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## Influenza in Singapore: To Vaccinate or Not?

By Dr Wong Sin Yew, Dr Lam Mun San

Influenza in a tropical country such as Singapore, occurs throughout the year. Every year, there are seasonal increases rather than epidemic peaks and these usually occur from the months of March to May and around December. These increases coincide with peak incidences of influenza in the Northern and Southern hemispheres.

Whilst there have been definitive national recommendations for influenza vaccination in temperate countries, similar recommendations are not available in tropical countries. In Singapore, much of the influenza vaccination has previously been given to a small segment of population who travel frequently for holidays, religious reasons and businesses.

Should influenza vaccination be given to the population at large and the recommendations promulgated by those from governmental agencies in temperate countries be adopted? There is no straightforward answer. In September 2003, there has been a change in the approach from the Ministry of Health, Singapore. The Health Promotion Board has begun a public health education campaign to advise influenza vaccination to travellers visiting countries that had SARS. Most recently, the Ministry has advised that healthcare workers, and elderly patients in chronic care facilities be vaccinated against influenza. In this article, we will review the frequently asked questions and attempt to provide some answers to help you understand the issues better.

Unless stated, the discussion on influenza vaccine applies to the inactivated trivalent vaccine.

### INFLUENZA VIRUS AND ANNUAL VACCINE FORMULATION

There are three types of influenza virus – A (multiple subtypes based on Haemagglutinin and Neuraminidase), B and C. The influenza syndrome (acute febrile illness with respiratory and systemic symptoms), caused by influenza A and B, results in annual epidemics, and occasionally, pandemics. Influenza C causes a short febrile illness and does not cause epidemics. The latter will not be discussed any further.

The influenza viral antigens undergo continual change and this is termed as antigen drift. This is the reason for which the various influenza virus strains incorporated in vaccine are changed annually. The World Health Organisation (WHO) and other health authorities including the Centres for Disease Control (CDC) in Atlanta update the predicted predominant influenza A and B strains for the next influenza season. Vaccine companies then incorporate these recommended strains in their vaccine formulation for the upcoming influenza season. Suffice to say that clinical protective immunity conferred by vaccination is highly dependent on the antigenic match between the vaccine strains and the circulating strains.

For the influenza season 2003-2004 in the Northern and Southern hemispheres, the vaccines should contain the following:

- A/New Caledonia/20/99 (H1/N1) like virus
- A/Moscow/10/99 (H3N2) like virus
- B/Hong Kong/330/2001 like virus

It should be noted that in other seasons, there may be a difference in the strains recommended for the Northern and Southern Hemispheres. This is particularly important for travellers and residents in specific geographic locales.

If the viral antigen undergoes a major change, termed as antigen shift, the global population would not be immune and this may result in an influenza pandemic.

### TYPES OF VACCINE AVAILABLE

There are seven registered influenza vaccines in Singapore.

The common vaccines used are the inactivated split trivalent vaccine (Fluarix by Glaxo Smith Kline, Vaxigrip and Vaxigrip Paediatric by Aventis).

Subunit vaccines with (Fluad) ME 49 adjuvant or without (Aggripal S1) are produced by Chiron. The subunit vaccine with adjuvant produces better seroconversion rates with higher antibody titers but this is associated with increased adverse reactions including local pain, erythema, and systemic complaints such as fever and myalgia.



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**ADMINISTRATION OF VACCINE**

Influenza vaccine, when indicated, should be administered on an annual basis.

Vaccine protection usually starts eight to ten days after vaccination. After a single administration, the antibody titer will peak in two to four weeks and slowly wanes over time.

**SHOULD WE USE THE NORTHERN OR SOUTHERN HEMISPHERE VACCINE FORMULATION FOR SINGAPORE RESIDENTS?**

In Singapore, influenza transmission occurs throughout the year. For prevention of influenza, patients should be administered on an annual basis using either the Northern or Southern Hemisphere formulation. At this time, there are no requirements for the administration of both the vaccines in a single year. The rule of thumb when the patient attends your clinic is to vaccinate with the most current vaccine available.

**WHAT ARE THE CONTRAINDICATIONS FOR VACCINATION?**

The major contraindication to the inactivated trivalent vaccine is egg and chicken protein allergy. For those who have a bleeding tendency, the subcutaneous route of administration is recommended. The smallest gauge needle (25G) should be used for vaccination and pressure applied to the injection site for 15 to 30 minutes. Patients who are on daily low molecular weight heparin should omit the heparin one day prior to vaccination.

