Overview and management of Colds and Flu

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Abstract

The common cold is a viral infection that requires symptomatic treatment. It is usually self-limiting. Influenza is often referred to as the flu. There are several differences between the common cold and the flu, including the onset of the condition as influenza is typically more acute in onset and more debilitating. Treatment of both these conditions requires a symptomatic approach that should be evidence-based, including herbal remedies, over-the-counter medicines, antiviral agents and analgesics for pain and fever. This will be discussed in more detail in the ensuing section.

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Introduction

Every year, adults dread the winter months, especially because they don't want to "catch a cold". The common cold is not so uncommon, and adults experience a cold 2-4 times annually. What causes colds and why do we get infected so easily? The rhinovirus, coronavirus and the adenoviruses are responsible for this self-limiting upper respiratory tract infection. These viruses spread very easily and quickly, especially through close proximity to infected persons via hand-to-hand contact, or by inhalation of airborne droplets through sneezing or coughing.[1]

Once the virus has invaded the nasal cavity and bronchial epithelia, it causes damage to the ciliated cells, which, in turn, release inflammatory mediators and cause inflammation of the nose tissue lining. Oedema is the result of the increased permeability of the capillary cell walls. This effect is experienced as nasal congestion and sneezing by the infected person. A postnasal drip, which is the nasal mucous fluid running down the throat, may also be present, and can spread the virus and cause a sore throat and cough.[2]

The cold should easily resolve with symptomatic treatment within 7-10 days, but sometimes it can be complicated by a bacterial infection.[1] Symptoms include a sore throat, a stuffy nose, sneezing, mild to moderate fever (38.9°C), minor headaches, muscle aches and coughing. Nasal discharge is normally clear and runny, and may become thick and turn a yellow colour after a few days.[3]

Influenza, also known as the flu, is a viral illness with high rates of mortality and hospitalisation in persons aged 65 years and older.[4]

People often confuse flu with a common cold. However, there are subtle differences between the two. Influenza occurs especially between the months of December to March, but can also take place at any time of the year. People all over the world are apprehensive about acquiring flu because they immediately think of "swine" or "bird flu", and fear that they may die. Influenza epidemics can become very serious, and even fatal, when a new strain evolves.[3]

A flu virus also spreads quickly through direct contact with infected persons, or through close contact with infected persons who are sneezing or coughing. The virus spreads from one day before the onset of symptoms in healthy people and usually continues to spread for five days after the symptoms have developed, but patients who are immunocompromised can shed the virus for weeks to months.[3]

The flu virus manifests in different strains. The virus is a cluster of genes connected together in a protein membrane, and covered with glycoprotein molecules. The different flu strains develop according to the number of membranes of which they consist, and also the type of glycoprotein that is present.[3] Refer to Table I for an overview of the different influenza strains with regard to severity and who may become infected.

Table I: Differences between the two influenza strains with regard to severity and who may become infected[3]

Influenza strain	Who will get infected?	Severity
Influenza A	Animals and humans	Causes major pandemics
Influenza B	Only humans	Less common and less severe than influenza A

People who are infected with influenza have distinctly different symptoms to those with a common cold. The flu virus has a rapid onset, with fever, headaches, myalgia, malaise, a non-productive

cough, a sore throat and rhinitis. Flu symptoms resolve within 4-5 days, but the coughing and malaise may persist for 14 days or longer.[3] Refer to Table II for a checklist of symptoms to be used to differentiate between a common cold and the flu.

Table II: Checklist of symptoms to differentiate between a cold and the flu[2,4]

Symptoms	Cold	Flu
Fever	Mild to moderate (38.9°C)	Moderate to high (38.9-40°C)
Headaches	✗	✓
General aches and pains	✗	✓
Fatigue, exhaustion and weakness	✗	✓
A stuffy nose	✓	✓
Sneezing	✓	✓
A sore throat	✓	✓
Chest discomfort and coughing	✓	✓
Postnasal drip	✓	✓

Management of the common cold 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 as a pathogen, 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 flu. (Each of these recommendations will be discussed separately):[1,3,5]

- A flu vaccine is recommended by the Centers of Disease Control and Prevention as a preventative measure against the acquisition of the influenza virus
- Combinations of active ingredients, e.g. decongestants, cough suppressants and paracetamol, are available for use as over-the-counter (OTC) products
- *Drinking plenty of fluids:* 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)
- Antiviral drugs, e.g. N-methyl D-aspartate receptor antagonists (amantadine and rimantadine)
- Other [orally inhaled anticholinergics, inhaled corticosteroids, herbal solutions and nonsteroidal anti-inflammatory drugs (NSAIDs)].

