

Colds and flu – an overview of the management

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Abstract

The common cold and flu are two very different viruses that share very similar symptoms. The common cold is a self-limiting upper respiratory tract infection and it is caused by the rhinovirus, coronavirus or the adenovirus. It usually resolves within 7-10 days. The flu is caused by the influenza virus and usually presents with headaches, myalgia, fever and body aches. There is no place for antibiotic usage in colds and flu and there is no clinical evidence which suggests that using antibiotics alters the course of the disease or prevents secondary infection. Treatment is mainly symptomatic and includes many over the counter medicines, antivirals and herbal treatment.

Keywords: colds, flu, rhinovirus, coronavirus, adenovirus, influenza, upper respiratory tract infections, herbal medicine, antivirals, over-the-counter medicine

Introduction

The common cold, otherwise known as a self-limiting upper respiratory tract infection, is caused by the rhinovirus, coronavirus or the adenovirus¹. Symptoms like sneezing, nasal congestion, coughing, sore throat and a low grade fever are often experienced during the winter season². A person may be contagious after being infected with the virus, but before they present with symptoms, and until after all the symptoms have subsided³. The viruses in question are airborne and spread quickly via hand-to-hand contact, or via the inhalation of airborne droplets from sneezing and coughing¹.

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 lining¹. The increase in permeability of the capillary cell walls results in oedema. Oedema is responsible for symptoms like sneezing and nasal congestion^{1,3}. A postnasal drip may develop and is responsible for spreading the virus, which leads to a sore throat and coughing¹.

Common colds are self-limiting and resolve within 7-10 days without the use of antibiotics. However, some people may develop a secondary bacterial infection².

The common cold is often confused with the flu. However, the flu is a viral illness that is caused by the influenza virus and has a high mortality and hospitalization rate⁴. Influenza can occur all year round but is seen more from May through winter. Due to the

Hand-to-hand contact: Self-infection by touching a person or object that is infected with the virus.

Droplet transmission: Inhalation of airborne droplets.

Close contact with infected persons: Infection by disposition of large air droplets from sneezing.

Figure 1: Transmission of viruses that cause colds².

constant evolution of the influenza strains there a higher fatality rate associated with the virus¹.

The influenza virus is transmitted via air droplets when a person comes into close contact with an infected person or via self-infection when a person comes into direct contact with an infected person or object⁵.

Table 1: Types of influenza strains and their differences¹.

Virus Strain:	Influenza A	Influenza B
Who can become infected:	Animals and Humans	Humans
Severity of infection:	Causes pandemics, like swine flu and bird flu.	Less severe than Influenza A.

A rapid onset of fever, headaches, myalgia, 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^{1,2}. Influenza-like illness (ILI) is an acute respiratory infection that presents with a fever greater than 38°C, coughing or pharyngitis. The diagnosis of influenza-like illness is rarely based on the patient's clinical picture. Laboratory diagnosis usually includes⁶:

- Virus isolation in cell culture
- A polymerase chain reaction (PCR) test
- Antigen detection.

Management of common colds and flu

Pharmacotherapy is directed at alleviating associated 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 as a preventative measure. The following measures can be used to either prevent or treat the symptoms of a common cold and the flu (each of these recommendations will be discussed separately)^{1,5}:

- A flu vaccine is recommended by 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 lubricate the mucous membranes
- Vitamins and minerals, 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, such as orally-inhaled anticholinergics, inhaled corticosteroids, herbal solutions and nonsteroidal anti-inflammatory drugs (NSAIDs).

Vitamins and Minerals

The prophylactic use of vitamin C has been shown to reduce the risk of developing a cold or flu in certain populations, e.g. athletes, with a reduction of approximately 6% in the disease duration. However, the evidence that supports the use of vitamin C in high dosages to reduce the severity of a cold or flu is lacking and inconclusive.

Zinc may inhibit viral growth, and could possibly reduce the duration of cold symptoms. However, not enough high-quality trials support the routine and high-dosage use of zinc in preventing a cold or flu. Some reports have been lodged with the US Food and Drug Administration (FDA) that nasal preparations containing zinc may cause loss of smell. Zinc may also reduce the absorption of certain antibiotics. Food containing calcium and phosphorus can impair the absorption of zinc⁷.

