

Can the natural course of allergy and asthma be changed by allergen vaccinations?

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Asthma, allergic rhinitis, atopic eczema and other diseases were allergic manifestations play an important role are increasingly common in infants and children. Asthma is the most common chronic disease in childhood. Decision makers should be aware of the impact of allergic diseases and act to improve the situation for those already allergic and asthmatic and, even more important, institute measures to prevent development of new allergies and new patients with asthma (1). Most children who start having allergic rhinitis seem to go on having symptoms up to adulthood except the few who are mono-sensitised and allergen elimination and avoidance are possible (2).

A link between allergic rhinitis and allergic asthma is evident from epidemiological, pathophysiological and clinical studies. Dysfunction of the upper and lower airways frequently coexists; they appear to share key elements of pathogenesis. Data from epidemiological studies indicates that nasal symptoms are experienced by as many as 28 to 78% of patients with asthma and that asthma is experienced by as many as 19 to 38% of patients with allergic rhinitis. It has been reported that 25 to 43% of a population of rhinitic patients develops asthma over a period of 8 to 10 years (3, 4). Bronchial asthma is said to develop in about 50% of children suffering from allergic rhinitis. Studies also have identified a temporal relation between the onset of rhinitis and asthma, with rhinitis frequently preceding the development of asthma. Upper and lower airway allergy develop simultaneously in 25% of patients, and of the remaining 75% half develops asthma first and half rhinitis first (3, 4).

When inhalant allergy expresses its symptoms, the nature of the allergic inflammation is always IgE-mediated, no matter what target organ is involved. Up to 50% of patients with allergic rhinitis and no clinical evidence of asthma exhibits non-specific bronchial hyperresponsiveness. It has

To cite this article:

Valovirta E. Can the natural course of allergy and asthma be changed by allergen vaccinations?
Allergy 1999, 54, 27-29.

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ISSN 0108-1675

been suggested that the patients with allergic rhinitis and bronchial hyperresponsiveness are those most likely to develop asthma. The prognosis of childhood asthma is poorer if the child has had severe asthma in childhood and/or concurrent allergic disease. Furthermore, the prognosis is poorer if the child has IgE-mediated allergy or a family history of asthma. About 50% of asthmatics are symptom-free about 20 years after the diagnosis has been established, but many of them still show bronchial hyperreactivity and at least 25% of them will get back symptoms within years (1). Thus early and intense treatment of the allergic disease in childhood is most important. The key question is how to stop the development of allergic rhinitis to asthma.

Treatment strategies must focus on the underlying IgE-mediated inflammation to control the symptoms and to reduce the development of complications. Of particular interest to the clinicians are the studies showing that treatment of allergic rhinitis reduces the incidence and severity of asthma. In fact, it has become evident that the control of the upper airways is necessary for controlling the lower airways.

Three techniques for the reduction and control of the allergic inflammation are used:

- 1) Avoidance of the offending allergens,
- 2) Selection of appropriate pharmaceuticals, and
- 3) Introduction of allergen specific immunotherapy, allergen vaccinations.

Early appropriate treatment of the underlying inflammation saves patients of related airway diseases, reduces the overall costs of care and improves the quality of life of the patient and the family (5). Allergen specific immunotherapy, allergen vaccination, is the only form of treatment which has been shown to have influence on the allergic disease, on its symptoms and bronchial hyperreactivity up to at least five years after the cessation of the treatment (6).

Allergen specific immunotherapy, allergen vaccination, has a systemic anti-inflammatory effect on the IgE-mediated inflammation. In the WHO Position Paper: Allergen Immunotherapy: Therapeutic Vaccines for Allergic Diseases from 1998 (7), it is discussed that the indications for immunotherapy have been separated into rhinitis and asthma respectively in some guidelines. This artificial separation has led to unresolved questions, possibly because an IgE-mediated reaction has not been considered as a multiple organ involvement. It is therefore important to consider immunotherapy based on the allergen sensitization rather than on a particular disease manifestation. The

EAACI Immunotherapy Position Paper from 1993 (8) indicates that immunotherapy should be started early in the disease process, meaning rather early in the lives of most patients. The International Consensus Report on the Diagnosis and Management of Rhinitis from 1994 (9) gives guidelines for the use of immunotherapy in the treatment of allergic rhinitis: Immunotherapy should be considered if there is a history of allergic rhinitis for at least two seasons (seasonal allergic rhinitis) or six months (perennial allergic rhinitis) when pharmacotherapy insufficiently controls the symptoms.

Already, as early as 1968 the study of Johnstone and Dutton showed that children receiving immunotherapy had asthma significantly less than the children receiving placebo (10). In a recent study by Jacobsen et al. from 1997 (11) it was shown that none of the adult patients allergic to birch, alder and hazel suffering from allergic rhinitis developed asthma over the 6-year period of follow-up after the 3 years course of allergen specific immunotherapy. This indicates that allergen specific immunotherapy not only prevents the onset of asthma in a risk group of rhinitic patients, but also produces a long-term reduction of asthma risk. The results of the immunotherapy study for asthma in allergic children by Adkinson et al. from 1997 (12) showed that the subgroups in which there was a tendency towards a benefit from allergen vaccination were children with mild disease and the younger children, under the age of 8.5 years in this study. Future investigations should focus on the prophylactic use of immunotherapy in children with allergic rhinitis, who are at high risk for asthma, or in highly allergic children with the recent onset of mild asthma. It is possible that the prophylactic use of immunotherapy early after the onset of asthma alters the natural history of the disease by suppressing airway inflammation at a time when a child is only intermittently symptomatic. In the on-going European multi-center study Preventive Allergy Treatment (PAT) Study (13, 14) the preliminary results clearly show that after three year period of allergen specific immunotherapy and after five years' follow-up the risk of the onset of asthma is reduced in children from 5 to 13 years of age suffering from birch and/or timothy pollen induced allergic rhinoconjunctivitis. The PAT Study is a prospective study with the total follow-up time up to the year 2003.

Allergen specific immunotherapy in children monosensitized to house dust mite has shown to alter the natural course of allergy in preventing the development of new sensitizations (15). In this prospective, nonrandomized case-control study ten of 22 children monosensitized to house dust mite who were receiving immunotherapy did not have

new sensitivities in the skin prick testing or in the measurement of allergen specific IgE in serum compared with zero of 22 children in the control group. These results cannot be extended to polysensitized children, because it has been shown that the rate of sensitization is unaltered by the administration of allergen specific immunotherapy.

In the WHO Position Paper on Allergen Immunotherapy it

is concluded that immunotherapy is the only treatment that affects the natural course of allergic diseases. It has a capacity to stop the development of new sensitizations in mono-allergic children and a possibility to prevent the development of asthma in selected patients with allergic rhinitis. It is valuable to introduce allergen vaccination to the patients in the early phase of their allergic disorder.

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