

# Influenza: prevention, prophylaxis and treatment

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## Abstract

Influenza spreads rapidly to affect 515% of the global population on an annual basis. It is estimated that influenza causes between three and five million cases of severe illness and between a quarter and half a million deaths every year. In South Africa during the period from 1997 to 2001, influenza and pneumonia combined was one of the top five causes of death for both males and females.<sup>1</sup> Influenza illness causes substantial morbidity and mortality, with healthcare costs and lost productivity due to absenteeism resulting in both direct and indirect costs and, ultimately, a formidable economic burden.<sup>2</sup>

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## Introduction

The general practitioner's role in flu prevention and treatment extends much further than simply providing a convenient and accessible cold-chain outlet of flu vaccines and offering symptomatic treatment. Early flu patients present often to the pharmacists or clinic nurse first and these health care workers should be educated to refer patients to the family practitioner for early antiviral treatment. Early antiviral treatment (within 48 hours) can be given to patients with flu to reduce secondary complications, reduce the spread of influenza to high-risk patients and to shorten the duration of illness. It can also reduce the severity of flu, even in vaccinated individuals who have developed flu. It can also be given as post-exposure prophylaxis in high-risk patients.

## More about the influenza virus

The influenza virus, which causes influenza, is a single-stranded, helical-shaped, RNA virus that belongs to the orthomyxoviridae family. Nuclear material of the virus determines the antigen types of A, B and C. The influenza virus has surface antigens haemagglutinin (H) for viral attachment to host cells, and neuraminidase (N) for viral penetration in host cells. These H and N surface antigens denote the different subtypes. Influenza A tends to cause moderate to severe illness in all age groups, and can infect humans and animals, including birds. Influenza B causes milder disease only in humans, primarily in children. Influenza C has rarely been reported to affect humans. The problem with the influenza virus is that it undergoes antigenic drift, which means that new strains evolve that are related to those circulating during previous epidemics. Antigenic shift refers to the emergence of a new virus that possesses novel haemagglutinins with/ or a novel neuraminidase. This virus is distinct from earlier viruses and arises through mutations.<sup>3,4,5</sup>

Influenza is a highly infectious disease that primarily attacks the respiratory system. It is transmitted by inhalation of microdroplets,<sup>3</sup> after which the virus attaches to and penetrates the respiratory epithelial cells in the trachea and bronchi where viral replication occurs to destroy the host cell.<sup>4</sup>

## Symptoms and signs

The symptoms of influenza begin after an incubation period of between one and four days, and resemble the common cold at first with a sore throat and rhinorrhoea. Sudden onset chills, fever, malaise, generalised body aches and pains signify typical influenza in adults. Associated symptoms include photophobia and headache. The respiratory symptoms tend to progress from a scratchy sore throat, substernal burning and non-productive cough to persistent, raspy and productive cough. The cough, weakness, sweating and fatigue can last for a couple of weeks. Pneumonia, a complication of influenza, is suggested by worsening cough with bloody or purulent sputum, or dyspnoea.<sup>6</sup> Influenza in young children is difficult to diagnose as it is often indistinguishable from other respiratory infections because there are no unique symptoms specific to influenza.<sup>7</sup> Children can, however, present with prominent nausea, vomiting and abdominal pain during an episode of influenza.<sup>6</sup> The influenza virus is found to circulate with the respiratory syncytial virus (RSV), and thus children who present with influenza-like symptoms may have more than one virus present simultaneously. The complications that arise from influenza may be a consequence of the influenza or due to secondary bacterial infections. The complications include febrile convulsions, bronchiolitis, pneumonia, croup, acute otitis media and encephalitis. Influenza is highly contagious in children due to a short viral replication cycle and prolonged viral shedding.<sup>7</sup> See Table I for flu and cold symptoms.

## Vaccination

The influenza vaccination is an important factor in combating influenza and is advocated for the primary prevention of influenza in people who have not been infected with the strain of influenza currently in circulation. The vaccines that are currently available in South Africa are all inactivated vaccines and they consist of 1) whole virus vaccines prepared from formalin-inactivated whole virions grown in embryonated chicken eggs, 2) split vaccines produced the same way as whole virus vaccines, but the virus particles are disrupted using detergents, and 3) subunit vaccines that consist of purified HA and NA proteins with the rest of the viral components removed.<sup>5</sup>

**Table 1:** Flu and cold symptoms

Symptom/Sign	Flu	Cold
<b>Fever</b>	Common A fever of more than 39°C is more likely to be flu	Rare If the patient's temperature is normal it is more likely to be a cold
<b>Aches</b>	Common and severe, prominent headache	Slight, rarely headaches
<b>Coughs</b>	Common and severe	Less common, mild to moderate
<b>Tiredness</b>	Common and severe Causes absenteeism: "I cannot go to work"	Mild Causes absenteeism: "I do not want to go to work"
<b>Speed of onset</b>	Sudden	Gradual

Adapted from www.fluworld.com

A Cochrane review of vaccination against influenza in healthy adults failed to demonstrate a beneficial effect with regards to reducing the spread of the virus, and showed limited effects on reducing working days lost, morbidity and hospitalisations. The authors, therefore, concluded that routine vaccination of healthy adults should not be advocated based on current evidence. However, in the elderly, especially those that are deemed high risk, vaccinations help to reduce the risk of being hospitalised for complications such as pneumonia.<sup>8,9,10</sup> Another Cochrane review of the influenza vaccine in healthy children showed little evidence for routine vaccination in this group. Some of the studies may have indicated a decrease in acute otitis media and absenteeism from school. The authors concluded that further studies are required to evaluate the effects of the vaccine with regards to efficacy and other mentioned end-points. From this information it can be seen that vaccination should be limited to those in the high-risk group.<sup>11</sup>

