Rhinitis and asthma
it's one airway after all

The concept of 'united airways disease' – that allergic asthma and rhinitis are manifestations of a single inflammatory airways disease – is supported by laboratory and epidemiological studies and by treatment responses.

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Allergic rhinitis and asthma are two common global health problems with high prevalences. Allergic rhinitis is a disease of the upper airways, whereas asthma is a disease of the lower airways. It has been suggested that both allergic asthma and rhinitis are manifestations of a single inflammatory airways disease, and the concept of 'united airways disease' is supported by laboratory and epidemiological studies and by treatment responses.

This article explores the relation between rhinitis and asthma, considering epidemiology, pathophysiology, environmental influences (such as infections), allergens and treatment responses. It also highlights that treatment of one entity will change the course of the other, and that optimal treatment of upper airways disease can offer opportunities to maximise treatment benefits and even prevention of asthma.

Epidemiology links

Although asthma is a common condition affecting up to 12% of adults, rhinitis is more common still, affecting up to 40% of individuals in some studies. The prevalence of asthma in those with rhinitis is two to three times that of the general population, and almost 80% of those with asthma have rhinitis.[1] Indeed, rhinitis is an independent predictor of at least a five-fold risk for asthma in both atopic and nonatopic individuals.[2] Thus, rhinitis and asthma are linked by these epidemiological findings, where rhinitis is a risk factor for asthma occurrence. Such epidemiological findings also suggest the inflammatory responses in each condition have common origins.

Function of the nose

Inspired air is usually warmed to body temperature and completely humidified before reaching the lower airways. In nose breathing, nearly all of this conditioning takes place in the nose, which achieves this through its structure of leaves of mucosal-covered bone (the turbinates) over which the air flows, closely regulated by venous sinuses. In mouth breathing, however, the trachea and proximal bronchi humidify and warm inspired air, and in hyperventilation (such as in exercise) the

IN SUMMARY

- **Asthma and allergic rhinitis are described as two different presentations of a common disease process. Understanding the relation between them will greatly influence the care of patients suffering from either condition.**
- **The term 'united airways disease' has been proposed to describe the airway problems in patients with significant allergic respiratory disease.**
- **About 80% of patients with asthma also have rhinitis. There is evidence that treatment of rhinitis in asthma by inhaled corticosteroids reduces asthma exacerbation rates.**
- **Specific allergen immunotherapy delivered by either the subcutaneous route or the sublingual route has been shown to reduce the subsequent development of asthma in children with allergic rhinitis.**

involvement of more distal bronchi is necessary for the incoming air to reach body conditions.

The loss of the humidifying properties of the upper airways can have a significant impact on the lower airways. For example, patients with permanent tracheostomies lose the humidifying effects of the upper airways and often suffer considerable morbidity from chronic bronchitis occurring through the inhalation of unconditioned air.

The nose also acts as a filter for inspired particles. Particles greater than about 8 μm in diameter are captured in the upper airways, whereas most particles about 5 μm or less will penetrate to the lower airways. The upper airways therefore act as a barrier to the inhalation of particulate matter such as allergens, infectious agents and pollutants. This can have pathological consequences. For example, grass pollen-related allergy causes seasonal rhinitis rather than asthma as pollen grains are of a size such that they are normally trapped by the upper airway and do not penetrate the lower airways except in special circumstances. Other allergens, such as house dust mite, are less than 5 μm in diameter and, therefore, are associated with lower as well as upper airway disease, causing asthma.

Inflammation

The inflammatory changes consistent with allergic inflammation are similar in both upper and lower airways, with eosinophil and lymphocyte infiltration being characteristic. Moreover, the upper and lower airways may be linked in that the upper airways have the capacity to stimulate inflammatory processes in the lower airways. Stimulation of the nasal mucosa by an allergen can cause inflammatory processes that feed back to the bone marrow, causing differentiation and release of eosinophils, which may secondarily home in on pulmonary tissue. Also, as neural pathways link the nose and the lung, stimulation of the nasal mucosa by cold air or an allergen can induce reflex bronchoconstriction.

Airway immune responses and the effects of chronic airway inflammation are discussed in the box on page 54.[3,4]

Response to infection

Over 75% of childhood asthma exacerbations and 55% of adult hospital admissions for asthma are due to viral infections, typically caused by rhinoviruses, which predominantly affect the upper airways. It is also clear from experimental studies that respiratory virus infections of the upper airways can have very significant effects on the lower airways.

PHOTOLIBRARY

Figure. About 80% of patients with asthma also suffer from rhinitis.

