

Sensitization to Cat: Why Not Use Molecular Diagnostics instead of the Nasal Challenge in Clinical Practice?

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Dear Editor,

We read with interest the article of Al-Ahmad et al. [1] reporting the results of a nasal challenge test (NCT) carried out in patients suffering from perennial allergic rhinitis (PAR) due to cat allergy in order to determine useful criteria for prescribing allergen immunotherapy (AIT). Although the NCT may be considered the gold standard for detecting the culprit allergen in PAR, from a theoretical point of view, this procedure has some important limitations in “real life.” As recognized by authors, the NCT is a complex and time-consuming procedure requiring reliable performance and quality training of the staff. This is the reason why the NCT is not easily organized in clinical practice. In contrast, its use is highly recommended in research settings to demonstrate the efficacy of antiallergic drugs/AIT [2, 3], to identify basic immunological and neural mechanisms, or to investigate local allergic rhinitis [4]. Moreover, although several different approaches to provocation exist, a universal consensus on the optimal methods is lacking. Therefore, we would like to suggest other possible methods of realizing a “personalized” diagnosis of cat allergy without the use of such a complex procedure as the NCT.

Firstly, the authors have not specified if their patients were sensitized exclusively to cat allergens (in this case, would it be necessary to perform an NCT?) or also to other allergens inducing persistent respiratory symptoms. This is an important issue in polysensitized patients. Although involvement of the bronchial airways (also with minimal or no symptoms) may be common in patients suffering from PAR [5], no mention of this has been made by the authors. The peak expiratory flow (PEF) testing performed preliminarily may be inadequate to point out a latent bronchial hyperreactivity, thus increasing the risk of bronchial obstruction after accidental penetration of allergens into the lower airways. We believe that measuring the FEV₁ and the FEV₁/FVC ratio with forced spirometry before and during the NCT would be a more correct procedure, and this is particularly true during a cat allergen challenge in subjects never exposed to a methacholine challenge to exclude asthma. The risk should not be neglected, also considering the characteristics of cat allergen-carrying particles. Several studies have demonstrated that about 25% of cat allergens are carried by

submicronic particles (<1–2 µm in diameter) which easily become airborne with natural air ventilation. These particles are able to penetrate into the deep airways, inducing persistent allergenic stimulation and prolonged small-airway obstruction in already sensitized individuals [6, 7]. In fact, Zeidler et al. [8] showed that naturalistic exposure to cat allergens (using a cat room challenge) results in significant small-airways obstruction and hyperresponsiveness which persists for at least 23 h as measured by pulmonary function testing and high-resolution computed tomography. Although the NCT may be considered a safe procedure when carried out by well-trained medical staff in adequate health facilities such as those reported by Al-Ahmad et al. [1, 9, 10], the same situation is unlikely to occur in outpatient health facilities in “real life.” Thus, it is not clear why the authors did not consider component-resolved diagnostics (CRD) before undertaking a potentially “unsafe” in vivo procedure such as the NCT.

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We believe that the cat's allergens are among those better characterized in comparison with other inhalant allergens, thus not making it necessary to use a "more invasive" diagnostic approach to establish the real clinical significance/correlation. Although at least 8 cat allergens have been identified so far, it is well known that Fel d 1 (a secretoglobulin) is the major allergen being recognized by 66–100% of cat-sensitized individuals [11, 12]. Another crucial aspect is that secretoglobins are not involved in any significant cross-reaction with other described animal allergen families. As a consequence, heeding clinical considerations (e.g., evident worsening of respiratory symptoms after direct cat contact or after prolonged absence of cat exposure), skin prick test (SPT) results, and CRD positivity for Fel d 1 and negativity for other animal "pan-allergens" (lipocalins and albumins), we are likely able to "personalize" the diagnosis of cat allergy and to provide information on AIT prescription. In contrast, the utility of the NCT is much more pronounced in cases in which the suspected culprit allergens stem from dogs, since in dog allergy, many different (at least 7) allergens may be involved in the development of respiratory symp-

toms [13]. These allergens belong to different protein families (including some pan-allergens) which can cross-react with pan-allergens of several other furry animals [14]. Using an in vivo model (SPT) and an in vitro model (the microarray technique ImmunoCAP ISAC; Thermo Fisher Scientific – ImmunoDiagnostics, Uppsala, Sweden), we have shown that exposure and allergic sensitization to common pets (in particular, dog) increase about 14-fold the risk of developing sensitization to other furry animals, suggesting a possible predisposition to develop multiple sensitization to animal allergens [15, 16]. Therefore, CRD constitutes an important means of distinguishing a "true dog allergy" from a multiple-IgE response to several furry animal allergens [17, 18]. These difficulties may justify in vivo stimulation of the nasal mucosa to establish the culprit dog allergen(s), and, consequently, to prescribe dog AIT [13].

In conclusion, we believe that CRD may be a reliable procedure, in addition to clinical data and results from SPTs, to obtain information for a "personalized" diagnosis of cat allergy and, if necessary, for AIT prescription without the use of the NCT in "real life."

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Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

G. Liccardi conceived the idea of the letter and wrote the first draft of the manuscript; all co-authors (L. Calzetta, M. Milanese, M.B. Bilò, and P. Rogliani) drafted the manuscript, gave their input, and agreed on the final submitted version. All authors read and approved the final manuscript.

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