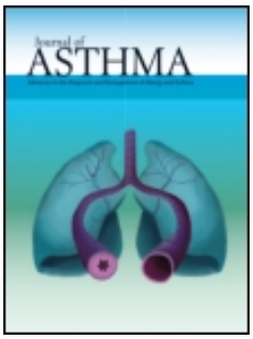

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EDITORIAL

Asthma and Immune Deficiency Syndromes

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The association of asthma and respiratory infections has been recognized by clinicians for decades. Viral infections precipitate wheezing in children with bronchiolitis and are associated with increased asthma in many adults. Unfortunately, the precise mechanisms involved in triggering asthmatic symptoms remain unknown. The association of viral respiratory infections and asthma has been studied extensively (1–3). There is little doubt that viral infections in children are a prominent trigger in the induction or perpetuation of reactive airways disease. Postulated mechanisms of increased bronchial hyperresponsiveness have included (a) the induction of primary and secondary inflammatory mediators that result in increased immediate and late-phase asthmatic responses; (b) subsequent increased exposure to submucosal irritants and/or allergens; (c) induction of viral-specific IgE antibodies; (d) damage to nerve endings resulting in a decreased threshold of reactivity; (e) deleterious effect on stability of mast cells and their products by viral agents. Although the association with respiratory syncytial virus infection is clear, it is unclear whether these observations can be generalized to other viral respiratory infections.

Although bacterial infections of the upper and lower respiratory tract are extremely uncommon in asthmatics, they are infrequently proven to be a definite trigger to the symptomatic expression of asthma or the precise causation of the de novo appearance of asthma. Two notable exceptions to this observation appear to be *Mycoplasma pneumoniae* and *Chlamydia* infections of the lung. The association with purulent rhinosinusitis in asthma is well known to the clinician (4). We frequently encounter patients whose asthma control improves when definitive antimicrobial and/or surgical therapy of the paranasal sinus disease is undertaken. This clinical observation appears to be particularly relevant for the patient with aspirin idiosyncracy syndrome.

The immunodeficient patient presents particularly difficult diagnostic and therapeutic challenge to the asthma specialist. In this issue of the *Journal of Asthma,* Silk reviews the pathological and clinical presentation of primary immunodeficiency states and their potential association with asthma. He notes that patients with primary humoral deficiency states frequently present with purulent sinobronchial infections. These infec-

tions may first present with symptoms of cough, nasal and sinus congestion, and rhinorrhea suggesting allergic mechanisms such as may occur with allergic rhinitis and many cases of asthma. A particularly difficult clinical dilemma exists in early childhood when transient IgA, IgG, and IgG subclass deficiency may be associated with increased risk of infection, but which may normalize with age. Unfortunately, structural abnormalities of the paranasal sinuses, middle ear, and lung may persist for years and may lead to further anatomical barriers to a normal immune response and control of infection. These changes may explain the greater incidence of asthma and impaired lung function in individuals with IgA, IgG, or IgG subclass deficiencies (5–7).

Silk describes an interesting and informative group of patients in a consultative pediatric allergy and asthma practice. The association of impaired antibody production to pneumococcal immunization is intriguing in this group. A deficiency in primary antibody production occurred in 38 of 69 patients (55%) with recurrent sinopulmonary infection. This represents a higher than expected incidence of immune dysfunction despite the selection bias of a consultative allergy and asthma practice. These findings suggest that the prevalence of abnormal primary humoral responses in the asthmatic and atopic population is substantial. Clearly, this observation requires confirmation in a prospective multicenter study. To derive meaningful incidence figures, it is essential to study individuals presenting with these symptoms in a large primary care setting. Furthermore, this observation, while suggesting a causal link of infection in asthma, does not suggest that correcting impaired antibody response, even if plausible, would affect the natural history of the associated bronchial asthma.

The use of intravenous gamma globulin in clinical practice continues to be controversial. While its role in therapy of primary humoral deficiency such as common variable hypogammaglobulinemia and Bruton's hypogammaglobulinemia is unquestioned, its role in the treatment of IgG subclass deficiency and/or isolated impaired antibody response to polysaccharide antigen is less clear. Owing to the expense and invasive nature of this procedure, the clinician needs to be cautiously optimistic when interpreting published data, which are most likely to report positive clinical findings. In addition, research protocols investigating the use of high-dose intravenous gamma globulin as an immunomodulatory agent in the treatment of severe childhood asthma, while potentially exciting, should also be cautiously interpreted (8–10). This group of patients is extremely difficult to study in that there is extreme variability in the natural history of the underlying disease as well as a significant placebo effect in any study that evaluates patients with severe and often steroid-dependent asthma. While it is appropriate to be cautious, intravenous gamma globulin also represents a potentially very exciting area of therapy for the asthma specialist. In young children, the expense of intravenous gamma globulin may be much less significant than in the adult. High-dose intravenous gamma globulin therapy may cost many thousands of dollars in an adult; such therapy may cost hundreds of dollars in a child. Furthermore, if one can potentially prevent serious infection and subsequent impaired lung function, the primary cost saving to the individual as well as the secondary cost saving to society can be substantial.

In summary, Silk's review in this issue of the *Journal of Asthma* reminds clinicians who treat patients with asthma of the importance of recognizing primary and sometimes subtle forms of immune dysfunction. Patients who present with recurrent sinobronchial infections that may be associated with the induction and/or perpetuation of asthmatic symptoms need to be evaluated for potential immune dysfunction. This can be done quite simply and inexpensively in a clinical practice with routine measurements of IgA, IgG, and IgG subclasses when indicated. In those individuals who may have a strongly positive history suggestive of severe and recurrent sinobronchial infections, it is certainly reasonable to further test their humoral response to primary and/or secondary immunization. While the role for antibody replacement ther-

apy in these patients continues to be defined, there are patients who will clearly benefit from immunorestoration with intravenous gamma globulin.

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