

Understanding flu vaccination

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Abstract

Circulating influenza (flu) viruses are continuously undergoing change, which makes the public more vulnerable to contracting flu. While anyone may develop complications from influenza, there are certain high-risk groups who are more vulnerable to life-threatening complications. Healthcare workers are in the ideal position to identify high-risk groups and to recommend annual flu vaccination. Carefully explaining the benefits and allaying certain misconceptions regarding flu vaccination will help increase the number of people receiving the flu vaccine annually, thereby decreasing the high morbidity and mortality rate due to influenza.

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Introduction

Key to understanding the influenza (flu) vaccine and how it is developed is having an idea as to the structure of the flu virus and how it mutates. This article will briefly explain the latter and focus on answering many of the commonly asked questions regarding the influenza vaccine.

Structure and mutation of the influenza virus

Influenza 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 of flu.¹ The influenza C virus may cause mild infection of the respiratory tract, but is generally of little concern.^{1,2}

The two proteins on the surface of the envelope surrounding the virus, haemagglutinin (H) and neuraminidase (N), determine the subtype of the influenza A virus.² 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.^{1,3} Within the envelope is the influenza genome consisting of a single strand of RNA divided into eight segments (influenza A and B only), while the C virus has seven segments.^{1,4}

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.²

Influenza A viruses may undergo a process called antigenic shift which has resulted in new subtypes or strains causing epidemics and pandemics. Major genetic changes occur in H and N. A large variety of animals, most commonly birds, pigs and humans, may be hosts to influenza A viruses and this leads to a "mixing" of genetic information and new subtypes emerging. These new subtypes may infect humans who have not developed resistance, leading to pandemics.¹ 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 that humans had not been exposed to before.⁵ This strain no longer causes pandemics, but is now one of the prevalent circulating strains responsible for seasonal influenza.³

Seasonal influenza occurs due to minor changes in the virus antibody-binding sites over a period of time as the ribonucleic amino acids (RNA) mutate. This process is called antigenic drift. Both influenza A and B viruses undergo antigenic drift.¹

Which organisation selects the composition for the following season's flu vaccine?

The World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS) is a global network that meets twice a year, in February (to recommend which viruses should be included in the flu vaccine for

the upcoming Northern Hemisphere's flu season) and September (to recommend the Southern Hemisphere's flu season vaccine composition).^{6,7} Due to tropical areas having no distinct flu season, each individual national and regional authority would make a decision based on epidemiological studies as to which vaccine, February or September, would be appropriate.^{5,7}

How does the GISRS make a recommendation as to which viruses should be included in the flu vaccine?

The influenza viruses need to be monitored continuously due to their constant evolution. The GISRS base their recommendations on data collected globally throughout the year. Informal consultations have been held in Geneva in 2010, 2011 and 2014 with the aim of improving this vaccine selection process.⁸

The recommendations also take into consideration the antibody responses to the influenza virus, how well vaccinated people are able to mount an attack against circulating influenza 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.⁶

An interesting observation is that it may be possible to predict the next flu season's predominant strains by monitoring children's seroconversion rates to the current circulating influenza viruses in the preceding season.⁵

When is the Northern Hemisphere's flu season and what was the recommended composition for the 2018/2019 flu vaccine?

The Northern Hemisphere's flu season typically runs from November through April.⁹ The World Health Organization recommended, as of February 2018, that the trivalent flu vaccine for the 2018/2019 flu season contain the following:

- an A/Michigan/45/2015 (H1N1)pdm09-like virus;
- an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus;
- a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage).

If a quadrivalent vaccine is to be produced, WHO recommends that it contain the above viruses as well as a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).¹⁰

When is the Southern Hemisphere's flu season and what is the recommended composition for the 2019 flu vaccine?

Flu season in the Southern Hemisphere is normally between April and September.⁹ The recommended trivalent vaccine for the 2019 flu season is:

- an A/Michigan/45/2015 (H1N1)pdm09-like virus;

- an A/Switzerland/8060/2017 (H3N2)-like virus; and
- a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage).

The WHO recommends that if a quadrivalent vaccine is produced, a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) be added in addition to above viruses.¹⁰

How does the flu virus spread?