Importance of Hydration

Fluid (especially water) helps to lubricate the mucous membranes of patients suffering from the common cold or influenza. However, some literature contradicts this by suggesting that the provision of extra fluid to patients with acute respiratory conditions may cause hyponatraemia and fluid overload, because of antidiuretic hormone. This hormone is released in adults and children with lower respiratory tract infections and causes water reabsorption from the renal collecting duct. The combination of the increased production of the antidiuretic hormone and extra fluid may lead to fluid overload. Research has not clearly illustrated this in upper respiratory infections yet and water hydration still remains of importance in common colds and flu^{1,8,9}.

Other strategies used to treat the common cold and flu

Anticholinergic agents, such as inhaled ipratropium bromide, may be used to treat a cough caused by the common cold. Nasal preparations have shown some efficacy in reducing rhinorrhoea and sneezing. Inhaled corticosteroids can be used to reduce the swelling and inflammation of the nasal mucosa, but have not been shown to provide any benefit in patients diagnosed with a common cold¹.

Conflicting evidence has emerged about the use of nasal irrigations. Nasal irrigations constitute a mechanical intervention. It is not classified as a decongestant and does not improve ciliary function. Studies have shown that nasal preparations that contain a certain preservative, namely benzalkonium chloride, may worsen symptoms and infections. Nasal washes that contain a lot of fluid and minimal salt can be used to remove mucus from the nose, removing bacterial products, and improving sinonasal function. Nasal irrigations can be used prior to the administration of topical therapies to ensure true sinus distribution^{1,10}.

There are several different OTC medications that can be used to alleviate pain and fever associated with the common cold and flu. The typical active ingredients are aspirin, paracetamol and caffeine. Aspirin, however, is contraindicated in children who have a viral infection as they are at risk of developing Reye's syndrome^{1,2}.

The use of codeine or hydrocodone as a cough suppressant has not been found to be any more beneficial than a placebo¹.

Herbal products and supplements include substances like Echinacea, Chinese herbal cold and allergy products, elderberry extracts, *Andrographis paniculata*, *Pelargonium sidoides* and *Acanthopanax senticosus*^{1,11}.

Probiotics were more effective than placebo in reducing the number of episodes as well as the rate of episodes of upper respiratory tract infections¹¹.

The flu or influenza vaccine

Influenza 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 vaccine¹². It is for this reason that recommendations are based on the World Health

Table 2: Herbal products and supplements^{1, 11}.

Herbal product	Evidence supporting the use of the medicine	Adverse effects
Echinacea	No evidence supports the use of this product in the treatment of colds and flu.	People who are allergic to Echinacea develop erythema nodosum, which features tender, red nodules under the skin
Chinese herbal cold and allergy products	No evidence supports the use of this product in colds and flu	These products also pose the risk of renal damage and cancer as they contain aristolochic acid.
Elderberry extracts	Some evidence supports the use of these extracts in shortening the duration of flu symptoms. <i>However this has yet to be confirmed by bigger studies.</i>	These extracts are unsafe when the leaves, stems, unripe fruit or uncooked fruit is consumed.
Pelargonium sidoides (commonly known as African geranium) and Acanthopanax senticosus	Literature has confirmed a reduction in the duration of 10 different flu symptoms.	There are isolated reports of liver toxicity; however, no causative relationship has been linked to the herb itself.

Organization’s accredited regional laboratories, and changes are made to the composition, in terms of strains of influenza every year^{13, 14}. This is also the reason why the vaccine that is released in September every year in the Northern Hemisphere is not always exactly the same as that released in February in the Southern Hemisphere.

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%¹⁴. If a family member or house mate has already developed the flu, vaccination of other members, within 36-48, hours will still provide effective protection against the virus¹⁴.

Table 3: List of individuals who would require the flu vaccine as a matter of priority¹.

