Two of a Kind?
Treating both rhinitis & asthma

By Jacques Hébert, MD

In this article:

1. How are rhinitis and asthma linked?
2. Which treatments improve symptoms of both rhinitis and asthma?
3. What are the recent studies on upper and lower respiratory tract disease?

Allergic rhinitis is a health problem that has been on the rise for several decades.[1,2] It is often associated with upper respiratory tract problems, particularly asthma. In the last few decades, rhinitis and asthma have, in fact, been considered unrelated conditions that were evaluated and treated independently by different professionals. As a consequence, both conditions have been generally undertreated.

A number of recent observations allows for the re-evaluation of rhinitis and asthma as separate entities.[1,2] The notion of them as unique diseases of the respiratory tract with variable manifestations seems to have been instilled. These manifestations range from pure rhinitis, and rhinitis associated with bronchial hyperactivity, to full-blown asthma. The goal of this research is to gather evidence that supports the concept that allergosis, as a whole, consists of rhinitis and asthma. A good understanding of this reality will allow more precise diagnosis and better treatment of upper or lower respiratory tract disease.

What are the links?

Evidence of the links between rhinitis and asthma comes from several perspectives, namely epidemiology, embryology, anatomy, physiology, immunopathology, and therapy. A review of the immunopathologic and therapeutic evidence will illustrate the importance and logic of this concept.

What is the immunopathologic evidence?

The same cells are involved in both rhinitis and asthma (Table 1). Inflammatory cells carrying immunoglobulin E (IgE) receptors, derived from

a common denominator from the bone marrow, seem to circulate from the systemic circulation to the respiratory tracts, where they are recruited by local inflammatory transmitters. Inflammatory cells are found in patients with allergic rhinitis and asthma.[3] The atopic immune response is identical for rhinitis and asthma. The IgE plays a dominant role; the same cytokins and inflammatory cells are found.[3-6]

The concept of common pathophysiology is supported by studies dealing with specific nasal and pulmonary inducement tests. In fact, the Braunstalhl et al. group demonstrated that, after nasal provocation localized with an allergen (making sure there is no evidence of pulmonary contamination), both an objective and subjective nasal clinical response, as well as a pulmonary clinical response, can be observed.[7] Both nasal and pulmonary responses are accompanied by local inflammatory responses.

Table 1
Cells involved in both rhinitis and asthma

- antigen-presenting cells including epithelial cells
- Langerhans or dendritic cells
- immunocompetent cells such as activated T lymphocytes and B lymphocytes
- cells involved in inflammation, including eosinophils, mast cells and neutrophils

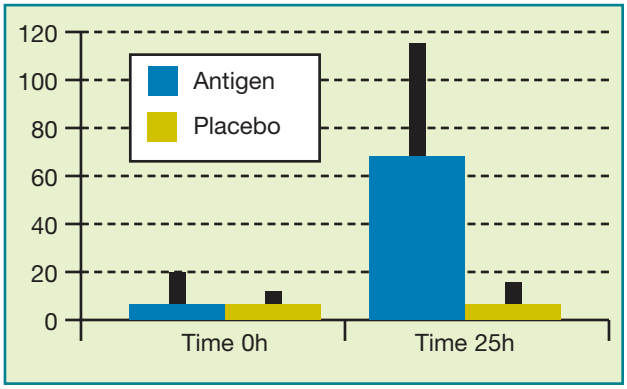

Figure 1. Nasal inflammatory cells (eosinophils) after segmentary pulmonary provocation (mean +/- standard error).

Table 2
Meta-analyses for rhinitis and asthma

Rhinitis:

16 studies: 759 patients

Parameters: improvement of symptoms (nose/eyes); usage of emergency medication; at least 35 days without symptoms

Odds ratio 1.81 ($p < 0.05$)

Asthma:

54 studies

Odds ratio (<1 prefer SIT)

Increase in specific HRB	0.28
Increase in the use of medication	0.32
Increased symptoms	0.26
Increase in non-specific HRB	0.22
Impairment of pulmonary functions	0.56

The same group also demonstrated the reverse correlation: a segmentary bronchial provocation resulted in significant pulmonary and nasal changes (Figure 1).[8]

What is the therapeutic evidence?

The only difference in the treatment of rhinitis and asthma lies in the adrenergic monitoring, where adrenergic agonists produce vasoconstric-

