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 Early allergenic food introduction for all infants

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The Learning Early About Peanut (LEAP) study triggered a paradigm shift in the field of food allergy prevention.1 In high-risk infants aged 4 to 10 months with either significant eczema and/or an egg allergy, peanut consumption three times a week achieved an 81% reduction in the prevalence of peanut allergy at five years of age.1 However, the majority of cases of peanut allergy come from non-high-risk infants. An extrapolation of the LEAP study to the Irish population demonstrated that 4.8% of Irish infants fulfil the LEAP enrolment criteria.2 Implementing the LEAP intervention would prevent 29% of the annual incidence of peanut allergy, as 59% of the cases of peanut allergy occur in the non-high-risk infants.2

Post LEAP, infant feeding guidelines around the world have changed, now advocating early introduction, with some countries restricting such guidance to peanut alone and emphasising risk status3 and others recommending a broader range of allergenic food introduction in the general population of infants.4 Concerns have been expressed on two grounds: firstly, the validity of changing general infant feeding recommendations on the basis of the high-risk LEAP study, and secondly, commencing early introduction before six months of age in breach of the current WHO recommendation of 6 months exclusive breastfeeding,5 given the average age of enrolment onto the LEAP study was 7.8 months.6 However, food allergy can emerge before six months of age.7

So what about early allergenic food introduction for the 95.2% of non-high-risk infants? The EAT study attempted to answer this by introducing six allergenic foods from 3 months of age and observed a 20% reduction in food allergy by three years of age to one or more of the six foods but was not statistically signficant.8 Per-protocol reductions in allergy to any food or to specific foods were statistically significant but subject to the criticism of bias and to the low level of adherence achieved to the intervention: 34% for all food and 52% for peanut.8

The seminal study by Håvard Ove Skjerven and colleagues in *the Lancet* answers the question.9 The Preventing Atopic Dermatitis and ALLergies in Children (PreventADALL) study is a large pragmatic trial of 2397 newborn infants recruited from the general population in Norway and Sweden. The study had a cluster-randomised 2 x 2 factorial design with a food intervention of introducing peanut, milk, wheat and egg from 3 months of age and/or a skin intervention of regular oil baths and facial cream from 2 weeks of age. Early introduction of the four foods was found to result in a statistically significant reduction in the primary outcome of allergy to any interventional food at 3 years of age: 2.6% (31/1170) in the no food intervention groups and 1.1% (13/1224) in the food intervention groups, a 60% reduction.

The overall protective effect of the intervention was driven by the peanut allergy results: 2.0% (23/1170) in the no food intervention groups and 0.7% (9/1224) in the food intervention groups, a 63% reduction. Egg allergy rates at 3 years were very low in both groups (no food intervention groups 0.6% and food intervention groups 0.4%). The efficacy observed for peanut was remarkable on two counts. Firstly, the EAT and LEAP peanut intervention was 2g of peanut protein per dose (consumed three times weekly in LEAP and twice weekly in EAT). PreventADALL, in complete contrast, did not stipulate consumption dosages at all. Families were asked to feed their infant “tastes” of each food on at least four days per week. Consumption monitoring recorded frequency of consumption, but no data on dose being consumed. Notably only 13% (78/599) of the food intervention group were achieving consumption of peanut 4 times a week or more during the key early introduction period from 3 to 6 months of age. Despite no dose being stipulated, PreventADALL adherence in the key early introduction period through to 6 months of age in the food intervention group was remarkably similar to the EAT study: 35% (227/641) for full protocol adherence to at least 3 of the 4 early introduction foods and 39% (251/641) for peanut.

Secondly, peanut consumption in the food intervention group diminished dramatically after the early intervention period. Half of the food intervention group had ceased peanut consumption completely between 6-9 months (49%, 195/396) and 9-12 months (46%, 185/403) of age. Hence the PreventADALL study’s significant findings appear to be derived from an infant consuming, in all likelihood, a small dose of peanut, on average between 1 and 3 times a week, through to six months of age.

Whilst the prevalence of egg allergy was too low to determine the efficacy of early egg introduction, consistent with EAT, per-protocol consumption in PreventADALL strongly suggests significant efficacy if such consumption can be achieved. Of the 387 infants achieving full adherence to the food intervention regimen, only one developed a peanut allergy and one an egg allergy.

The PreventADALL regimen consisted of normal foods. It was cheap and safe. Like the EAT study it had no deleterious impact on breastfeeding at the end of the key early introduction period at 6 months of age. Whilst the desire for the interventions to be pragmatic was understandable, families not recording the actual amount of allergenic food consumed has left a residual uncertainty as to the dose of food required to induce tolerance. The prevalence of food allergy in the general population is not high and further studies to attempt to resolve the issues of dose and duration of consumption required to induce tolerance would have to be prohibitively large. Furthermore, arguably they are unnecessary, with PreventADALL now providing robust evidence to support early allergenic food introduction for the 95.2% of infants who generate the majority of food allergy.

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