

INFLUENZA VACCINATIONS

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ABSTRACT

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. Influenza vaccine, when indicated should be administered on an annual basis. Seven registered vaccines are available in Singapore. The rule of thumb is to choose the most current vaccine. In the future, we can look forward to newer vaccines that will be more efficacious and hopefully eliminate the need for annual vaccination. The efficacy and safety of the influenza vaccine in the elderly and working populations have been demonstrated in numerous studies.

INTRODUCTION

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 were not available in tropical countries. In the past in Singapore, influenza vaccination had been given to a small segment of population who travel frequently for holidays, religious reasons and businesses.

Since September 2003, there has been a change in the approach from the Ministry of Health, Singapore. The Health Promotion Board began a public health education campaign to advise influenza vaccination to travelers visiting countries that had SARS. Subsequently, the Ministry advised that health care workers, elderly patients in chronic care facilities and those with underlying medical conditions be vaccinated against influenza.

In this article, I have highlighted some frequently asked questions and issues and have attempted to provide some answers. Unless stated, the discussion on influenza vaccine applies to the inactivated trivalent vaccine.

INFLUENZA VIRUS AND ANNUAL VACCINE FORMULATION

There are 3 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) is caused by influenza A & B and results in annual epidemics and occasionally pandemics. Influenza C causes a short febrile illness and does not cause epidemics and 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. WHO and other health authorities including Centres for Disease Control (CDC), Atlanta update the predicted predominant influenza A&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 2005-2006, the Northern and Southern hemispheres, the vaccines should contain the following:-

Southern Hemisphere 2005

- o A/New Caledonia/20/99 (H1N1)
- o A/Wellington/411/2002 (H3N2)
- o B/Shanghai/361/2002

Northern Hemisphere 2005/2006

- o Both H1N1 and B are the same
- o A/California/7/2004

In this year, there is a difference in the strains recommended for Northern and Southern Hemispheres. This is particularly important for travelers 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 a influenza pandemic.

TYPES OF VACCINES AVAILABLE

There are 7 registered influenza vaccines in Singapore. The common vaccines used are the inactivated split trivalent vaccine (Fluarix by Glaxo Smith Kline and Vaxigrip, 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, myalgia.

ADMINISTRATION OF VACCINE

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

Vaccine protection usually starts 8-10 days after vaccination. After a single administration, the antibody titer will peak in 2-4 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 Northern and Southern Hemisphere vaccine 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 15-30 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. Recommendations from Ministry of Health, Singapore are similar. Priority of vaccination is for the elderly and those groups at highest risk of developing complications. Another major group that are targeted for vaccination are those who may transmit the infection to those at risk e.g. health care workers, close relatives of patients at risk etc. These recommendations target the following groups for vaccination with the inactivated trivalent vaccine.

1. Elderly >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. Health care 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 70-90% 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, hospitalizations, school absenteeism and the use of antibiotics.

The split trivalent vaccines may be used in children aged 6 months and above. Young children aged 9 years and below who have not received the vaccine previously, will need to receive 2 doses at least 4-6 weeks apart. Thereafter, they only require an annual vaccine.

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 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 5-49 years only. It is noteworthy that it is not approved for use in the very young, the elderly and those may have an underlying immune deficiency. In USA, it is also more expensive than the standard inactivated trivalent vaccine.

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 RELEVANT IN ASIA?

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.

Two recent publications have also highlighted the importance of influenza in Asia. In Hong Kong, a 4 year study (from 1996 to 1999) by Wong et al reported that influenza accounted for 78 to 102 excess deaths per 100,000 elderly population with cardio-respiratory disease. From January 2001 to June 2001, 88, 000 elderly patients were monitored in Kaoshiung County, Taiwan. The rate of influenza vaccination was 58% in high risk group and 29% in low risk group. In both groups, influenza vaccination reduced hospitalization in all patient groups (with lung, heart, liver, renal diseases, stroke, DM, cancer etc). For those

that were hospitalized, vaccination decreased ALOS by 2.4 days for all patients and 4.9 days for those with lung disease.

SUGGESTED READING

1. Ng et al. Influenza in Singapore: Assessing the burden of illness in the community. *Ann Acad Med Singapore* 200; 31:182-8.
2. Wong et al. Influenza associated mortality in Hong Kong. *Clin Infect Dis* 2004; 39:1611-7.
3. Wang et al. Reducing hospitalization rates and shortening hospital stays after influenza vaccination. *Clin Infect Dis* 2004; 39:1604-10.

LEARNING POINTS

- o Influenza in a tropical country such as Singapore, occurs throughout the year.
 - o Every year, there are seasonal increases rather than epidemic peaks and these usually occur from the months of March to May and around December.
 - o These increases coincide with peak incidences of influenza in the Northern and Southern hemispheres.
 - o Influenza vaccine, when indicated should be administered on an annual basis.
 - o Seven registered vaccines are available in Singapore. The rule of thumb is to choose the most current vaccine. In the future, we can look forward to newer vaccines that will be more efficacious and hopefully eliminate the need for annual vaccination.
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