

# Understanding the influenza vaccination

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**Keywords:** flu vaccination, influenza, Southern Hemisphere, WHO

## Abstract

Circulating influenza (“flu”) viruses are continuously undergoing change, which makes the public more vulnerable to contracting flu. While anyone can develop complications from flu, certain high-risk groups are more vulnerable to life-threatening complications. Pharmacists are in an ideal position to identify high-risk groups and to recommend an annual flu vaccination. Carefully explaining the benefits of and allaying certain misconceptions about the flu vaccination helps the number of people wishing to receive the flu vaccination annually to increase, thereby decreasing the high morbidity and mortality rate due to flu.

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S Afr Pharm J 2016;83(2):14-19

## Introduction

Having an idea of the structure of the influenza (“flu”) virus, and how it mutates, is key to understanding the flu vaccine and how it is developed. This article briefly explains the latter, and answers many commonly asked questions about the flu vaccine.

## Structure and mutation of the influenza virus

Flu viruses can be divided into three distinct types, A, B and C. While the influenza A virus is responsible for most cases of flu, especially epidemics and pandemics, the B virus is responsible for local outbreaks.<sup>1</sup> The influenza C virus may cause mild infection of the respiratory tract, but is generally of little concern.<sup>1,2</sup>

The two proteins on the surface of the envelope surrounding the virus, haemagglutinin and neuraminidase, determine the subtype of the influenza A virus.<sup>2</sup> There are 18 different haemagglutinin proteins and 11 different neuraminidase proteins, the arrangement of which determines the different subtypes, e.g. influenza A(H1N1) and A(H3N2), which are the current circulating influenza A subtypes.<sup>1,3</sup> Within the envelope is the influenza genome, which consists of a single strand of ribonucleic acid (RNA) divided into eight segments (influenza A and B only), while the C virus comprises seven segments.<sup>1,4</sup>

Influenza B viruses are classified according to where they originated from and their strains. Presently, the influenza B strains in circulation originate from the Yamagata and Victoria areas, i.e. B/Yamagata and B/Victoria.<sup>2</sup>

Influenza A viruses may undergo a process called antigenic shift, which has resulted in new subtypes or strains that cause epidemics and pandemics. Major genetic changes occur in the haemagglutinin-neuraminidase protein. A large variety of animals, most commonly birds, pigs and humans, may be hosts to influenza A viruses. This leads to the “mixing” of genetic information and new subtypes emerging. These new subtypes may infect humans who have not developed resistance, leading to a pandemic.<sup>1</sup> An example of this is the 2009 H1N1 pandemic, which was caused by a new reassortant human-swine-avian strain of the influenza A (H1N1) virus to which humans had not previously been exposed.<sup>5</sup> This strain no longer causes pandemics, but is now one of the prevalent circulating strains responsible for seasonal flu.<sup>3</sup>

Seasonal flu occurs because of minor changes in the virus antibody-binding sites over a period as the RNA mutates. This process is called antigenic drift. Both influenza A and B viruses undergo this.<sup>1</sup>

## Which organisation selects the composition of the following season's influenza vaccine?

The World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS) is a global network whose personnel meet twice a year in February to recommend which viruses should be included in the flu vaccine for the upcoming flu season in the Northern Hemisphere, and in September to recommend the flu season vaccine composition in the Southern Hemisphere.<sup>6,7</sup> Because there is no distinct flu season in tropical areas, each individual national and regional authority makes a decision based upon epidemiological studies as to which vaccine (February or September) would be the most appropriate.<sup>5,7</sup>

# Influenza is a serious threat...



## ...to life

3 to 5 million cases of severe influenza illness result in 250 000 to 500 000 deaths per year<sup>1</sup>.

## ...to society

The economic impact of influenza because of healthcare costs and lost productivity is considerable<sup>2</sup>.

Vaccination results in a significant reduction in hospitalization due to chronic respiratory conditions and pneumonia.  
Overall mortality – a decrease of up to 50%<sup>3</sup>

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[S2] Influvac Subunit 2016. Composition: Each 0,5 ml Influvac Subunit 2016 influenza vaccine contains influenza virus surface antigens (haemagglutinin and neuraminidase) of strains: A/California/7/2009 (H1N1) pdm09-like strain used (A/California/7/2009, X-181) 15 µg HA; A/Hong Kong/4801/2014 (H3N2)-like strain used (A/New Caledonia/71/2014, X-257A) 15 µg HA; B/Brisbane/60/2008-like strain used (B/Brisbane/60/2008, wild type) 15 µg HA. Abbott Laboratories S.A. (Pty) Ltd, Reg. No. 1940/014043/07, Abbott Place, 219 Golf Club Terrace, Constantia Kloof, 1709. Tel No.: 011 858 2000 For full prescribing information refer to the package insert approved by the medicines regulatory authority. Date of publication: March 2016 Promotional Review Number: ZAEINF150254.

