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Risks of milk formulas containing peanut oil contaminated with peanut allergens in infants with atopic dermatitis

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Four cases of infants with atopic dermatitis are reported. In all cases, a sensitization to peanut is demonstrated. Any ingestion of peanuts can be excluded, with the exception of a daily consumption of peanut oil, contained in milk formulas. Oral challenges with peanut oil induce a rash, and elimination of these brands is followed by the disappearance of eczematous lesions. The presence of residual allergenic proteins in peanut oil is thus suspected. Owing to the growing incidence of peanut hypersensitivity, the elimination of peanut oil from all milk formulas, food for babies, and ointments, seems to be highly advisable.

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Food allergy plays an important part in causing and prolonging atopic dermatitis (AD) in infants (1–4). The food allergy spectrum mainly concerns eggs, fish and peanuts. In three American centres, as in France, peanut allergy accounts for 13% of food allergy cases (4–5). It seems that this severe allergy does not vanish with time (6). Furthermore it is the primary cause of lethal or near lethal anaphylaxis to food (7–12).

In recent studies (4–6, 13) the children were, on average, about three years of age when the allergy is detected, but a worrying increase in its incidence may be noticed in the first months of an infant's life. This raises the question not only of the origin of this sensitization but also of the form in which the allergen is ingested. Since infants do not eat peanuts, the possibility of peanut allergens being hidden allergens has to be put forward (4–6). Indeed, the important risk of hidden allergens, present in trace amounts in food, has already drawn attention (8, 12, 14–16).

Four cases are reported, which incriminate milk formulas containing peanut oil as being capable of inducing allergic reactions in infants who are sensitized to peanuts.

Clinical investigations

A careful questioning of the parents was complemented by one week's food diary including all labellings, the aim of which was to establish all types of food intake. AD was diagnosed according to Hanifin's criteria (17). The severity was evaluated by a clinical score, modified, from Molkhou (18). Briefly, the clinical evaluation was made by considering 20 areas of skin surface. A score on a 0- to 3 scale was recorded for each area rating. Moderate lesions: 1. Intermediate severity: 2. Severe lesions: 3. The maximal score is 60.

The skin tests and challenges were carried out with a standard peanut extract (Stallergènes-Pasteur, Fresnes, France), and with peanut butter and virgin peanut oil.

Prick skin tests were performed on the volar part of the forearm, and compared to a 9% codeine phosphate control and to a negative saline control. The criterion of positivity for the test was a wheal diameter equal to or greater than three mm (19–20).

Specific IgE were detected by Phadebas RAST CAP or by MAST-CLA (DHS). The labial challenge (LC) consisted in placing a drop of peanut butter, or

Table 1. Clinical aspect and biological tests in four infants with peanut-induced atopic dermatitis

Case	Age (months)	Time onset of AD	Breast feeding	Peanut Oil (%) in fats	Rast to peanut (KU/l)	Prick-tests			Labial test			Oral test	
						Peanut extract	Peanut butter	Peanut oil	Peanut proteins	Peanut butter	Peanut oil	Peanut proteins	Peanut oil
1	4 m	1 m	no	80	1.7	+	+	+	nd	+	+	nd	+1 ml
2	13 m	1 m	no	67	4.5	nd	nd	nd	-	nd	+	nd	+5 ml
3	8 m	15 d	no	80	1.2	+	nd	nd	-	nd	nd	+(350 mg)	+1 ml
4	61/2 m	3 m	<8 d	80	19	++	++	nd	nd	+	nd	nd	+1 ml

Legend:
m = month
d = day
nd = not done

oil, or peanut powder on the lower lip. The result was observed after ten minutes. Positivity resulted in oedema of the lip, sometimes in erythema or urticaria of the neighbouring skin and conjunctivitis. 19 tests in control subjects were negative (21).

A single-blind oral challenge (SBOC) was carried out with the informed consent of the parents with peanut oil or kernel powder, with increased doses every thirty minutes: 1 ml, 5 ml, 10 ml for the oil; 100 mg then 250 mg for the powder. These amounts were disguised in 10 g of stewed apple. The SBOC was thought to be sufficient, according to the age of the patients, and the fact that objective signs only were taken into account.

Case history

Case 1 – K.C. was examinated at four months for AD which appeared when she was one month old. The AD was severe, evaluated at 50/60 according to the modified Molkhou's score, despite dermo-corticoid treatment. She was not breast-fed but given milk formula Milumel® in which peanut oil accounts for 80% of the lipids. During pregnancy, her mother had often eaten peanuts and peanut oil.

