

WHAT SHOULD WE KNOW ABOUT HYPERSENSITIVITY TO PEANUTS IN TOPICAL PREPARATIONS

The rising prevalence of food allergies poses an increasingly important clinical problem. Peanut is one of the most potent allergens, and allergic reactions to peanuts may even be fatal. A great proportion of hypersensitive individuals manifest allergic reaction on their first exposure to peanut containing food, pointing to pre-existing sensitization. Therefore, the question arises whether peanut containing topical preparations are safe or epicutaneous sensitization is still possible.

A considerable increase in the prevalence of allergic diseases has been recorded in the past few decades, in industrialized countries in particular. This increasing tendency primarily refers to type I allergic diseases such as allergic asthma, allergic rhinoconjunctivitis and atopic dermatitis. Such a significantly rising tendency has not been recorded for other types of allergic disease such as cytotoxic reactions (type II), immune complex diseases (type III) and delayed immune response reactions (type IV) (1).

The rise in the prevalence of food allergies poses a major clinical problem. Considering various foodstuffs, peanut is one of the most potent allergens, as 1% of the Western world populations suffer from peanut hypersensitivity (2). Clinical manifestations of peanut allergy are variable, from urticaria, gastrointestinal and respiratory discomforts through severe clinical manifestations such as anaphylactic shock (3). Peanuts account for as many as 63% of fatal food allergic reactions (4).

Peanut contains proteins that are responsible for its high allergenic potency. A number of proteins have been isolated and identified as peanut allergens, designated Ara h 1 – Ara h 8 (4) after the Latin name of the plant, *Arachis hypogaea* (5). Some of these protein clones have now been synthesized (6). The minimal amount of the protein considered adequate to cause allergic reaction is 50-100 mg (7). Peanut oils may pose great problem in sensitized individuals due to residual protein they contain, depending on the manufac-

turing technology. Refined oils contain 100 times less protein than non-refined ones (5,7). In a study conducted in Great Britain, none of the 60 subjects with known peanut allergy showed allergic reaction upon refined oil intake, whereas six (10%) individuals developed allergic reaction upon non-refined oil intake (7). Similar studies were performed with soybean oils, and none of the study subjects developed allergic reaction (8).

Although one could infer thereof that refined oils are safe for use by individuals allergic to peanuts, great caution is warranted because of the possible "contamination" of these products through their repeated use in food preparation, due to residual protein from the previously prepared food (7). Cases have been described of anaphylactic reaction caused by the use of peanut contaminated objects or through contact between peanut contaminated hands and saliva in individuals with known peanut hypersensitivity (9).

When talking about peanut hypersensitivity, the possible cross reaction with soy should always be borne in mind. Peanut and soy are botanically related plants, and there is some overlapping between their allergenic components, thus IgE antibodies to peanut may cross react with soy proteins. In Sweden, six fatal cases of anaphylactic food reactions, two of them peanut allergy and four soybean allergy, were recorded during the 1993-1996 period. Allergic reaction to soy proteins was not previously known in any of the four cases of soybean allergy, while peanut allergy was previously known in all these subjects (10). In 72%-81% of cases, the individuals with peanut allergy manifest it upon the first intake of this allergen (11,12). As it is an IgE-mediated allergic reaction (type I), which requires previous allergen sensitization, the question arises of the possible sensitization by some other than oral route.

Sensitization *in utero* may be possible, however, there are no studies to demonstrate it. In a study carried out in Toronto, Canada, in 1999-

2000, peanut proteins were detected in breast milk of lactating women taking peanuts, thus sensitization *via* breast-feeding is considered as one of the possible routes of sensitization (11). The more so, there are some controversial studies (13), and an open question is whether breast-feeding may even have an unfavorable effect in families with atopic predisposition (13).

The safety of the use of peanut based topical preparations has lately been strongly challenged, pointing to the possible epicutaneous sensitization in allergy predisposed individuals. Besides its wide use in food industry, peanut oil (*oleum arachidis*) is frequently used in pharmaceutical industry as an excipient in products intended for topical, oral or parenteral administration. In cosmetic industry, peanut oil is used in the manufacture of soap, cream and other consumer goods. The beneficial effect of peanut oil in the form of oil baths, free from any side effects recorded, was especially pronounced in the treatment of very dry and damaged skin (e.g., eczema) both in adults and in children (3). However, the official statement of the European Agency for the Evaluation of Medicinal Products (EMA) from January 12, 2006, presents reports of skin reactions that may have been related to the use of oil baths containing peanut or soybean oil (14). A retrospective British study (15) demonstrated the association between type I hypersensitivity reaction to peanut and previous skin exposure, i.e. use of topical preparations based on peanut oil. It is considered that as many as 95% of individuals with peanut hypersensitivity have a history of previous exposure to topical preparations containing peanut oil, especially in the first six months of life. The study does not specify the products and their amount used, etc.

As peanut containing topical preparations are mostly used by individuals with already damaged skin barrier, in search for an answer to the issue of the possible epicutaneous sensitization and subsequent induction of Th-2 immune response we refer to the experimental model employed by Strid *et al.* (12). In this study, mice were administered a topical peanut based preparation following epidermal damage caused by self-adhering tape, corresponding to the skin with protective barrier impairment. The levels of IL-4 and IgE showed a considerable increase when the mice started receiving peanut based chow. Initially, the level of IFN- γ was also elevated, indicating that the immune response was still of a mixed Th-1 and Th-2 type, with subsequent predominance of Th-2 type response. In addition, the development of

otherwise expected oral peanut tolerance was prevented, with impairment of the already achieved oral tolerance. In adults, even daily washing, shaving, frequent use of exfoliating preparations, depilation preparations, etc. may lead to impairment of the protective skin barrier (12).

Although the EMA statement is that skin reactions which can be related to the use of topical preparations containing peanut oil may be interpreted as contact allergic dermatitis, and considering that the studies reported point to the possible induction of allergic reaction upon their use, these preparations should be referred to as allergens. Therefore, the general statement of the EMA is that topical preparations containing peanut oil or soybean oil should not be used in individuals with known peanut and soybean allergy (14).

In conclusion, peanut sensitization is an important and increasing clinical problem due to the severe allergic manifestations that may threaten the life of sensitized individuals. Topical preparations containing peanut oil have proved efficient in the treatment of very dry and damaged skin in children and adults with atopic diseases. Epicutaneous sensitization is one of the potential routes of sensitization; therefore great caution is warranted in individuals with allergic predisposition.

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