

An overview of cold and flu management

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Abstract

Common colds and flu are caused by very different viruses but share similar symptoms. The common cold is a self-limiting upper respiratory tract infection and it is typically caused by a rhinovirus, coronavirus or adenovirus. It usually resolves within 7–10 days. The flu is caused by the influenza virus and typically presents with headaches, myalgia, fever and generalised body aches. In South Africa deaths related to colds and flu are at least three times higher when compared to the USA. The burden of infections with the human immunodeficiency virus (HIV) and tuberculosis (TB) in our country, heightens the risk of severe flu-related illness. However, treatment remains mostly symptomatic.

Keywords: colds, flu, rhinovirus, coronavirus, adenovirus, influenza virus, upper respiratory tract infection, flu vaccine, antivirals, neuraminidase, novel coronavirus (2019-nCoV), coronavirus disease (COVID-19)

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Introduction

The common cold is a self-limiting upper respiratory tract infection that is typically caused by a rhinovirus, coronavirus or adenovirus.² Symptoms like sneezing, nasal congestion, coughing, sore throat and a low-grade fever are often experienced during the late autumn and winter season, from about early-May to August in South Africa.³ A person may be contagious after being infected with the virus.⁴ The viruses in question are airborne and spread quickly via hand-to-hand contact, or via the inhalation of airborne droplets from sneezing and coughing (also refer to Figure 1).²

After the virus enters the nasal cavity it damages the ciliated cells resulting in the release of inflammatory mediators and causing inflammation of the nasal tissue lining.² The increase in permeability of the capillary cell walls results in oedema. Oedema is responsible for symptoms like sneezing and nasal congestion.^{2,4} A postnasal drip may develop and is responsible for spreading the virus. This also leads to a sore throat and coughing.²

Common colds are typically self-limiting and resolve within 7–10 days without the use of antibiotics. However, some people may end up developing a secondary bacterial infection.³

The common cold is often confused with influenza (or the so-called flu). However, influenza is a viral illness that is caused by the influenza virus and has a high mortality and hospitalisation rate.⁵ Influenza can occur all year round but is seen more often from May through winter. The modes of transmission are similar to those that are involved in the transmission of the common cold (see Figure 1).

Influenza in a nutshell

There are four main types of influenza virus, namely A, B, C and D (also refer to Table I). However, only A and B are typically associated with human flu and influenza outbreaks. Influenza A viruses may be further sub-categorised, based on the specific subtype of haemagglutinin (H) and neuraminidase (N) surface proteins they carry. For example, influenza A (H3N2) carries the

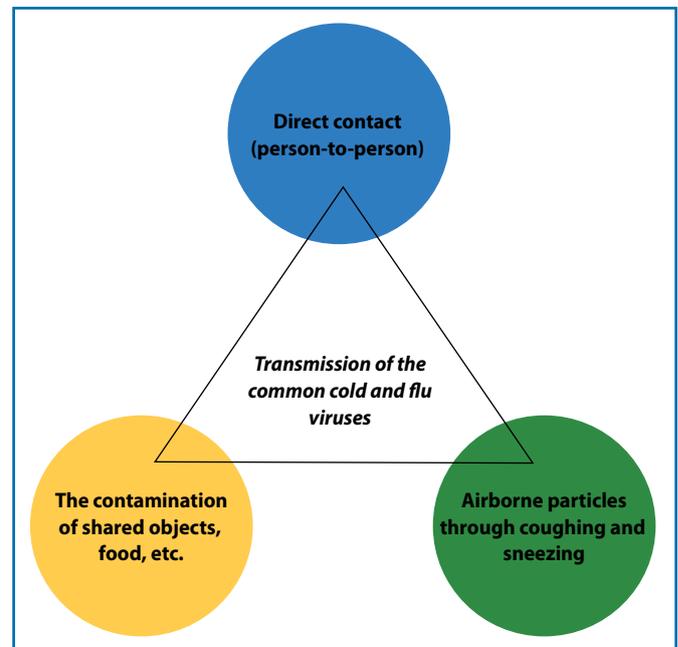


Figure 1: Transmission of viruses that cause common colds and flu³

third haemagglutinin subtype and the second neuraminidase subtype; currently there are 18 subtypes of the former, and 11 of the latter. Conversely, instead of subtypes, influenza B currently belong to one of two lineages (as opposed to being divided into subtypes), namely B/Yamagata and B/Victoria.^{1,6}

