Allergic rhinitis

Prevalence and epidemiology
The prevalence of allergic respiratory diseases in the population is increasing. Fleming and Crombie showed that in England and Wales, the number of rhinitis, firstborn children increased temporally increasing. The late 1970s and early 1980s have been a period of marked increase in the prevalence of both rhinitis and asthma. Frick et al. showed that the onset of allergic disease in infants with allergic parents was related temporally to preceding viral infections such as respiratory syncytial virus and parainfluenza. Furthermore, several investigators have shown that total concentrations of circulating IgE are raised during the acute phase of viral infections.

INHERITANCE OF ATOPY
Recent genetic studies suggest that atopy (the ability of a person to produce high concentrations of IgE directed against common allergens) may be inherited, carried on chromosome 11 as an autosomal dominant characteristic with variable penetrance. Certainly most allergic children have a strong family history of allergy, and concordance for symptoms of allergy is increased in monozygotic compared with dizygotic twins.

ENVIRONMENTAL INFLUENCES
Many environmental factors probably contribute to the sensitisation of an allergy prone subject in early life. Children born in spring in Scandinavia have an increased risk of birch pollen rhinitis, and grass pollen has the same effect in the United Kingdom. Sibbald and Rink, however, have recently shown that rhinitis in non-atopic subjects is also associated with birth during the summer months, suggesting that other factors, such as winter respiratory tract infection at a time when transferred maternal immunoglobulin concentrations have fallen below protective levels, may promote the development of rhinitis. Parental smoking is certainly associated with wheezing in children, but also with risk of rhinitis. In a large study in rural Sweden the relative risk of rhinitis increased to 1.8 in children who lived in damp homes and had parents who smoked. The effects of damp and passive smoking were synergistic, neither factor being a significant independent risk. Modern energy efficient 'tight' buildings may encourage the growth of house dust mites and moulds, thus increasing environmental exposure to potential allergens.

Industrial environmental pollution is also likely to be a contributory factor. Comparative studies between developed and developing countries suggest a lower prevalence of allergic diseases in the latter. Furthermore, studies of urban and rural populations suggest that urban dwellers are more prone to rhinitis. Pollen grains in urban areas are contaminated by pollutants, and such deposits on inhaled pollen may act as adjuvants to sensitisation.

Nasal responsiveness
It is not surprising that nasal responsiveness has similar characteristics to bronchial responsiveness, given that the nose is contiguous with the rest of the respiratory tract. Nasal airways resistance can be measured and increased non-specific nasal responsiveness can be induced with agents such as histamine and other mediators, although the range of responsiveness in rhinitis is less clear cut than that of bronchial responsiveness in asthmatic patients. The lower repeatability of measurements of nasal airways resistance compared with that of forced expiratory volume in one second (FEV₁) together with the absence of a smooth muscle constrictor response, contributes to this difference. The response to methacholine seems to be entirely secretory, in contrast to the highly correlated methacholine and histamine responses in the lower airways. The absence of smooth muscle in the nose almost certainly accounts for the difference.

Early and late phase allergic responses may also be induced in the nose. Late phase responses occur in about half the patients between two to eight hours after challenge, but only produce small rises in nasal airways resistance. The late phase response is less pronounced than in the lower airway, firstly because there is no smooth muscle, and secondly because the response may be masked by the nasal cycle in which there is an increase in nasal airways resistance in alternate nostrils every two to four hours.
Pathogenesis

MAST CELLS

Studies of the nasal mucosa in patients with rhinitis have shown that total numbers of mast cells are increased compared with patients without rhinitis.20 Furthermore, there is a significant increase in the numbers of mast cells and eosinophils during the pollen season.21 There is also evidence that the number of circulating mast cell/basophil progenitors is increased in such patients and that their numbers fall during the pollen season, suggesting the possibility of recruitment to the site of allergic inflammation.22 It is likely that atopic subjects are predisposed to produce the cytokines necessary for basophil/mast cell and eosinophil differentiation.22 Plaut et al showed that murine mast cells triggered by cross linkage of Fc,RI receptors secrete interleukins 3 (basophil activation), 4 (IgE synthesis), and 5 (eosinophil activation), which suggests that there is a positive feedback mechanism amplifying the inflammatory response.23

