

6. Busse W. New directions and dimensions in the treatment of allergic rhinitis. *J ALLERGY CLIN IMMUNOL* 1988;82:890-900.
7. van Megen YJ, Klaassen AB, Rodrigues de Miranda JF, van Ginneken CA, Wentges BT. Alterations of muscarinic acetylcholine receptors in the nasal mucosa of allergic patients in comparison with nonallergic individuals. *J ALLERGY CLIN IMMUNOL* 1991;87:521-9.
8. Meredith SD, Raphael GD, Baraniuk JN, Banks SM, Kaliner MA. The pathophysiology of rhinitis. III. The control of IgG secretion. *J ALLERGY CLIN IMMUNOL* 1989;84:920-30.
9. Devillier P, Dessanges JF, Rakotosihanaka F, et al. Nasal response to substance P and methacholine in subjects with and without allergic rhinitis. *Eur Respir J* 1988;1:356-61.
10. Meltzer EO, Orgel HA, Bronsky EA, et al. Ipratropium bromide aqueous nasal spray for perennial allergic rhinitis patients: a study of its effect on their symptoms, quality of life and nasal cytology. *J ALLERGY CLIN IMMUNOL* (in press).
11. Kirkegaard J, Mygind N, Molgaard F, et al. Ordinary and high-dose ipratropium in perennial nonallergic rhinitis. *J ALLERGY CLIN IMMUNOL* 1987;79:585-90.
12. Simons FER. Anticholinergic drugs and the airways: Time future contained in time past [Editorial]. *J ALLERGY CLIN IMMUNOL* 1987;80:239-42.
13. Milford CA, Mugliston TA, Lund VJ, Mackay IS. Long-term safety and efficacy study of intranasal ipratropium bromide. *J Laryngol Otol* 1990;104:123-5.
14. Mygind N, Borum P. Intranasal ipratropium: literature abstracts and comments. *Rhinology* 1989;(suppl 9):37-44.
15. Bok HE, van Wijngaarden HA, Cornelissen PJG. Intranasal ipratropium bromide for paroxysmal rhinorrhoea. *Eur J Respir Dis* 1983;64(suppl 128):486-9.
16. Malmberg H, Grahne B, Holopainen E, Binder E. Ipratropium (Atrovent) in the treatment of vasomotor rhinitis of elderly patients. *Clin Otolaryngol* 1983;8:273-6.

A double-blind, placebo-controlled study of the safety and efficacy of ipratropium bromide nasal spray versus placebo in patients with the common cold

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*Ipratropium bromide (IB) has been found to reduce secretions in the upper respiratory tract; this is accomplished through competitive inhibition of acetylcholine at muscarinic receptors that control rhinorrhea production. This study compared the safety and efficacy of IB with placebo in the symptomatic relief of rhinorrhea in patients with the common cold. Human subjects with symptoms of a common cold, primarily rhinorrhea, were enrolled and treated with either IB (84 µg/nostril) or placebo; each was administered as two sprays per nostril, four times a day, for 4 days. Primary efficacy analyses were in-clinic measurements of nasal discharge weights over a 3-hour period after administration on days 1 and 2 and assessment of rhinorrhea symptoms by use of a subjective patient-completed visual analog rating scale. IB significantly reduced rhinorrhea an average of 18% over placebo for days 1 and 2 ($p = 0.01$). Visual analog scale scores showed an average improvement in rhinorrhea of 22% over placebo ($p = 0.001$). When patients with relatively minor rhinorrhea (baseline weight of nasal discharge ≤ 1.0 gm) were excluded, IB produced an average reduction in nasal discharge of 23% over placebo for days 1 and 2 ($p = 0.003$). (*J ALLERGY CLIN IMMUNOL* 1992;90:1076-82.)*

Key words: Common cold, rhinorrhea, ipratropium bromide, nasal discharge

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The common cold is the most frequently occurring infectious problem in humans. In particular, it is the most common upper respiratory tract infection. The etiologic agents most clearly associated with common colds are the rhinoviruses, which comprise three genera of the family of picornaviruses. At least 50 anti-

genically distinct serotypes of infectious rhinoviruses have been identified. However, on the basis of viral isolation studies of nasal secretions, rhinoviruses account for only 25% to 35% of colds experienced by adults and probably 10% to 25% of those in children. Thus the etiologic agents responsible for most common colds have not been identified.

