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The Common Cold: What Pharmacists Need to Know

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Respiratory tract infections are the most common type of infectious disease in the United States, with the common cold being the second most frequent cause of this type of infection.¹ Children under five years of age experience four to nine episodes of upper respiratory tract infections (URTI) per year, while children aged five to nine have an annual frequency of four to six episodes. Incidence of URITs in children increase as they are exposed to more people, particularly other children in childcare facilities.^{2,3,4} Adults have fewer colds, only about one to two per year. The morbidity associated with the common cold has a major impact on the health care budget. The total costs associated with the common cold are estimated to be approximately \$24 billion dollars per year. This includes both direct and indirect costs, such as expenditures for drugs or treatments to relieve symptoms, lost days of work, and decreased productivity.⁵ Specifically, an estimated 23 million days of work are lost each year, which is an average of almost 7 days per person in the U.S.⁶

Etiology

The leading cause of the common cold is the rhinovirus, which is responsible for more than 30% of all colds and consists of over 100 serotypes. Additionally, coronavirus is the second leading cause of colds and accounts for about one-fifth of this type of infection.^{7,8} Influenza is another type of respiratory tract virus, but it is not a cause of the

common cold. Other viruses that cause cold symptoms include respiratory syncytial virus (RSV) and parainfluenza. In adults, these viruses often cause a mild self-limiting disease, but in infants with underlying pulmonary or cardiac problems, RSV can lead to death. Contrary to popular belief, a cold environment does not increase the risk of contracting the common cold. Another common myth is that people with a weakened immune system are more likely to develop a cold compared to healthy people. In fact, the opposite may be true. Healthy people are more likely to be symptomatic from a cold because they can mount a better cytokine response than immunocompromised individuals.

Pathophysiology

Modes of cold virus transmission include inhalation by airborne nasal droplets, ingestion of saliva directly or indirectly from sharing food or drink, and direct contact with an infected individual followed by rubbing the nose or eyes. Smoking and psychologic stress may increase susceptibility to viral upper respiratory infections. Once infected with a cold virus, individuals can be asymptomatic for approximately 48 to 72 hours during the viral incubation period. Although individuals may be asymptomatic during the incubation period, they may still be contagious. Inflammatory mediators, including histamine, kinins, and interleukins, are released in the nasal passages. Host responses to these mediators cause rhinitis, nasal secretions, nasal congestion, sneezing, sore throat, and cough. Nasal secretions may contain virus for up to one week after the overt symptoms of the cold are gone.⁹

Patient Assessment

The initial symptom of the common cold is generally a sore throat, followed by nasal symptoms, watering eyes, sneezing, and then cough. These symptoms are usually self-limiting, and resolve within 1-2 weeks regardless of treatment. The key to differentiating between a cold, the flu, and a bacterial infection is to assess the symptoms. (Table 1) For example, an abrupt onset of fever and chills without sneezing or itchy eyes is most likely the flu.

Treatment Options

Since there is no cure for the common cold, all treatment modalities are aimed at alleviating symptoms. In addition to any pharmacologic treatment that is instituted, non-pharmacologic measures should always be considered. These include rest and maintaining adequate fluid intake. Humidifiers or vaporizers may also be useful to alleviate symptoms. (Table 2)

Pharmacologic Treatment

When helping the patient select an appropriate product, the pharmacist should not overlook the value of the patient's prior OTC use and experience. Past product use may be obtained from the patient profile or a quick interview with the patient.

Analgesics/Antipyretics – Fever, Sore Throat, Aches/Pains

While patients may complain of feeling feverish, high fevers are rarely seen in patients with the common cold, and, if a fever persists, the patient should be referred to a physician. Some patients, however, may experience slightly elevated temperatures or mild myalgia, which may be relieved with OTC analgesics or antipyretics. While all the OTC products are effective for these symptoms, the choice of acetaminophen, aspirin, or an NSAID depends on the age of the patient and the presence of any co-existing diseases or drug therapies. For example, children should not take aspirin while they have a viral infection due to the potential for Reye's Syndrome.

