Clinic Rev Allerg Immunol (2011) 41:1–3
DOI 10.1007/s12016-011-8270-2

Novel Challenges for the Allergist

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Published online: 15 April 2011

Abstract The last years have witnessed novel findings with exciting developments in the field of allergy-related diseases including asthma, bronchial hyperresponsiveness, eczema, and atopy that have enormously increased over the past few years. This issue of the *Reviews* is timely dedicated to comprehensive articles discussing the current trends in the study of these conditions. In particular, the impact of new data in genomics, environmental factors through epigenetics and proteomics will be reviewed and critically discussed.

Keywords Allergy · Asthma · Biologics

The widespread interest on the mechanisms and treatments of allergic phenotypes is witnessed by the amount of peer-reviewed publications that can be retrieved with a PubMed search over the past years. Indeed, the keyword "allergy" returned 11,207 articles in 2010, compared to 10,692 in 2005, and 8,767 in 2000. In a parallel fashion, our knowledge of allergy-related diseases such as asthma, bronchial hyperresponsiveness, eczema, and atopy has enormously increased over the past few years. For this reason, the present issue of *Clinical Reviews in Allergy and Immunology* is timely and, based on comprehensive review articles, encompasses the current trends in the study of allergy-related conditions.

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The study of genomics in allergy stemmed from earlier observations reported in monozygotic twins in which a largely incomplete concordance was reported [1] thus supporting the multifactorial origin of allergy-related conditions. This is the ideal setting for the novel high-throughput studies to determine the associations of complex diseases with single nucleotide polymorphisms (SNP) through genome-wide association studies (GWAS)[2]. Such large-scale approaches recently led to the identification of genes associated with asthma [3], bronchial hyperresponsiveness [4], and atopy [5] with previous findings extensively reviewed elsewhere [6]. Of note, GWAS in allergy-related phenotypes appear to be more advanced compared to rare conditions based on the fact that significant associations were independently replicated [7] and that is has easier access to large numbers of patients and controls compared to other immunological diseases [8, 9]. Similarly, intriguing data have been reported over the past years on the epidemiology of allergy-related phenotypes, as illustrated by the significant increase in the incidence of peanut allergy worldwide and by a large study performed in the Australian Capital Territory [10]. Conflicting data, on the other hand, were reported from Sweden where the incidence of allergic rhinitis was found to be increasing, different from asthma [11]. Epidemiological evidence provides an ideal basis to investigate the environmental factors leading to specific phenotypes and data were recently reported for the association of asthma with ethnicity [12], reproductive factors [13–16], viral infections [17], and dietary habits [18, 19]. In the present journal issue, Dr. Andersen and colleagues studied whether some characteristic disease entities could be identified in Europe for allergy to *Rosaceae* fruits and identified five allergy patterns involving the allergen families PR-10, LTP, and profilin [20].

The hygiene hypothesis has been proposed to determine the risk of allergy-related disorders, and the exposure to infectious agents appears to be inversely related to the manifestation of atopic diseases such as asthma and hay fever. A recent study took advantage of data from schoolchildren living in predominantly rural areas of Central Europe: the German population of the Prevention of Allergy—Risk Factors for Sensitization Related to Farming and Anthroposophic Lifestyle (PARSIFAL) study and the Bavarian population of GABRIELA (Multidisciplinary Study to Identify the Genetic and Environmental Causes of Asthma in the European Community [GABRIEL] Advanced Study) [21]. The authors compared the prevalence rates of asthma and atopy in children from farms and in other children living in the same areas serving as controls and rigorously analyzed the diversity of the microbial exposure in these groups using two complementary approaches, i.e., single-strand conformation polymorphism analysis in the PARSIFAL study and culture techniques in GABRIELA. The gathered data supported the role of infectious agents in the development of childhood asthma as subjects living on farms were exposed to a wider range of bacteria and this difference accounted for part of the inverse relation between asthma and growing up on a farm [22]. An additional mechanism that was derived from epidemiological observations is based on the association during pregnancy or infancy between fish oil intake and atopy development, as extensively illustrated in the present issue by Dr. Kremmyda and colleagues [23]. The intake of polyunsaturated fatty acids (PUFA) from fish oil during pregnancy may be inversely correlated with sensitization to common food allergens and reduce the risk of atopic dermatitis in the offspring [24], thus contributing to disease onset [25]. To date, several epidemiological studies supported this link, but there is not a full agreement on the issue. Studies investigating the impact of infant fish oil intake also failed to prove definitive associations with allergy and atopy.

More hot topics in the field of allergy-related diseases have been proposed in the past years and are addressed in this issue. First, new molecular tools, as in the case of proteomics for immune-mediated diseases [26], apply to food allergy [27, 28] and are expected to improve food allergy diagnosis, therapy, and allergenic risk assessment, but the high current costs do not allow a routine use of high-specificity methods towards personalized medicine [29]. Second, the availability of sensitive laboratory methods has significantly modified our approach to asthma [30–32], as in the case of exhaled carbon monoxide in the meta-analysis by Shaoquin et al. [33]. Third, significant developments have been obtained from the study of epigenetics in determining the susceptibility to immunological disorders [34–36]. Fourth and possibly most importantly, our knowledge of the pathogenesis of asthma and allergy has significantly progressed with new players recognized in the classical immune-mediated pathways [37, 38]. The case of chemokines, for example, is representative of this trend for allergy [39] and other immunological conditions [40–42]. These recent developments are currently raising interest based on the putative therapeutic implications of chemokine antagonists [43]. While current and more classical treatments warrant adequate knowledge, as in the case of intranasal steroids for rhinitis [44] or histamine targeting [45], new therapeutic molecules are expected to revolutionize the management of patients with allergy-related phenotypes. In particular, immunotherapies based on biologics such as anti-IgE antibodies and soluble interleukin 4 receptors [46] are currently under advanced clinical evaluation.

In conclusion, it is now established that allergy, eczema, asthma, and other related conditions are to be considered as complex and it would be naïve to expect that one pathogenetic model or one therapeutic approach may fit all, particularly in the rapidly growing field of targeting specific immunological pathways using monoclonals or other cutting-edge approaches [47]. We are convinced that allergy will thus prove as the ideal setting to practice translational medicine in which data coming from genomics, epidemiology, in vitro studies will equally contribute to prepare new tools to prevent and treat the plethora of clinical phenotypes.

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