**WHO SHOULD BE VACCINATED?**

There are numerous recommendations for influenza vaccination and the most comprehensive are those from CDC Atlanta and WHO. Priority of vaccination is for the elderly and those groups at highest risk of developing complications. Another major group that is targeted for vaccination are those who may transmit the infection to those at risk e.g. healthcare workers, close relatives of patients at risk, and so on. These recommendations target the following groups for vaccination with the inactivated trivalent vaccine.

1. Elderly above 65 years of age – CDC now recommends that all those above 50 years should receive vaccination.
2. Residents of nursing and long term care facilities.
3. Adult and children with chronic pulmonary and cardiovascular diseases. The largest patient population in this group are asthmatics.
4. Adult and children with renal and metabolic diseases.
5. Children receiving long-term aspirin therapy and therefore at risk of developing Reye’s syndrome if they are infected with influenza.
6. Family members of (1) – (5) as they are at risk of transmitting influenza.
7. Healthcare workers and allied health personnel.

Vaccine efficacy varies according to age, underlying immunocompetency and the antigenic match between the

vaccine and epidemic strains. In young adults, with a good antigenic match, levels of protection of 70% to 90% have been reported. A recent meta-analysis of published cohort observational trials derived an estimate of 56% for the level of vaccine efficacy in the elderly.

WHO has set goals of attaining vaccination coverage of the elderly to at least 50% by 2006 and 75% by 2010.

**SHOULD CHILDREN BE VACCINATED?**

There are numerous studies which have reported that vaccination of schoolchildren reduces febrile illnesses, cases of otitis media, hospitalisations, school absenteeism and the use of antibiotics.

The split trivalent vaccines may be used in children aged six months and above. Young children aged nine years and below who have not received the vaccine previously, will need to receive two doses at least four to six weeks apart. Thereafter, they only require an annual vaccine.

**HOW DOES IT HELP IN SARS?**

The recent global outbreak of SARS has heightened concerns about respiratory diseases which have symptoms similar to those seen in SARS.

In the early phase of infection due to SARS-Coronavirus, the symptoms may be difficult to differentiate from infections caused by other respiratory viruses such as influenza. In fact, a small outbreak of influenza B occurred at the Institute of Mental Health in Singapore in the midst of the SARS crisis. There was initial concern that this fever outbreak was due to SARS.

When clusters of fever and respiratory symptoms occur, especially in the healthcare setting, they raise suspicion of SARS. This will result in disruption of healthcare as well as institution of costly precautionary measures and investigations.

By vaccinating target groups like healthcare workers, the elderly and travellers, it would help to reduce the cases of febrile respiratory tract illnesses that may be confused with SARS.

**NEW VACCINES**

The current influenza vaccines have to be administered annually because they do not provide long-standing immunity and do not provide cross protection against different strains. There is extensive ongoing research to provide better formulations including DNA vaccines that should induce both T and B cell protective immune responses.

A trivalent, live attenuated vaccine (Flumist™) administered intranasally has recently received regulatory approval by Food and Drug Administration, United States of America. This vaccine obviates the need for parenteral administration but still has to be given on an annual basis. The indications are restricted to immunocompetent persons aged five to 49 years only. It is noteworthy that it is not approved for use in the very young, the elderly and those who may have an underlying immune deficiency. In USA, it is also more expensive than the standard inactivated trivalent vaccine.

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In the future, we can look forward to newer vaccines that will be more efficacious, and hopefully, eliminate the need for annual vaccination.

### **IS INFLUENZA VACCINATION COST EFFECTIVE IN SINGAPORE?**

The safety and efficacy of the influenza vaccine in the elderly and working populations have been demonstrated in numerous studies. In an article published in 2002 in the *Annals Academy of Medicine*, Ng et al from the Department of Community, Occupational and Family Medicine, National University of Singapore have estimated the disease burden of influenza in Singapore. Based on the likelihood that 15%

of patients with influenza like illness were positive for influenza, they estimated that there were 630,000 cases of influenza virus infection a year, giving rise to 520,000 sick visits and 315,000 days of sick absence from work. With an estimated overall vaccine efficacy of 56%, the potential benefit of influenza vaccination in Singapore is expected to be substantial. ■

#### **Note:**

*Influenza vaccines are available from the following suppliers*  
 (1) *Glaxo Smith Kline (Fluarix) – Samantha Foo 6232 8366*  
 (2) *Aventis Pastuer (Vaxigrip and Vaxigrip Paediatrics) – Alvin Tan 9790 4418*  
 (3) *Pacific Biosciences (Fluad, Aggripal S1) – Billy Ong 9695 0546.*

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