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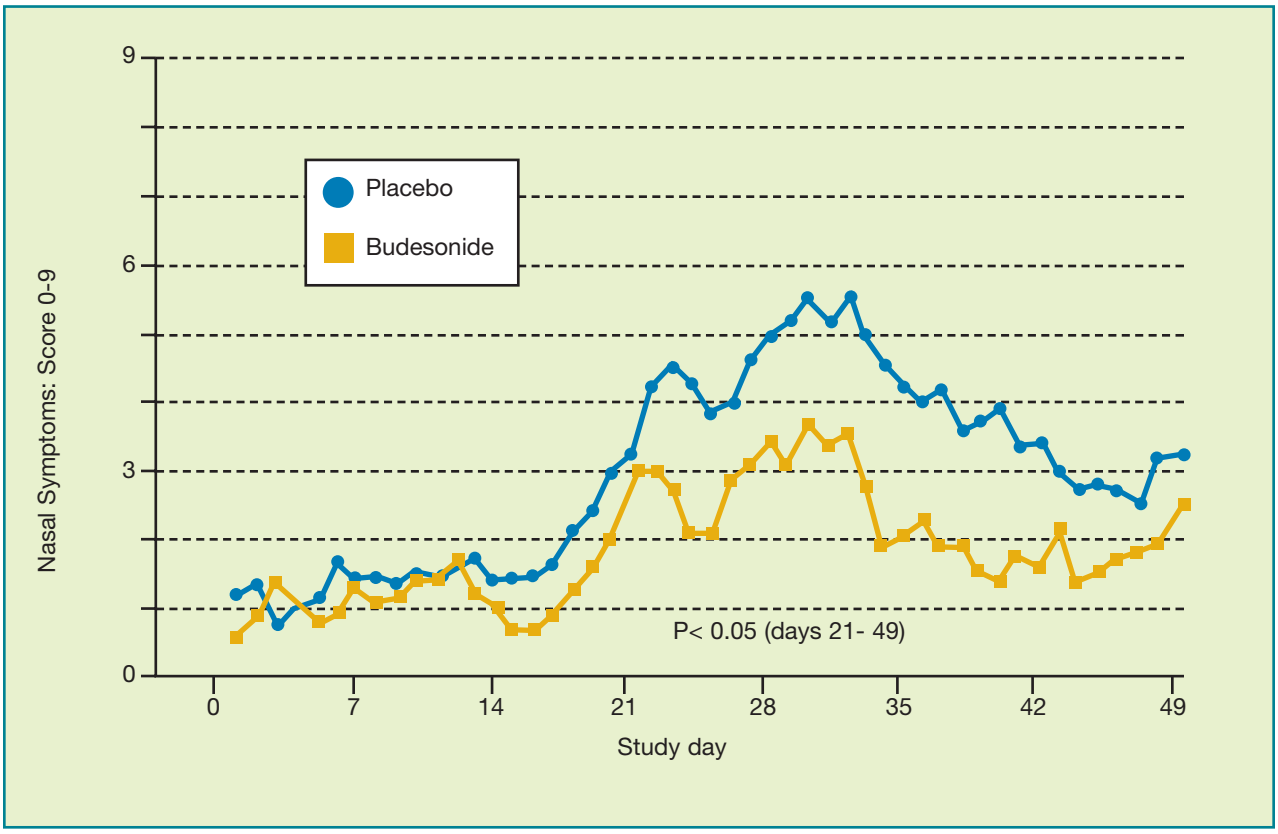

Figure 2. Treatment of patients with light asthma and seasonal allergic rhinitis with an inhaled steroid only (budesonide) and the effects on the clinical nasal response. Patients treated with inhaled steroids show significant clinical nasal improvements.

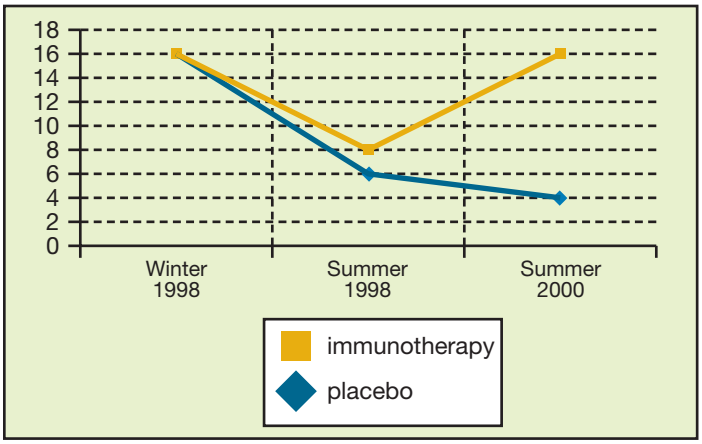

Figure 3. Effects of specific immunotherapy on bronchial hyperactivity where A = before therapy when the patient is asymptomatic; B = when patient is symptomatic during the pollen season; and C = two years after therapy, during the pollen season.

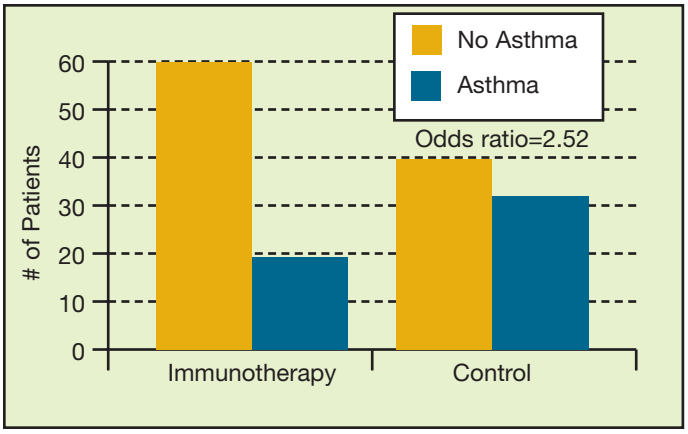

Figure 4. Number of patients with or without asthma after three years of immunotherapy. The 151 patients did not have asthma at the beginning of the study.

tion, and beta-adrenergic drugs induce pulmonary bronchodilatation.[9-11] The same drugs are used for both conditions for the same purpose. Furthermore, treatment of one condition favourably affects the other.

