ANTIVIRAL TREATMENTS FOR EXISTING INFECTION

Two specific antiviral drugs are now available for the treatment of established influenza infection. Zanamivir ('Relenza') and oseltamivir ('Tamiflu') both interfere with the access of influenza A and influenza B virus into cells and the escape of virus from cells. Zanamivir is administered as a twice daily inhalation to adults and children aged five years and over. Oseltamivir is administered as a twice daily capsule to those aged 13 years and over and as a suspension formulation for children one year and older, and adult patients who cannot swallow capsules.

Dr Dominic Dwyer, medical virologist at Westmead Hospital in Sydney, said the drugs are effective for laboratory-confirmed influenza infection, reducing the severity and duration of infection. 9,10 "Both treatments need to be commenced within 36-48 hours of the first symptoms, and they are not effective against other viruses such as RSV, adenovirus, parainfluenza and metapneumovirus which can cause similar symptoms," Dr Dwyer said. "We need to educate patients about the need to seek early treatment, rather than just spending the first few days at home in bed."

Most trials of zanamivir and oseltamivir have been in relatively healthy people. Effects in reducing the duration of illness are more pronounced in people with additional risk factors.

PLANNING VACCINES FOR THE INFLUENZA SEASON

The formulation of influenza vaccines for Australians is based on information from an international surveillance and monitoring program coordinated by the World Health Organization. Four Collaborating Centres for Influenza, in Atlanta, London, Melbourne and Tokyo, integrate information from 110 centres in 80 different countries. Mr Alan Hampson. Convener of the ISG. said the network meets twice yearly to make recommendations for vaccines for the following Northern and Southern hemisphere seasons.

"Influenza is a 'moving target' for vaccines," Mr Hampson said. "Continuing antigenic drift, which is an evolutionary response by this easily-mutated RNA virus to host immunity, means that we have to make a prediction each year about the strains that will be most prevalent."

Recommendations from WHO are taken to the Australian Influenza Vaccine Committee, within the Therapeutic Goods Administration, in October each year for approval and implementation, allowing manufacture of vaccines to commence. Vaccines normally contain two influenza A strains and one influenza B strain, and are developed from clearly-characterised laboratory stocks of the virus.

Epidemics of influenza among poultry flocks in Asia have made headline news, but the implications for human infection are still uncertain. Influenza A is fundamentally a virus of birds, with infection of humans and the establishment of distinct and self-perpetuating human strains an incidental occurrence, according to Alan Hampson. Influenza A has 16 H (haemagglutinin) types and nine N (neuraminidase) types. Only three H types (H1, H2 and H3) and three N types (N1, N2, N8) have been known to occur as self-perpetuating infections in humans.

Recent outbreaks originating in Asian countries have involved an H5N1 type, and human infections and deaths have been reported. "The concern is that the virus will adapt to the human host, either through mutation or genetic reassortment by mixing with a human strain," Mr Hampson said. "This type of antigenic shift is the basis of influenza pandemics." A vaccine seed virus has been produced by the UK. This is a Vietnamese strain of the H5N1. Trials testing this vaccine strain have commenced in the USA and Australia will also trial vaccines using this same strain. A concern is that if the virus changes considerably in adapting to humans that this vaccine may no longer be immunogenic.

The ongoing spread of the Avian influenza into Mongolia and Russia continues to heighten the threat that a pandemic may result. WHO is sponsoring the effort to prepare and coordinate an international response.

INFLUENZA SPECIALIST GROUP

The Influenza Specialist Group consists of medical and scientific specialists as well as professional and patient groups from around the country. It cooperates with state and federal governments in educational activities about influenza. In conjunction with other organisations including the Australian Medical Association, Royal Australian College of General Practitioners, WHO Collaborating Centre for Reference and Research on Influenza, Pharmaceutical Society of Australia, National Asthma Council, Diabetes Australia and the National Heart Foundation it runs the annual Influenza Awareness Program. The Program, launched in 1992, informs key audiences about the consequences of influenza and the importance of preventing and treating infection.

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Vaccination against influenza safely and effectively reduces the risk of infection, and treatments are now available to alleviate the duration and severity of symptoms if infection occurs. Although Australia has made excellent progress in targeting those aged 65 and older, the majority of younger at-risk individuals - including many who are active in the workforce - remain unprotected. This publication, from the Influenza Specialist Group, reviews current issues in the prevention and treatment of influenza - at a time when awareness of viral respiratory infections has been heightened by the occurrence of SARS and the recent spread of avian influenza, originating in South-East Asia, highlighting the threat of a potential worldwide pandemic.

