia is expected to be seen over the next 5 years. Surveillance of influenza is undertaken in many regions throughout Asia but still requires considerable development.

Failure to vaccinate against influenza will have devastating consequences not just in Asia but for the entire world

The 1957 outbreak of 'Asian flu' demonstrated the devastating effects of avian-derived influenza. The Asian region is of particular concern as it is experiencing a population explosion and an influenza pandemic would infect a large number of people. Administration of influenza vaccine will help to reduce the chance of a new virus being generated and, therefore, the likelihood of an influenza pandemic. Continued influenza surveillance will allow early control of influenza and provide a warning system. A lot of effort is required in Asia in order for it to catch up with the level of influenza control that exists in the USA and Europe.

Dr Ingerani Sujana Prawira

Ingerani Sujana Prawira is Director of the Disease Research Centre and Development at the National Institutes of Health Research and Development in Indonesia. She is a member of several regional and international organisations, including the International Hospital Federation and the International Health Law Association.

World focus

Current influenza-related news from around the globe, including outbreaks, research and development, and new recommendations.

Peramivir ineffective against influenza

Disappointing results from preliminary phase III testing of peramivir, an investigational oral influenza neuraminidase inhibitor, have been released by BioCryst Pharmaceuticals, Inc., USA. The agent was being developed for the treatment of influenza A and B, and the objective of the phase III trials was to evaluate its safety and efficacy in otherwise healthy adults. Peramivir was administered to a total of 1246 adults over a period of four flu seasons. Results showed that no significant difference was seen in the primary efficacy endpoint, i.e. the length of time from the first dose to the onset of clinically significant influenza symptoms, between individuals treated with peramivir and those treated with placebo. Development of peramivir has now been discontinued.

[BioCryst Pharmaceuticals, Inc., 25 June 2002]

New avian influenza viruses may result in next pandemic

The June issue of the *Proceedings of the National Academy of Sciences* reported that the ongoing evolution of avian influenza virus provides cause for human pandemic concern. In 1997, the Hong Kong bird influenza outbreak, associated with H5N1 viruses, caused the death of six people and the subsequent slaughter of millions of birds. Although these viruses

Avian viruses have pandemic potential.

are no longer detected, new precursors have arisen that have crossed from waterfowl to chickens and other poultry. These viruses have been found to be lethal in mice, and the pace at which they are being generated is causing investigators to worry.

[Guan Y, Peiris JS, Lipatov AS *et al.* Emergence of multiple genotypes of H5N1 avian influenza viruses in Hong Kong SAR. *Proc Natl Acad Sci* 2002; 99: 8950–5]

Recommendations of the Hong Kong Avian Flu Investigation Team

Following isolation of H5N1 influenza viruses in poultry, the Hong Kong Avian Flu Investigation Team has proposed a number of recommendations to reduce the incidence of future avian influenza outbreaks. The new recommended measures include improving farm biosecurity, enhancing measures relating to poultry transport cages, reducing the volume of trade in live poultry, introducing an additional 'rest day' to break virus cycles in retail markets, and enhancing surveillance tools and monitoring for new emerging viruses.

[Hong Kong Special Administrative Region (HKSAR) Government, 24 May 2002]

Respiratory virus infection – a cause of hospitalisation in chronic lung disease patients

A recent investigation of individuals with chronic lung disease has shown that influenza and respiratory syncytial virus (RSV) infection account for a high percentage of acute respiratory hospitalisations. In children and adults with chronic lung disease, influenza and RSV caused 15–33% and 7–9% of hospitalisations, respectively. The highest numbers of influenza- and RSV-associated hospitalisations were seen in children aged <5 years and persons aged ≥65 years. In the older age group, 9% of deaths were related to either influenza or RSV. Both viruses were associated with an excess of outpatient visits in children and antibiotic prescriptions in all age groups.

[Griffin MR, Coffey CS, Neuzil KM *et al.* Influenza- and respiratory syncytial virus-related morbidity in chronic lung disease. *Arch Intern Med* 2002; 162: 1229–36]

Update from the WHO

Global agenda

At the recent World Health Organization (WHO) Consultation on Global Priorities in Influenza Surveillance and Control meeting held 6–7 May 2002, in Geneva, Switzerland, final additions were made to the global agenda. Many leading influenza and communicable disease experts shared their individual approaches to influenza surveillance and control.