As a consequence, effective preventive or curative therapies for colds remain elusive, although symptomatic relief can often be provided. The well-known clinical manifestations of the common cold include sneezing, watery nasal discharge, which becomes thicker and assumes a yellowish and semipurulent appearance over several days, and a subjective feeling of general malaise. Fever is usually absent, and cough is not common early in the infection. During the initial phase of a cold, the nasal mucous membrane is edematous and has a boggy appearance. The nasal mucosa is primarily innervated by the parasympathetic nervous system. Therefore this system plays an important role in the production of rhinorrhea by the mucous and seromucous glands.

In a study of experimental rhinovirus colds,¹ intranasally administered atropine methonitrate, 125 µg sprayed twice into each nostril four times daily for 5 days, was shown to reduce nasal mucous production and result in subjective reports of nasal drying. Nasal "symptoms" and patency remained unaffected. In both noninfected and infected volunteers, dosage was accompanied by side effects such as dry mouth, dry eyes, and systemic phenomena. Bleeding sites in the nasal mucosa were observed in 33% of infected patients and in 20% of noninfected volunteers. Lower atropine dosage did not significantly reduce nasal symptoms or mucous production compared with placebo.

The secretory response to methacholine during a common cold is stronger the first 2 days; this parallels the degree of spontaneous hypersecretion in patients with a common cold. Forty patients, each of whom had a naturally acquired common cold, participated in a study. All patients were randomly assigned to receive placebo or 80 µg of IB four times a day for 7 days 5 minutes after the administration of an intranasal vasoconstrictor (xylometazoline 0.1%). The nasal discharge was significantly reduced by IB, and the effect was most pronounced during the first few days when the secretions were mainly watery. During this time the use of paper handkerchiefs in the group receiving IB was one half of that in the placebo group. There was no difference in the number of sneezes per day. Seven subjects in the placebo group and 10 in the IB group had slight local side effects of dryness in the nose and throat during the last days of the

Abbreviations used

IB: Ipratropium bromide
VAS: Visual analog scale

treatment when the hypersecretion had almost ceased. Because of the changing secretory activity during the first week of the disease and the rapid onset of IB activity, varying doses and frequency of administration of an anticholinergic agent appear to be the most appropriate treatment regimen for a viral rhinitis.²

Experimentally induced viral rhinitis was also examined to determine the effect of anticholinergic medications in the reduction of nasal hypersecretion. For 5 days beginning 24 hours after challenge with rhinovirus type 39, 80 µg of IB was sprayed intranasally three times a day. Most volunteers in both the active treatment (73%) and control groups (79%) developed infections as determined by viral shedding. However, clinical colds occurred in 50% of the volunteers receiving IB compared with 76% of the placebo recipients ($p < 0.05$). The mean nasal mucous weights, rhinorrhea score, and tissue counts also tended to be lower in the group receiving IB. Although side effects occurred more often in volunteers receiving medication (dry nose and dry mouth), intranasal IB was generally well tolerated.³

The anticholinergic atropine methonitrate was also assessed for the treatment of experimental rhinovirus colds. A dose of 125 µg three times daily had no effect on symptoms or signs. A higher dose of 250 µg administered by nasal spray four times daily for 5 days beginning 24 hours after challenge with rhinovirus type 39 was associated with subjective drying and a reduction in nasal mucous production. Atropine methonitrate had no effect on nasal patency.