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

Symptoms of flu and those at greatest risk of complications

Flu viruses are continually evolving.¹¹ For this reason, millions of people contract a new influenza infection annually. While many cases of influenza are uncomplicated, there are high-risk groups who are more likely to be susceptible to complications arising from contracting flu.¹¹

Symptoms of uncomplicated flu include:

- Fever
- Muscle fatigue
- Headache
- Sore throat
- Dry cough
- Runny or blocked nose
- Malaise
- *Note:* Gastrointestinal symptoms may occur in children¹

These symptoms are generally self-limiting and resolve within five to seven days. However, muscle fatigue may persist for more than two weeks.¹¹

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

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.
- Worsening of chronic illnesses, especially in those with metabolic, pulmonary and cardiac conditions.¹¹

People at highest risk of developing complications from

flu include: pregnant women, (including up to two weeks after delivery); children under five years of age (especially under two years of age); the elderly over the age of 65 years; people with chronic illnesses (including chronic neurological illnesses); immunocompromised people; children under the age of 19 years receiving chronic aspirin therapy and morbidly obese (BMI ≥ 40) people.¹²

The best way to prevent flu is by vaccination with the annual flu vaccine.¹² The vaccine is generally most effective in healthy people between the ages of two and 65 years of age.¹¹ The flu vaccine will not protect against all strains of flu viruses, e.g. influenza C viruses, nor will it protect against infections caused by other viruses which may present with flu-like symptoms.²

Although the overall efficacy of the flu vaccine is dependent on there being a good correlation between the vaccine and the circulating flu viruses that season, as well as the age and immunocompetency of the person vaccinated, the vaccine will still provide protection.¹¹

Which flu vaccines will be available in South Africa?

South Africa is expecting to have a trivalent, as well as a quadrivalent, inactive influenza vaccine available this year.^{10,13}

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

Pregnant women

During pregnancy, women are at a higher risk of developing severe complications from influenza.¹⁴ This is due to the cardiovascular, pulmonary and immune system changes that occur as a result of the pregnancy, leading to a greater risk of hospitalisation.¹¹ This risk continues throughout pregnancy and including two weeks after birth.¹¹ As a consequence of influenza in pregnancy, babies may also be born prematurely, have lower birth size, weight and an increased risk of mortality.¹⁴

The inactive flu vaccine has been found to be effective and well-tolerated in pregnant women through any stage of their pregnancy.¹⁴ 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.^{11,12}

Elderly (65 years and over)

Elderly patients, with or without chronic illnesses, are at a much higher risk of death from complications of influenza, especially if hospitalised for pneumonia.⁵ In industrialised countries, most deaths from influenza occur in people over the age of 65 years.⁹ The severity of influenza 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.⁵

Adults over the age of 65 may not have an optimal response to the inactivated flu vaccine compared to younger individuals.^{11,15} In a study conducted in 2010, it was shown that antibody titres rapidly declined six months after the flu vaccine was administered in this age group.¹⁵ However, even when taking this into account, the flu vaccine offers protection in this patient population.¹¹ However, there is no benefit to receiving a second flu vaccination in the same season.¹⁶

A study done over three years showed that flu-related hospitalisations decreased by 61% in people over 50 years who had received the flu vaccine.¹² It is important to note that delaying flu vaccination in the elderly in order to provide better immunity later in the flu season, may result in losing the opportunity to vaccinate and also having a larger volume of people to vaccinate within a limited time period.¹⁵ In addition to vaccinating all adults over 65 years against the flu, it is also recommended that people living in retirement facilities, chronic care and rehabilitation institutions also receive the flu vaccine.¹⁷

Children aged six months to 59 months

Children under the age of five years often need medical attention because of influenza. Of particular concern for complications from influenza, is the under-two-year age group. Annually over 20 000 children under five years are hospitalised due to influenza complications.¹⁸

A better response to the inactivated flu vaccine is seen in children from two years of age as opposed to the under-two-year age group, who tend to have a poorer immune response. However, even with taking this into account, the flu vaccine will still offer protection for this age group.¹⁷ Babies under six months cannot be vaccinated against flu and are particularly vulnerable to serious complications from influenza.¹⁴ This vulnerable age group may be best protected by vaccinating all adults and children who are close contacts of the infant.¹¹

Table I. Dosage requirements for children from six months to their ninth birthday (trivalent vaccine)

Adults and children nine years of age and older	Adult dose (0,5 ml) IMI single dose
Children three years to their ninth birthday	Adult dose (0,5 ml) IMI 1 or 2 doses*
Children six months up to 35 months	0.25 ml (half an adult dose) IMI 1 or 2 doses*

*All children aged six months to ninth birthday who have never received a flu vaccine before, require two influenza vaccinations separated by four weeks in order to mount a proper immune response.¹¹

Table I illustrates the dosage requirements for children from six months to their ninth birthday (trivalent vaccine)*.

