The Natural History of Allergic Diseases and Its Management

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The epidemiologic studies report that the allergic diseases of children has increased considerably in the last 30yrs, those finding being prominent in the developed counties (Table 1) The prevalence of the allergic diseases in Korea is comparable to those of European countries. It is important to prevent the acute exacerbation and the occurrence of these diseases to reduce the burden of socioeconomic cost because the course of the allergic diseases is chronic through childhood. To reach those goals, it is necessary to understand the natural course of the allergic diseases which are characterized by so called ‘allergic march’ (Fig. 1, Fig. 2).

The aim of this review is to comprehend the

Table 1. Atopic diseases in childhood. Prevalence of disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food allergy</td>
<td>7–8</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>15–20</td>
</tr>
<tr>
<td>Asthma/recurrent wheezing &lt;5 yr</td>
<td>31–34</td>
</tr>
<tr>
<td>Asthma &gt;5 yr</td>
<td>7–10</td>
</tr>
</tbody>
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Fig. 1. Allergic March. From Ann Allergy Asthma Immunol 2010;105:99-106.

Fig. 2. The prevalence of current eczema, allergic rhinitis, and asthma estimated from compiled data over the age span of birth to 70 years. From Ann Allergy Clin Immunol 2009;103:282-9.
allergic march, distinctive figure of allergic disease and the management to control the course of diseases.

**Allergic Diseases and Its Natural Course ‘Allergic March’**

Allergic (atopic) diseases consist of atopic dermatitis, asthma, allergic rhinitis and food allergy, etc. The atopic march or allergic march is a term that describes the progression of atopic diseases, from atopic dermatitis to allergic rhinitis, asthma during the first several years of life. Atopic dermatitis is generally considered the entry of allergic march.

AD has its onset during the first 6months of life in 45% of children, and before 5 years of age in at least 85% of affected individuals.

The features of atopic dermatitis (AD) is the chronicity of the disorder, itching, and the age-specific rash-pattern and distribution of lesions. The grade of involvement might range from mild limited flexural area to severe generalized. AD has been divided into 3 phases based on the age of the patient and distribution of lesion: the infantile, childhood, and the adult phase. The infantile phase reflect the period from birth to 2 years of age. The erythematous papules, vesicles initially appear on the cheeks, forehead and scalp, might extend to trunk, the extensor of extremities. The character of this phase is the tendency to manifest edema of affected areas, leading to oozing, crust and scaling and easily get aggravated due to allergens or irritants such as drooling and infection. The childhood phase is during the period from 2 year to puberty. While children are less likely to have the exudative lesions of infancy, the more lichenified papules and plaques representing the more chronic diseases are exhibited. The flexural areas of extremities are the common localization site. Facial involvement tends to localized to periorbital and perioral areas. The adults phase begins at puberty. Common sites of the disease are flexural fold, face and neck, and hand etc. The adult phase begins at puberty and frequently continues into adulthood. Flexural areas including hand, foot and extremity and face are prominent areas that is characterized by dry scaling erythematous papules and the formation of large lichenified from lesional chronicity.

But all infants with atopic dermatitis don’t have these courses and the number and percentage of patients outgrow their disease. In the questionnaire study to be followed the 205 patient for 25year from 6~36 month of age, 60% was resolved, with the patients with severe AD reporting a longer time to resolution. The study report in UK report the prevalence of AD is peak at 20% of children by 1year of age and declined to approximately 5% after 22 year. Meanwhile, the prevalence of allergic rhinitis slowly increased over time from 3% to 15%, in the prevalence of wheezing, 5% to 40% and increased rate of aeroallergen sensitization. The German study followed up a birth cohort of infants more than one thousand and that classified the outcome into 3 groups (intermittent, persistent, resolution). At 7 years of age, 43% were in complete remission, 38% in intermittent and 19% in persistent. Risk factors for persistent AD were the initial severe AD and atopic sensitization (Fig. 3). Early atopic dermatitis might predict allergic rhinitis and
Fig. 3. Natural course of AD up to age 7 years with early manifestation of diseases (<2 yr). From J Allergy Clin Immunol 2004;113:925-31.

Fig. 4. Percentage of patients developing asthma. Higher incidence of asthma in severe AD.

Fig. 5. Development of allergic disease. From Pediatr Allergy Immunol 2004;15Suppl16:9-32.

The mechanism of allergic march

The development of allergic disease depend on a complex interaction between genetic and several environmental factors such as environmental exposure to food, inhalant allergen, and non-specific adjuvants factors, such as air pollution (Fig. 5). The considerable number of culprit genes are common in these:

- Genetic predisposition
- Early sensitization
- Allergen exposure
  - +
  - +/−
  - Immune modulation (b)
    - infections
    - intestinal microflora
    - other factors
  - Development of clinical allergy

wheezing episode by 7 years of age. In the another 8 year-followup study, 90% of patients with atopic dermatitis out-grew their disease and the patient with severe atopic dermatitis showed asthma in 43%, and the prevalence was higher risk factor than mild AD (Fig. 4).
allergic diseases belonging to the allergic march.

In the mouse experiment, mice developed inflammatory dermatitis after epicutaneous sensitization to the ovalbumin that subsequently progressed to airway hyperresponsiveness and bronchial inflammation on a single exposure to inhaled ovalbumin. Experimental data in animal AD model suggest that the impaired barrier function of the AD epidermis allows epicutaneous sensitization, enhanced by rubbing and scratching of inflamed atopic skin, and can lead to systemic allergic response and airway sensitization. Severe AD patients tend to have exaggerated airway responses to inhalation challenge with allergen or direct stimuli such as methacholine (Fig. 6).

The Management and Prevention of Allergic Disease

Primary prevention: addresses healthy children with the aim to prevent development of allergic disease
Secondary prevention: addresses already diseased children with the aim to prevent symptoms and further progression.
Tertiary prevention: addresses patient with chronic disease in order to prevent progression and deterioration.

1. Diet.

Absolute breast feeding has the effect to prevent the occurrence of atopic dermatitis and asthma until 5 years of age. In the high risk infants with allergic family history, absolute breast feeding until 4 month of age and weaning after the 4-6 month of age has the preventive effects on the development of atopic dermatitis and food allergy. Complete hydrolyzed milk or amino acid based formula reduces the allergic symptoms and signs. Probiotics and vitamin remain undetermined.

2. Modification of environment

Genetically predisposed infants are more easily at risk to allergic disease about exposure to tobacco smoke and indoor allergen. The severity of atopic dermatitis is improved and allergic sensitization is less likely by active avoidance of house dust mite in infants with AD.

3. Specific Immunotherapy under investigating

References