The published literature contains several reports on the safety and efficacy of intranasally administered IB, a quaternary isopropyl derivative of atropine, in the relief of symptoms of the common cold.⁴⁻⁹ The objective of the present study was to assess the safety and efficacy of 0.06% IB nasal spray compared with placebo in the symptomatic relief of rhinorrhea associated with the common cold. IB is a quaternary ammonium anticholinergic compound that reduces secretions in the upper respiratory tract through a competitive inhibition of acetylcholine at muscarinic receptors. Because of its chemical structure, minimal systemic absorption of IB occurs when it is administered by the inhalation (topical) route; this results in a favorable safety profile.¹⁰

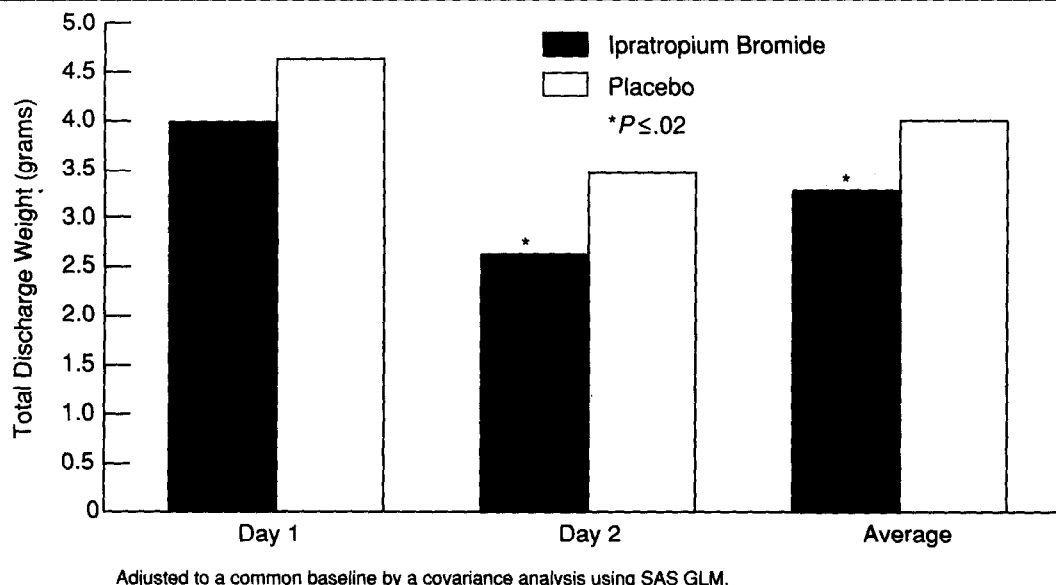


FIG. 1. Mean weight of nasal discharge by treatment ($N = 301$ patients).

The low absorption levels of IB and its therapeutic action when applied directly to the target organ suggest that IB may be an ideal choice for symptomatic relief of rhinorrhea in the common cold. In two studies nasal discharge was significantly reduced in patients receiving intranasal IB compared with placebo. No effects were noted on sneezing or nasal congestion.^{10, 11}

MATERIAL AND METHODS

Study design

The study was timed to end before the onset of the allergy season. A parallel rather than a crossover design was used for this trial because of the short-term nature of the condition under study. In this design each patient receives only one treatment, and comparisons are made between treatment groups. The primary drawback to a parallel design is that each subject cannot act as his or her control. Comparisons between treatment groups may be subject to more variability than in a crossover design, and consequently a larger sample size is required for a parallel study.

Study participants

The study was a double-blind, placebo-controlled, multicenter trial in which 321 participants were enrolled (159 received IB and 162 received placebo). Of these, 317 were included in the intent-to-treat analysis, and 301 were included in the full efficacy analysis. The mean age of participants was approximately 29 years. Males and females represented about 45% and 55% of the total, respectively. Age, sex, height, and weight of the participants were comparable in the active drug and placebo groups.