Environmental control

Environmental control, which means eliminating allergenic factors which may contribute to the symptomatology from the environment, improves not only upper respiratory tract symptoms, but also lower respiratory tract symptoms.[12,13]

Corticosteroids

Locally administered nasal and pulmonary corticosteroids have been used widely as treatment in the last few decades, resulting in high efficacy without any side effects.[14] This approach has been totally effective in reducing morbidity due to both rhinitis and asthma. These results, however, may have also contributed to an unrealistic separation of the two diseases. We quickly noticed therapeutic effects that spread beyond the treatment application site. Administering intranasal steroids not only sharply reduced nasal symptoms, but also concurrently improved asthma and bronchial hyperactivity without directly filling the lungs, as demonstrated in radioisotopic studies.[15,16]

Antihistamines

Antihistamines that are very efficient in the treatment of allergic rhinitis are, in general, considered to be of little use and even dangerous to treat asthma, unless it is administered at very high doses (incurring side effects). However, several recent studies have shown that when standard therapeutic doses for allergic rhinitis are administered, there is also significant improvement in both light pulmonary symptoms and associated pulmonary functions.[17,18] Two retrospective studies involving more than 25,000 patients support the fact that adequate treatment of rhinitis improves asthma.[19,20]

Topical Steroids

It has also been proven that treatment of light asthma with a topical intrapulmonary steroid could not only improve pulmonary symptoms, but also improve clinical symptoms of allergic rhinitis (Figure 2).[21,22]

Oral Drugs

Several oral drugs have been administered over the years to treat both rhinitis and asthma. The impact of these drugs on the respiratory tract system has often been underestimated or disregarded. Theophylline has been used for decades to treat asthma, but is generally recognized to be of little efficacy in treating allergic rhinitis. Several studies have, however, suggested this treatment could also prevent allergic rhinitis.[23] It is also the case for new anti-phosphodiesterase drugs, such as roflumilast, which is efficient for asthma and chronic obstructive pulmonary disease, as well as for allergic rhinitis.[24,25] The same observation can be applied to antileukotriene drugs which improve asthma as well as rhinitis. As a result, the indication of antileukotrienes will also be approved for the treatment of rhinitis.[26]

Specific Immunotherapy

Specific allergies are also treated with specific immunotherapy (SIT), or repeated allergen injections to improve the patients' tolerance to them. This approach has definitely proven to be effective in several nasal studies.[27,28] Table 2 summarizes a meta-analysis of the efficacy of immunotherapy for the treatment of rhinitis.[29]

SIT also significantly improves the associated pulmonary condition, regardless of the parameters studied.[27] Table 2 reports the results of a meta-analysis on the efficacy of the SIT in the treatment of asthma.[30] The SIT significantly improves the clinical parameters of asthma: specific and non-specific hyperactivity; clinical symptoms of asthma; and pulmonary functions.

The effects of SIT on bronchial hyperactivity are especially convincing in a recent study that measured off-season hyperactivity (Figure 3). During pollen season, patients had measurable hyperactivity which disappeared in those who were treated, but not in those who were not treated.[31]

Figure 3 shows bronchial hyperactivity expressed in doses of metacholine (in mg), inducing a drop of forced expiratory volume in one second (FEV1) of 20% (PC20 [provocative concentration]). It was measured before any treatment, off-season, during allergy season, and after two years of treatment during pollen season. In this study, a certain degree of bronchial

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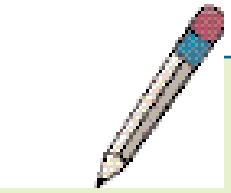

- Evidence supports the concept of global respiratory disease, with symptoms that range from the mouth and nasopharynx to the end of the alveoli.
- Rhinitis and asthma cannot be disassociated, both from a physiological and mechanistic perspective.
- One disease cannot be treated without treating the other.
- As rhinitis and asthma have been traditionally considered unrelated conditions, they have both been generally undertreated.

hyperactivity is noted during pollen season in all patients, although the problem is corrected in patients who receive treatment ($p<0.01$), which is significantly different than for patients who are not treated ($p<0.04$).

Immunotherapy is unequivocally efficient in controlling and treating lower respiratory symptoms. These symptoms are quite often the first things to improve after immunotherapy. Numerous studies have confirmed that SIT may also prevent the development of asthma. In a recent study, allergic patients without asthma were given immunotherapy or placebo, and observed for three years. In this study, the incidence of asthma in patients who were treated was significantly lower (Figure 4).[32] CME

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