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## How do Global Influenza Surveillance and Response System personnel make a recommendation as to which viruses should be included in the influenza vaccine?

Flu viruses need to be monitored continuously because they constantly evolve. GISRS personnel base their recommendations on data collected globally throughout the year. Informal consultations were held in Geneva in 2010, 2011 and 2014, with the aim of improving this vaccine selection process.<sup>8</sup>

Antibody responses to the flu virus, how well vaccinated people are able to mount an attack against circulating flu viruses, the genetic character of the viruses, whether or not these viruses are susceptible to available antiviral drugs, the efficacy of current vaccinations, and the availability of the culture medium, are also taken into account when compiling the recommendations.<sup>6</sup>

Interestingly, it may be possible to predict the next flu season's predominant strains by monitoring children's seroconversion rates to the current circulating flu viruses in the preceding season.<sup>5</sup>

## When is the influenza season in the Northern Hemisphere, and what is the recommended composition of the 2015/2016 influenza vaccine?

The flu season in the Northern Hemisphere typically runs from November through to April.<sup>9</sup> As of February 2015, the WHO recommended that the trivalent flu vaccine for the 2015/2016 flu season should contain the following:

- An A/California/7/2009 (H1N1)pdm09-like virus
- An A/Switzerland/9715293/2013 (H3N2)-like virus
- An B/Phuket/3073/2013-like virus.

If a quadrivalent vaccine is to be produced, the WHO recommends that it contains the above viruses, as well as a B/Brisbane/60/2008-like virus<sup>10</sup> (not available in South Africa).

## When is the influenza season in the Southern Hemisphere, and what is the recommended composition of the 2016 influenza vaccine?

The flu season in the Southern Hemisphere is between April and September.<sup>9</sup> The recommended trivalent vaccine for the 2016 flu season comprises:

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

The WHO recommends that if a quadrivalent vaccine is produced, that a B/Phuket/3073/2013-like virus should be added, in addition to the previously mentioned viruses.<sup>10</sup> Quadrivalent vaccines are not available in South Africa.

## How does the influenza virus spread?

During the cold winter months, people tend to spend more time indoors, and in close proximity to one another.<sup>1</sup> The flu virus is an airborne virus, and is transmitted from person to person through infected sputum by sneezing or coughing.<sup>1</sup> The infected droplets are inhaled, or may be spread through contact with contaminated surfaces.<sup>11</sup>

## Influenza symptoms and those at greatest risk of complications

Flu viruses continually evolve.<sup>11</sup> Millions of people contract a new flu infection annually for this reason. While many cases of flu are uncomplicated, high-risk groups are more likely to be susceptible to complications arising from flu.<sup>11</sup>

The symptoms of uncomplicated flu include:

- Fever
- Muscle fatigue
- Headaches
- A sore throat
- A dry cough
- A "runny" or blocked nose
- Malaise.

Gastrointestinal symptoms may also occur in children.<sup>1</sup>

These symptoms are generally self-limiting, and resolve within 5-7 days. However, muscle fatigue may persist for > 2 weeks.<sup>11</sup>

Complications from flu can be severe, and usually require hospitalisation. The progression from uncomplicated to complicated flu may not be distinct, but can include the progressive deterioration of symptoms, such as persistent fever, vomiting and difficulty breathing.<sup>11</sup>

Complications arising from flu include:

- Viral pneumonia
- Secondary bacterial or viral infections
- Multi-organ failure
- Rarely: encephalopathy, myocarditis, transverse myelitis, pericarditis and Reye's syndrome (rarely)
- Worsening of chronic illnesses, especially in those with metabolic, pulmonary and cardiac conditions.<sup>11</sup>

People at highest risk of developing flu complications include pregnant women (including up to two weeks after pregnancy), children aged < 5 years (especially those aged < 2 years), the elderly (aged > 65 years), people with chronic illnesses (including chronic neurological illnesses), immunocompromised people, children aged < 19 years receiving chronic aspirin therapy, and the morbidly obese with a body mass index (BMI) > 40 kg/m<sup>2</sup>.<sup>12</sup>

The best way of preventing flu is by vaccination with an annual flu vaccine.<sup>12</sup> The vaccine is generally most effective in healthy people

between the ages of 2 and 65 years.<sup>11</sup> The flu vaccine will not protect against all strains of flu viruses, e.g. the influenza C virus, nor will it protect against infections caused by other viruses which may present with flu-like symptoms.<sup>2</sup>