Table I: Types of human influenza strains and their major differences²

Virus strain*	Influenza A	Influenza B
Who can become infected:	Animals and humans	Humans
Severity of infection:	Could cause pandemics, like swine flu and bird flu	Less severe than influenza A

* Influenza C only results in mild respiratory illness and type D is known to be a bovine virus that does not infect people.⁶

A rapid onset of fever, headaches, myalgia, general body aches and pains, sore throat and rhinitis (runny nose) are associated with the flu. These symptoms generally last for 4–5 days and then disappear; however, a person may experience coughing and malaise for more than 14 days.^{2,3} Influenza-like illness (ILI) is an acute respiratory infection that presents with a fever greater than 38 °C, with coughing and/or pharyngitis. The diagnosis of influenza-like illness is used in influenza surveillance around the globe.⁶ Laboratory diagnosis usually includes:⁷

- virus isolation in cell culture,
- a polymerase chain reaction (PCR) test, and
- antigen detection.

Potentially pandemic influenza A (H1N1) is commonly referred to as swine flu, and (H5N1) as bird flu.

Management of common colds and flu

Pharmacotherapy is mostly directed at alleviating the symptoms. Antibiotics are often prescribed erroneously, and in the absence of a secondary bacterial infection. Antibiotics should only be administered when a bacterial infection has been identified and should not be used prophylactically in this setting. The following measures can be used to either prevent or treat the symptoms of a common cold and the flu:^{2,6}

- A flu vaccine is recommended by, amongst others, the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), in the United States of America, as a preventative measure against the acquisition of the influenza virus.
- Selected over-the-counter (OTC) products contain a combination of active ingredients which help with symptomatic relief.
- Drinking plenty of fluids, especially water; water has been shown to be the best fluid with which to hydrate mucus and lubricate the mucous membranes.
- Vitamins and mineral supplements, e.g. vitamin C and zinc sulphate.
- Antiviral drugs, e.g. neuraminidase inhibitors (zanamivir and oseltamivir), as well as N-methyl D-aspartate receptor antagonists (amantadine and rimantadine).
- Other remedies, such as orally-inhaled anticholinergics, inhaled corticosteroids, herbal solutions and nonsteroidal anti-inflammatory drugs (NSAIDs).

The flu or influenza vaccine

The influenza vaccine is developed each year to protect people against the most prevalent strains of the influenza virus. At present, for the 2020 southern hemisphere influenza season, this would be influenza A (H1N1) and (H3N2), with the addition of one or two influenza B viruses.¹ A flu vaccine that contains the two required A-strains for the season in question, plus only one B-strain (currently from the B/Victoria lineage), is referred to as a trivalent flu vaccine, and one that includes both B-strains, is called a quadrivalent vaccine. The WHO recommendations make provision for both types to be used.¹ Flu vaccines then provoke an immune response to the antigen found on the surfaces of the viruses. Antigenic drift can occur in the viruses, causing resistance

to the vaccine.⁸ It is for this reason that recommendations are based on the World Health Organization's accredited regional laboratories, and changes are made to the composition, in terms of the specific strains to be included in the vaccine, every year. This antigenic drift is the reason why the vaccine that is released in September every year in the northern hemisphere is not always exactly the same as the one that is released in February in the southern hemisphere.^{8–10}

Antibodies usually develop within two weeks of the vaccine being administered. A peak in immunity occurs four to six weeks after vaccination, which then gradually wanes again. It therefore does not convey lasting immunity against the influenza virus. Immunisation reduces the likelihood of the flu developing in healthy adults by approximately 70–90%. If a family member or household contact has already developed the flu, vaccination of other members of the household within 36–48 hours will still provide effective protection against the virus.^{1,2,10} Table II lists those high-risk individuals that need to be prioritised for annual flu vaccination.

