

Influenza in children

Influenza, caused by influenza A or B virus, produces a spectrum of disease ranging from mild to severe illness. **Seasonal influenza** is common; in South Africa, the influenza season usually lasts from April until August. The World Health Organization estimates that 3 - 5 million cases of seasonal influenza occur every year, with around 250 000 - 500 000 deaths. The annual attack rate in developed countries is estimated at between 10% and 20% of adults but is higher in children, with approximately 1 in 3 children infected annually.¹ In South Africa, seasonal influenza is estimated to cause 6 000 - 10 000 deaths every winter.

Pandemic influenza occurs at regular periods when a circulating influenza strain or strains undergoes genetic reassortment or antigenic shift. This has recently occurred, leading to the current pandemic from influenza A H1N1 virus or swine flu. The causative virus, a novel influenza A H1N1 virus, seems to have originated in pigs; however, spread is predominantly between people. A pandemic has occurred because humans have little or no immunity to the new virus and it is easily transmitted from human to human.

Influenza viruses are spread from person to person mainly through droplet spread. Adults are infectious from the day before symptoms for approximately 5 days thereafter, but children can be infectious for longer periods, shedding virus for 10 or more days after the onset of symptoms.¹ Immunocompromised people can continue to shed virus for weeks or even months. Children are often the primary means of spread within the family

Clinical presentation and complications

Influenza illness is characterised by the **acute onset** of systemic and respiratory signs.^{1,2} The abrupt onset and systemic signs should enable influenza to be distinguished from a simple upper respiratory tract infection or common cold. Common signs of influenza include fever, myalgia, malaise, a non-productive cough, a sore throat, rhinitis, nausea and vomiting, and headache.

In infants and neonates nonspecific signs or fever alone may be the only presenting feature. For most children under 2 years of age, a clinical case definition includes sudden onset of **high fever, cough and rhinorrhoea during the influenza season or during a pandemic.**^{2,4} For children older than 2 years of age, sudden onset of **fever, cough, pharyngitis and headache during the influenza season or during a pandemic** have a sensitivity and specificity of approximately 80% each for the diagnosis of influenza.^{2,4} Other symptoms and signs include fatigue, occurring in 51 - 75% of cases, chills in 76 - 100% and conjunctivitis in 26 - 50%.

Young children or people with underlying chronic illness are at higher risk of developing complications.^{1,2,4} (Table I). The complication rate is higher in children than in adults, with approximately 20 - 30% of children under 2 years of age developing complications. Common complications include febrile convulsions, otitis media, sinusitis, bronchiolitis, croup and pneumonia.² Pneumonia may be caused by the influenza virus or by a secondary bacterial infection. Rates of hospitalisation and death are increased in young children under 2 years of age, especially in those under 6 months.

TABLE I. CHILDREN AT RISK OF COMPLICATIONS FROM INFLUENZA

- Chronic respiratory disease
- Immunodeficiency (including HIV)
- Chronic cardiac disease
- Chronic renal disease
- Chronic liver disease
- Diabetes
- Malignancy
- Haemoglobinopathy
- Chronic neurological disease, e.g. diseases with muscle weakness
- On chronic aspirin therapy

Reye's syndrome, encephalitis, pericarditis and myocarditis rarely occur as complications of influenza infection.^{2,4} Infection with the influenza virus may exacerbate an underlying chronic illness.

The symptoms and clinical presentation of children infected with the pandemic influenza A H1N1 influenza virus (swine flu) are similar to and indistinguishable from seasonal influenza. Fortunately the clinical illness currently occurring in those who do not have an underlying illness is mild, with case fatality rates reported to be approximately 100 times lower than those for seasonal influenza.⁵

Distinguishing illness caused by other respiratory viruses may be difficult on the basis of signs and symptoms and laboratory diagnostic confirmation may be useful.