The prick skin tests were positive for standard extract, peanut butter and peanut oil, and negative for cow's milk, casein, β-lactoglobulin and alpha lactalbumin. Eosinophilia was raised to 4400/mm^3. IgE was 15 KU/L. Phadebas CAP-RAST were positive for peanut: 1.7 KU/L – egg white: 7.1 KU/L, egg-yolk: 1.1 KU/L. The LC was positive for peanut oil and peanut butter with the onset of labial oedema. The SBOC with peanut oil (1 ml) brought on a widespread rash located in the same place as the eczematous lesions (Table 1).

The milk formula was replaced by cow's milk. After two weeks the clinical score had gone down from 50 to 8. Milk formula was then reintroduced. The skin lesions re-appeared 36 h later. The child was then fed with milk formula containing no peanut oil, and Oxatomide was prescribed for one month. Skin lesions have resolved. A further SBOC, was performed with 1 ml of peanut oil, six months later, and was negative.

Case 2 – F.B., 8 months old, developed AD two weeks after birth. He was not breast-fed, and was given several brands of milk formula, in the first of which peanut oil accounted for 67% of the total lipid content (Nidal®). The AD was severe. The score was 47/60. The food regimen included large intakes of vegetable-oil based biscuits flavoured with vanilla and synthetic vanillin.

The prick skin tests carried out for 35 food allergens were positive for peanut and egg-white. The total IgE was 41 KU/L. Specific IgE to peanut was detected by DHS-CLA. Phadebas RAST was 1 KU/L for egg-white. The LC with peanut proteins was negative. The SBOC with kernel powder (350 mg) was positive, showing a rash on the right thigh and neck (Table 1).

The infant was placed under oxatomide for one month, with elimination limited to egg. The clinical score decreased from 47 to 15/60. Then a SBOC was carried out with 1 ml of peanut oil. The test was positive causing the appearance of a rash on the abdomen 15 min after absorption.

A strict diet was then imposed, involving the elimination of all products containing vegetable fats, the exclusion of peanut oil and treatment with ketotifen and oral disodium cromoglycate. After four months the results was excellent since the clinical score had gone down from 15 to 2/60 (slight lesions in the skin folds at the elbows).

Case 3 – K.Y., a 13-month-old male infant, developed AD at the age of one month. He was not breast-fed, but was given the same milk formula as Case 1. At a very early age, he ingested cereals containing egg (Blédiscuit Nestlé). This mother had eaten peanuts during pregnancy. At five months, food allergy to egg was revealed by Prick, RAST (1.7 KU/L for egg-white) and labial and oral challenges. Despite elimination of egg and treatment with ketotifen and DSCG (Nalcron), the atopic der-

matitis did not improve. Molkhou's clinical score was 37/60. No skin test possible. The LC with peanut extract was negative. The LC with peanut oil caused labial oedema. The SBOC with 5 ml of peanut oil was positive: a rash appeared on the thorax, abdomen and thighs (Table 1). With the elimination of peanut-based products, associated with a ketotifen and DSCG treatment, the infant's condition improved.

Case 4 – S.C., a 6½ month-old female infant, developed AD at the age of three months. After having been breast-fed for a few days, she was given the same milk formula as Cases 1 and 3. From the age of four months onwards, she has been given a varied diet including chicken, turkey meat and biscuits containing egg.

The prick skin tests were extremely positive with the standard peanut extract, kernel powder and peanut butter. The RAST for peanut was 19 KU/L, and 6.4 KU/L for egg-white. The LC with peanut butter was positive (labial oedema). The SBOC with 1 ml of peanut oil brought on a generalized rash over the whole abdomen after 30 min (Table 1).

The infant was placed under Oxatomide, associated with an elimination of all products containing vegetable fats or peanut oil. The atopic dermatitis disappeared and a normal skin was observed within the following year.

Discussion

These four children presented with AD at a very early age, from two weeks to three months after birth. A simultaneous sensitization to egg and peanut was brought to the fore. The frequency of sensitization to these food allergens is well known (13, 22–24).

In these four babies sensitised to peanut, the ingestion (from birth) of milk formula containing 67% to 80% of these lipids in the form of peanut oil led to its being suspected of causing the AD. The fact that peanut oil is capable of bringing about a skin reaction is documented by the oral challenge tests. The DBPCFC was not used though it is considered the gold standard for the diagnostic evaluation of food sensitivity (25). We prefered to test peanut oil openly, insofar as we performed this kind of challenges without any reference prior to our study. We felt that due to the young age of the babies, there were no risks of any psychological reaction. On the other hand, we took the rule of recording only objective signs, such as the labial oedema or an erythematous rash in the predilection sites for atopic dermatitis.