Patients were excluded from the study if they had sig-

nificant cardiovascular, renal, hepatic, endocrine, metabolic, neurologic, pulmonary, or other systemic disease, or if they had a history of asthma or other chronic respiratory disease, perennial rhinitis, nasal polyps, glaucoma, or unresolved prostatic hypertrophy. Patients with allergic rhinitis were excluded if their allergen was in season or ubiquitous in their environment (e.g., animal dander). Participants were not admitted to the study if they had a positive *Streptococcus* culture, the presence of rales or rhonchi suggestive of a lower respiratory tract infection, a temperature greater than 102° F, or a history of frequent complications associated with upper respiratory tract infections. Also excluded were lactating women, women with a positive pregnancy test, or women of childbearing potential who did not use a medically approved method of contraception; persons judged unable to adequately maintain a symptom record form; and those persons who could not tolerate anticholinergics or were sensitive to benzalkonium chloride.

To enroll in the study, patients were required to have moderate rhinorrhea for less than 36 hours and swollen, erythematous nasal mucosa on examination. At baseline, the mean duration of rhinorrhea among study participants in the placebo group was 23.9 hours; among those in the active drug group it was 22.8 hours. Mean weights of nasal discharge for 1 hour at baseline were comparable in the two groups—2.56 gm in the placebo group and 2.76 gm in the group receiving active treatment.

Drug administration

The duration of the study was 5 days. Medication (IB) or placebo was administered by nasal spray four times a day for the first 4 days. Each spray of active drug delivered 42 µg of IB; at each dose two sprays were delivered to each nostril for a total of 84 µg per nostril per dose or 672 µg

(0.672 mg)/day. Participants' supplies of medication were weighed at each visit to verify that doses were being taken as instructed. Previous studies in patients with chronic rhinitis and the common cold have shown IB doses ranging from 40 to 200 µg per nostril as an inhaled aerosol have been effective in reducing rhinorrhea.¹²

Concomitant medications

Over-the-counter analgesics such as acetaminophen, aspirin, or ibuprofen were permitted. The only cough medications allowed during the study were Robitussin and Robitussin-DM (A.H. Robins Company Inc., Richmond, Va.). For 24 hours before study entry and during the study, patients were not allowed to take any antiasthma medications or other medications for relief of cold symptoms. Anticholinergics, including tranquilizers and antidepressants with anticholinergic effects, and investigational drugs other than the study medication were not permitted.

Data collection

On day 1 before randomization to either drug or placebo, participants underwent nasal and general physical examinations and completed a baseline subjective self-assessment of the severity of their symptoms with the use of a VAS. The VAS is a 0- to 10-point scale that participants were instructed to mark to rate the severity of their cold symptoms. A score of 0 represented no symptoms, and 10 represented unbearable discomfort requiring additional treatment, which forced the patient to withdraw from the trial. Intermediate degrees of discomfort were defined as *very mild*, doubtful, trivial, or just noticeable; *mild*, present but not uncomfortable; *moderate*, present and somewhat uncomfortable or annoying; and *severe*, present and definitely uncomfortable or annoying.

After randomization, patients undertook a 1-hour baseline collection of nasal secretions. They were instructed not to sniff to clear their noses but to collect all secretions in previously weighed paper tissue handkerchiefs that were kept in a plastic bag to minimize evaporation. After this baseline collection, the first dose of medication or placebo was administered, and the weighed medication container was given to the patient.

Measurements of rhinorrhea (paper handkerchief weights) and subjective assessments of symptoms were repeated on day 1 at 1, 2, and 3 hours after drug administration and again on the second day at 1, 2, and 3 hours after drug administration. Before patients left the study site on day 1, they were given symptom record forms to be completed daily. Participants underwent repeat nasal examinations on the second and last days of their study participation. At the time of the last visit, usually on day 5, participants had not taken any study medication at all for approximately 24 hours. (Some patients returned for their last visit on day 7 and had consequently been without medication for longer periods.)