Although the WHO has a long-standing Influenza Surveillance Network, established in 1948, it was thought that more should be done to encourage wider input and participation. The global agenda has been created to address many existing issues relating to influenza surveillance and control – most importantly, morbidity and mortality due to annual influenza epidemics, and preparing for the next influenza pandemic.

There are four major themes in the global agenda.

(continued on page 11)

Influenza in the Asia-Pacific region

At a meeting of the Asia-Pacific Advisory Committee on Influenza (APACI) in February 2002, members from Hong Kong, Australia, Indonesia, Malaysia and New Zealand presented overviews on influenza in their respective countries.

Australia

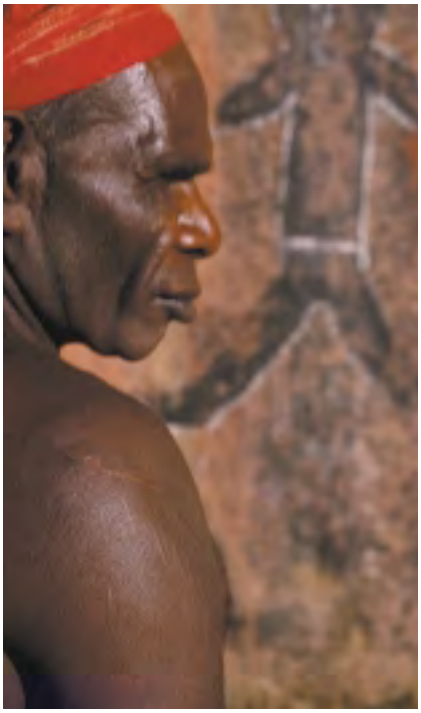
Influenza is a significant cause of morbidity and mortality in Australia, Clinical Associate Professor David Smith, Clinical Director at the Western Australia Centre for Pathology and Medical Research, told the meeting. Influenza affects 10–20% of the population annually, causing between 20,000 and 40,000 hospitalisations, 1500 deaths and 1.5 million lost work days. The total economic costs of the disease are estimated to be almost AUD$1 billion each year.

The incidence of influenza is highest in adults in the 15–44-years age group. Annual epidemics occur in winter, usually beginning between April and June, and finishing between August and October. Epidemics tend to spread geographically from New Zealand, to the east and then west coasts of Australia.

Mortality is proportionally higher in at-risk groups, that is the very young, the elderly and those with pre-existing cardiovascular or respiratory disease. Australia's influenza vaccination policy recommends vaccination for these groups, as well as residents of nursing homes and other long-term care facilities, and families of those who are at risk.

Vaccination is free of charge for those aged >65 years, and for indigenous Aboriginal and Torres Strait Islanders aged >50 years. For others aged <65 years who are at risk, it is either free or subsidised (this varies from state to state). Vaccination rates for those aged >65 years are above 70%, but there is room for further improvement.

Rates for the risk groups aged <65 years are poor and have been targeted for improvement. Every year in Australia, an Influenza Awareness Campaign is launched to coincide with the annual release of influenza vaccine. The campaign is a joint effort by Australia's Commonwealth and State governments, the National Pharmaceutical Association and the Australian Medical Association.



Vaccination is available free of charge in Australia for indigenous people aged >50 years.

New Zealand

Dr Lance Jennings, Canterbury Health Laboratories, Christchurch, New Zealand, began his presentation by explaining that in New Zealand, epidemics of influenza occur every winter – usually between May and September – beginning in the North Island and then moving to the South Island.

New Zealand's influenza mortality data per head of population are similar to Australia's. There is a proportionally higher hospitalisation rate among New Zealand's Maori population compared with the European population.

Free influenza vaccine was made available to those aged ≥65 years from 1997, and since 1999, to those <65 years with certain ongoing medical conditions. However, vaccination rates have not reached the 75% target, with only 59% of the population ≥65 years being vaccinated in 2001. The New Zealand government has initiated an Influenza Awareness Programme, which is aimed at increasing awareness of the dangers of influenza and encouraging vaccination of those at risk.

Indonesia

Dr Ingerani Sujana Prawira, Ministry of Health, Jakarta, told the meeting that in Indonesia, only limited epidemiological data are available on influenza. In Jakarta, the peak incidence occurs from September to December, corresponding with the rainy season.