The irritated or sore throat that frequently accompanies the common cold may result from local inflammatory mediators. Unless contraindicated, NSAIDs may be preferred over acetaminophen or regular dose aspirin. In patients with colds, experimental evidence suggests that acetaminophen and aspirin lower serum neutralizing antibody titers and increase the duration of viral shedding in nasal secretions.¹⁰ In addition, OTC lozenges, gargles, and sprays containing topical anesthetics, such as benzocaine, dyclonine, and phenol, may be used every 3-4 hours for temporary, symptomatic relief of a sore throat.

Decongestants – Nasal/Ocular Congestion

Decongestants are the mainstay of treatment for the common cold. They are alpha-adrenergic agonists which constrict blood vessels throughout the body, particularly the nasal and ocular vasculature.

Decongestants may be given orally or topically, including both intranasal and ophthalmic preparations (Table 2). Topical decongestants are minimally absorbed, decreasing the incidence of systemic side effects. Drainage into the stomach may occur when excess drops are applied to the nose (nasopharynx to the stomach) or eyes (nasolacrimal duct to the nasopharynx to the stomach), resulting in systemic absorption. Rebound congestion (Rhinitis Medicamentosa), manifesting as increased nasal congestion after decongestant cessation, may occur after only three days of use. This phenomenon is more common with shorter acting topical decongestants than longer acting agents.

Systemic decongestants, such as pseudoephedrine and phenylpropanolamine, constrict the alpha adrenergic vascular beds and stimulate the central nervous system. Cardiac side effects include increased blood pressure, increased heart rate, and palpitations. Nervousness, irritability, restlessness, and insomnia may also occur. Diseases potentially aggravated by decongestants include high blood pressure, heart disease, diabetes mellitus, hyperthyroidism, benign prostatic hyperplasia, and angle-closure glaucoma. In addition, decongestants are contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), which may further intensify the alpha-adrenergic effects of the decongestants. Therefore, when selecting a decongestant, pharmacists should question patients about the presence of concomitant diseases and the

use of other medications. An understanding of decongestant effects on various organ systems will aid in determining precautions and contraindications (Table 3).

The OTC decongestants are all Category C agents and, therefore, should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Additionally, lactating women should use decongestants with caution since it is unknown how much is excreted into breast milk following topical or systemic administration.¹¹ Topical saline drops are very safe and may be used in place of topical decongestants in pregnancy, lactation, and in infancy.

Expectorants/Mucolytics/Antitussives - Cough

The common cold can cause either a dry, hacking cough or a productive cough that results in the expectoration of sputum. A productive cough is the mechanism by which the body clears the lungs and airways of unwanted materials.

Nonprescription cough products contain expectorants, such as guaifenesin, or cough suppressants, such as dextromethorphan. Expectorants may thin sputum, increase volume, and facilitate expulsion. Guaifenesin is thought to expel respiratory tract secretions by reflex gastric stimulation. In 1992, the FDA warned against the use of OTC expectorants in children under 12 years of age if there is a persistent or chronic cough, such as occurs with asthma, or if the cough is accompanied by excessive mucus. The key to successful use of guaifenesin is to drink plenty of fluids to lower the viscosity of the sputum and aid in expectoration.

Antitussives, which inhibit or suppress the act of coughing, are most effective for dry coughs. Centrally acting agents suppress the medullary centers of the brain, decrease the sensitivity of respiratory system cough receptors, or interrupt the transmission of cough impulses. If they are given to a patient with a productive cough, more mucus is retained and may ultimately result in pneumonia.¹² Dextromethorphan, an isomer of levorphanol, is generally well tolerated at therapeutic dosages, however drowsiness and GI upset may occur. While at recommended doses addiction potential is low, doses exceeding 120 mg can result euphoria with bizarre behavior as a result of its opiate and phencyclidine (PCP) activities.¹³ In addition, concomitant use with monoamine oxidase inhibitors is not recommended due to the potential for hypertensive crisis.