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Avian influenza

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- Antiviral treatments for existing infection
- Planning vaccines for the influenza season

RISKS OF INFLUENZA AND BENEFITS OF VACCINATION

Risks

Influenza is a potentially fatal disease, and a number of studies have shown that deaths directly attributed to the infection are a substantial under-estimate of the true mortality. A Dutch study, for example, estimated the mortality rate was four times higher than that recorded in death certificates, with many deaths attributed to secondary cardiovascular and respiratory complications. An actuarial study in Australia suggested the death rate could be eight times higher than that officially recorded.2 In addition, while people 65 years and older are at high risk, nearly a quarter of all deaths occur in younger age groups (Table 1).

An Australian study estimated that influenza was responsible for a million medical consultations, 20,000-40,000 hospitalisations, 1,500 deaths and 1.5 million days off work each year, and a total economic cost of about \$600 million annually.3

Benefits of vaccination

Influenza vaccination is about 70% effective against laboratory-proven, symptomatic disease, according to Dr Heath Kelly, Head of the Epidemiology Unit at the Victorian Infectious Diseases Reference Laboratory, "There are special difficulties in assessing the effectiveness of influenza vaccination in 'real world' settings, and data from studies need careful interpretation," Dr Kelly said. Vaccinations against other viral infections such as measles

Continued from page 1...

are targeted at a stable virus, while the match between the vaccine and circulating strains of influenza virus is not always perfect. In addition, only about 40% of 'influenza-like' respiratory viral infections, characterised by rapid onset, fever and malaise, are in fact caused by the influenza virus.

A number of analyses have addressed specific outcomes, and identified pronounced benefits in terms of proven influenza infection: Table 2 provides a representative example. In the frail elderly and those with underlying conditions, prevention of hospitalisation and death may be the main aim, while in younger healthy people the focus may be on decreasing time off work or reducing complications from pre-existing chronic diseases.

Contraindications to vaccination include hypersensitivity to the vaccine components and current febrile illness.

AUSTRALIAN VACCINATION RATES: GOOD PROGRESS BUT ROOM FOR IMPROVEMENT

Dr Rosemary Lester, Manager of the Prevention and Perinatal Health Section at the Department of Human Services in Victoria, said there has been good progress in vaccinating older Australians against influenza but room for significant improvement in protecting younger people considered at risk.

"There is no vaccination register for influenza, but vaccination rates in Australians over 65s are fairly stable with latest research from the AIHW demonstrating uptake rates of 79% in this group," Dr Lester said.

The NHMRC recommends vaccination in adults and children older than 6 months with chronic pulmonary or circulatory disease, including severe asthma, and other chronic illness that required regular medical follow-up or hospitalisation in the preceding year. In these at risk groups, latest research has shown that only 42% of people are getting vaccinated annually.

"Influenza vaccination is a proven lifesaver for older people and those at risk for other reasons." Dr Lester said.

Table 1: Estimated influenza deaths in the United Kingdom - 10 year period

65 years and older	21,900
40-64	6,100
15-39	280

Table 2: Efficacy of influenza vaccination in preventing outcomes in elderly patients⁵

All respiratory diseases	56%
Pneumonia	53%
Hospitalisation for any cause	50%
Death from any cause	68%

HEALTH AUTHORITIES SUPPORT VACCINATION IN CHRONIC ILLNESS

Representatives of three leading health authorities have supported the benefits of influenza vaccination in people with an underlying chronic illness that increases their vulnerability to the infection and its complications.

Greg Johnson, Chief Executive Officer of Diabetes Australia in Victoria, noted that NHMRC guidelines recommend vaccination for adults and children older than 6 months who have chronic illnesses that require regular medical follow-up. This includes diabetes. "We believe all people with diabetes, regardless of their age, should be aware of this recommendation and discuss their individual needs with their doctors," Mr Johnson said. "Diabetes is a rapidly growing problem, affecting Australians of all ages. Influenza can exacerbate the problems of diabetes, and it is sensible to take steps to avoid it."

The NHMRC also recommends vaccination for people with severe asthma. Kristine Whorlow, Chief Executive Officer of the National Asthma Council, said the effects of influenza and the risks of complications could be more problematic in the presence of underlying asthma and other chronic respiratory illnesses. "We define 'severe' asthma as asthma which causes persistent or frequent symptoms including night-time asthma, limits physical activity, needs emergency

department visits or hospital admission, or requires treatment with high doses of inhaled corticosteroids or oral corticosteroids," Ms Whorlow said. "There are a number of myths about influenza vaccination in people with asthma. It does not trigger asthma attacks, although it may cause a slight increase in symptoms in a minority of people. If this occurs, then it's appropriate to increase the use of a preventer medication in line with the individual's written asthma management plan. Most people, though, notice no difference in their asthma symptoms after influenza vaccination."