Vitamins and minerals

Evidence supporting the use of high dosages of vitamin C to reduce the severity of the disease is lacking and inconclusive.[3,6] The prophylactic use of vitamin C has only been shown to produce a marked reduction in the risk of developing a cold or flu in defined populations, e.g. athletes, with a reduction of approximately 6% in the disease duration.[3,7]

High dosages of vitamin C also provide the following challenges:

- Intestinal and urinary problems, with a higher tendency to develop headaches
- Vitamin C enhances the absorption of iron, and patients with certain blood disorders, such as haemochromatosis, thalassaemia or sideroblastic anaemia, should avoid high dosages
- High dosages of vitamin C may also interfere with anticoagulant medication, and blood tests used in diabetes and stool tests.

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.[3,6] Zinc may also reduce the absorption of certain antibiotics. Food containing calcium and phosphorus can impair the absorption of zinc.

Hydration for the common cold and flu

Contradictory literature exists for the recommendation of hydration for the common cold and flu. Some studies have suggested that providing extra fluid to a patient with an acute respiratory condition may cause hyponatraemia and fluid overload, because of the release of the antidiuretic hormone. This hormone is released in adults and children with lower respiratory tract infections. The combination of increased production of the antidiuretic hormone and extra fluid may lead to hyponatraemia and fluid overload.[8] It has not been as clearly illustrated in upper respiratory tract infections, and extra fluid (water still remains the first choice) may help to lubricate the membranes in these patients.[3,6]

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 cold".[9]

There has been conflicting evidence on the use of nasal irrigations with hypertonic saline or a nasal wash. Some studies have shown that nasal preparations that contain benzalkonium chloride as a preservative may worsen symptoms and infections. Traditional nasal washes that do not contain baking soda may be used (plentiful fluid and minimal salt) to remove mucus from the nose.[6,9]

Medication used to alleviate the pain and fever associated with the common cold and flu includes aspirin, ibuprofen, naproxen or paracetamol. Aspirin should only be used in adults, and not in children, as there is a risk of the latter acquiring Reye's syndrome; especially in children with a viral infection.[6,9]

The use of codeine or hydrocodone as a cough suppressant is not supported by the literature, and has been demonstrated to be no more effective than placebo.[3,6,9]

Herbal products and supplements include substances like Echinacea, Chinese herbal cold and allergy products, elderberry extracts, *Andrographis paniculata, Pelargonium sidoides* and *Acanthopanax senticosus.* Supplements that contain these agents are not formally regulated by the Medicines Control Council of South Africa or even the FDA. Thus, these products are sold by manufacturers without the permission of regulating authorities.

The following should be noted with regard to these products:[3,6,9]

- *Echinacea:* There is no solid evidence that this product can be used to treat or prevent a common cold. Some people are allergic to Echinacea and develop a skin reaction called *erythema nodosum* which features tender, red nodules under the skin
- Chinese herbal cold and allergy medication can be harmful, and can cause renal damage and cancer as it may contain aristolochic acid. Other herbal remedies imported from Asia sometimes contain other pharmaceutical drugs, such as phenacetin and steroids (with toxic metals), and should not be used
- Small studies have shown some efficacy in the use of elderberry extract, with a shortened duration of flu symptoms. This needs to be confirmed by larger studies
- *Pelargonium sidoides* has been shown to reduce the duration of 10 different cold symptoms in the literature, and may be of some benefit. This holds true for *Andrographis paniculata* too.