Although the overall efficacy of the flu vaccine is dependent upon a good correlation existing between the vaccine and the circulating flu virus that season, as well as the age and immunocompetency of the person vaccinated, the vaccine still provides protection.<sup>11</sup>

### Which influenza vaccines are available in South Africa?

Although different flu vaccines are available globally, currently only a trivalent inactivated split influenza virus vaccine is available in South Africa. The vaccine is cultivated on embryonated eggs.<sup>13</sup>

### Which high-risk groups would benefit from receiving the influenza vaccine?

#### Pregnant women

During pregnancy, women are at higher risk of developing severe complications from flu.<sup>14</sup> This is owing to the cardiovascular, pulmonary and immune system changes which occur as a result of pregnancy, leading to a greater risk of hospitalisation.<sup>11</sup> This risk continues throughout pregnancy, and up to two weeks after birth.<sup>11</sup> As a consequence of flu during pregnancy, infants may be born prematurely, be of low birth size and weight, and at increased risk of mortality.<sup>14</sup>

The inactivated flu vaccine has been found to be effective and well tolerated in pregnant women through any stage of their pregnancy.<sup>14</sup> It has also been shown that vaccinating pregnant women against the flu virus induces passive immunity in the infant, and may continue to protect the baby up to six months after birth.<sup>11,12</sup>

#### Elderly (aged > 65 years)

Elderly patients, with or without chronic illnesses, are at a much higher risk of death from complications from flu, especially if hospitalised for pneumonia.<sup>5</sup> Most deaths from flu in industrialised countries occur in people aged > 65 years.<sup>9</sup> The severity of flu infections in the elderly may be exacerbated by a decrease in the strength and capacity of the respiratory system, as well as a decrease in the immune response to new antigens.<sup>5</sup>

Compared to younger individuals, adults aged > 65 years may not have an optimal response to the inactivated flu vaccine, as was shown in a study in 2010.<sup>11,15</sup> It was demonstrated that antibody titres rapidly declined six months after the flu vaccination was administered in this age group.<sup>15</sup> However, even after taking this into account, the flu vaccine was shown to offer protection in this patient population.<sup>11</sup> It has been demonstrated that there is no benefit to receiving a second flu vaccination in the same season.<sup>16</sup>

It was shown in a study carried out over three years that flu-related hospitalisations decreased by 61% in people aged > 50 years who had received the flu vaccine.<sup>12</sup> It is important to note that delaying flu vaccination in the elderly in order to provide better immunity later in the flu season could result in the opportunity to vaccinate being lost, and a larger number of people needed vaccination within a limited period.<sup>15</sup> In addition to vaccinating all adults aged > 65 years against the flu, it is also recommended that people who live in retirement facilities, chronic care and rehabilitation institutions should receive the flu vaccine.<sup>17</sup>

#### Children aged 6 months to 59 months

Children aged < 5 years often need medical attention because of flu. Complications from flu in the age group < 2 years is particularly concerning. Annually, over 20 000 children aged < 5 years are hospitalised because of flu complications.<sup>18</sup>

A better response to the inactivated flu vaccine is seen in children aged > 2 years, as opposed to those aged < 2 years, who tend to mount a poorer immune response. However, even after this was taken into account, the flu vaccine still offered protection in this age group.<sup>17</sup> Infants aged < 6 months cannot be vaccinated against flu, and are particularly vulnerable to serious complications therefrom.<sup>14</sup> Infants in this vulnerable age group may be best protected by vaccinating all adults and children who are in close contact with them.<sup>11</sup>

Table I illustrates the flu vaccine dosage requirements for children aged 6 months through 8 years.<sup>11</sup>

**Table I:** Influenza vaccine dosage requirements for children aged 6 months through 8 years<sup>11</sup>

Adults and children aged > 9 years	Adult dose: 0.5 ml intramuscularly (a single dose)
Children aged 3–8 years	Adult dose: 0.5 ml intramuscularly (1 or 2 doses)*
Children aged 6 months through 2 years	Child dose: 0.25 ml (half an adult dose) intramuscularly (1 or 2 doses)*

\* Children aged 6 months through 8 years who have never received a flu vaccine before require two influenza vaccinations, separated by four weeks, in order to mount a proper immune response<sup>11</sup>

#### Children on long-term aspirin therapy

Owing to the increased risk of Reye's Syndrome, flu vaccination is recommended in children aged < 18 years while taking aspirin.<sup>11</sup>