The National Heart Foundation also encourages people with a range of cardiovascular diseases to have an annual influenza vaccination. "It's been estimated that up to two-thirds of people hospitalised with influenza are younger than 65 and have conditions such as heart disease, lung disease or diabetes," according to Dr Andrew Boyden, the Foundation's Medical Affairs Manager. "Although this group suffers a significant proportion of the total burden of the disease, only about 40% of Australians aged between 40 and 65 who have such high-risk conditions are protected through immunisation." An acute influenza infection predisposed people with heart disease not just to a higher risk of respiratory complications, but also risked exacerbating their underlying cardiovascular problem.

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WORKPLACE VACCINATION

Vaccinating healthy working adults against influenza will generate cost savings 95% of the time. The exact economic outcomes may vary from year to year, depending on factors such as the illness rate in each season, the absenteeism that results, and the hourly rate of pay of employees who are affected.

It has also been demonstrated that vaccination has benefits beyond protecting employees against influenza. A study in healthy employees aged between 18 and 64 found those who were vaccinated against influenza had:

- 25% fewer episodes of upper respiratory tract illness
- 43% fewer days off work because of upper respiratory illness
- 44% fewer visits to doctors because of upper respiratory illness.

In one Australian company, vaccination benefits were calculated to be over two and a half times the cost of the program.⁶ This finding is also supported by international studies, with cost savings estimated at an average of \$US47 for every person vaccinated in a study published in 1995.⁷

The benefit of workplace vaccination cannot be predicted each year, as it is influenced by the extent and virulence of the epidemic. A recent review⁸ suggests employers need to make individual decisions on whether to implement a workplace influenza vaccination based on factors including:

- the ease of organising a vaccination program
- the ease of transmission in a workplace
- the potential impact of an epidemic.

"In organisations where delivery of the vaccine is relatively easy and sudden rises in absence would be catastrophic, the cost-benefit equation may favour vaccination," the review stated. "Alternatively, where vaccine delivery is logistically difficult (for example, wide geographical spread, multiple bases) and the impact of an epidemic on productivity would be less severe, the case for vaccination is not as strong." In health and social care settings, the risk of transmission from employees to clients, and vice versa, also needs to be taken into account.

IMPLEMENTING A WORKPLACE INFLUENZA VACCINATION PROGRAM

Influenza vaccination programs have been implemented successfully in workplaces for many years, according to Dr Brandon Carp, managing director of the Unified Healthcare Group. "Each program should be individualised, with the promotion to staff, the arrangements for funding and other issues being determined according to the circumstances," he said. "The programs are very well received because staff and employers both benefit from protecting employees' health, reducing the risks of transmission in the workplace, and decreasing the time lost from work." Employers considering an influenza prevention program should assess it like other investments, accounting for the potential direct savings of reduced sick leave and lost productivity, as well as the indirect advantages of offering a staff benefit.

Influenza vaccination programs now tend to be undertaken by contractors rather than in-house personnel. Consultants are able to assist with promotion of the program, education about the health consequences of influenza and information about the efficacy and safety of vaccination. "It is vital that a flu vaccination program is provided through a professional and comprehensive service using well-trained professionals, that the quality of the vaccines is preserved by following strict 'cold chain' measures, and that any adverse reactions can be dealt with appropriately," Dr Carp said.

Workplace vaccination is an excellent method for protecting younger people with underlying chronic diseases against influenza. "A large proportion of this age group are in the workforce but mightn't necessarily have the opportunity to discuss it with their GP," Dr Carp said. "They often view themselves as healthy, and might not be aware of the special advantages of vaccination."

IS IT INFLUENZA?

Some people call any cold or other upper respiratory tract infection 'the flu'. It's important to realise that influenza is a specific illness caused by the influenza virus. Some of the features of influenza are listed in Table 3.

Table 3: Influenza or the common cold?

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Spectrum of illness	Systemic	Local - nose and throat	
Speed of onset	Sudden	Gradual	
Fever	Usually high	Usually mild	
Other symptoms	Chills, muscle aches, malaise, cough, sore throat	Sneezing, nasal congestion, sinusitis	
Severity	Severe - confined to bed	Usually mild	
Course of illness	May be protracted	Usually brief	

^{*}Note: some other respiratory viruses may cause influenza-like illness

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