Children on long-term aspirin therapy

Influenza vaccination is recommended due to the increased risk of Reye's syndrome in children under 18 years developing flu while taking aspirin.¹¹

Immunosuppressed patients and those with chronic medical conditions

People with certain chronic illnesses and/or who are immunosuppressed are at high risk of influenza, as well as developing serious complications from influenza.¹⁴ During the 2009 pandemic, people who were immunosuppressed, as well as those with chronic respiratory and neurological diseases, had the highest mortality rate.¹⁴

The flu vaccine is of benefit to young and old with chronic health conditions.¹² Chronic illnesses include (list is not exhaustive): asthma, blood disorders, chronic lung diseases, diabetes, cardiovascular diseases, kidney disorders, liver disorders, neurological disorders as well as morbid obesity (BMI \geq 40).¹²

Immunocompromised individuals due to disease (e.g. HIV patients with CD4 counts $>$ 100 cells/ μ L), or on treatment (e.g. chemotherapy), should receive the inactivated flu vaccine.^{11,14} 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 influenza as well.¹⁴

Certain conditions causing immunosuppression require that vaccines be given at a certain time (e.g. stem cell, solid organ transplant and asplenic patients). It is best to refer to specific guidelines or the attending physician regarding the selection and timing of vaccination for individual conditions.^{14,15}

Healthcare workers

Vaccinating against influenza not only protects the healthcare worker, but also their patients.¹¹ This reduces the incidence of absenteeism due to illness and acts as a barrier for the spread of influenza.¹¹

Any person over six months should receive the annual influenza vaccine to reduce the risk of influenza

When is the best time to vaccinate?

The flu season typically coincides with the winter season in the Northern and Southern Hemispheres.⁷ In South Africa, the flu season usually starts around the beginning of June and lasts for approximately 12 weeks. The start and duration of the flu season may, however, also vary from these averages.¹¹ It takes about two weeks to develop a protective immune

response to the flu vaccine, therefore vaccinating before the onset of the flu season is optimal.¹¹

Why do we need a flu vaccine 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.¹⁴

Who should *not* get the flu vaccine?

Egg allergy: Egg allergy is no longer a contraindication to receiving the influenza vaccine.¹⁹ Adults and children who have experienced only hives after eating egg can receive the flu vaccine without following any additional special precautions. Adults and children who have experienced an anaphylactic reaction after ingestion of egg, should be vaccinated in a controlled medical setting, such as a doctor's office, where severe allergic reactions may be recognised and managed should they occur.¹⁹

As there have been no safety studies in children under six months of age, the flu vaccine is contraindicated in this age group.¹¹

Caution should be exercised for 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.¹¹

Can the flu vaccination cause flu?

The flu vaccination available in South Africa is inactivated and therefore cannot cause flu.¹⁶ There are many viruses circulating during the winter season with symptoms similar to flu. Since the vaccine can only protect against the flu virus, it cannot offer protection against any other viruses. There are also different flu viruses circulating 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 takes two weeks), may lead to the person contracting flu. For some people, especially those over 65 years or the immunocompromised, the flu vaccine may not offer sufficient protection against flu.¹⁶

Flu vaccine tips for travellers

People travelling to tropical areas should bear in mind that these areas have no distinct flu season. Cruise ships have had summertime outbreaks of flu in the Northern and Southern Hemispheres. A flu vaccine would be recommended to travellers who have not already timeously received the previous flu season vaccine.⁵

Travellers should consider flu vaccination if:

- In a high risk category (see above) and entering another hemisphere's flu season (note that the flu vaccine for that

hemisphere may not be available in country of origin, therefore they may only be able to receive the vaccine once arriving at destination)⁹

- Attending the Hajj⁹
- The patient falls into a high-risk group and is going on a cruise⁹
- Travelling with high-risk groups in order to prevent possible disruptions due to influenza⁹

Conclusion

While the efficacy of the flu vaccine is dependent on there being a good “match” between the circulating virus and vaccine, as well as the immune status of the patient, the best way to prevent complications such as hospitalisation from flu in the general population is through receiving the annual flu vaccine.¹²