Data analysis

This trial was designed to determine whether rhinorrhea was reduced in patients given IB compared with patients

given placebo. Three endpoints were established to evaluate the change in rhinorrhea: (1) average weight of nasal discharge over 3 hours on days 1 and 2 of drug administration compared with baseline; (2) change from baseline of patients' evaluation of rhinorrhea symptoms using the VAS over 3 hours on days 1 and 2 and for both days averaged versus baseline; and (3) change from baseline in rhinorrhea symptoms as evaluated by patients using the VAS, averaged over days 1 and 2 and separately averaged over days 3 and 4. As secondary measures of efficacy, patients also made daily VAS assessments of sneezing and stuffy nose, each of which were averaged separately for the first 2 days and the second 2 days.

RESULTS

Overall, the study demonstrated that IB significantly reduced the rhinorrhea associated with the common cold, as measured by weight of nasal discharge and patients' subjective assessment of rhinorrhea severity using the VAS. Patients in both the active treatment (IB) and the placebo groups experienced improvement in symptoms that was greater on day 2 of the study than on day 1. It should be noted that amelioration of symptoms was expected on placebo, because the placebo was not an innocuous vehicle.

The weight of nasal discharge was significantly decreased; both the IB and placebo groups showed progressive reduction in discharge weight from baseline through day 1 to day 2. The IB group experienced a significantly greater improvement than did the placebo group (Fig. 1). Among patients included in the full efficacy analysis, a 14% difference occurred in mean discharge weight between patients receiving IB and placebo on day 1, 23% on day 2, and 18% for the average of the 2 test days. These differences were statistically significant on day 2 ($p = 0.01$) and for the average of both days ($p = 0.02$).

When patients with relatively minor rhinorrhea (baseline weight of secretions <1 gm) are excluded, the difference between treatment groups becomes more pronounced (Fig. 2). On day 1 the difference was 19%; patients taking IB had significantly less nasal discharge than did placebo patients ($p = 0.03$). On day 2 the difference between groups was 28%, which was also significant ($p = 0.003$), as was the average for the 2 days (23%, $p = 0.003$). Thus symptomatic improvement was more marked in patients whose rhinorrhea was initially more severe.

A parallel change was observed in patients' subjective assessment of change in rhinorrhea as rated on the VAS. Again, there was significantly more improvement with IB than with placebo on both days and improvement increased from day 1 to day 2 (Fig. 3). Improvement with IB was 19% more than improvement with placebo on day 1, 23% more on day

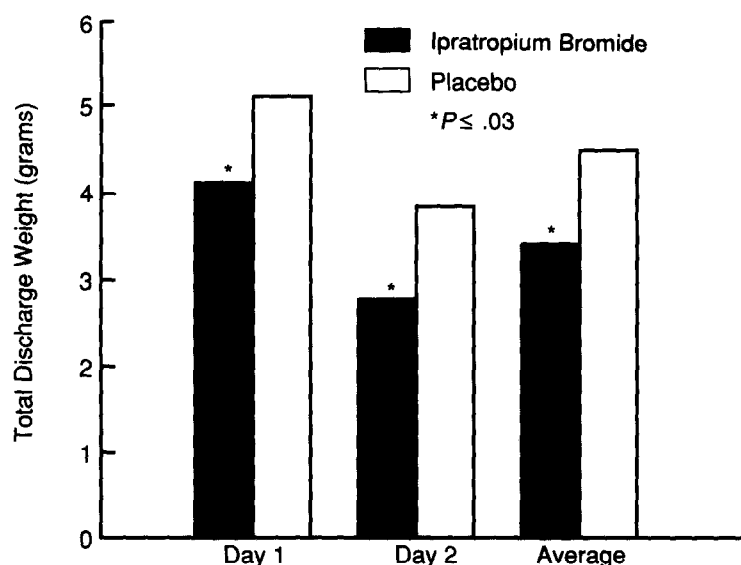


FIG. 2. Mean weight of nasal discharge by treatment. ($N = 253$ patients with baseline discharge weight ≥ 1.0 gm).