Several studies have shown that experimental nasal rhinovirus infection causes marked increases in both allergen-specific and nonspecific lower airway hyper-responsiveness, suggesting further linkage between upper and lower airway inflammatory responses.[5]

Further work with experimental rhinovirus infections has revealed the presence of viral particles in the lung despite these being primarily upper respiratory infections. Lower airway findings associated with experimental rhinovirus infections include denudation of epithelium, which is likely to render the airways more susceptible to exogenous influences such as allergens because the normal structural defence mechanisms will be impeded.[6]

More recently, primary abnormalities have been observed in cultured bronchial epithelium from individuals with asthma. There appears to be a constitutive abnormality in the asthmatic epithelium related to virus killing, enabling greater virus replication in the lower respiratory tract and, therefore, increased susceptibility to viral infection.[7] While such abnormalities have yet to be observed in epithelium derived from the upper airway, the similarities in histology suggest that this constitutive abnormality is likely to

More on inflammation in the airways

Airway immune responses

Recent studies in mice have shown that immune stimulation of the upper and lower airways results in active T-cell-mediated immune responses that lead to asthma and allergic rhinitis. Antigenic stimulation of any part of the respiratory mucosa seems to have ripple effects along the entire airway, thus supporting the concept of united airways disease.[3]

Effects of chronic airway inflammation

Although the epithelial lining of both the upper and the lower airways is pseudostratified columnar epithelium, these regions differ in their responses to chronic inflammation.

In asthma, the concept of an 'epithelial–mescenchymal trophic unit' is well established, whereby the epithelium is a primary organ in lower airway (pulmonary) inflammatory processes, driving chemokine and inflammatory mediator release in response to infection and other stimuli. Primary abnormalities of the asthmatic epithelium (increased inflammatory responses) are thought to be responsible for much of the collagen, vascular and smooth muscle remodelling that is a key component of asthma.

The effects of chronic inflammation in the nasal passages are not so well established as those in the lower airways. In the nose, the epithelial–mesenchymal trophic unit overlies a vascular rather than a muscular submucosa, and the airway wall remodelling that is characteristic of asthma is virtually absent in the nose compared with the bronchi, despite the presence of similar inflammation.[4] Airflow through the nasal passages is closely regulated by congestion of venous sinuses, which can cause differential tissue oedema and alternately induce airflow through each nostril to obtain maximal humidification and warming of inspired air. Therefore, chronic inflammation in the nasal epithelium is likely to affect the regulation of the vascular nasal pathways and lead to nasal obstruction.

be a problem in both upper and lower airways.

Thus there may be a pathophysiological reason for people with asthma to experience more lower respiratory tract infections than those without asthma, and for these infections to be prolonged and associated with significant increases in airway reactivity.[8]

Upper airway infections are, therefore, a major influence on the significant morbidity associated with severe asthma attacks.

Response to treatment

The links between upper and lower airway diseases are probably best explored in the relation between the treatments for asthma and rhinitis. Pharmacological and allergen-specific (allergen avoidance and immunotherapy) treatments have effects on both upper and lower airways, and can be used to enable optimal treatment for or even prevent both conditions.

Corticosteroids

Topical corticosteroid treatments are effective in both rhinitis and asthma. In asthma, inhaled corticosteroids are effective in improving lung function and decreasing asthma exacerbation rates, and their use appears to be protective against asthma death. Topical nasal corticosteroids (aqueous formulations) are the treatment of choice for allergic rhinitis. In a large and unselected group of individuals with asthma, the risk of severe asthma exacerbations was almost halved in those prescribed intranasal corticosteroid therapy in addition to other asthma treatments.[9]

In children, there is further evidence that treatment of seasonal allergic rhinitis with topical corticosteroids can be protective against the development of allergic asthma. Best practice, as recommended by Taramarcaz and Gibson, is to treat asthma conventionally with intrabronchial corticosteroids and β_2-agonists and to add intranasal corticosteroids to treat specific rhinitis symptoms.[10]

Immunotherapy

Allergen-specific immunotherapy (using allergen extracts) remains the only treatment currently available that can change the underlying immunological basis of allergic diseases.

The use of allergen immunotherapy for allergic rhinitis is well established, with the earliest trials reported in 1911 indicating the therapy has significant efficacy. The use of allergen-specific immunotherapy for asthma is more controversial because of its potential to cause severe allergic reactions, and deaths have been attributed to its use. However, there is now an excellent evidence base for the safe use of subcutaneous allergen immunotherapy in asthma, with effectiveness in the prevention of both asthma exacerbation and the increasing use of asthma medications, and in the improvement of airway hyper-responsiveness.[11]

Allergen immunotherapy for the treatment of asthma is favoured for younger patients as the airway wall remodelling responsible for much of the constitutive airway hyper-responsiveness in asthma is likely to be irreversible by the time patients become middle-aged. A recent randomised study in 205 children aged 6 to 14 years with seasonal allergic rhinitis investigated the use of subcutaneous immunotherapy with grass and/or birch pollen allergens and followed up the children with respect to asthma outcomes.[12] While the immunotherapy was effective in treating the rhinitis, an unexpected benefit was the apparent prevention of the development of asthma in those children undergoing active treatment.

At follow up, the odds ratio for developing asthma in the treated group was reduced threefold. During the period of follow up, the actively treated group also acquired significantly fewer new allergen sensitisations, suggesting that the immunotherapy was effective in preventing the onset of new allergic sensitisations.