Individuals that require the vaccine as a matter of priority	✓
Pregnant women, and women who are planning to fall pregnant during winter	
Patients younger than 18 years of age on chronic aspirin therapy	
HIV infected patients (CD4 cell count >100 cells/uL).	
Patients who suffer from any other disease which leaves them immune compromised	
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 staying in old age homes, frail care facilities and rehabilitation centres	
Healthcare workers who have direct contact with patients on a daily basis	
Patients who are on glucocorticosteroid therapy for long periods of time	

In the southern hemisphere, it is recommended that the vaccine be given in April; however, it can be given throughout the winter season. Figure 2 below depicts the adverse effects that are associated with the flu vaccine¹.

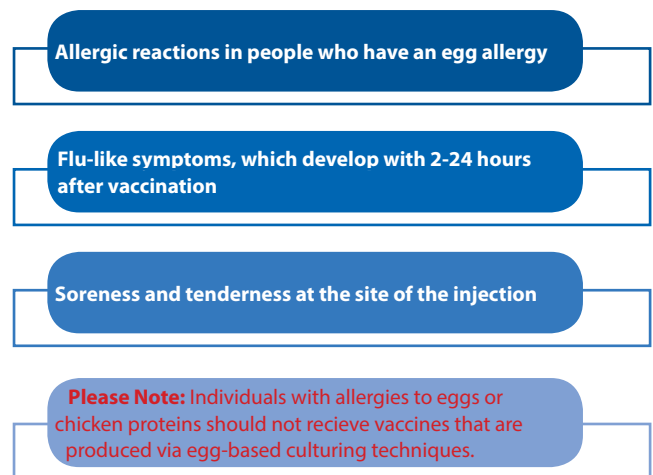


Figure 2: Adverse effects of flu vaccines^{12, 13, 14}.

Combination Products used for common colds and flu

Antitussive agents (cough suppressants)

Antitussive agents should only be given for a non-productive, dry, irritating cough (refer to Table IV). Care should be taken when giving antitussive agents as the coughing mechanism serves as a protective function of 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.

Certain classes of drugs are able to suppress the coughing mechanism, such as opioid analgesics and opioid derivatives (codeine phosphate, methadone, etc.)^{1, 13}.

Table 4: Over-the-counter medicine for the treatment of colds and flu^{1,13}.