Zinc

One of the most controversial and popular natural remedies for the common cold is zinc. Zinc lozenges and lollipops are widely available in pharmacies and supermarkets. Of ten randomized, controlled studies of zinc lozenges for the common cold, five showed positive results and five showed negative results.¹⁴ The exact mechanism of action of zinc is unclear, but it may inhibit viral binding to epithelial cells in the upper respiratory tract

Past clinical trials do not consistently support the efficacy of zinc gluconate lozenges to treat the common cold. The formulation of the lozenge, though, appears to be important because the addition of citric acid or tartaric acid in some preparations may actually reduce efficacy by chelating the zinc ion.¹⁵ The benefit appears to be maximal if

the lozenges are started immediately after the onset of symptoms. Common side effects include unpleasant taste, mouth irritation and nausea. Patients should be instructed to take one lozenge every 2 hours while awake and continue for the duration of the illness. To minimize the incidence of nausea, the lozenges should not be taken on an empty stomach. Additionally, citrus containing juices should be avoided within an hour of taking a lozenge to reduce the possibility of chelation of zinc ions.¹⁵

If a patient decides to use zinc, the pharmacist should advise the patient on conventional OTC medications that are effective for symptom management. Pediatric use should be discouraged until more information on safety and efficacy are available. Common OTC products containing zinc include Cold-Eeze and Zicam.

Vitamin C

The use of vitamin C to prevent or treat the common cold remains a controversial topic. The proposed mechanism of action is that vitamin C, an antioxidant, neutralizes the large amounts of oxidizing compounds released by neutrophils. An extensive review of 61 trials published between 1940 and 1991 concluded that vitamin C, even in gram doses per day, cannot prevent a cold.¹⁶ However, it has been suggested that large doses, 1-4 grams per day, may decrease the duration and severity of symptoms by 10-29%.¹⁷ The patient should be cautioned that large doses of ascorbic acid could lead to diarrhea and renal stones.

Herbals

Herbal products have recently gained increasing interest with the public as a remedy for the common cold. Studies of efficacy using double-blind, placebo-controlled methods are rare. However, some of the more widely used products will be studied in the near future under the sponsorship of the National Institutes of Health. (Table 4)

Homeopathy

Homeopathy is based on the theory similars. For example, large doses of drugs that produce symptoms of a disease in healthy people will cure the same symptoms when administered in extremely small amounts.¹⁸ After the many dilutions required for potency, these products probably contain no measurable active ingredient. Although some studies report positive findings, well-designed, clinical trials have yet to be conducted.¹⁹ The lack of valid clinical evidence has not deterred the public from purchasing these products to the tune of millions per year. One popular product is *oscillococcinum*

Oscillococcinum is a common remedy used by practitioners of homeopathic medicine as well as the public for the treatment of symptoms of the common cold and flu. It contains extremely diluted constituents of autolysed duck heart and liver with literally no “active” ingredient detectable.^{19,20} One placebo-controlled study conducted in France in patients with influenza-like symptoms demonstrated a significantly greater number of

patients recovering within 48 hours after initiation of oscillococinum compared to placebo. However, this study was significantly flawed by multiple factors, rendering the results useless.²⁰

Future

Current drug therapy is aimed at ameliorating the symptoms of the cold, not eliminating the causative virus. Pleconaril is a new investigational antiviral drug with activity against picornoviruses, including rhinoviruses and enteroviruses, a cause of viral meningitis.²¹ Initial trials of Pleconaril versus the common cold did not demonstrate a dramatic decrease in cold symptoms, but subsequent trials may show otherwise.

Conclusion

Despite the numerous OTC products available for symptomatic treatment of the common cold, a definitive cure remains to be discovered. Supportive care remains the mainstay of therapy. Therefore, as pharmacists, it is important that we assess each patient individually, taking into account other disease states and current drug therapy, as we target our counseling and recommendations to the individual's specific symptoms.