The quantity ingested is quite compatible with the daily intake of milk formula, which is estimated to be a few ml per day. It was proven beyond doubt in Case 1 by the disappearance of the lesions when the milk formula was replaced by cow's milk and by their reappearance 36 h after the same milk formula was reintroduced. The resolution of the AD with cow's milk confirmed the negativity of the tests with cow's milk proteins. Similarly milk was not responsible for the symptoms in Cases 2 and 3. Both milk formulae ingested by the children had in common peanut oil constituting 80% and 67% of the total lipids. In Case 1, it was certain that no egg protein had been ingested. In the two other cases, it was observed that the elimination of egg led only to a partial improvement in the lesions, but that the disappearance of the AD followed a strict diet eliminating all products containing peanut oil. However, the improvement could be partially associated with therapy using an antihistaminic drug (ketotifen) and DSCG, since both drugs might provide some improvement in condition that respond to the elimination of the offending allergens (18).

Increased reactivity of peanut proteins contained in peanut butter has been demonstrated by RAST inhibition (26). At equal quantities, higher RAST inhibition is obtained with peanut butter than with peanut kernel. It has been suggested that the heating of the proteins exposed reactive epitopes. We commonly observe that prick skin tests to peanut butter are more positive than prick skin tests to peanut extract (data not shown). The fact that the LC was positive to peanut oil, and negative to peanut extract (Case 2) might possibly be explained by this hypothesis.

Peanut oil generally has been considered to be devoid of allergenicity (27). Some adult subjects allergic to peanut did not react upon ingestion of 30 ml of peanut oil (28). However, according to Sampson's comments, to be 95% certain that 95% of peanut allergic patients will not react to peanut oil, 58 individuals would have to be challenged to peanut oil with no reactions (4). Only 10 subjects have been studied (27). In fact, nothing is known about the threshhold level of sensitivity in allergic patients, and specifically in highly atopic infants. Accidental anaphylaxis with hidden allergens in food leads to the conclusion that tiny amounts are sufficient (15). The example of peanut sensitive individuals exhibiting symptoms by inhalation of allergen when the lid is removed from a jar of peanut butter, leads us to estimate that micrograms quantities could be sufficient to elicit a reaction (7). Soy, maize, sesame, sunflower, and peanut oils contain very low quantities of protein (29–30). Unrefined peanut oil contains from 150 to 550 mcg of proteins per litre (30). As peanut oil is heated to 200° for deodorization purposes, we suggest that these traces of residual proteins are made highly allergenic by this heating process. The isolation and characterization of the

residual proteins in peanut oil, and their allergenicity, is currently under study in our laboratory. In fact, several cases of allergic reactions to oils have been recorded; two cases of anaphylaxis to sesame oil have already been described (31–32) and a case of anaphylaxis to peanut oil was published in the ancient times, when adrenalin was injected in peanut oil. In that case, a positive skin test was even obtained to peanut oil (33).

The cases we present seem to indicate the possibility of AD linked to peanut allergy caused by these milk formulas. They prompted us to inquire into the origin of vegetal oils contained in 45 brands of infant formula; 11 milk formulas of 45 contain a variable proportion of peanut oil that can reach up to 80% of total lipids. It is possible that the ignorance of the role played by this masked allergen could explain the apparent failure of eviction diets concerning egg, milk or fish, when these food allergens have been identified.

In very young infants with AD systematic prick skin tests to peanut may be carried out. A positive test would make it advisable to ban all foodstuffs containing vegetable fat (with no details of origin), all those containing peanut butter and all foods containing peanut oil (many cereal-based products), as well as some brands of margarine, dermatologic creams, bath-oils, etc... (34). In any event, peanut oil should be banned from milk formula (35–36). The possibility that an early diagnosis and a careful avoidance of trace amounts of allergens could lead to the loss of sensitivity, or to a lessened sensitivity, has to be kept in mind. Indeed, the SBOC became negative in Case 1, following the eviction diet during six months. However, the result of a higher provocative dose in this case remains speculative.

The question of the origin of the peanut sensitization in these infants remains open. The role of peanut oil in milk formulas or other foods is to be debated. *In utero* sensitization can not be excluded (36–38). This hypothesis is under study at the present time. The frequency and the severity of allergy to peanut requires clarification of this possibility in order to establish an effective prophylactic protocal since the first attempts of immunotherapy have been hampered by the occurrence of a fatality (39).

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