The Indonesian government's priorities are focused on controlling malaria, tuberculosis, dengue fever, haemorrhagic fever and measles rather than influenza. However, respiratory tract infections, of which the influenza virus is one of the causative agents, are the third leading cause of death in Indonesia. Preventing death from pneumonia is a high priority for the government. No government policy exists yet for influenza vaccination, but with the influenza vaccine becoming available in 1999, public awareness and demand for influenza vaccination has begun to increase in the private sector. At least 200,000 Hajj pilgrims (15–40%) are immunised each year before leaving for Mecca.

Malaysia

Associate Professor Ilina Isahak, University of Kebangsaan, Malaysia, explained to the Committee members that Malaysia is similar to other tropical countries in that it has two peaks of influenza incidence, which occur from December to March and from June to July.

In Malaysia, the effect of influenza can best be gauged from studies of pneumo-

Clinical Associate Professor David Smith

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nia prevalence and mortality since in 13% of pneumonia cases, influenza is the cause, according to a study conducted at the Hospital University of Kebangsaan, Malaysia. The majority of deaths from pneumonia occur in infants <1 year of age.

Since 1992, there has been a decreasing trend in the death rate from pneumonia, from 450,000 in 1992 to 200,000 in 1997. Influenza vaccination is largely perceived as a travel vaccine for cold countries, such as European nations and the USA in winter. Prior to 1998, fewer than 10,000 Malaysians underwent vaccination even though public awareness of influenza vaccination has increased since 1998.

Along with pneumonia and meningitis vaccines, influenza vaccine is recommended to Hajj and Umrah pilgrims. It is also recommended for healthcare workers and patients undergoing cardiac operations.

Hong Kong

Professor John Tam, Director of Virology at The Prince of Wales Hospital, Hong Kong, told the Committee members that because of its high population density, the influenza virus spreads easily in Hong Kong.

There are two peaks of activity – January to March each year and a smaller outbreak in July, said Professor Tam. Most influenza A cases occur in children <5 years of age. The pattern for influenza B is similar to influenza A, but with a tendency to occur in peak years. Viral respiratory infection is the leading cause of morbidity in Hong Kong, particularly amongst children. In an epidemiological study of viral respiratory tract infections in patients (86% of whom were children <10 years of age) at Hong Kong's Prince of Wales Hospital studied over a 5-year period, influenza A and B together accounted for 44% of all cases.

Hong Kong's population is at increased risk from influenza.

Info-net

FluNet

FluNet (http://oms2.b3e.jussieu.fr/flunet) is the official website of the World Health Organization (WHO) Global Influenza Surveillance Network. The site was created in collaboration with the Institute for Medical Research and Health. In addition to maps and graphs of recent influenza activity, the site features weekly country reports and a global situation summary.

The Australian WHO Collaborating Centre for Reference and Research on Influenza

The website of one of the WHO's global collaborating centres, which can be found at www.influenzacentre.org, focuses on influenza data from Australia and South-East Asia. General influenza information can be found alongside electron micrograph images of the influenza virus. Surveillance maps and up-to-date regional news reports are also available.

Member's diary

Influenza – Asian Focus speaks to Professor John Tam, Chairman of the Asia-Pacific Advisory Committee, about his recent presentation entitled 'Avian influenza A virus infection in Hong Kong' at the San Lazaro Hospital in Manila, the Philippines, in July 2002.

During 1997, an avian H5N1 influenza A virus outbreak occurred in chickens in Hong Kong. This was of particular concern as H5N1 influenza A virus is able to infect numerous animal species. It can also infect many organs within the body, such as the brain, kidneys and liver, unlike other types of influenza virus, which primarily infect only the respiratory tract. The first case of this virus in humans was seen in a 3-year-old boy, who died 10 days after presenting with symptoms. A total of 18 cases were noted during 1997, with six deaths. Since 1997, the avian H9N2 influenza A virus has been detected in poultry, and two cases in humans were reported in 1999. Pandemic human influenza viruses are thought to evolve from genomic reassortment during the co-infection of avian and human influenza virus in an intermediate host (Figure 1). Pigs are likely to be a significant intermediate host in the southern China region (as discussed in the Feature Article of the current issue of *Influenza – Asian Focus*). However, the outbreak of H5N1 and H9N2 influenza A virus in Hong Kong appeared to be a direct transmission of the viruses from poultry to human.