Flu vaccine and the influenza vaccine

Vaccines administered during autumn contain an inactive virus, thus designed to 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. It is for this reason that recommendations are based on the World Health Organization-accredited regional laboratories, and changes are made every year.[3,7] This is also the reason why the vaccine that is released in September every year in the Northern Hemisphere is not 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 4-6 after vaccination, which then gradually wanes. Immunisation reduces the likelihood of the flu developing in healthy adults by approximately 70-90%.[3]

If flu has already developed in one family member in the household and is accurately diagnosed, vaccination in the other members of the household within 36-48 hours provides effective protection.[3]

Table III provides an overview of people for whom vaccination against the influenza virus is a priority.

The vaccine is best administered in April, but can be given throughout the winter months. Some adverse effects that may be experienced include allergic reactions in people who are allergic to eggs, soreness at the injection site, and flu-like symptoms which develop within 2-24 hours of the vaccination being administered as a response to the virus proteins in the vaccine.[3,7] Individuals with allergies to egg or chicken protein should not receive vaccines that are produced via egg-based culturing techniques.[3,7]

Table III: Priority individuals who require vaccination against the influenza virus[3,7]

Condition
Pregnant women or those who plan to fall pregnant in the flu season
People with underlying medical conditions, such as chronic lung disease, including asthma, COPD, heart disease, sickle cell anaemia, diabetes, chronic liver disease and other chronic conditions
People aged 18 years and younger on chronic aspirin therapy
HIV-infected persons with a CD4 count above 100 cells/µl
People diagnosed with cancer and other conditions that might lead to a weakened immune system
People on long-term steroid treatment for any condition
Everyone who is older than 65 years of age
Front-line healthcare workers who have direct contact with patients
Children aged 6-49 months of age
People staying in old age homes, chronic care facilities and rehabilitation institutions

COPD: chronic obstructive pulmonary disease, HIV: human immunodeficiency virus

Combination products

Cough suppressants (also referred to as antitussive agents)

The fact that the coughing reflex fulfils an important protective function should always be kept in mind when giving consideration to the use of a cough suppressant. Coughing clears the back of the throat and lower respiratory tract, i.e. the trachea, bronchi and bronchioles, of secretions and foreign particles. Care should be taken to only suppress dry, irritating and non-productive coughs, and only once this has been established as safe and desirable (Table IV). Coughing that is due to bronchoconstriction or bronchospasm (which may be found in asthmatic patients, for example) should be managed with appropriate bronchodilators. Infections of the lower respiratory tract must be suitably treated with antimicrobial agents. Drugs that are capable of suppressing this reflex include the opioid analgesics and opioid derivatives, such as dextromethorphan, pholcodine, codeine phosphate, methadone and noscapine.[10]

Expectorants and mucolytic agents

Expectorants and mucolytic agents are drugs that promote the coughing up of sputum by decreasing the viscosity of the bronchial secretions. This may ease a productive cough by making it easier for the patient to expel the mucus from the lower respiratory tract.

There are two ways of achieving this through pharmacological intervention:[10]

- By using expectorants to increase the volume of bronchial secretions and produce more fluid-like mucus, i.e. increased secretions with decreased viscosity. Guaiphenesin, sodium