Other mast cell products released in the acute phase after allergen administration include histamine, prostaglandin D2, kinins and tryptase, which are likely to be responsible for many immediate symptoms.24 The release of these mediators shows the features of priming—that is, repeated allergen challenge within the same day is followed by an augmented response.

Mast cell heterogeneity has been found in nasal polyp tissue, with tryptase positive mucosal type cells predominating in the epithelium and connective tissue type (chymase and tryptase positive mucosal type) cells predominating in the lamina propria.25 Such heterogeneity has also been noted in bronchial biopsy specimens,26 whereas the predominant type in the skin and submucosa of the gut is the connective tissue type. Tryptase positive mucosal type cells do not stain with safranin O, indicating that the proteoglycan component is not heparin, nor do they degranulate in response to polyamine 48/80. The morphological differences may explain the lack of effect of sodium cromoglycate on the allergic response in the skin compared with the good response in the upper and lower airways.27 It is likely that mast cells migrate from the mucosa to the epithelium and differentiated to become the cells that produce cytokines derived from clonal differentiation (CD4+ T helper cells, fibroblasts, and epithelial and endothelial cells.22

EOSINOPHILS

Numbers of eosinophils are increased in patients with rhinitis and rise during the pollen season in those who are sensitive to pollen.20 Eosinophils show a transient increase in numbers in the nasal mucosa 30 minutes after an allergen challenge,28 but numbers in nasal secretions are persistently raised, peaking at seven to 10 hours,29 suggesting an efflux from the mucosa into the secretions. The chemotaxants taking part in this process have not yet been identified, though they may include leukotriene B4, platelet activating factor, and intercellular adhesion molecules. The eosinophils are activated, as evidenced by hypodense granules and the expression of EG2 (eosinophil granule) positive activation markers (SR Durham, unpublished observations). Recent studies from our department have shown the effect of activated eosinophils on bronchial epithelial cells in vitro; cultured bronchial epithelial cells show evidence of damage, with reduced ciliary beat frequency (JL Devalia, unpublished observations). In addition, they express intracellular adhesion molecules that may be essential to the attraction of eosinophils to tissue sites. As cultured bronchial epithelial cells are morphologically similar to nasal mucosal explants it is likely that they respond similarly. Release of toxic granule products from eosinophils, particularly eosinophil peroxidase and major basic protein, may contribute to the inflammatory features of the late phase response.

T CELLS

There seems to be an imbalance in cytokine production from T cells in atopic subjects, who have a tendency to produce more of interleukins 4 and 5 and less interferon gamma. The numbers of dendritic cells at the surface of the nasal epithelium are increased in rhinitics and these may bind allergenic peptides. Interaction of these dendritic cells with T cells may promote differentiation towards the helper type of T cells (Th2) that produce interleukins 4 and 5, which promote B cell IgE production and eosinophil activation, respectively.30 In situ hybridisation studies show that T cells from atopic and asthmatic patients express messenger RNA for interleukins 4 and 5.30 31

Effect of treatment

VASOCONSTRICTORS

α-Adrenergic agonists such as ephedrine act on the smooth muscle of the venous system in the nasal mucosa. They are highly effective in immediately increasing nasal patency. There is a low risk of rebound congestion with compounds such as xylometazoline and naphazoline, but fears of 'rhinitis medicamentosa' have limited their use to one to two weeks periods only.32