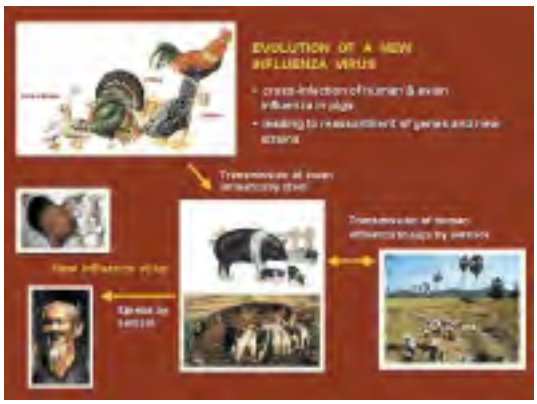

Figure 1. The evolution of a new influenza virus.

Avian influenza is thought to originate in waterfowl and passes easily to chickens. Since 1997, the Hong Kong government has authorised the slaughter of poultry on three separate occasions because of the presence of avian influenza viruses. In order to reduce the likelihood of human infection, new control measures have been set up in Hong Kong. The segregation of poultry and waterfowl has been encouraged and outbreak scans are regularly undertaken in poultry farms. Border controls have been introduced to inspect poultry imported into Hong Kong from mainland China; all batches of chickens entering Hong Kong must now complete quarantine screening and any evidence of infection leads to the rejection of birds for importation.

The Hong Kong government has also taken measures to raise awareness of avian influenza. Guidelines have been issued on the handling of live chickens bought in local markets and on the preparation of chickens for meals. The government has also reduced the number of live chickens for sale in markets.

Associate Professor Jen-Ren Wang

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

...Update from the WHO, continued from page 8

1. Improving the quality and coverage of virological and epidemiological influenza surveillance.
2. Improving the understanding of the health and economic burdens of influenza, including benefits of epidemic control and pandemic preparedness.
3. Expanding the use of existing vaccines, particularly in developing countries and in high-risk groups, and accelerating the introduction of new vaccines.
4. Increasing national and global epidemic and pandemic preparedness, including supplies of vaccine and other pharmaceuticals.

The global agenda will act as a guide for those involved in research and development, influenza surveillance and control, policy development, advocacy and fund raising.

New influenza vaccine composition

The vaccine content for the northern hemisphere 2002–3 season was also decided at the Geneva meeting. The WHO has recommended the following viruses for influenza production next year:

- A/New Caledonia/20/99(H1N1)-like virus
- A/Moscow/10/99(H3N2)-like virus*
- B/Hong Kong/330/2001-like virus.

The recommendation was based on available surveillance data from the worldwide network of national influenza centres and WHO collaborating centres. Already, representatives from all the major influenza vaccine companies have been invited to discuss this recommendation in order to allow sufficient time for production of the vaccine before the onset of the 2002–3 influenza season.

* The widely used vaccine strain is A/Panama/2007/99.

Associate Professor Chantapong Wasi

Chantapong Wasi is Associate Professor of Microbiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand, and President of the Virology Association, Thailand. She is a member of a number of national and international organisations including the WHO Expert Panel in Viral Diseases, and the Asia-Pacific Association of Medical Virology.

Other members of the APACI will be profiled in future issues of *Influenza – Asian Focus*.

Upcoming meetings

International

World Vaccine Congress 2002
Lyon, France — 30 September–2 October 2002
www.pharma-rd.net/WVC_Lyon2002

48th International Respiratory Congress
Florida, USA — 5–8 October 2002
www.aarc.org/headlines/register_early

1st European Influenza Conference
St Julians, Malta — 20–23 October 2002
www.jades.nl/malta

Western Pacific Congress of Chemotherapy and Infectious Diseases
Perth, Australia — 1–5 December 2002
www.icms.com.au/wpccid

Regional

1st Asian Congress of Paediatric Infectious Diseases
Pattaya, Thailand — 10–13 November 2002
www.pidst.org/acpid2002

In the next issue...

Topics that will be covered in the next issue of *Influenza – Asian Focus* include:

- What is influenza? Exploding the myths
- Childhood influenza: children as a high-risk group in Asia
- Influenza and travellers
- An update from the World Health Organization
- Influenza outbreak in Madagascar
- APACI highlights: influenza in the Asia-Pacific region

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