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Letter to the Editor

Earlier than early exposure to allergenic food and prevention of allergic sensitization in young children

Exposition plus que précoce aux aliments allergènes et prévention de la sensibilisation allergique chez le jeune enfant

Keywords: Allergic sensitization; IgE; Peanut intake; Preconception; Pregnancy; Mother-child cohort

Mots clés : Sensibilisation allergique ; IgE ; Consommation de cacahuètes ; Préconception ; Grossesse ; Cohorte mère-enfant

While for decades, the prevailing advice to parents was to avoid introducing early in life certain known allergenic foods such as egg, peanut and cow's milk in children's diet, to prevent from allergic sensitization and subsequent development of allergies, current recommendations are shifting towards the need to introduce these foods in early-life to promote tolerance [1]. This has been recently shown by Perkin et al. [2] who found in a per-protocol that a 2-g peanut protein intake/week in 3-month children was associated with a significantly lower prevalence of childhood peanut allergy than was a lower intake. However, the trial did not show the efficacy of early introduction of allergenic foods in an intention-to-treat analysis. One possible explanation for the lack of significance in this analysis may be due to the low rate of adherence, which could be associated with parents' concern about choking in children with immature oral motor abilities.

While further investigations may find potential solutions to improve the food preparations to be easier to administer to infants, alternative strategies for allergy primary prevention might be considered. Indeed, a sooner timing and a less demanding route of specific food exposures may be beneficial for allergic sensitization and subsequent allergy prevention in children. During gestation, food allergens ingested by mothers cross the placental barrier [3] and may influence fetal immune development [4]. Very few studies have analysed associations between maternal peanut intake and childhood allergic sensitization. A protective effect of maternal gestational [5] peanut intake against peanut allergy was recently found.

Data from our EDEN birth cohort study of 1140 mother-child pairs drawn from the general population (<http://www.eden.vjf.inserm.fr/>) followed-up during 5 years [6] support the hypothesis that preconceptional and pregnancy periods may be important time frames to consider in allergies development. The mothers completed two food frequency questionnaires. The first FFQ was completed at the time of

recruitment, before the 24th week of amenorrhea, indicating their usual dietary intake during the year before the pregnancy. The second FFQ was completed in the first days after delivery, and concerned their usual intake during the three final months of pregnancy, which can be expected to reflect diet during pregnancy and which is a period during which mothers are less likely to experience vomiting. The FFQ completed by the mothers was very similar to the one developed for the Fleurbaix-Laventie Ville Santé study [7], which was validated using a series of 24-hour recalls [8].

Four categories of maternal peanut consumption were created: low (consumed < once/month), medium (1–3 times/month), high (once a week or more) and no intake.

Because of the possibility that diets recorded by the mothers before and during pregnancy may vary, we examined how the consumption of peanuts changed from the diet that was recorded before pregnancy to the diet recorded during pregnancy. Among the women, 90.5% reported either no change or minor change (increase or decrease), indicating that peanut consumption is relatively stable between the preconception and pregnancy period. In addition, no child reported intake of peanuts during their first year.

Total IgE were assessed using ImmunoCAP-technology (Thermo-Scientific/Phadia) in a subsample of 247 children with available serum at 5 years. Total IgE were considered positive when > 60 IU/mL, which is considered as an indicator of atopic sensitization [9] and a predictor of allergic diseases.

In multivariable-adjusted logistic regression models, we found that high maternal peanut consumption before pregnancy significantly decreased the risk of allergic sensitization at 5 years (Table 1). Increasing levels of maternal peanut consumption before pregnancy were significantly inversely associated with total IgE (aOR: 0.64, $P=0.02$). Similar trends ($OR < 1$) were observed for high and medium (versus no intake) maternal peanut consumption before pregnancy (aOR: 0.38, $P=0.17$ and aOR: 0.43, $P=0.10$, respectively).

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Table 1
Relationships of maternal peanut intake before and during pregnancy to allergic sensitization as assessed by total IgE > 60 IU/mL (positivity to total IgE) in children of 5 years.

	Before pregnancy			During pregnancy		
	aOR (95% CI) ^a	P [*]	P-interaction ^b	aOR (95% CI) ^a	P	P-interaction ^b
Positivity to total IgE at 5 years (n = 247) (36.18%)						
Peanut intake (% before/% during pregnancy)						
No intake (12.15/27.24)	1 [reference]			1 [reference]		
Low (40.08/34.15)	1.03 (0.39; 2.71)	0.98	0.99/0.38	0.44 (0.21; 0.95)	0.03	0.53/0.73
Medium (38.46/27.24)	0.43 (0.16; 1.19)	0.10	0.92/0.50	0.48 (0.21; 1.09)	0.08	0.77/0.70
High (9.31/11.38)	0.38 (0.10; 1.51)	0.17	0.97/0.55	0.27 (0.08; 0.84)	0.02	0.67/0.82
Increasing intake of peanuts	0.64 (0.44; 0.94)	0.02	0.22/0.89	0.66 (0.48; 0.90)	0.009	0.61/0.68

^a aOR and 95% confidence interval: adjusted odds ratio for city, mother's age, pre-pregnancy maternal BMI, maternal intake of fruits and vegetables before and during pregnancy, familial history of asthma or allergies, any smoking during pregnancy, environmental tobacco smoking exposure (0–5 years), caesarean birth, exclusive breastfeeding (≥ 6 months), number of siblings, season of child's birth and newborn's sex.

^b Interaction term between maternal/familial history of asthma or allergies and peanut consumption (before or during pregnancy).

^{*} P-value.

During pregnancy, high maternal intake of peanuts was associated with a 73% reduced odds of having positive total IgE (aOR: 0.27, $P=0.02$). In addition, increasing levels of maternal peanut consumption during pregnancy were significantly inversely associated with total IgE (aOR: 0.66, $P=0.009$).

No effect modification by maternal or familial history of asthma or allergies was observed (interaction terms with maternal peanut consumption were not significant (Table 1)).

An original aspect of the present study is our examination of the relationship between childhood total IgE and maternal peanut intake during the year preceding the pregnancy. In our study, we showed that maternal preconceptional and gestational peanut exposures may be beneficial for allergy prevention. Therefore, it may be possible that dietary intake of peanuts associated with allergy already exert their influence during the preconceptional period. This observation raises the hypothesis that maternal dietary exposure to peanuts or other allergenic foods during the periconceptual period and in particular the preconceptional period may have an impact on the epigenetic programming involved in the prevention of allergy. One study showed that maternal supplementation with micronutrients during the periconceptual period was associated with changes in the epigenome of newborns [10]. These epigenetic changes seem to be transmitted to the fetus during pregnancy, modifying genes involved in the development of the immune system, particularly in utero and in early childhood [10].

In our study, we showed that preconceptional and gestational exposure of peanuts may be beneficial for allergy prevention. Providing women desiring pregnancy and pregnant women with specific and personalized recommendations on diet may represent a possible approach to contribute to allergy prevention in early childhood.

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Disclosure of interest

The authors declare that they have no competing interest.

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