ANTIHISTAMINES

The development of potent, long acting antihistamines do not easily cross the blood-brain barrier has resulted in their wider usefulness. The newer ones such as cetirizine combine rapid action with a half life of nine hours and minimal sedative effect. Recent studies on skin windows showed that cetirizine has additional anti-inflammatory properties in that it inhibits eosinophil chemotaxis in response to anti-IgE, platelet activating factor, and the tetrapeptide N-formyl methionyl leucyl phenylalanine (N-FMLP), whereas terfenadine has little or no effect.33 34

ANTI-INFLAMMATORY TREATMENT

Nedocromil sodium seems to be considerably more potent than sodium cromoglycate as an anti-inflammatory agent. In vitro studies have shown that nedocromil sodium inhibits histamine release from mast cells, eosinophil activation, and neutrophil cytotoxicity against schistosomula with a tenfold greater potency than sodium cromoglycate.35 In vivo nedocromil sodium significantly inhibited the accumulation of mast cells in the nasal mucosa during the pollen season in patients with rhinitis who were sensitive to grass pollen.36

Topical application of anti-inflammatory corticosteroids is the most effective treatment for symptoms of nasal blockage. Newer compounds have recently been developed that minimise suppression of the hypophyseal pituitary-adrenal axis. Fluticasone propionate has a fivefold higher relative potency than beclomethasone dipropionate but hardly inhibits the hypophyseal pituitary adrenal axis, because it is quickly metabolised in the liver.37 Preliminary results showed that fluticasone propionate significantly reduced the numbers of activated eosinophils in nasal mucosal biopsy specimens from patients with rhinitis who were sensitive to grass pollen and who were challenged with grass pollen outside the pollen season; it is also effective in reducing symptoms in such patients during the pollen season.38

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Routine measurement of blood pressure in schoolchildren

Undergraduate and postgraduate medical students learn that the measurement of blood pressure is part of routine clinical examination. This would seem a reasonable assertion; however, as will be shown in this article, it requires a thorough understanding of the factors involved in the production of a valid measurement in order to interpret blood pressure meaningfully in children.

Apart from research endpoints, the measurement of blood pressure must be to identify some pathology. That pathology may be a disease causing secondary hypertension, in which case it is important that the clinician should know how to deal efficiently with abnormal findings, probably referring those with severe hypertension to tertiary centres. Otherwise it may be perhaps a more subtle tendency towards essential hypertension, in which case there should be provision for long term follow up, including the difficult period around adolescence, and later, when transfer to adult care is necessary. In both cases, it is important neither to miss a treatable condition nor create unnecessary anxiety to parents and child by failing to recognise normality. This article addresses some of the factors leading to valid assessment of blood pressure.

When to measure blood pressure

The most important hurdle to overcome in relation to blood pressure measurement in children concerns the decision actually to take the blood pressure. The recent working party of the British Hypertension Society did not recommend the routine screening of the paediatric population for blood pressure. Blood pressure in children is very variable, and so regression to the mean, which has long been a problem in trials of antihypertensive treatments in adults, is likely to cause even greater problems in children. Thus although the phenomenon of ‘tracking’ of blood pressure allows some prediction of later hypertension, the correlation coefficients between initial and final blood pressure measurements in a number of studies are relatively low and insufficiently consistent to allow predictions of future blood pressure levels from initial recordings, especially in young children.

The situation becomes more unclear when considering the child with a family history of hypertension. While it would seem prudent to follow up a child with a strongly positive family history, the power of observations made before adolescence is debatable. The position may be different during adolescence when there is probably greater overall predictive value, but traditionally this is a period when medical input is at a minimum.

At the other end of the range, there seems little doubt that blood pressure should be measured in all children presenting to clinicians when ill or when illness is suspected. This would be expected practice. What is then uncertain is why it should not be applied to children. The following groups of children should also have regular routine blood pressure measurements because of the known association between certain pathological states and hypertension: those with any form of renal or cardiovascular disease, urological abnormalities, meningomyelocele, diabetes mellitus, and neurofibromatosis. Also those with headaches, visual