TABLE I. Frequently occurring adverse events ($N = 321$ patients)

Type of adverse event*	% of patients	
	IB	Placebo
All	16.4	13.6
Epistaxis (nosebleed, blood-tinged mucus)	6.3	1.9
Rhinitis (nasal dryness, crusting)	4.4	3.1
Headache	2.5	3.7
Dry mouth	1.3	0.0
Otitis media	0.0	1.2

*Lists only adverse events affecting $\geq 1\%$ of patients in either group.

2, and 22% more for the 2 days averaged ($p < 0.02$). Although improvement continued with further treatment so that patients in both groups rated their symptoms reduced still further on days 3 and 4, the difference between the groups did not reach the same level of statistical significance. No significant difference was noted between the two treatment groups in sneezing and nasal congestion.

Adverse events

The overall incidence of adverse events was similar in the two treatment groups. Adverse events were

experienced by 16.4% of IB-treated patients and 13.6% of placebo-treated patients. No adverse events were considered serious. The most frequently occurring side effects included epistaxis, headache, and rhinitis, which was described as nasal dryness and crusting. Adverse events are summarized in Table I.

Nasal examinations

Nasal mucosal color and edema, quantity, color, and consistency of rhinorrhea and the presence of postpharyngeal secretions were examined at each patient visit. Most patients experienced improvement in all these characteristics. However, 8 of 157 patients receiving IB and 12 of 159 patients taking placebo experienced a worsening of symptoms, that is, a color change from normal to red or red to pale, a change in edema from mild to moderate, or an increase in rhinorrhea. Of 316 patients in the study who had exit physical examinations, 11 had physical changes regarded as worsening from baseline. Such changes included the development of wheezing, rhonchi, and rales, worsening of the nasal condition, otitis, pharyngitis, and conjunctivitis. Such changes are not inconsistent with the continuation or progression of a common cold.

DISCUSSION

IB nasal spray has been previously shown to decrease the production of nasal secretions from rhinorrhea caused by the common cold. This effect is

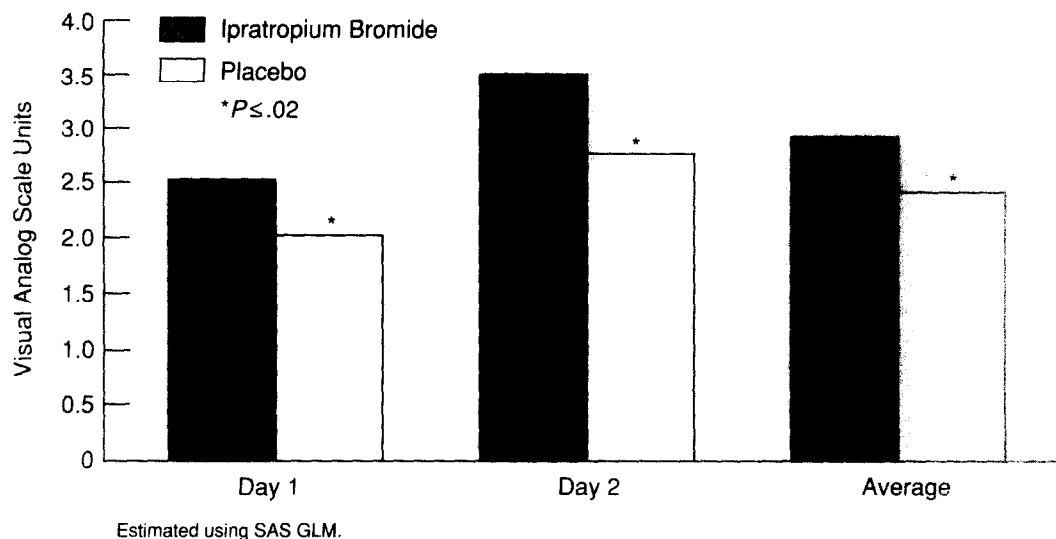


FIG. 3. Improvement in rhinorrhea by treatment as assessed by VAS ($N = 301$ patients).