Newer developments in immunotherapy are related to the increasing recognition of sublingual immunotherapy (SLIT) as an effective alternative to subcutaneous immunotherapy.[13] The advantages of SLIT are the ease of administration (it is administered at home), the low overall incidence of side effects and the negligible occurrence of serious adverse effects. The key to success of SLIT appears to be the delivery of a sufficient dose of allergen, and this makes it an expensive alternative to subcutaneous immunotherapy. However, follow up of children receiving SLIT suggests that the occurrence of asthma is reduced in those receiving this mode of therapy. In a 10-year follow up study of children sensistised to house dust mite (most of whom also had asthma), the asthma rate was reduced by 90% in those receiveing SLIT but unchanged in controls.[14] The acquisition of new sensitisations was not affected in this study. Another study, a three-year follow up of children, about half of whom had undergone SLIT with grass pollens for seasonal allergic rhinoconjunctivitis, revealed a 3.8-fold reduction in the risk of asthma onset in the actively treated group.[15]

Thus, both subcutaneous and sublingual immunotherapies provide promise of reducing asthma occurrence in allergic children receiving specific allergen immunotherapy. While the clinical availability of SLIT in Australia is currently limited, it is worth remembering that few other treatments have shown safety and efficacy in preventing asthma onset or providing durable remission of asthma occurrence, and these study results deserve confirmation. The suggestion that SLIT may provide a safe method of preventing asthma occurrence may support its more widespread clinical use in young adults and children.

Other therapeutic modalities

Other treatments for allergic diseases have also shown promise in affecting the subsequent development of allergic diseases. In particular, treatment of children with eczema with non-sedating antihistamines seems to delay, although not prevent, the development of asthma, as shown by a study of 18 months' cetirizine treatment for atopic dermatitis in young children.[16] The use of H_1-antihistamines for early onset allergic diseases is worthy of further study.

Montelukast (Singulair), a potent leukotriene receptor inhibitor, is approved for the treatment of asthma and is also effective in allergic rhinitis. The newly developed IgE inhibitor omalizumab (Xolair) has been reported to have efficacy in both rhinitis and asthma.

Thus, various therapeutic options are available to treat asthma and rhinitis at the same time. This multilateral clinical efficacy of anti-inflammatory drugs supports the 'one airway–one disease' hypothesis.

Conclusion

The upper and lower airways are linked physiologically and pathologically due to a common epithelium and structural similarities. As the nose is likely to be the first organ exposed to respirable influences, it will be the first to respond, but recent evidence confirms that nasal responses are likely to influence the lower respiratory tract through both direct reflexes and bloodborne mechanisms. Treatment of nasal disease is, therefore, a significant feature in gaining control of lower airway disease. Probably the most appropriate

A case study

Gabriel is a 29-year-old computer consultant who presents in November with night-time cough and wheeze. On reflection, he recalls experiencing similar symptoms in preceding years during spring and summer, and they were always accompanied by symptoms of hay fever. Although he reports having a runny nose during spring and summer, for him the most troubling hay fever symptoms have been itchy and watery eyes, which have been particularly difficult because he wears contact lenses. In the past, he has self-treated his hay fever with antihistamine tablets and some eye drops bought from the local pharmacist, and has found these provided reasonable symptomatic relief. The remainder of the year he is generally well and does not have any asthma or hay fever symptoms.

Assessment

On examination, Gabriel's chest is clear and his peak flow rate is 490 L/min, which is within the predicted range. Blood specific IgE testing reveals high levels of ryegrass-specific IgE, and a total IgE level of 130 IU/L.

Gabriel's symptoms are likely to be due to his grass pollen allergy, which involves allergic rhinoconjunctivitis and now seasonal symptoms of asthma.

Treatment

Treatment of Gabriel's rhinitis with intranasal corticosteroids is likely to improve both ocular and nasal symptoms and may prevent the involvement of his lower respiratory tract in the allergic process. In the longer term, Gabriel would be an ideal candidate for allergen immunotherapy with ryegrass pollen extract, which would treat both his rhinoconjunctivitis and his asthma.

Consultant's comment

I urge every general practitioner to think carefully about the message in this important article. For too long the individual organs involved in allergy have been treated in isolation, without a real appreciation of the impact of the involvement of one organ on another. Allergy is essentially a multisystem disease. Patients with asthma will often tell you that exacerbations follow sneezing and nasal symptoms. So, every patient with asthma should have the benefit of treatment for their (almost) inevitable allergic rhinitis. Every patient with allergic rhinitis is a candidate for bronchospasm and the development of asthma.

Times have changed!

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practice is to treat persistent asthma conventionally with intrabronchial corticosteroids and β_2-agonists, and to add intranasal corticosteroids to improve specific rhinitis symptoms.[10]

In the longer term, specific allergen immunotherapy offers some protection against asthma exacerbations and the development of asthma in those with allergic rhinitis, suggesting that this treatment should be considered more frequently than at present, particularly in younger patients. MT

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Further reading

1. ARIA (Allergic Rhinitis and its Impact on Asthma), an international collaborative on allergic rhinitis, has various documents and resources available on its website (www.whiar.com) concerning the evidence-based management of allergic rhinitis in conjunction with asthma.

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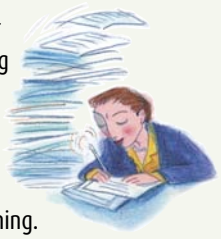

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