### High-risk groups

- Individuals (adults and children) with chronic medical conditions such as pulmonary, cardiac, renal and metabolic diseases such as diabetes mellitus. Vaccinations of diabetics results in a reduction in hospitalisations for reasons of diabetic control.<sup>12</sup>
- Immunosuppressed adults, including those with HIV infection with CD4 counts between 200 and 500 cells/ $\mu$ l.<sup>13</sup> It has been shown that the influenza vaccine is safe in HIV-infected children, therefore its annual use should be advocated.<sup>14</sup> Immunosuppression includes patients with asplenia and splenic dysfunction.
- Inhabitants of chronic care and rehabilitation institutions, as well as old age homes.
- Healthcare personnel responsible for the care of the above-mentioned patients.
- Family members of the above-mentioned patients.
- All people over the age of 65 years.
- Women who will be in their second and third trimesters of pregnancy during the influenza season. Immunisation at any stage of pregnancy is recommended for women with chronic medical conditions.
- Any individuals who wish to protect themselves.
- Children on long-term aspirin therapy.<sup>5,13</sup>

### Patients with HIV

Patients infected with HIV have a much higher influenza-attributable mortality rate than the general population and the hospitalisation rates

are similar to those of other high-risk groups. Thus annual vaccination is important in these patients. There are no long-term effects on the CD4 count, HIV RNA levels or progression to AIDS in those patients who use the vaccine, thus healthcare professionals should not hesitate to vaccinate this group of high-risk patients to prevent complications. The live attenuated form of the influenza vaccine is contraindicated in HIV-positive patients.<sup>15</sup>

Dosages for each vaccine should be administered as indicated by the manufacturer guidelines and it should be noted that children below the age of eight years who have previously not been vaccinated need a second dose four weeks apart. Vaccines should be administered timeously, as a protective antibody response takes about two weeks to mount. The vaccine is contraindicated in people with an allergy to eggs and should also preferably be avoided during the first trimester of pregnancy and during a febrile illness.<sup>13</sup> Adverse effects of the vaccine are minimal, and include pain, redness and swelling at the site of injection, fever and a rash that may last a day or two. Vaccines are extremely safe and hypersensitivity reactions are rare.<sup>5,12,16</sup>

The vaccines to be used in the 2008 season (southern hemisphere winter) should contain the following strains of influenza virus:

- A/Solomon Islands/3/2006 (H1N1)-like virus
- A/Brisbane/10/2007 (H3N2)- like virus
- B/Florida/4/2006 – like virus<sup>2</sup>

Studies have shown that there are four factors that influence why patients remain unvaccinated. These are concern regarding side effects (i.e. believing that the vaccine causes influenza), lack of concern that the illness has any significance, feeling impervious to influenza and lack of healthcare provider directive. It is thus imperative that pharmacists be proactive and encourage especially high-risk patients to be vaccinated.<sup>17</sup>

### Post-exposure prophylaxis and treatment

Treatment of influenza is chiefly symptomatic, with currently utilised modalities including rest, hydration and occasional anti-pyretics. It should be noted that the use of aspirin is not advised in children during a viral illness. Oseltamivir is an oral antiviral agent (neuraminidase inhibitor) and is effective against influenza A and B. It can be used in the treatment of acute influenza to shorten the duration of disease, to reduce the severity and to prevent other complications such as pneumonia. It is also effective for post-exposure prophylaxis. It is registered for the treatment of patients above one year of age provided it is started within 48 hours of the commencement of symptoms.

Oseltamivir is also recommended for post-exposure prophylaxis in high-risk people who have had contact with another person who exhibits influenza-like symptoms and who have not been adequately protected by vaccination. Once again, prophylaxis needs to be commenced within 48 hours. It should be taken after meals to reduce nausea and vomiting.

Zanamavir is another neuraminidase inhibitor and inhibits a wide range of influenza viruses type A and B. It is administered through an inhaler and advocated for the treatment of patients above 12 years of age.<sup>12,18</sup>

Amantadine and rimantadine specifically inhibit the replication of the influenza A virus by blocking the proton pump of the M2 protein in the virus, but has no activity against influenza B. Both these antivirals are

relatively effective in the prophylaxis and treatment of influenza A. However, a Cochrane review recently indicated that these two antivirals should be kept for emergency situations when all other measures have failed. The NICE (National Institute for Clinical Excellence) guidelines recommended that amantadine should not be used for seasonal or post-exposure prophylaxis. The adverse effects of amantadine include light-headedness, hallucinations, insomnia, dizziness, headache and falls, particularly in the elderly. Drug resistance emerges rapidly with the use of amantadine. Rimantadine, not currently available in South Africa, is not routinely recommended due to its extensive neurological adverse effects, particularly in the elderly.<sup>19,20</sup>

#### Box 1: Summary of flu prevention, prophylaxis and treatment

##### Flu vaccination


- All people over the age of 65 years
- Individuals with chronic medical conditions
- Immunosuppressed adults and children
- Inhabitants of chronic care institutions
- Healthcare personnel treating high-risk people
- Family members of high-risk people
- Pregnant women
- Any individuals who wish to protect themselves
- Children on long-term aspirin therapy

##### Antiviral therapy

- Patients who present early with flu
- Any patient with acute flu (to reduce duration, severity and spreading)
- High-risk individuals with flu (to reduce duration and severity)
- High-risk patients exposed to flu

#### Conclusion

Influenza can be a devastating disease. However, timely vaccination of the afore-mentioned groups will help to combat the complications produced by this disease. Alternative strategies for prevention and

treatment exist but effectiveness, cost and side-effect profiles need to be kept in mind before recommendations can be made. 

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