Preparation	Active ingredient	Indication
Topical decongestants		
Illiadin®	Oxymetazoline (0.100 mg/ml)	Short-term symptomatic relief of nasal congestion
Drixine®	Oxymetazoline (0.5 mg/ml)	Short-term symptomatic relief of nasal congestion
Nazene® Adult Nasal Metered Spray	Oxymetazoline (0.5 mg/ml)	Short-term symptomatic relief of nasal congestion
Otrivin®	Xylometazoline (1 mg/ml)	Short-term symptomatic relief of nasal congestion
Sinutab® Nasal Spray	Xylometazoline (1 mg/ml)	Short-term symptomatic relief of nasal congestion
Vibrocil-S®	Phenylephrine and dimethindene (250 mg/100 g)	Short-term symptomatic relief of nasal congestion
Topical Corticosteroids		
Avamys®	Fluticasone furoate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Beclate Aquanase®	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Beconase®	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Clenil® Aq Nasal Spray	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Flomist®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Flonase®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Nexomist®	Mometasone furoate (50 µg)	Maintenance therapy for allergic rhinitis
Rinelon®	Mometasone furoate (50 µg)	Maintenance therapy for allergic rhinitis
Topical antihistamines/anti-allergic agents		
Rhinolast®	Azelastine (0.14 mg/spray)	Short-term intermittent allergic rhinitis
Sinumax Allergy Nasal Spray®	Levocastastine (0.5 mg/ml)	Short-term intermittent allergic rhinitis
Vividrin®	Cromoglicic acid (2.6 mg/spray)	Intermittent or persistent allergic rhinitis
Other nasal preparations		
Mistabron®	Mesna (50 mg/ml)	Nasal obstruction owing to thick secretions
Systemic nasal decongestants with antihistamines		
Actifed®	Pseudoephedrine HCl (30 mg) Triprolidine HCl (1.25 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Betafed Be-Tabs®	Pseudoephedrine HCl (30 mg) Triprolidine HCl (1.25 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Demazin Syrup®	Phenylephrine HCl (2.5 mg/5 ml) Chlorpheniramine (1.25 mg/5 ml)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Demazin NS®	Pseudoephedrine sulphate (120 mg) Loratidine (5 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Systemic decongestant and/or analgesic and/or antihistamine combinations		
Efferflu C® Cold and Flu	Paracetamol (500 mg) Chlorphenamine maleate (2 mg) Vitamin C (250 mg)	Symptomatic relief of colds and flu
Benylin® for colds	Pseudoephedrine HCl (30 mg) Ibuprofen (200 mg)	Symptomatic relief of colds and flu
Nurofen® Cold and Flu	Ibuprofen (200 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu
Sinuclear®	Paracetamol (325 mg) Phenylpropranolamine HCl (18 mg)	Symptomatic relief of colds and flu
Sinugesic®	Paracetamol (500 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu
Sinumax®	Paracetamol (500 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu
Sinustat®	Paracetamol (325 mg) Phenylpropranolamine HCl (18 mg)	Symptomatic relief of colds and flu
Sudafed® Sinus Pain	Paracetamol (500 mg) Pseudoephedrine HCl (60 mg)	Symptomatic relief of colds and flu
Cough preparations		
Mucolytic		
Solmucol®	N-Acetylcysteine	To reduce viscosity of secretions
Mucatak®		
Amuco 200®		
ACC200®		
Betaphlem®	Carbocisteine	To reduce viscosity of secretions
Bronchette®		
Flemex®		
Lessmusec®		
Mucospect®		
Bisolvon®	Bromhexine HCl	To reduce viscosity of secretions
Expectorants		
Benylin Wet Cough Menthol®	Guaifenesin	Cough alleviation
Cough suppressants		
Benylin® Dry Cough	Dextromethorphan	Symptomatic relief of a non-productive cough
Dilinct® Dry Cough		
Nitepax®	Noscapine	
Pholtex® Forte	Pholcodine	
Pholtex Linctus®	Pholcodine 15 mg/10ml Phenyltoloxamine (10 mg/10 ml)	

Antihistamines

The first-generation antihistamines, such as chlorpheniramine, brompheniramine and promethazine, are used to reduce certain symptoms of a cold, 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. Literature has stated that antihistamines used alone are of very little benefit in treating symptoms of the common cold and flu, but they do offer symptomatic relief when used in combination with decongestants and antitussive agents⁵.

Please note: In 2007 promethazine-containing medicines were contraindicated in children under the age of two years¹⁵.

Expectorants and mucolytic agents

Expectorants and mucolytic drugs are used to alter the viscosity of mucous and bronchial secretions, thereby making it easier to cough up sputum^{1, 16}. There are two ways of achieving this through pharmacological action:

- 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 an antihistamine, should rather be avoided.
- By using mucolytic agents, which act by altering the structure of mucus, thus resulting in a low mucus viscosity. Examples are: carbocisteine, bromhexine and N-acetylcysteine. Dornase alfa (recombinant human DNase) 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 now mainly available in combination in South Africa⁵. Oral decongestants should only be used for a short period of time and as symptomatic relief for acute coryza, as part of flu and influenza. Topical agents are preferred as they have reduced systemic side-effects¹. Clear warnings should be given to patients about the use of oral decongestants with alcohol or certain drugs like sedatives^{13, 17}.

Nasal decongestants:

Nasal congestion, a result of vasodilation and oedema of the nasal mucosa, can be alleviated using alpha-1 adrenergic agonists topically (nasal sprays) or orally. These topical decongestants are actually vasoconstrictors and compared to a placebo have shown a reduction in airway resistance^{1, 5, 13, 17}.

