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# Timing of Allergenic Food Introduction and Risk of Immunoglobulin E–Mediated Food Allergy

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## BASED ON ARTICLE

JMAPediatrics | Original Investigation

Roberta Scarpone, MD, MPH; Parisut Kimkool, MD; Despo Ierodiakonou, MD, PhD; Jo Leonardi-Bee, PhD; Vanessa Garcia-Larsen, PhD; Michael R. Perkin, MD, PhD; Robert J. Boyle, MD, PhD, Timing of Allergenic Food Introduction and Risk of Immunoglobulin E–Mediated Food Allergy, A Systematic Review and Meta-analysis, JAMA Pediatrics May 2023 Volume 177, Number 5 (Reprinted) jamapediatrics.com

## SUMMARY

**Importance** Earlier egg and peanut introduction probably reduce the risk of egg and peanut allergy, respectively, but it is uncertain whether food allergy as a whole can be prevented using earlier allergenic food introduction.

**Objective** To investigate associations between the timing of allergenic food introduction to the infant diet and risk of food allergy.

**Data sources** In this systematic review and meta-analysis, Medline, Embase, and CENTRAL databases were searched for articles from database inception to December 29, 2022. Search terms included infant, randomized controlled trial, and terms for common allergenic foods and allergic outcomes.

**Study selection** Randomized clinical trials evaluating age at allergenic food introduction (milk, egg, fish, shellfish, tree nuts, wheat, peanuts, and soya) during infancy and immunoglobulin E (IgE)–mediated food allergy from 1 to 5 years of age were included. Screening was conducted independently by multiple authors.

**Data extraction and synthesis** The Preferred Reporting Items for Systematic Reviews and meta-analysis guideline was used. Data were extracted in duplicate and synthesized using a random-effects model. The Grading of Recommendations, Assessment, Development, and Evaluation framework was used to assess the certainty of evidence.

**Main outcomes and measures** Primary outcomes were risk of IgE-mediated allergy to any food from 1 to 5 years of age and withdrawal from the intervention. Secondary outcomes included allergy to specific foods.

**RESULTS** Of 9283 titles screened, data was extracted from 23 eligible trials (56 articles, 13 794 randomized participants). There is moderate-certainty evidence from 4 trials (3295 participants) that introduction of multiple allergenic foods from 2 to 12 months of age (median age, 3-4 months) was associated with reduced risk of food allergy (risk ratio [RR], 0.49; 95%CI, 0.33-0.74; I<sup>2</sup> = 49%). The absolute risk difference for a population with 5% incidence of food allergy was -26 cases (95%CI, -34 to -13 cases) per 1000 population. There was moderate-certainty evidence from 5 trials (4703 participants) that the introduction of multiple allergenic foods from 2 to 12 months of age was associated with increased withdrawal from the intervention (RR, 2.29; 95%CI, 1.45-3.63; I<sup>2</sup> = 89%). The absolute risk difference for a population with 20% withdrawal from the intervention was 258 cases (95%CI, 90-526 cases) per 1000 population. There is high-certainty evidence from 9 trials (4811 participants) that the introduction of eggs from 3 to 6 months of age was associated with reduced risk of egg allergy (RR, 0.60; 95%CI, 0.46-0.77; I<sup>2</sup> = 0%) and high-certainty evidence from 4 trials (3796 participants) that the introduction of peanut from 3 to 10 months of age was associated with reduced risk of peanut allergy (RR, 0.31; 95%CI, 0.19-0.51; I<sup>2</sup> = 21%). Evidence for timing of the introduction of cow's milk and risk of cow's milk allergy was very low certainty.

**Conclusions and relevance** In this systematic review and meta-analysis, earlier introduction of multiple allergenic foods in the first year of life was associated with lower risk of developing food allergy but a high rate of withdrawal from the intervention. Further work is needed to develop allergenic food interventions that are safe and acceptable for infants and their families

### Key Points

**Question** Is the timing of the introduction of allergenic foods to infants associated with their risk of developing immunoglobulin E--mediated food allergy?

**Findings** This systematic review and meta-analysis of 23 randomized clinical trials with 13 794 participants found moderate-certainty evidence that introducing multiple allergenic foods from 2 to 12 months of age was associated with reduced risk of any food allergy but increased risk of withdrawal from the intervention. There was high-certainty evidence that earlier introduction of egg or peanut was associated with reduced risk of egg or peanut allergy, respectively. **Meaning** In this study, earlier introduction of multiple allergenic foods was associated with a reduced risk of food allergy but with significant rates of withdrawal from the intervention.

**Research** Original Investigation Timing of Allergenic Food Intro

## COMMENTARY

### Message

1. Earlier introduction of multiple allergenic foods is associated with reduced IgE-mediated allergy to any food
2. Earlier egg and peanut introduction are associated with a lower risk of each respectively.
3. Multiple foods introduction is difficult to adhere
4. It cautions against the use of multiple allergenic food protein powders for food allergy prevention.

## Problems:

It is against WHO guidelines of introduction at 6 months as against the introduction between 3 to 6 months.

## Importance in Indian Context:

As per our tradition, it has been customary to exclusively breastfeed for the first 4 to 6 months and they introduce the protein and carbohydrate-based weaning diet in a ceremonious way. This may be one of the many reasons for protecting us against food allergies which is rampant in Indian children born in Westernized societies. Hence, we need to rethink before jumping blindly on the bandwagon of the Westernized ways of feeding.