#### Immunosuppressed patients and those with chronic medical conditions

People with certain chronic illnesses, and/or who with immunosuppression, are at high risk of flu, as well as developing serious complications therefrom.<sup>14</sup> During the 2009 pandemic, the highest mortality rate was recorded in people with immunosuppression, as well as in those with chronic respiratory and

neurological diseases.<sup>14</sup>

The flu vaccine is of benefit to young and old patients with chronic health conditions.<sup>12</sup> Chronic illnesses include (the list is not exhaustive) asthma, blood disorders, chronic lung diseases, diabetes mellitus, cardiovascular diseases, kidney, liver and neurological disorders, and the morbidly obese (BMI > 40 kg/m<sup>2</sup>).<sup>12</sup>

Individuals who are immunocompromised due to disease, e.g. human immunodeficiency virus patients with a CD4 count of > 100 cells/μl, or on treatment, e.g. chemotherapy, should receive the inactivated flu vaccine.<sup>11,14</sup> Immunosuppressed individuals may not mount a full immune response to the vaccine. It is of benefit for caregivers and close contacts to be vaccinated against flu as well.<sup>14</sup>

Vaccines must be given at a certain time to patients with certain conditions that cause immunosuppression, e.g. to stem cell, solid organ transplant and asplenic patients. It is best to refer to specific guidelines or to the attending physician with regard to the selection and timing of vaccination for individual conditions.<sup>14,15</sup>

### Healthcare workers

Vaccinating against flu not only protects healthcare workers, but also their patients.<sup>11</sup> This reduces the incidence of absenteeism due to illness, and acts as a barrier against the spread of flu.<sup>11</sup>

### When is the best time to vaccinate?

The flu season typically coincides with the winter season in the Northern and Southern Hemispheres.<sup>7</sup> The flu season usually starts around the beginning of June and lasts for approximately 12 weeks in South Africa. However, the start and duration of the flu season may also vary.<sup>11</sup> It takes approximately two weeks to develop a protective immune response to the flu vaccine. Therefore, vaccinating before the onset of the flu season is optimal.<sup>11</sup>

### Why is the influenza vaccine needed every year?

Revaccination every year is important as protection levels from the flu vaccine wane after one flu season. The circulating flu virus may also have changed from the previous season.<sup>14</sup>

### Who should not receive the influenza vaccine?

Any person who has had an anaphylactic reaction to egg protein or to any component of the flu vaccine should not be vaccinated.<sup>14</sup> As safety studies have not been conducted on the flu vaccine in children aged < 6 months, the flu vaccine is contraindicated in this age group.<sup>11</sup>

Caution should be exercised with respect to vaccinating any person who developed Guillain-Barré syndrome within six weeks of receiving the flu vaccine. It is also best to delay vaccinating a

person with a moderate illness, with or without a fever, until the person is asymptomatic.<sup>11</sup>

### Can the influenza vaccination cause influenza?

The flu vaccination that is available in South Africa is inactivated, and therefore cannot cause flu.<sup>16</sup> Many viruses circulate during the winter season with symptoms that are similar to those that accompany flu. Since the vaccine can only protect against the flu virus, it cannot offer protection against any other viruses. Different flu viruses also circulate which are not included in the flu vaccine, which may give rise to flu. Exposure to a flu virus before the vaccine has been able to mount an immune response in the body (usually two weeks) may lead to the person contracting flu. The flu vaccine may not offer sufficient protection against flu in some people, especially those aged > 65 years or in the immunocompromised.<sup>16</sup>

### Influenza vaccine tips for travellers

People travelling to tropical areas should bear in mind that these areas have no distinct flu season. Summertime outbreaks of flu have occurred on cruise ships in both the Northern and Southern Hemispheres. A flu vaccine is recommended in travellers who have not already timeously received the flu vaccine from the previous season.<sup>5</sup>

Travellers should consider flu vaccination if:

- They fall into a high-risk category and are entering another hemisphere during the flu season. (Note that the flu vaccine for that hemisphere may not be available in the country of origin. Therefore, travellers may only be able to receive the vaccine once they have arrived at their destination)<sup>9</sup>
- They are attending the Hajj<sup>9</sup>
- They fall into a high-risk category and are going on a cruise<sup>9</sup>
- They are travelling with a high-risk group.<sup>9</sup>

### Conclusion

While the efficacy of the flu vaccine is dependent on a good “match” existing between the circulating virus and vaccine, as well as the immune status of the patient, the best way of preventing complications in the general population, such as hospitalisation from flu, is by receiving the annual flu vaccine.<sup>12</sup>

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