Antiviral Agents

Neuraminidase inhibitors

Zanamivir and oseltamivir are currently available. These drugs are registered for the prophylaxis of the influenza A and B virus, and should be used within the first 24 hours of the onset of the symptoms. These agents act by inhibiting the enzyme involved in viral replication, neuraminidase. Important information regarding the use of these agents is listed in Figure 3 below^{1, 18}:

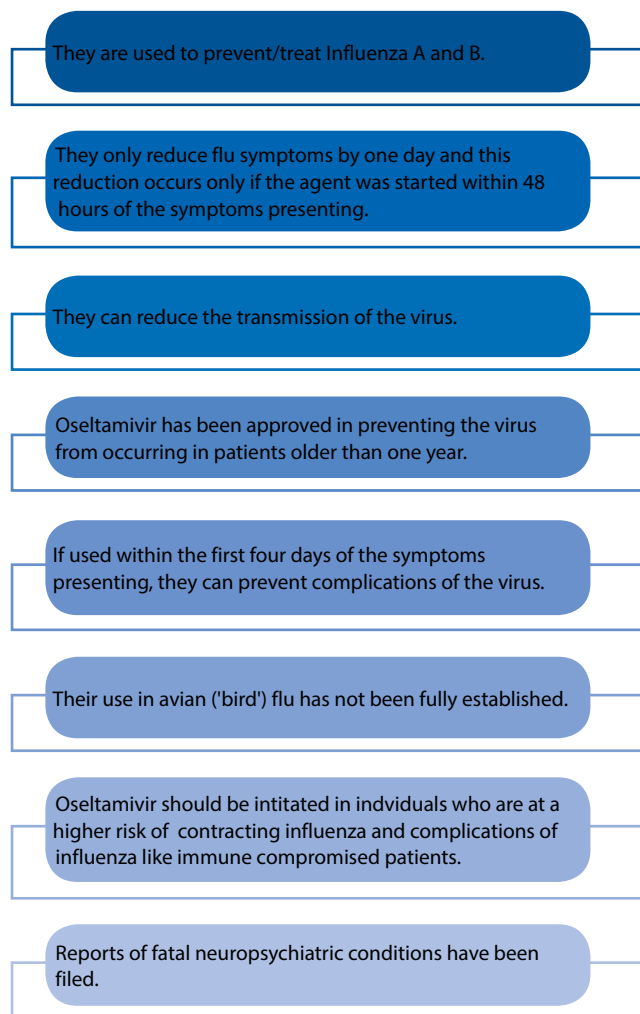


Figure 3: important information regarding the use of oseltamivir and zanamivir^{1, 18}.

Table 5: Important differences between zanamivir and oseltamivir^{1, 18}.

Zanamivir	Oseltamivir
Administered through an inhaler.	Available as a suspension and a capsule. It has minor side effects like nausea and vomiting.
May provide a challenge to older patients and patients with a lung disorder.	Dosage adjustments in patients with renal impairment.

N-methyl D-aspartate receptor antagonists

Amantadine is an antiviral drug that is commonly associated with the treatment of Parkinson's disease. 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 the neurons. Amantadine is currently not recommended for treatment or use as an antiviral agent as there is wide-spread resistance to the drug^{1, 13, 18}.

If the drug is being used for minor sensitive strains the following should be noted:

- Initiation of amantadine should occur within 2 days after contracting influenza A as it may reduce the duration of the disease.
- It cannot be used against influenza B.
- There is no literature which supports the drug preventing complication of influenza A.

Conclusion

Antibiotics should never be used to treat the common cold or flu, unless there is a secondary bacterial infection. There is insufficient evidence in the literature to support the use of OTC products for the prevention of these viral infections; however, vitamin C and zinc can be used as prophylaxis. Receiving the influenza vaccine may reduce the risk of acquiring seasonal influenza. Treatment is symptomatic; however, the use of many of the OTC medicines is not supported by literature. Certain herbal remedies like *P. sidoides* extract, *A. paniculata* and elderberry may be effective, although a person should always read the safety profile of these remedies first. Codeine and antihistamines may be used in combination therapies to treat coughs and other cold symptoms. Medicines, such as paracetamol and other NSAIDs, may be used to manage pain and fever in adults. Antivirals, such as the neuraminidase inhibitors, can be used in the prevention and treatment of both influenza A and B.

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