Table IV: Over-the-counter medication for the common cold and flu

Over-the-counter medication			
Preparation	**Active ingredients**	**Indications**	**Price**
Topical decongestants			
Illiadin®	Oxymetazoline (0.100 mg/ml)	Short-term symptomatic relief of nasal congestion	R31.90
Drixine®	Oxymetazoline (0.5 mg/ml)	Short-term symptomatic relief of nasal congestion	R32.26
Nazene® Adult Nasal Metered Spray	Oxymetazoline (0.5 mg/ml)	Short-term symptomatic relief of nasal congestion	R35.99
Otrivin®	Xylometazoline (1 mg/ml)	Short-term symptomatic relief of nasal congestion	R53.71
Sinutab® Nasal Spray	Xylometazoline (1 mg/ml)	Short-term symptomatic relief of nasal congestion	R35.00
Vibrocil-S®	Phenylephrine and dimethindene (250 mg/100 g)	Short-term symptomatic relief of nasal congestion	R37.19
Topical corticosteroids			
Beclate Aquanase®	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis	R55.70
Beconase®	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis	R107.66
Clenil® Aq Nasal Spray	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis	R51.35
Flomist®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis	R73.92
Flonase®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis	R68.40
Nexomist®	Mometasone furoate (50 µg)	Maintenance therapy for allergic rhinitis	R170.74
Rinelon®	Mometasone furoate (50 µg)	Maintenance therapy for allergic therapy	R74.81 (60 metered sprays) R174.57 (140 metered sprays)
Topical antihistamines/antiallergic agents			
Rhinolast®	Azelastine (0.14 mg/spray)	Short-term intermittent allergic rhinits	R51.30
Sinumax Allergy Nasal Spray®	Levocabastine (0.5 mg/ml)	Short-term intermittent allergic rhinitis	R69.51
Vividrin®	Cromoglicic acid (2.6 mg/spray)	Intermittent or persistant allergic rhinitis	R34.58
Other nasal preparations			
Mistabron®	Mesna (50 mg/ml)	Nasal obstruction owing to thick secretions	R101.97
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	R19.54
Betafed Be-Tabs®	Pseudoephedrine HCl (30 mg) Triprolidine HCl(1.25 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu	R17.05
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	R39.52
Demazin NS®	Pseudoephedrine sulphate (120 mg) Loratidine (5 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu	R26.51
Systemic decongestant and/or analgesic and/or antihistamine combinations			
Benylin® for colds	Pseudoephedrine HCl (30 mg) Ibuprofen (200 mg)	Symptomatic relief of colds and flu	R41.44
Nurofen® Cold and Flu	Ibuprofen (200 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu	R47.66
Sinuclear®	Paracetamol (325 mg) Phenylpropanolamine HCl (18 mg)	Symptomatic relief of colds and flu	R33.61
Sinugesic®	Paracetamol (500 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu	R22.54
Sinumax®	Paracetamol (500 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu	R45.31
Sinustat®	Paracetamol (325 mg) Phenylpropanolamine HCl (18 mg)	Symptomatic relief of colds and flu	R21.16
Sudafed® Sinus Pain	Paracetamol (500 mg) Pseudoephedrine HCl (60 mg)	Symptomatic relief of colds and flu	R14.23

Cough preparations			
Mucolytic			
Solmucol®	N-Acetylcysteine	To reduce viscosity of secretions	R93.39 (20 sachets/200 mg) R161.24 (30 sachets/400 mg)
Mucatak®			R51.59 (25 **effervescent** tablets/200 mg)
Amuco 200®			R43.77 (20 **effervescent** tablets/200 mg)
ACC200®			R58.86 (25 **effervescent** tablets/200 mg)
Betaphlem®	Carbocisteine	To reduce viscosity of secretions	R17.93 (250 mg/5 ml, 200 ml)
Bronchette®			R15.23 (250 mg/5 ml, 200 ml)
Flemex®			R69.81 (250 mg/5 ml, 200 ml)
Lessmusec®			R26.01 (375 mg, 30 caps)
Mucospect®			R24.02 (250 mg/5 ml, 200 ml)
Bisolvon®	Bromhexine HCl	To reduce viscosity of secretions	R67. 54 (10 mg/5 ml, 50 ml)
Expectorants			
Benylin Wet Cough Menthol®	Guaifenesin	Cough alleviation	R18.70 (200 mg/10 ml, 50 ml) R27.93 (100 ml)
Cough suppressants			
Benylin® Dry Cough	Dextromethorphan	Symptomatic relief of a non-productive cough	R32.81 (15 mg/5 ml, 100 ml) R65.65 (200 ml)
Dilinct® Dry Cough			R23.13 (15 mg/5 ml, 100 ml) R46.27 (200 ml)
Nitepax®	Noscapine		R55.89 (25 mg/5 ml, 100 ml) R111.79 (200 ml)
Pholtex® Forte	Pholcodine		R37.80 (15 mg/5 ml, 100 ml)
Pholtex Linctus®	Pholcodine 15 mg/10ml Phenyltoloxamine (10 mg/10 ml)		R40.58 (100 ml)

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.[10]

- By using mucolytic agents, such as carbocisteine, bromhexine and N-acetylcysteine. These drugs are capable of changing the structure of the mucus itself, resulting in decreased viscosity. Dornase alfa (recombinant human DNase) is used in patients with cystic fibrosis.[10]