Laboratory diagnosis

Laboratory testing of mild illness is *not* recommended by the National Institute of Communicable Diseases, as it provides little advantage to the clinical management of individual patients.⁶ Testing for pandemic influenza A (H1N1) is only recommended in the following circumstances:⁶

- Patients who have severe infections where a laboratory diagnosis will assist in management or patients hospitalised for a lower respiratory tract infection, where there is no other cause for their illness and influenza is part of the differential diagnosis.
- Patients with co-morbid disease and at risk for serious complications and who are symptomatic, to guide clinical management.
- Clusters of cases where a diagnosis of the cause of the outbreak is needed.
- When an individual has died and pandemic influenza A (H1N1) is suspected to be the cause of death.

A swab collected from each nostril and a throat swab pooled into the same container of viral transport medium is the specimen of choice.⁵ Nasopharyngeal swabs may be collected instead of nose and throat swabs as this provides a good specimen for viral detection and provides a higher yield than a throat swab.¹ Swabs or aspirates should be placed in a vial of viral transport medium that is stored and transported at 4°C and delivered promptly to the laboratory.⁶

Available diagnostic tests for influenza virus include viral culture, rapid antigen detection, immunofluorescence assays and polymerase chain reaction (PCR) testing; these are done on respiratory secretions. The sensitivity and specificity of testing depends on the test, the laboratory, the specimen and the timing of collection. The sensitivity of rapid tests (approximately 70%) is lower than that of culture. Rapid tests are least reliable when there is a low prevalence of circulating influenza viruses. However, rapid testing may provide a result within 30 minutes while culture takes 3 - 10 days. Consideration should be given to confirming a negative rapid test with culture or other means, given the lower sensitivity of rapid testing.^{1,4,5}

Treatment

Supportive and symptomatic therapy should be given to children.^{2,4,5} For those requiring hospitalisation, oxygen is a mainstay of treatment in hypoxic children. Children with secondary bacterial infection or who are severely ill with pneumonia requiring hospitalisation should also be treated with an antibiotic for community-acquired pneumonia according to national guidelines.^{2,7}

Antiviral agents with activity against influenza are effective for treatment. Possible agents include amantadine, rimantadine, zanamivir and oseltamivir.¹ Amantadine and rimantadine are effective only against influenza A virus. Because of high levels of resistance and the rapid emergence of resistance, these agents are not usually recommended for therapy for seasonal influenza.¹ The pandemic influenza A (H1N1) virus is resistant to amantadine and rimantadine.^{4,5}

Zanamivir and oseltamivir are neuraminidase inhibitors that are effective against both influenza A and B. Zanamivir is given intranasally, but is only approved for treatment in children from 12 years of age in South Africa. Oseltamivir is the only oral formulated neuraminidase inhibitor and is licensed for the treatment of influenza in children from 1 year of age. Although some seasonal influenza strains have been reported to be resistant to oseltamivir, the pandemic influenza A (H1N1) virus is currently sensitive to oseltamivir. Oseltamivir may reduce the complication rate from influenza in children by up to 40%, reduce the need for hospitalisation, the duration of hospitalisation in children already hospitalised and the duration of illness.⁸⁻¹¹ **Early diagnosis is essential, as treatment with oseltamivir should be initiated within the first 48 hours after the onset of illness.**^{2,8,11} However, for children hospitalised with pandemic influenza A (H1N1) virus, oseltamivir may be recommended for use for up to 5 days after the onset of illness.²

Indications for oseltamivir in children

Oseltamivir is indicated for treatment of influenza in children older than 1 year of age to reduce the risk of complications and severity of illness. Oseltamivir is specifically indicated in children:^{4,5, 8-11}

- with life-threatening influenza illness, *or*
- who are at high risk for complications of influenza.

Dosage of oseltamivir in children

Oseltamivir is available as a capsule (75 mg) or syrup (12 mg/ml). The recommended dosage is shown in Table II.