more marked during the early stages of the infection because hypersecretion and production of watery rhinorrhea tend to become displaced by more mucopurulent secretions as the illness continues.¹⁰ IB has also been found to be effective in relieving watery rhinorrhea associated with perennial rhinitis, as well as rhinorrhea associated with exposure to cold air or ingestion of hot, spicy soup.² It has also proved effective in inhibiting experimentally induced nasal mucosal hypersecretion produced by intranasal instillation of methacholine.³ However, because of its route of topical administration as a nasal spray and its lack of systemic effect, it can be expected to relieve rhinorrhea arising only in the nasal mucosa and not, for example, in the paranasal sinuses or other sites.²

In a study by Gaffey et al.,¹¹ rhinovirus was instilled into the nasal cavity to provide an experimentally induced infection. The dosage of IB was 80 μg three times daily intranasally (a total of 240 μg or 0.240 mg/day), beginning 24 hours after the initial viral challenge. Results of this study were similar to those in the present study involving naturally acquired infections, with both active drug and placebo providing relief but with significantly greater relief associated with IB treatment. However, it was also found that after 5 days of treatment, approximately 75% of the placebo-treated patients continued to shed rhinovirus, whereas viral shedding was observed in only 50% of the group treated with IB. Although it is reasonable to expect relief of symptoms to accompany a reduction in viral shedding as the infection resolves, the connection between these observations and the use of IB

was not made explicit. Further investigation may be indicated to show whether IB can reduce the length of an actual rhinovirus infection, in addition to providing relief of symptoms.

CONCLUSION

In conclusion, it was found that IB significantly reduced rhinorrhea associated with the common cold, as measured by weight of nasal discharge and by patients' subjective assessments of severity of rhinorrhea. The treatment was found to be safe and well tolerated, with a low incidence of side effects. Ongoing studies are planned to clarify the effects of slightly higher doses of IB as well as the effects of the placebo alone.

REFERENCES

1. Gaffey MJ, Gwaltney JM, Jr, Dressler WE, Sorrentino JV, Hayden FG. Intranasally administered atropine methonitrate treatment of experimental rhinovirus colds. *Am Rev Respir Dis* 1987;135:241-4.
2. Mygind N, Borum P. Anticholinergic treatment of watery rhinorrhea. *Am J Rhinology* 1990;4:1-5.
3. Borum P. Intranasal ipratropium: inhibition of methacholine induced hypersecretion. *Rhinology* 1978;16:225-33.
4. Milford CA, Mugliston TA, Lund VJ, Mackay IS. Long-term safety and efficacy study of intranasal ipratropium bromide. *J Laryngol Otol* 1990;104:123-5.
5. Mygind N, Borum P. Intranasal ipratropium: literature abstracts and comments. *Rhinology* 1989;9(suppl):37-44.
6. Kirkegaard J, Mygind N, Milgaard F, et al. Ipratropium treatment of rhinorrhea in perennial nonallergic rhinitis: a Nordic multicenter study. *Acta Otolaryngol* 1988;449(suppl):93-5.
7. O'Dwyer TP, Lee RJ, Kaye J, Fennell G. Ipratropium bromide

in the treatment of the rhinorrhea syndrome. *J Laryngol Otol* 1988;102:799-801.

