Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Infection, asthma and bronchial hyperresponsiveness

Many asthmatics attribute their exacerbations to infection and will request antibiotic therapy in preference to an increase in anti-inflammatory therapy. However, it is viral and not bacterial infection which is associated with wheezing episodes in asthmatics. Viral isolation is strongly associated with asthma exacerbations but bacterial isolation is as frequent in wheezing as in asymptomatic periods (1,2). Horn and co-workers (3) studied 146 children during 446 wheezing episodes. In 26% of cases, a viral infection was identified by culture and serology. Forty-six percent of these were rhinovirus infections. Parainfluenza, coxsackie A and B and influenza A accounted for most of the remaining cases. Viral isolation rates depend on the techniques used and until recently, it has been particularly difficult to identify rhinovirus infection satisfactorily using standard culture and serology because of the numerous different serotypes. Viral isolation rates have ranged from 11–26% (3–5).

The use of the polymerase chain reaction (PCR) has allowed the identification of a greater proportion of infections. In one recent study (6), a virus was identified in 64% of asthmatic children with exacerbations due to colds. Fifty-nine percent of these (40% of the exacerbations) were due to rhinovirus infection and were detected by PCR. The remaining cases were attributed to influenza A (7%), parainfluenza (7%), coronavirus (7%) and respiratory syncytial virus (RSV). A similar virus isolation rate of 57% in adult asthma exacerbations has been shown by Ireland and co-workers (7) using a PCR for rhinoviruses and enteroviruses, culture and serology (D. Ireland, personal communication). Twenty-nine percent of the respiratory viral infections were identified by PCR alone. Although the technique is highly sensitive, no asymptomatic individuals demonstrated false positive PCR tests in this study, although Johnston and co-workers (6) found positive PCR results in 4–6% of asymptomatic individuals.

These high incidences of viral isolation during exacerbations of asthma suggest a role for respiratory viral infection and specifically rhinoviruses in the pathogenesis of asthma. Peak flow variability and bronchial responsiveness both increase during colds (8–10). These parameters classically correlate with bronchial inflammation (11,12), yet it is possible to show increased bronchial responsiveness in normal individuals with colds (8) and influenza (13). Epidemiological data collected in general practice show that the effect of colds on bronchial responsiveness in the community can be variable between consecutive winters and this may best be explained by epidemics of particular viral serotypes (14).

A further link of respiratory viral infection with airway inflammation is suggested by the finding that non-asthmatic, ragweed-sensitive rhinitics have an increased tendency to a late asthmatic response (LAR) to inhaled ragweed allergen following experimental rhinovirus infection (15). Eight of ten individuals developed an LAR, compared to one of ten prior to infection. The simplest explanation of the pro-inflammatory effect of viruses is the effect of damage to the epithelium. This may release mediators from the epithelium, expose cholinergic nerve endings, promote the penetration of antigen, remove inhibitory epithelial components such as epithelial derived relaxant factor and reduce epithelial uptake and degradation of mediators (16). However, the cytopathic effect of rhinoviruses on nasal epithelial cells in culture is negligible compared to the destruction of the monolayer caused by influenza A and adenovirus (17). Nevertheless, shedding of nasal epithelial cells occurs *in vivo* after experimental rhinovirus infection (18). There have been few bronchial biopsy studies in viral respiratory tract infection. An early uncontrolled study commented on the features of influenza infection (19): there was evidence of oedema, epithelial cell loss and an inflammatory infiltrate composed predominantly of lymphocytes and histiocytes but including some eosinophils. Additionally, there was thickening of the basement membrane, a feature associated with asthma (20,21). These findings were, however, subjective. Similar features have recently been demonstrated following mycoplasma and influenza infection (22).

Release of inflammatory mediators such as histamine and bradykinin is increased during rhinovirus infection but such mediators cannot produce ongoing allergic inflammation (23). Production of specific T-helper cell subsets by interaction with the major histocompatibility complex on antigen-presenting cells could provide the stimulus to the inflammatory process. Th1 clones expressing mRNA for interleukin-2 (IL-2) and interferon-γ (IFN-γ) are associated with viral infection, whereas Th2 clones (expressing mRNA for IL-4 and IL-5) are found in allergic inflammation (24,25). Peripheral blood mononuclear cells show increased release of IL-2 and IFN-γ in response to phytohaemagglutinin following rhinovirus infection (26), indicating the presence of Th1 subsets. The numbers of circulating T-helper (CD4) cells is reduced, suggesting recruitment to the site of inflammation (27).

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Recent studies have suggested an increase in allergic inflammation in atopic individuals in viral infection. Eosinophil activation can be shown *in vitro* following rhinovirus and influenza infection (28) and the eosinophil response to segmental bronchial allergen provocation is increased following experimental rhinovirus infection in atopic rhinitics (29). Finally, specific IgE is raised to respiratory syncytial virus in infants and its presence is correlated with increased severity of the illness and a higher risk of persistent wheeziness later in life (30–32). Interferon-γ release from Th1 cells following viral infection would be expected to inhibit rather than promote B-cell IgE production.

At present there is clearly some difficulty in finding a unifying mechanism to explain the association of viral infection and allergic airway inflammation. Adhesion molecules may, however, have an important role. The major receptor for 90% of rhinoviruses is the intercellular adhesion molecule (ICAM-1) (33). ICAM-1, expressed on many cell types, including epithelial cells, is up-regulated in allergic airway inflammation and by cytokines such as IL-1, IFN-γ and tumour necrosis factor-α (34). The major ligand for ICAM-1 is LFA-1, which is expressed on inflammatory cells. ICAM-1 is essential to the development of an inflammatory infiltrate and its expression is increased in the bronchial mucosa of asthmatics. There is thus a potential feedback mechanism by which IFN-γ may increase ICAM-1 expression, allowing increased rhinovirus and leucocyte binding. Further detailed immunopathological study of respiratory viral infection is indicated.

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