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The common cold: Current therapy and natural history

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Despite its prevalence, the common cold is complicated and can be difficult to treat, even symptomatically. There is still no cure for the myriad of viruses that cause the common cold. Many of the most popular remedies are either ineffective or counterproductive. This paper reviews the causes and course of upper respiratory infections, and discusses treatment options, including a new anticholinergic aqueous formulation for controlling rhinorrhea. (J ALLERGY CLIN IMMUNOL 1995;95:1133-8.)

Key words: *Common cold, upper respiratory infection, epidemiology, etiology, pathophysiology, treatment*

As new data emerge regarding the pathophysiology of upper respiratory infections (URIs), we continue to gain new insight into their treatment and possible complications. It has been estimated that the average preschool child experiences six to ten URIs, or "colds," per year; the average adult has two to four.[1] The effects of the common cold can be uncommonly disruptive, forcing otherwise normal individuals to miss work, school, or other important activities. Individuals who are at increased risk, such as those with bronchitis or asthma, may also experience a life-threatening exacerbation of their underlying conditions. The average annual expenditure for various cold treatments exceeds $2 billion in the United States. This statistic becomes even more provocative when we consider that one of every three individuals with a confirmed infection has no apparent symptoms of a cold.

Abbreviation used
URI: Upper respiratory infection

EPIDEMIOLOGY AND ETIOLOGY

Viruses that cause colds can be spread through contact with inanimate surfaces,[2] as well as by hand-to-hand contact.[3] Seasonal variations in cold patterns have long been recognized. Generally there are fewer colds in the warm summer months and more colds during periods of crowding, particularly the fall. In spite of the nomenclature, exposure to cold temperatures per se does not seem to be a significant factor in cold epidemiology. Folklore is somewhat at odds with modern science over this issue; there are many cultures where youngsters who have a "cold" are dressed sufficiently to keep them warm on the coldest winter night, even when the outside temperature is tropical.

Colds are caused by a wide variety of viruses (Table I). The rhinoviruses, which account for more than 30% of colds in adults, have more than 100 antigenically different types. Coronaviruses also appear to be responsible for a large percentage of colds, but precisely what that percentage is compared with parainfluenza or respiratory syncytial viruses has not yet been well established. Certain viruses appear to be more common in children than adults, but in general, viruses appear in roughly the same proportions in both populations. Some viruses may be associated with more severe symptoms than others, for example, the exacerbation of asthma seen with respiratory syncytial virus. However, the most significant factor in the severity of a viral infection seems to be the incubation period.[4]

Various factors are thought to increase susceptibility to URIs. There seems to be a relationship between colds and stress. In assessing the differences between symptomatic and asymptomatic individuals with confirmed viral infections, Stone

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TABLE I. Infectious agents associated with the common cold

Category	Agents	Type or subtype
The usual perpetrators	Rhinovirus	1-100+
	Parainfluenza	1-4
	Respiratory syncytial virus	2
	Coronavirus	Numerous
Occasional culprits	Adenovirus	~31
	Enterovirus	Coxsackie A (1-24) and B (1-6), echovirus (1-34)
	Influenza	A, B, C
	Reovirus	1-3
	Mycoplasma pneumoniae	
Rare offenders	*Coccidioides immitis*	
	Histoplasma capsulatum	
	Bordetella pertussis	
	Chlamydia psittaci	
	Varicella	
	Rubeola	
	Epstein-Barr virus	
	Herpes simplex	

et al.[5] found a correlation between the manifestation of colds and life events involving major stress. Cohen et al.[6] found an association similar to a dose-response between psychologic stress and increased risk of acute infectious respiratory illness; the risk involved increased rates of infections rather than frequency of symptoms after infection. Smokers are at greater risk than nonsmokers to develop both infections and symptoms after infection.[6] It also appears that certain drugs may increase susceptibility to colds. Aspirin and acetaminophen suppress sero-neutralizing antibody response ($p < 0.05$) and are associated with increased nasal symptoms and signs. There is a trend towards longer duration of virus shedding with both of these medications.[7]

PATHOPHYSIOLOGY

Common cold viruses characteristically cause an infection that is self-limited and of short duration. Although shedding of rhinovirus has been shown to last 3 weeks in young adults with experimentally induced colds,[8,9] rhinoinfections with coronavirus are usually detected for only a few days. Most colds are not associated with cell necrosis or significant mucosal damage, but there may be some sloughing of columnar epithelial cells.[10] Initially there is an increase in vascular permeability,[11] followed later by glandular secretions, both of which may have implications with regard to the timing and effectiveness of treatment.