(Table 5)

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Table 1 Influenza vs. Common Cold vs. Bacterial Infection

Characteristic	Influenza	Common Cold	Bacterial
Presentation	Generalized	Local-nose & throat	Systemic
Onset	Sudden	Gradual	Gradual-sudden
Fever	High (>100°F)	Mild	High (>100°F)
Differential symptoms	Headache Chills Muscle pains Nonproductive Cough Sore throat Anorexia	Sneezing Nasal congestion Sore throat Productive cough	Chills Chest pain Productive cough Tachycardia Tachypnea
Fatigue, weakness, & exhaustion	Extreme	Mild	Extreme
Duration	1-5 days high fever; 1-3 weeks symptoms	1 week; rapid recovery	variable
Complications	Pneumonia; bronchitis	Earache	Sepsis

Table 2 Symptomatic OTC Treatment of the Common Cold

Symptom	Treatment
Nasal congestion and discharge	Decongestants Systemic Ephedrine Phenylephrine Phenylpropanolamine Pseudoephedrine Inhalers Desoxyephedrine Propylhexedrine Topical (duration) Short Acting (4-6 hours) Ephedrine Epinephrine Naphazoline Phenylephrine Tetrahydrazoline Intermediate Acting (8-10 hours) Xylometazoline Long Acting Oxymetazoline Ophthalmic Epinephrine Naphazoline Oxymetazoline Phenylephrine Tetrahydrazoline
Cough	Hydration Antitussives Expectorants Cool mist/steam vapors
Sore throat	Saline gargles Local anesthetics Systemic analgesics
Feverishness and headache	Systemic analgesics

Adapted from reference 23

Table 3 Adverse Effects and Potential Contraindications of Decongestants

Target Symptoms	Systemic Effects	Adverse Effects	Potential Contraindications
Blood vessels	Constricts	Hypertension	Hypertensive patients MAOI use within past 2 weeks
Heart	Stimulates	Tachycardia	Arrhythmia Cardiovascular disease
Eye	Constricts radial muscle	Increase intraocular pressure	Glaucoma
Genitourinary tract	Constricts bladder sphincter	Obstructs urinary flow	BPH
Exocrine glands	Stimulates	Hyperthyroidism Hyperglycemia	Hyperthyroidism Diabetes
Central nervous system	Stimulates	Excitability	Seizures

Table 4 Herbal Products

Herb	Use	Clinical Considerations
Echinacea	Supportive therapy for colds and chronic infections of the respiratory tract; immunostimulant	<ul style="list-style-type: none"> • Cross sensitivity in patients allergic to sunflower seeds • Caution in patients with autoimmune disease, AIDS, or leukemia because of T-cell and macrophage stimulation • Not recommended for chronic use
Ephedra (Ma Huang)	Bronchial asthma (produces bronchodilation, vasoconstriction, and reductions in bronchial edema)	<ul style="list-style-type: none"> • Avoid in patients with cardiac conditions, HTN, diabetes, or thyroid disease • Side effects: nervousness, insomnia, palpitation • Avoid concomitant use with decongestants, weight control products
Goldenseal	Antimicrobial, astringent, and antihemorrhagic activity in the treatment of mucosal inflammation	<ul style="list-style-type: none"> • Absolute Contraindicated in pregnancy
Horehound	Expectorant, antitussive	<ul style="list-style-type: none"> • FDA declared ineffective as a cough suppressant and expectorant

Adapted from reference 22

Table 5 Patient Counseling Tips

- Select medications that treat only the symptoms you have.
- Don't take medicines longer or in higher doses than the label recommends. If symptoms persist, see a physician.
- If the label says use two teaspoons, use a measuring spoon, or a dosing cup marked in teaspoons, or an oral syringe, instead of a common kitchen spoon.
- Find out if the patient has other medical conditions (diabetes, hypertension, hyperthyroidism) or is currently taking any prescription or nonprescription medications that should be considered in selecting a product.
- Determine what products have been tried and the outcome of prior therapy.
- Select a product that is most convenient for the patient to take to enhance compliance.