DRUG ALERT

Recommendations pertaining to the use of influenza vaccines and influenza antiviral drugs, 2016

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Vaccination is the most effective strategy to prevent influenza. It is recommended that influenza vaccine be administered each year before the influenza season, i.e. from March to June, although for individuals at increased risk of severe influenza in whom vaccination was missed, vaccine may be administered later. For a review of the 2015 influenza season and ongoing real-time updates of the 2016 influenza season when it starts, refer to the website of the National Institute for Communicable Diseases of the National Health Laboratory Service (www.nicd.ac.za). In this article we provide recommendations for the use of influenza vaccines in anticipation of the 2016 southern hemisphere influenza season. Guidance is based on available evidence to assist clinicians in making decisions regarding influenza vaccination. It should be noted that this article includes general recommendations for vaccination with influenza vaccines available in South Africa and may differ from groups targeted in specific vaccination programmes, e.g. the National Department of Health Programme.

S Afr Med J 2016;106(3):251-253. DOI:10.7196/SAMJ.2016.v106i3.10586

The burden of influenza in sub-Saharan Africa (and specifically in South Africa (SA)) is substantial, with some studies suggesting elevated influenza-associated mortality rates compared with other regions.[1-3] It is estimated that between 6 734 and 11 619 individuals die of seasonal influenza-associated illness in SA each year.[4,5] Approximately 5% of these deaths are in children aged <5 years. Among individuals aged ≥5 years, an estimated 50% of influenza-associated deaths are in the elderly and ~30% are in HIV-infected individuals.[4]

The highest rates of influenza-associated hospitalisation are in the elderly aged ≥65 years, HIV-infected individuals and children aged <5 years.[4-9] Influenza infection may trigger exacerbations of diabetes and pulmonary (e.g. asthma) and cardiovascular disease. For this reason, people with underlying chronic medical conditions are at high risk of serious influenza complications, often resulting in hospitalisation and even death. Surveillance data from SA showed that having underlying illnesses (other than HIV) was a risk for influenza-associated mortality (odds ratio 2.9, 95% confidence interval (CI) 1.2 - 7.3).[7] Pregnant women also represent an important risk group for influenza-associated mortality.[8] Among an estimated 646 - 1 428 seasonal influenza-associated deaths in women of childbearing age in SA in recent years, the majority (~90%) occurred in HIV-infected individuals and the influenza-associated mortality was three-fold higher (relative risk 2.8, 95% CI 7 - 3.9) in pregnant compared with non-pregnant women.[8] Studies suggest that individuals with underlying tuberculosis may also be at increased risk of influenza-associated death.[10,11]

Influenza circulation in SA is highly seasonal, and the influenza season falls in the winter months. The average onset of the influenza season is the first week of June.[12] However, the season has started as early as the last week of April and as late as the first week of July. The average duration of the influenza season is 12 (range 7 - 25) weeks. During the influenza season in SA government facilities, approximately 14% of patients hospitalised with lower respiratory tract infection and 25% of patients with influenza-like illness will test positive for influenza on polymerase chain reaction analysis.

Vaccinating individuals at risk of severe influenza may provide direct protection for these individuals. In addition, vaccinating individuals in close contact with people at risk for severe influenza may provide indirect protection through preventing transmission to high-risk individuals. This strategy is especially important for individuals in whom influenza vaccine is not indicated, such as children aged <6 months (who may be protected through maternal immunisation).[13] It may also be useful for individuals in whom the immune response may be poor, e.g. children aged <2 years and the elderly. The trivalent inactivated influenza vaccine (IIV) has reduced effectiveness in certain groups, e.g. the elderly and children aged <2 years; however, even for these individuals IIV still provides some protection. Other products, e.g. high-dose influenza vaccine and adjuvanted vaccines, have been shown to be more effective in certain groups,[14] but these vaccines are not available in SA. The trivalent IIV has been shown to provide protection in pregnant women and their infants[13,15,16] and in HIV-infected adults without severe immunosuppression.[17] Data are unclear as to the effectiveness in HIV-infected children aged <5 years.[18]

Recommended influenza vaccine formulation for 2016

Influenza vaccine is updated frequently because circulating influenza viruses continuously evolve. The following strains have been recommended by the World Health Organization (WHO) for the trivalent IIV 2016 southern hemisphere influenza season:

- an A/California/7/2009 (H1N1)pdm09-like virus
- an A/Hong Kong/4801/2014 (H3N2)-like virus
- a B Brisbane/60/2008-like virus.

These recommendations include a change in the A (H3N2) and B strains when compared with the composition of the trivalent IIV used for the southern hemisphere during the 2015 season.

Standard-dose IIV should contain 15 μg of each haemagglutinin antigen in each 0.5 mL dose.