In the Southern Hemisphere, it is recommended that the vaccine be given in April; however, it can be given throughout the winter season. Common adverse effects that are associated with the flu vaccine include:^{8–10}

- Allergic reactions in people who have an egg allergy (due to egg-based vaccine culturing techniques, where applicable).
- Flu-like symptoms, which develop within 2–24 hours after vaccination.
- Soreness and tenderness at the site of the injection.

Combination products used for common colds and flu

Treatment is mainly symptomatic and includes many over-the-counter medicines and herbal remedies. Various combinations of antitussive agents (i.e. cough suppressants), first-generation antihistamines, expectorants and mucolytic agents, as well as nasal decongestants may provide patients with some relief.²

Table II: List of individuals who would require the flu vaccine as a matter of priority^{2,10}

Individuals that require the vaccine as a matter of priority	✓
Pregnant women, and women who are planning to fall pregnant during the winter months	
Patients younger than 18 years of age on chronic aspirin therapy	
HIV-infected patients (CD4 cell count >100 cells/μL)	
Patients who suffer from any other disease which leaves them immunocompromised	
People who suffer from an underlying medical condition, e.g. diabetes mellitus, COPD, heart disease	
People older than 65 years of age, or infants between 6–49 months of age	
People living in old age homes, frail care facilities and rehabilitation centres	
Healthcare workers who have direct contact with patients daily	
Patients that are on glucocorticosteroid therapy for prolonged periods of time	

Antitussive agents (cough suppressants)

Antitussive agents should only be given for a non-productive, dry and irritating cough. Care should be taken when giving antitussive agents, because the coughing mechanism serves a protective function in the body. Coughing clears the throat and the lower respiratory tract of foreign particles and mucus. Coughing that occurs as a result of bronchoconstriction and bronchospasm (coughing in asthma and COPD patients) should be treated with bronchodilators. Coughing that is caused by a lower respiratory tract infection should be managed with appropriate antimicrobial agents.^{2,9,10}

Certain classes of drugs are able to suppress the coughing mechanism, such as opioid analgesics and opioid derivatives (codeine phosphate, methadone, etc.).^{2,9,10}

Antihistamines

The first-generation antihistamines, such as chlorpheniramine, brompheniramine and promethazine, are used to reduce certain symptoms of a common cold or flu, like rhinitis and sneezing. This is due to the anticholinergic effects of these drugs. Some of the first-generation antihistamines are also used for their antitussive action and are combined in cold medicines to help patients sleep. When used on their own, antihistamines offer little benefit in treating the symptoms of the common cold and flu, but they do offer symptomatic relief when used in combination with decongestants and antitussive agents.¹⁰ Note, however, that the use of promethazine is contraindicated in children under the age of two years.

Expectorants and mucolytic agents

Expectorants and mucolytic drugs are used to alter the viscosity of mucus and bronchial secretions, thereby making it easier to cough up sputum. There are two ways of achieving this through pharmacological action, namely:^{2,10,11}

- By using expectorants to increase the volume of bronchial secretions and reduce the viscosity of these secretions. Guaiphenesin, sodium citrate and ammonium chloride are examples of expectorants. For obvious reasons, the use of cough mixtures containing an expectorant, as well as an antitussive agent, or combined with a first-generation antihistamine, should rather be avoided.
- By using mucolytic agents, which act by altering the structure of the mucus, thus resulting in a low mucus viscosity. Examples of such agents include carbocysteine, bromhexine and N-acetylcysteine. Dornase alfa (recombinant human DNase, or rhDNase) is used in patients with cystic fibrosis.

Non-pharmacological methods, like maintaining a good fluid hydration status and inhaling steam, can also reduce the viscosity of mucous secretions.

Oral decongestants

Oral sympathomimetic, systemic decongestants, like pseudoephedrine, phenylpropanolamine and phenylephrine are mainly available as part of combination preparations in South Africa.^{9,10} Oral decongestants should only be used for a short period of time and as symptomatic relief only. Topical agents are preferred

Table III: Important differences between zanamivir and oseltamivir^{2,12}

Zanamivir (Relenza®)*	Oseltamivir (Tamiflu®)
Administered through an inhaler.	Available as an oral suspension and in a capsule formulation.
	It has minor side-effects like nausea and vomiting.
May provide a challenge to older patients and patients with lung disorders.	Dosage adjustments are required in patients with renal impairment.