8. Simons FE. Anticholinergic drugs and the airways: "time future contained in time past." *J ALLERGY CLIN IMMUNOL* 1987;80(suppl):239-42.
9. Kirkegaard J, Mygind N, Milgaard F, et al. Ordinary and high-dose ipratropium in perennial nonallergic rhinitis. *J ALLERGY CLIN IMMUNOL* 1987;79:585-90.
10. Borum P, Olsen L, Winther B, Mygind N. Ipratropium nasal spray: a new treatment of rhinorrhea in the common cold. *Am Rev Respir Dis* 1981;123:418-20.
11. Gaffey MJ, Hayden FG, Boyd JC, Gwaltney JM. Ipratropium bromide treatment of experimental rhinovirus infection. *Antimicrob Agents Chemother* 1988;32:1644-47.
12. Data on file, Boehringer Ingelheim Corp. (protocol).

Questions and answers

Dr. Spector. The pharmaceutical industry has been interested in antagonists for bradykinin in view of its presumed role with the common cold. Where do we stand as far as bradykinin antagonists, and are there antagonists for the vasoactive intestinal polypeptide?

Dr. Baraniuk. The problem with peptide antagonists has been that they are made out of peptides. Thus they are very good substrates for all the proteases that are present in the nasal mucosa and secretions.

That has been a real problem in functional studies. I think at the last meeting Dr. Proud presented the results of the use of an initial bradykinin antagonist with bradykinin nasal provocation. Despite very good studies in guinea pigs and in vitro, it turned out that the bradykinin antagonist had a half-life of about 30 seconds and had absolutely no effect on bradykinin-induced nasal provocation.

Faced with that, some of the drug companies have been a little bit reticent to develop any of these compounds. However, recently some breakthroughs have occurred in the development of novel amino acids that could be used that do not change the specificity of peptides for a specific receptor but make a given peptide very resistant to degradation.

As a result, in the next few years you will see studies with bradykinin and substance P antagonists. Later studies will be conducted with neurokinin A antagonists, because neurokinin A may play a role in bronchoconstriction. On the contrary, there may be some studies with neuropeptide Y agonists as vasoconstrictors.

Question. If muscarinic receptors are located on vessels, why don't methacholine challenges lead to nasal congestion?

Dr. Kaliner. To an extent, it does lead to nasal congestion. When you perform a methacholine challenge, you are really stimulating very superficially, and the blood vessels, as you may remember, are quite deep.

Thus endogenous acetylcholine release, which occurs deeper in the mucosa, would lead to vasodilation and vascular pooling. However, it is hard to reproduce that response with the topical methacholine nasal provocation system that we use.

Dr. Spector. Physiologically, we alternate breathing predominately from one side of the nose to the other at about 2- to 3-hour intervals. What is the explanation for this switchover effect? Is it neurologic? Are mediators involved?

Dr. Kaliner. It is vascular pooling, and the mechanism for that is presumably parasympathetic. However, what you are getting is tumescence, if you will, on the one side and then decongestion on the other side.

Dr. Spector. Are central pathways by way of the hypothalamus controlling it? What happens with disease? Has it been studied?

Dr. Kaliner. It is a congestion/decongestion cycle. The congestion stimulus is a parasympathetic-mediated response. You probably have had the experience of lying in bed at night on one side, and the side that is closest to the mattress becomes congested. You roll over and it decongests over a period of time.

That is not caused by gravity. It is mediated through the sympathetic/parasympathetic system and that phenomenon can be reproduced by putting a tennis ball under your arm and pressing very firmly on one side and the contralateral side will decongest.

A patient with Horner's syndrome may have intractable rhinitis caused by disruption of the sympathetic innervation on one side and loss of that decongestive pathway. As a result, you will have unopposed parasympathetic dilation.

Dr. Spector. Do we know what happens in others with disease? Does rhinitis per se alter the cycle? What about unilateral nasal polyps?

Dr. Kaliner. Usually people are unaware of the nasal cycle. Eighty percent of normal persons are supposed to have the nasal cycle, and you can demonstrate it easily. However, most of you here are totally