The constituents of the glandular secretions provide clues to their origins.[11,12] There is an elaboration of inflammatory mediators such as kinins. When these mediators accumulate along with polymorphonuclear cells, there is an increase in nasal symptoms.[13] Since bradykinin is a likely mediator,[14] we might expect that a bradykinin antagonist would be a useful treatment. It is therefore somewhat surprising that a study of a bradykinin antagonist in rhinovirus infections failed to demonstrate any positive results; the lack of effect may have been related to the dose administered.[15] Hsia et al.[16] postulated the activation of a systemic cellular immune response with a URI. For example, they found that a blastogenic response to the rhinovirus challenge correlated directly with mucus production ($p < 0.05$) and the number of days the virus was cultured from nasal washings ($p < 0.05$). Skoner et al.[17] also found induction of specific and nonspecific systemic cellular responses with a unique response pattern in subjects with allergic rhinitis. Production of interleukin-1 from nasal lavage fluid after rhinovirus infection is also thought to contribute to pathogenesis.[18] These interactions, as reviewed by Sperber and Hayden,[19] are seen in Fig. 1.

There are many potential complications to the common cold. Subjects with asthma (or bronchitis) may experience an acute exacerbation of their underlying disease after viral exposure.[20] Pneumonia may follow a URI associated with influenza; this lower-respiratory response would be unusual with other URI viruses. Sinusitis may accompany a

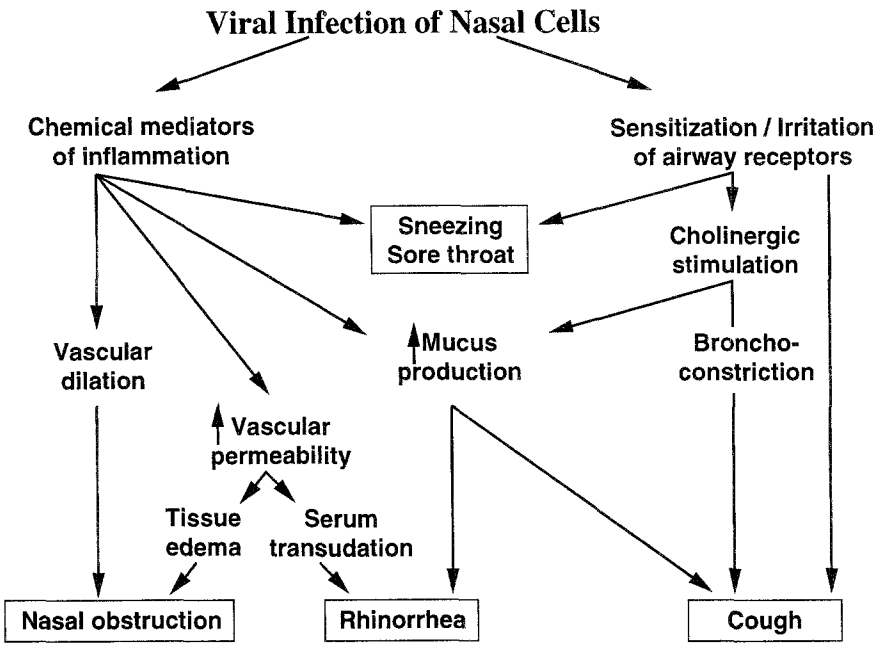

FIG. 1. Theoretical scheme of symptom pathogenesis in rhinovirus colds. (From Sperber SJ, Hayden FG. Antimicrob Agents Chemother 1988;32:409-19, by permission of The American Society of Microbiology.)