* No longer available on the local market.¹³

Table IV: Examples of commonly-encountered cold and flu remedies on the local market^{10,13}

Class	Examples*
Throat lozenges and gargles (for the relief of a sore throat)	Andolex® Andolex-C® Cepacol® Medi-Keel A® Strepsils®
Topical nasal decongestants	Iliadin® DriNasal® Drixine® Nazene® and Nazene Z® Otrivin® Sinutab Nasal Spray® Vibrocil-S®
Analgesics and decongestants (for the relief of pain, fever and nasal congestion)	Actifed® Advil Cold & Sinus® Benylin® Betafed® Brufen® Corenza Cold & Flu® Corenza Para-C® Coryx® Degoran Plus® Neurofen® Panado® Sinuclear® Sinugesic® Sinumax® Sinustat® Sinutab® Sudafed Sinus Pain®
Cough remedies (including expectorants and cough suppressants)	Cepacol® Coughcod® Dilinct® Duro-Tuss® Pholtex® Tussitot®
Immune system support	Immuenza® Viral Guard®

* Trade names are provided for illustrative purposes only.

as they have a reduced systemic side-effect profile compared to the systemic combination treatments.² Clear warnings should be given to patients about the use of oral decongestants with alcohol or certain drugs like sedatives.^{9,10}

Topical nasal decongestants

Nasal congestion, a result of vasodilation and oedema of the nasal mucosa, may be alleviated through the use of suitable alpha-1 adrenergic receptor agonists, applied topically (nasal sprays) or taken orally (see previous section). The topical decongestants are actually vasoconstrictors, and compared to a placebo, have shown a significant reduction in airway resistance (with fast and effective relief of a blocked or stuffy nose).^{1,8-10}

Antiviral agents

Two classes of antiviral agents may be used against the influenza virus, namely the neuraminidase inhibitors and N-methyl D-aspartate (NMDA) receptor antagonists. They play a major role in the treatment and prevention of both seasonal and avian influenza.^{2,12} Zanamivir and oseltamivir inhibit the neuraminidase (*syn.* sialidase) enzyme in both the influenza A and B virus and should ideally be used within the first 24–48 hours of the onset of symptoms. These drugs have the ability to limit the spread of the viral infection, but only provide a modest reduction in the duration of symptoms. Their use in avian or bird flu has not been fully established. Also refer to Table III.

Amantadine is an antiviral drug that is otherwise and possibly more commonly associated with the treatment of Parkinson's disease, because it is an NMDA-receptor antagonist with neuroprotective properties. It is however also used in the prevention and treatment of influenza A. Amantadine acts by increasing the amount of dopamine from the nigrostriatal pathway and inhibits the reuptake of dopamine by these neurons. In the case of the influenza virus, both amantadine and rimantadine (the adamantanes) block the M2 proton-selective ion channel of the influenza A virus but are not effective against influenza B.^{2,9,11,12}

Widespread viral resistance and unwanted side-effects limit the usefulness and effectiveness of the adamantanes. However, if the drug is being used for minor sensitive strains the following should be noted:^{2,9,11,12}

- Initiation of amantadine should occur within two days after contracting influenza A as it may reduce the duration of the disease.
- It cannot be used against influenza B.
- There is no evidence to suggest the effectiveness of this drug in preventing the complications of influenza A.

Two newer antiviral agents that are not available in South Africa yet, are baloxavir marboxil and peramivir. Table IV also lists some examples of cold and flu remedies that are available on the local market.

Conclusion

Antibiotics should never be used to treat the common cold or flu unless there is a secondary bacterial infection. The typical treatment of colds and flu is symptomatic. The neuraminidase inhibitors can be used in the prevention and treatment of both influenza A and B. Receiving the influenza vaccine reduces the risk of acquiring seasonal flu and remains the mainstay of all influenza prevention strategies. The importance of effective flu vaccination programmes cannot be overstated.

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