*Please refer to the package insert for the quadrivalent influenza vaccine for indications and dose recommendations, as these differ from the available trivalent influenza vaccine.²⁰

References

1. Davidson M. The Florida State University. The Influenza (Flu) Virus. [Online]. ©2015 [cited 2015 November 11]. Available from : <http://micro.magnet.fsu.edu/cells/viruses/influenzavirus.html>
2. Centers for Disease Control and Prevention. Types of Influenza Viruses. [Online]. [updated 2014 Aug 19; cited 2015 Nov 23]. Available from: <http://www.cdc.gov/flu/about/viruses/types.htm>
3. World Health Organization. Influenza virus infections in humans. [Online]. 2014 [cited 2015 Nov 26]. Available from: http://www.who.int/influenza/human_animal_interface/virology_laboratories_and_vaccines/influenza_virus_infections_humans_feb14.pdf
4. World Health Organization. Influenza. [Online]. [updated 2014 October 2; cited 2015 Nov 26]. Available from: <http://www.who.int/biologicals/vaccines/influenza/en/>
5. Dolin R. Epidemiology of influenza. In: UpToDate. [homepage on the internet]. ©2015 [cited 2015 Nov 23].
6. World Health Organisation. Questions and Answers. [Online]. [updated 2015 Oct 13; cited 2015 Nov 26]. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/201509_qanda_recommendation.pdf?ua=1
7. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2015-2016 northern hemisphere influenza season. ©2015 [cited 2015 Nov 26]. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/201509_recommendation.pdf?ua=1
8. World Health Organization. 4th WHO Informal Consultation on Improving Influenza Vaccine Virus Selection. [Online]. ©2015 [cited 2015 Nov 23]. Available from: http://www.who.int/influenza/vaccines/virus/4thmtg_improve_vaccine_virus_selection/en/
9. Health Protection Scotland, NHS National Services Scotland. Influenza. Travax. [updated 5 Nov 2018; cited 18 Feb 2019].
10. WHO recommendations on the composition of influenza virus vaccines. [Online]. 2019 [cited 18 Feb 2019]. Available from: <https://www.who.int/influenza/vaccines/virus/recommendations/en/>
11. NICD. Healthcare Workers Handbook on Influenza. [Online]. [updated 2015 May; cited 2015 Nov 23]. Available from: http://www.nicd.ac.za/assets/files/Healthcare%20Workers%20Handbook%20on%20influenza%20in%20SA_%205%20May%202015.pdf
12. Centers for Disease Control and Prevention. What are the Benefits of Flu Vaccination? ©2015 [cited 2015 Nov 23]. Available online: <http://www.cdc.gov/flu/pdf/freeresources/general/flu-vaccine-benefits.pdf>
13. Sanofi Pasteur. Vaxigrip® Prescribing Information October 2018 [from letter October 2018; cited 18 Feb 2019].
14. Influenza: the green book, chapter 19. [Online]. [updated 2015 Aug 28; cited 2015 Nov 26]. Available from: <https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19>
15. Grohskopf LA, Sokolow LZ, Olsen SJ, et al. Prevention and Control of Influenza with Vaccines: Recommendations of the ACIP, United States, 2015-16 Influenza Season. MMWR 2015 Aug 7;64(30):818-825. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6430a3.htm>
16. Centers for Disease Control and Prevention. Misconceptions about Seasonal Flu and Flu Vaccines. [Online]. [updated 2015 September 8; cited 2015 Dec 2] Available from: <http://www.cdc.gov/flu/about/qa/misconceptions.htm>
17. Walaza S, Cohen C. Recommendations pertaining to the use of influenza vaccines and influenza antiviral drugs: Influenza 2015. SAMJ 2015 Feb; 105 (2).
18. Children, the Flu, and the Flu Vaccine. In: CDC. [Online]. ©2015 [updated 2015 Aug 21; cited 2015 Nov 24]. Available from: <http://www.cdc.gov/flu/protect/children.htm>
19. Immunization Action Coalition. Ask the Experts. Influenza. [updated 16 Oct 2018; cited 20 Feb 2019]. Available from: http://www.immunize.org/askexperts/experts_inf.asp
20. VaxigripTetra® 2019 strains. Package Insert. Sanofi Pasteur SA. December 2018.