Maintaining an optimal hydration status and the use of steam inhalation also assists in decreasing mucous viscosity.[10]

Oral decongestants

Oral decongestants are available in many combination products that may also contain antihistamines. They should be used for the short-term only, and as symptomatic relief for acute coryza, as part of flu and influenza. Topical preparations are preferred as these reduce systemic side-effects.[3,6,7] The literature states that the use of combination products that contain oral sympathomimetic and antihistamines only provided a small marked improvement in general symptoms, with side-effects that may impair functioning, e.g. agitation, sedation, dizziness, a dry mouth and headaches. Systemic decongestants include sympathomimetic pseudoephedrine, phenylpropanolamine and phenylephrine. Explicit advice should be given to patients to avoid combinations of oral decongestants with alcohol and certain drugs, such as monoamine oxidase inhibitors and other sedatives.[3,6,7]

Nasal decongestants

A congested, i.e. a "blocked" or "stuffy" nose, is the result of vasodilatation and oedema of the nasal mucosa, which may be accompanied by inflammation, depending on the cause. Therefore, vasoconstrictors will alleviate congestion.[10] These decongestants are alpha-1 adrenergic agonists and may be applied topically or taken systemically.[10] Anti-inflammatory treatment with topical glucocorticosteroids may also be required, as well as suitable antihistamines, in the case of allergic rhinitis. Sodium cromoglycate nasal spray may also be used for the latter.[10]

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 drugs target and inhibit neuraminidase, an enzyme involved in viral replication. Both of them have shown only a modest reduction in illness duration.

Important information regarding the use of these drugs is as follows:[7,11]

- They may be used to treat both influenza A and B
- The reduction provided in the length of symptoms is only for approximately one day, and only when started within 48 hours of the symptoms presenting
- They may reduce transmission of the virus
- Oseltamivir has been approved in preventing the virus from occurring in patients aged one year and older
- They can be used to prevent the complications of the virus, but only when used within the first four days of the condition presenting
- Their use in avian flu has not been fully elucidated and requires further investigation
- Oseltamivir should be initiated promptly in individuals at high risk of complications of influenza and of contracting influenza, e.g. pregnant women and immunocompromised patients
- Reports of fatal neuropsychiatric conditions have been filed.

Important differences between oseltamivir and zanamivir are:[7,11]

- Zanamivir is administered through an inhaler and may provide challenges to older patients with regard to administration of the device, as well as to asthmatic patients and patients with lung disorders. The drug should only be used in its original inhaler device
- Oseltamivir is available as a liquid (suspension) and as a capsule with minor side-effects, e.g. nausea and vomiting. Dosage adjustments should be made in patients with renal impairment.

N-methyl D-aspartate receptor antagonists

Amantadine is an antiviral drug that is used to prevent and treat influenza A, but which can also be utilised in the treatment and management of Parkinson's disease. Amantidine increases the release of dopamine from the nigrostriatal neurons. It also inhibits the reuptake of dopamine by the neurons.[12] Only a minority of strains is still sensitive to amantadine, and it is currently not recommended for treatment or use as an antiviral agent.

If there is still sensitivity to the drug, the following is applicable.[3]

- It should be initiated within two days of contracting influenza A. It may shorten the duration of the disease and reduce its severity
- It is not effective against influenza B
- It has not been proved to prevent complications of influenza, e.g. pneumonia and bronchitis.

Conclusion

Antibiotics should not be used to treat a common cold or the flu. There is also not enough evidence to support the use of OTC drugs in the prevention thereof. Receiving an influenza vaccine may reduce the likelihood of acquiring seasonal influenza. Treatment is aimed at alleviating symptoms. However, many OTC medicines are not supported by evidence in the scientific literature. Herbal remedies may be effective, and include *P. sidoides* extract, *A. paniculata* and elderberry. The use of codeine and antihistamines as monotherapy is not effective in the management of coughs or other cold symptoms. Medications, such as paracetamol and other NSAIDs, may be used to manage pain and fever in adults. Antivirals, especially the neuraminidase inhibitors, can be utilised to treat and prevent influenza A and B, but should be used within two days of the correct diagnosis having been made. Large-scale resistance to amantadine by influenza has limited its usefulness.

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