Groups recommended for influenza vaccination

- Pregnant women irrespective of stage of pregnancy, or postpartum
- Individuals (adults or children) who are at high risk for influenza and its complications because of underlying medical conditions and who are receiving regular medical care for conditions such as chronic pulmonary (including tuberculosis) and cardiac diseases, chronic renal diseases, diabetes mellitus and similar metabolic disorders, individuals who are immunosuppressed and individuals who are morbidly obese (body mass index ≥40 kg/m^2)
- HIV-infected individuals
- Healthcare workers
- Residents of old-age homes and chronic care and rehabilitation institutions
- Persons aged >65 years
- Children aged 6 months - 59 months
- Persons aged 6 months - ≤18 years on long-term aspirin therapy
- Adults and children who are family contacts of individuals at high risk of severe influenza
- Any persons wishing to minimise the risk of influenza acquisition, especially in workplace settings where large-scale absenteeism could cause significant economic losses.

Table 1. Recommended dosages of influenza vaccine for individuals of different age groups

Age group*	Dose	Number of doses
Adults and children from 9 years of age	Adult dose (0.5 mL) IMI	Single dose
Children aged 3 - 8 years	Adult dose (0.5 mL) IMI	1 or 2 doses†
Children aged 6 - 35 months	0.25 mL (half an adult dose) IMI	1 or 2 doses†

*Note: influenza vaccine is not recommended for infants <6 months of age.
†For individuals who have not previously received a total of ≥2 doses before March 2016, or when vaccine status is unknown, 2 doses should be administered ≥1 month apart.

Table 2. Recommended dosages of influenza antiviral agents for treatment

Age group	Oseltamivir dosage*	Zanamivir dosage*
Adults	75 mg twice per day	Two 5 mg inhalations (10 mg total) twice per day
Neonates		
<38 weeks postmenstrual age	1 mg/kg twice per day	
38 - 40 weeks postmenstrual age	1.5 mg/kg twice per day	
Neonates and infants (1 day† - 12 months)	3 mg/kg twice a day	
Children		Two 5 mg inhalations (10 mg total) twice per day (only in children aged ≥7 years)
≤15 kg	30 mg twice per day	
>15 - 23 kg	45 mg twice per day	
>23 - 40 kg	60 mg twice per day	
>40 kg	75 mg twice per day	

*Recommended duration of treatment is 5 days. Zanamivir is recommended for treatment in children ≥7 years of age.
†US Food and Drug Administration approves >14 days old; however, experts agree should be used from 1 day.[19]

Dosage

Recommended dosages for individuals of different age groups are set out in Table 1.

Contraindications

Persons with a history of severe (anaphylactic) hypersensitivity to any components of the vaccine, including egg protein, or after a previous dose of any influenza vaccine.

Precautions

- Persons with moderate illness with or without fever should preferably be immunised after symptoms have disappeared. Having a mild upper respiratory illness is not a reason to defer vaccination.
- A history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.

Timing

Vaccines should be given sufficiently early to provide protection for the winter. A protective antibody response takes about 2 weeks to develop.

Antiviral chemotherapy

Antiviral therapy is recommended as early as possible, ideally within 48 hours, for any patient with confirmed or suspected influenza who has complicated or severe illness or is at high risk of influenza complications. At present influenza A(H1N1)pdm09, A(H3N2) and B viruses remain sensitive to oseltamivir and zanamivir. High levels of resistance to adamantanes among influenza A viruses has been detected in a number of countries. The use of amantadine and rimantadine in the treatment of influenza is therefore not recommended. The dosages for treatment with oseltamivir and zanamivir are set out in Table 2.

Antiviral chemoprophylaxis

Antiviral chemoprophylaxis for contacts of persons with influenza is currently not recommended. An annual influenza vaccination is the best way to prevent influenza because it can be given before the possible exposures to influenza occur, and it can provide safe and effective immunity throughout the influenza season. However, WHO recommendations also advise presumptive treatment for high-risk individuals (patients with severe immunosuppression or transplant patients) if any early signs of possible influenza infection are detected during the influenza season. Such individuals should be treated presumptively using the treatment regimen described above for a duration of 7 days, instead of the previously recommended long-term lower-dose chemoprophylaxis regimen.

For a more detailed description of antiviral management and chemoprophylaxis of influenza, please refer to the Healthcare Workers Handbook on influenza on the NICD website (http://www.nicd.ac.za/assets/files/Healthcare%20Workers%20Handbook%20on%20influenza%20in%20SA_%205%20May%202015.pdf).

For the full report on recommended composition of influenza vaccines, refer to the WHO website (http://www.who.int/influenza/vaccines/virus/recommendations/201509_recommendation.pdf?ua=1).

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Accepted 26 January 2016.