TABLE II. DOSAGE OF ORAL OSELTAMIVIR FOR TREATMENT OF INFLUENZA

Body weight	Dose
<15 kg	30 mg bd
15 - 23 kg	45 mg bd
>23 - 40 kg	60 mg bd
>40 kg	75 mg bd

Prevention of influenza

Immunisation

Immunisation is the most effective preventive strategy for seasonal influenza.^{1,4,12} Nevertheless, the rate of vaccination in South Africa is low, with only approximately 13% of adults vaccinated annually. Inactivated (killed) vaccine and live, attenuated vaccines have been produced, but only inactivated vaccines are currently available in South Africa. Inactivated vaccines may consist of whole virus, split products or viral subunit products. For children, split product or subunit vaccines are recommended. A specific vaccine formulation is recommended each year, according to the influenza strains that are predicted to be circulating that season, so annual vaccination is necessary.

Annual vaccination for seasonal influenza is recommended for children at high risk for influenza complications (Table I). In addition, annual routine immunisation of young children is recommended in some developed countries. In the USA, vaccination was routinely recommended for all children aged 6 months to 2 years; these recommendations have recently been extended to include all children under 5 years of age.¹ These recommendations were made because children aged under 2 years are at substantial risk for influenza-related hospitalisations, while those aged 2 - 5 years have an increased risk of influenza-related clinic and emergency department visits. Vaccination should also be recommended for family or household contacts of young children, particularly those under 6 months of age (who cannot be vaccinated but are at risk of more severe illness) and contacts of people at high risk of complications from influenza (Table III).¹² For example, all members living in a household with a HIV-infected child should be immunised to reduce the risk of transmission and the potential for severe illness in the child.

TABLE III. INDICATIONS FOR VACCINATION IN CHILDREN AND THEIR CAREGIVERS

- All children at high risk of complications from influenza (see Table I), including those with chronic pulmonary, cardiac, renal, hepatic, endocrine, neurological, metabolic or immunological disease
- Children on chronic aspirin therapy
- Adults and children who are family contacts of young children or contacts of high-risk people
- Caregivers older than 65 years
- Women in the second or third trimester of pregnancy during the influenza season
- Some countries recommend routine immunisation of all young children

Immunisation should be given according to the recommendations by the Department of Health and national guidelines.^{4,7,12} The recommended vaccine dosage is:

- children between 6 months and 9 years who have not previously been vaccinated require 2 immunisations of a single dose given 1 month apart
- children less than 3 years should receive half the adult dose on each of the 2 occasions
- children who are older than 9 years or those who have been immunised previously require only a single immunisation.

The vaccine is given intramuscularly. A protective antibody response takes approximately 2 weeks, so vaccination should ideally be given at the start of the influenza season.

As the vaccine contains inactivated virus, **it cannot cause influenza symptoms**. Side-effects most commonly reported are fever, rash or local reactions such as soreness or mild swelling at the injection site. In addition, seizures (most commonly febrile seizures) may occur.

Does the current seasonal influenza vaccine protect against swine flu?

The seasonal vaccine is effective only against seasonal influenza strains. The current vaccine contains the following 3 viruses – A/Solomon Islands/3/2006 (H1N1), A/Brisbane/10/2007 (H3N2) and B/Florida/4/2006.¹² Although the seasonal vaccine does contain an H1N1 strain, this differs from the swine H1N1 and therefore current seasonal vaccination does not offer substantial protection against pandemic influenza A (H1N1) virus.

Antiviral prophylaxis for swine flu in high-risk contacts

Antiviral post-exposure prophylaxis should only be offered to high-risk close contacts of suspected or confirmed cases of infection caused by pandemic influenza A (H1N1).^{5,6} For children, the dose of oseltamivir for prophylaxis is half the treatment dose, i.e. a daily dose of 30 mg, 45 mg, 60 mg or 75 mg depending on the child's weight.^{4,6} The duration of post-exposure antiviral chemoprophylaxis is 10 days after exposure to a case.

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