TABLE II. Incidence of epistaxis in the general population determined by telephone survey*

Treatment used	No.	Patients experiencing nosebleed (%)	Patients experiencing blood in tissues (%)
All patients	1533	7.4	15.8
No medication	290	7.2	9.0
OTC product	970	6.8	15.6
Prescription product	91	7.7	20.9
Both OTC and prescription product	181	11.0	25.4

OTC, Over-the-counter.
*R. Dockhorn, MD, unpublished data.

URI in more people than was previously realized, as is now becoming apparent with more sensitive techniques of detection.[21, 22] Digital tympanometry indicates that natural rhinovirus colds in adults are frequently associated with marked but transient middle-ear pressure abnormalities.[23] In a telephone survey of 1533 patients aged 18 years or older who had upper respiratory infections within the previous 6 months, it was found that the incidence of nasal bleeding was quite high (R. Dockhorn, unpublished data) (Table II). Although Doyle et al.[24] reported no increase in nasal responsiveness to an infectious trigger in allergic compared with nonallergic individuals, Bardin et al.[25] found that patients with allergic rhinitis had more severe colds independent of preinnoculation antibody. There is also an increased twitchiness of the tracheal bronchial tree following colds.[26]

TREATMENT

Sir William Osler has been quoted as saying, "There is just one way to treat a cold, i.e., with contempt." We seem to have made some progress in the treatment of URIs since this statement was made, due largely to a better understanding of the pathophysiology of colds, although there is certainly still room for improvement. Some treatments used today are better choices than others in terms of pathophysiology. As mentioned previously, both aspirin and acetaminophen may have a detrimental effect on cold treatment, neutralizing antibodies and increasing nasal symptoms.[27] In a

study by Sperber et al.,[28] naproxen did not alter virus shedding or serum neutralizing antibody in experimental rhinovirus cold, but it had a beneficial effect on such symptoms as headache, malaise, myalgia, and cough. Oral α-agonists relieve congestion in many individuals, although their effect is not dramatic.[29, 30] Topical decongestants may also help; unfortunately, if they are overused they may also be associated with rebound congestion or worsening of symptoms.

The role of antihistamines in the treatment of the common cold has been debated. Some antihistamines do not seem to be very effective,[31] whereas others may provide mild benefit. Antihistamine/decongestants do not appear to be effective in the treatment of URIs in children.[32, 33] Cromolyn sodium and nedocromil have both been studied; they do not cause a worsening of symptoms, but neither do they seem to provide any significant improvement.[34, 35] Apparently menthol cannot be positively demonstrated to provide a beneficial effect.[36] Interferon has been used in various studies with negative results.[37-39] Either intranasal or systemic steroids may suppress inflammation during the first days of infection, and would seem to merit further investigation.[40] Among the many nonpharmacologic therapies, steam has been shown by various authors to provide no beneficial effect;[41, 42] however, with proper timing, local hyperthermia[43] or sauna[44] may decrease the incidence of colds or provide slight relief. In general, the use of zinc has been disappointing and is associated with side effects.[45] Godfrey et al.[46] commented on the poor bioavailability of the older zinc products and found a statistically significant decrease in the duration of colds with their nonchelated formulations. Vitamin C may decrease the duration of cold symptoms.[47, 48] Of course, chicken soup is well known to provide benefit in the common cold (as long as it is one's mother's). In answer to the cynics who doubt such an assertion, chicken soup has been demonstrated to improve mucociliary clearance.[49]

There are new pharmacologic therapies on the horizon that may prove useful to the physician in the treatment of the common cold. Ipratropium bromide nasal spray, an anticholinergic therapy, has the unique property of specifically controlling rhinorrhea in URIs, as has been demonstrated in many studies.[50, 51] A novel attempt at antiviral therapy includes blockade of the receptor where the virus attaches.[52] Such a treatment may be useful against rhinoviruses that affect one or two common receptors but may not be applicable to less specific viruses.

SUMMARY

Modern research has demonstrated that URIs have myriad causes and complex effects. Although some time-honored treatments might have limited usefulness, novel attempts at ameliorating the symptoms of a common cold, such as the use of ipratropium bromide nasal spray or specific antiviral receptor therapy, might represent a significant advance. They are based on a better understanding of the pathophysiology of URIs.

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