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Food allergy and atopy patch tests

Dear Editor,

The review article by Ferreira et al.[1] is an appropriate tool for a better understanding on food allergies (FA), a difficult theme for patients and physicians, particularly pediatricians working in front line care.

The difficulties involved in diagnosis of cell-mediated FA are a problem for patient management. Oral challenge tests are complicated to carry out, because the symptoms may occur over the long time in cell-mediated hypersensitivity, which makes it very difficult to perform oral double-blind placebo challenges and could be a major confounding factor for dietary diaries. Although the authors mention that cutaneous contact tests, also known as atopy patch tests (APT), have low accuracy, atopic dermatitis and eosinophilic esophagitis are diseases in which these tests may be helpful in the diagnosis and treatment of patients.

Recently, the European Academy of Allergology and Clinical Immunology (EAACI) published a position paper related to aeroallergens and food atopy patch tests, in response to the large number of articles that have been published on the subject. That review concluded that for atopic dermatitis patients that do not respond adequately to initial treatment with skin moisturizing, emollients and taking care with irritants, a combination of skin prick tests (SPT) or specific IgE for foods and APT can be helpful in the diagnosis of food allergies associated with eczema.[2] The same article recommends the use of in natura foods while extracts are not yet standardized.[2]

In relation to eosinophilic esophagitis, particularly during childhood, there is a high level of association with FA. Patients develop an inflammatory process of the esophageal mucosa with the presence of eosinophils, 20 or more per high power field in biopsy of the lower third of esophagus. To control the inflammatory process, oral or swallowed corticosteroids are used together with exclusion of the food involved. In the absence of implicated foods it is necessary to make use of hydrolyzed proteins to control the inflammation.

Spergel et al.[3-5] have recently demonstrated, in a series of articles undertaken with appropriate methodology, that combining APT with SPT or specific IgE for foods increases the positive predictive value of the allergy tests, thereby achieving a greater number of FA diagnoses, and, consequently, a reduction in the use of hydrolyzed proteins due to exclusion of specific foods, improving patient quality of life by reducing their costs.

There is a small number of studies on the utility of APT for other conditions associated with cell-mediated FA. Recently, Fogg et al. described, in a pilot study, 16 cases of eosinophilic proctocolitis in babies with clinical diagnoses confirmed by APT.

Atopy patch tests employed in conjunction with specific IgE assays or SPT can be helpful in the diagnosis and treatment of patients with FA due to mixed mechanisms and, possibly, for exclusively cell-mediated. There is a need for larger studies in order to investigate what the best formulations might be for APTs, whether *in natura* or using protein extracts and, what is the best diluent, whether saline, water or petroleum derivatives, such as petrolatum. Despite this, the use of these tests has a growing basis in the literature and, furthermore, the EAACI's position is in favor of their use in these pathologies and in specific cases.

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Authors' reply

We want to thank Dr. Silva Segundo for his interest in our recent paper and for the pertinent review on the utility of atopy patch tests (APT) for the diagnosis of IgE-mediated food allergies. Indeed, there is evidence that APT can be helpful in predicting outcomes of double-blind placebo-controlled food challenges. However, most of such studies have been carried out in children with atopic dermatitis or allergic gastroenteropathies such as food-sensitive eosinophilic esophagitis. The majority of patients seen by pediatric gastroenterologists have food-sensitive enteropathies that are not associated with atopic dermatitis or eosinophilic enteropathies.

Moreover, several limitations exist with APT, even in carefully selected patients, as reviewed recently by the European Academy of Allergy and Clinical Immunology.[1] First and foremost are the limited and highly variable sensitivity and specificity of the APT. In the diagnosis of cow's milk allergy, the mean sensitivity (0.51) and specificity (0.86) of the APT are similar to those of skin prick tests. However, the sensitivity of the APT has been reported to vary enormously, from 0.18 to 0.89.[1]

Numerous factors may explain these limited results with APT. These include the potential lack of standardization of the test conditions: allergen source and concentration, vehicle employed, control material, duration of and material used for occlusion, and size of the chamber. Finally, even though the results of APT may correlate with the outcome of properly conducted food challenges, studies still need be carried out to show that the test results predict the outcome of food elimination diet on gastrointestinal symptoms.

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Salivary cortisol to assess the hypothalamic-pituitary-adrenal axis in healthy children under 3 years old

Dear Editor,

In the recent publication by Silva et al.,[1] a mean morning cortisol level of 558 nmol/L (range 77-1,620 nmol/L) in children was reported. This is remarkably higher than any of the previously published ranges for salivary cortisol in children. Although Silva et al. did not report the corresponding serum cortisol levels, their data contradict the notion that only the free cortisol component can pass into saliva, and therefore, under basal conditions, salivary cortisol equates to < 10% of total serum cortisol. Most institutions report morning cortisol levels of a much smaller magnitude, with mean morning salivary cortisol levels of < 30 nmol/L (Table 1).

The authors state that they were unable to locate reference salivary cortisol levels for children in the literature. For readers' information, we have included a summary of the previously published pediatric salivary cortisol literature (Table 1). Our group recently published salivary cortisol reference ranges for healthy children.[8] The range for morning cortisol was 0-25 nmol/L.[8]

Silva et al. used an in-house cortisol radioimmunoassay (RIA), using antibodies to cortisol-3-oxime conjugated with bovine albumin, quoting cross reactivity of 8.5% for cortisone and 7.9% for 11-deoxycortisol. These cross reactivities are higher than in commercially available RIAs. For example, the Orion Diagnostica Spectra Cortisol Coated Tube RIA product information quotes cross reactivity of 0.9% for cortisone and 0.3% for 11-deoxycortisol. However, the increased cross reactivity for cortisone and 11-deoxycortisol cannot explain why the results of Silva et al. are so discrepant from previously published data. This highlights the importance of establishing reference values for all methods and at each institution, as mentioned in the Editorial in the same edition of the journal.[9] However, to avoid misleading clinicians, particularly those who are unfamiliar with salivary cortisol, the au-