FactSheet

Vaccines, asthma and allergy

Vaccines have been implicated as a cause of the rising incidence of asthma and allergic disorders in developing countries.[1,2] The aetiology of allergic diseases such as asthma is multifactorial, with environmental, genetic and lifestyle factors all contributing and possibly interacting. It has been suggested that immunisation may result in some form of immunomodulation, which may affect the development of atopic disease. Some studies have suggested that vaccines increase the risk of atopy,[1-3] while others suggest that they decrease it[4-7] or are not associated with it.[8,9] The 'hygiene hypothesis' postulates a relationship between infection and allergy, whereby allergic diseases are prevented by infection in early childhood. This hypothesis has been used to explain the observed increased incidence of allergic disorders in developed countries, which is attributed to the reduction of childhood infection by vaccination and improved living standards.[10] This hypothesis was contrary to the previous view that infection acts as a trigger for allergy, and was not widely accepted until the early 1990s, when the distinction between different types of T helper (Th) cells was discovered.

Th cells play a key role in atopic disease, and are broadly categorised into two subtypes based on the cytokines they produce.[11] Th1 cells preferentially produce interleukin-2 (IL-2), interferon-gamma (IFN-gamma), and tumour necrosis factor-b (TNF-b), and are implicated in the development of delayed (type-IV) hypersensitivity reactions in chronic granulomatous diseases such as tuberculosis, leprosy, and sarcoidosis. Th2 cells, on the other hand, produce IL-4, IL-5, IL-9 and IL-13, but not IFN-gamma or IL-2. These cytokines are important in inducing synthesis of immunoglobulin E (IgE) and activating eosinophils, which have a role in the pathogenesis of asthma.[11] Th1 and Th2 cells are reciprocally regulated, and the IFN-gamma produced in the Th1 response strongly suppresses the Th2 response.

It is now accepted that asthma and allergic diseases are disorders with a predominant Th2 immune response. Some studies have highlighted the protective effect of mycobacterial infections, *Mycobacterium tuberculosis* (MTB) and BCG, all of which are associated with a predominant Th1 response, in the development of allergic diseases. Some researchers have found evidence that BCG vaccine, by increasing the Th1 response and suppressing the Th2 response, may reduce severity of asthma.[6,7] However, another study found that the prevalence of asthma and atopy does not differ in BCG vaccinated and unvaccinated children.[12]

The studies which implicated vaccination in the pathogenesis of asthma all included whole cell pertussis vaccine or DTP.[1-3] An immunological study of acellular pertussis vaccine found that, despite the enhancement of Th2 responses to *Bordetella pertussis* antigens, booster vaccination with acellular pertussis vaccine does not appear to be a risk factor for allergy, as the Th2 response is specific for the pertussis-related antigens.[13] Further, a randomised controlled clinical trial of pertussis vaccine showed no difference in atopy between vaccinated and unvaccinated children.[14] Data from the International Study of Asthma and Allergies in Childhood were used to perform an ecological analysis of national and local immunisation rates for tuberculosis, diphtheria and tetanus toxoids and pertussis (DTP), and measles and prevalence of atopic symptoms (asthma, allergic rhinoconjunctivitis and atopic eczema).[9] This study found no association between immunisation and atopy.[9] A recent large cohort study found no association between asthma and vaccination with diphtheria, tetanus, whole-cell pertussis, oral polio or measles-mumps-rubella (MMR) vaccines. It did, however, find weak, significant associations with hepatitis B and Hib vaccines, which the authors attributed to possible sources of bias.[15]

Influenza vaccine has also been studied for its role in asthma. Several studies have found that influenza vaccine does not exacerbate asthma, and may even protect against asthma.[4,5,16] The Institute of Medicine, an independent expert body in the United States, has conducted a review of the effect of multiple immunisations on the immune system.[17] This report highlights the fact that the individual studies have looked at different vaccines and different allergic outcomes, making comparison between studies fraught with difficulty. However, it concludes that "the epidemiological evidence regarding risk for allergic disease, particularly asthma, was inadequate to accept or reject a causal relationship".[17]

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