EDITORIAL COMMENT

Risk Factors Associated with the Development of Asthma

Ren-Bin Tang*

Department of Pediatrics, Taipei Veterans General Hospital, and National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

Prevalence of Allergic Diseases

Asthma and allergic rhinitis are 2 of the most common allergic diseases worldwide. The prevalence of these diseases appears to have increased significantly in the past 2 centuries, and, indeed, in the past few decades, a marked rise in the prevalence of allergic diseases has been noted in industrialized countries and in urban centers in less developed regions. Asthma has become the most prevalent chronic disease, especially in children.

In Taiwan, the prevalence of asthma and other allergic diseases has been increasing, with surveys documenting an asthma prevalence of 1.3% in 1974, 5.3% in 1987, and 8.7% in 2000. Trends towards an increasing occurrence of asthma have not been limited to Taiwan; indeed, such trends seem to be global, or at least common to the industrialized countries in which they have been studied. For example, reports have indicated an increased prevalence of allergic disease in Finland, Japan, Sweden, and the US. Findings from a behavioral risk-factor surveillance system indicate that approximately 7.2% of adults in the US currently have asthma, and the overall lifetime prevalence of asthma in adults is 11.0%.

Risk Factors for Asthma

Risk or trigger factors for asthma that are currently under investigation include the following: genetic atopic predisposition; early childhood allergen exposure and sensitization; viral respiratory infections in young children; maternal smoking during pregnancy; poor diet; lack of breast-feeding; childhood obesity; certain immunologic predisposition (Th2-prone); air pollution; and frequent immunization in childhood. It is most likely that the causes of allergic diseases are multifactorial. Risk factors for asthma have been studied extensively in school-age children; such evaluated factors included dietary fatty acid, number of older siblings, lack of breast-feeding, and atopy, which have all been associated with asthma in older children.

The Hygiene Hypothesis

The hygiene hypothesis suggests that childhood asthma develops as a result of decreased exposure to infectious disease and other stimuli. As Westernization occurs, the environment becomes cleaner, and we then lack the immunologic and infectious stimuli needed for our immune systems to shift from the helper T-cell Th2 to Th1 response. Seropositivity for food-borne and oro-fecal micro-organisms (e.g. hepatitis A virus, Helicobacter pylori, and Toxoplasma gondii), which are considered to be markers of poor hygiene, has been associated with a reduced prevalence of atopy. In contrast, colonization of the gut with Clostridium difficile, a potential intestinal bacterial pathogen, in early childhood may be associated with an increased prevalence of atopy. For mycobacteria, measles and respiratory viruses, studies demonstrate a significant increase in atopy or allergic disease, and parasite infections, which provide a strong Th2 stimulus, are associated with reduced rather than enhanced allergen sensitization. Nonetheless, available epidemiologic evidence does not support a mechanism of early life immune deviation. The principal environmental influences on atopic disease are likely to occur throughout life and involve interactions between microbes and non-infective and lifestyle factors.
Analyses of patterns of risk factors for allergic rhinoconjunctivitis and asthma in Europe have led to conjecture about causes of the allergic disease epidemic: the hygiene hypothesis. This hypothesis claims that hygiene has removed a protective influence against atopy and asthma that was once provided by exposure to infections in early life. However, the hypothesis has been questioned in the US, where allergic asthma since the 1970s has increased in minorities living in poverty and with suboptimal hygiene conditions (“inner-city asthma”). Such a recent increase in respiratory allergies among less-advantaged individuals in the US may be due to several factors linked to Westernization (e.g., declining exposure to food-borne and oro-fecal infections); these factors first affected the richest socioeconomic strata during the 19th century, expanded to the middle classes during the first half of the 20th century, and eventually cascaded down to affect less-advantaged Americans.

Vaccination

Anecdotal case reports and uncontrolled observational studies in the medical literature claim that vaccines cause chronic diseases such as asthma, multiple sclerosis, chronic arthritis, and diabetes. Several biologic mechanisms have been proposed to explain how vaccines might cause allergic or autoimmune diseases. For example, allergic diseases might be caused by the prevention of early childhood infections (the hygiene hypothesis), thus causing prolongation of immunoglobulin E (IgE)-promoting Th2 responses. However, vaccines do not prevent most common childhood infections, and large well-controlled epidemiologic studies do not support the hypothesis that vaccines cause allergies.

Testing for Allergens

Differentiating between allergic and nonallergic diseases involves detailed history taking, physical examination, and either in vivo or in vitro testing for relevant allergens. Skin testing is the most widely used diagnostic test for allergies. However, because of its high percentage of false positives, and certain contraindications such as skin problems and antihistamine interference, other diagnostic tests for allergies have been proposed. The multiple allergosorbent chemiluminescent assay, radioallergosorbent test, and Pharmacia CAP System (Pharmacia Diagnostics, Uppsala, Sweden), have all demonstrated good agreement with skin tests.

The house dust mites Dermatophagoides pteronyssinus and D. farinae, which are inhaled allergens, are the major allergens detected in Taiwan in both children and adults. A good correlation between the immunodot assay and skin testing was confirmed in asthmatic children. Further, the electroblotting technique is fast, convenient, and highly suitable for both allergen composition studies and screening for antibody specificity. Mean levels of mite-specific IgE were not significantly related to the age of onset and severity of asthmatic symptoms, but were significantly different between individuals with current asthma and those with previous asthma. Fungi are well known as allergens that cause allergic rhinitis and allergic asthma in Taiwan. Penicillium citrinum and Aspergillus fumigatus are prevalent indoor airborne fungal species that have been implicated in human respiratory allergic disorders.

In addition, pollen and food allergens both show significant differences in incidence among different age groups. Crab meat, milk, and egg white are all associated with a significantly greater incidence of allergic disease in the 2- to 6-year-old age group than other age groups.

Correlation Between Risk Factors and Asthma

The article by Chiang et al in this issue of the journal illustrates many of the difficulties that arise in a study attempting to evaluate the correlation between risk factors for and the development and severity of asthma. The article describes symptoms in 579 asthmatic patients of various ages, and documents that levels of specific IgE antibodies to house dust mites bear no relation to the severity of asthma. Nonspecific trigger factors were analyzed by questionnaire, but these factors were not well defined, because of a lack of symptom provocation by the factors or by inhaled allergens; generally, such symptom provocation is the most reliable way of demonstrating clinically relevant sensitization in atopic patients with asthma.

Asthma: A Multifactorial Condition

Asthma is a multifactorial lung disease that is often associated with familial, allergenic, socioeconomic,
psychologic, and environmental factors. Asthma affects proportionately more children than adults, but morbidity and mortality are, to some extent, preventable with improved medical, environmental, and self-management.

References


