

Elevated Specific IgE to Bystander Foods in Children with Peanut Allergy

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Abstract

Rationale: Circulating food-specific IgE (sIgE) levels are associated with the development of allergic responses. However, food-specific IgG4 (sIgG4) levels have been associated with tolerance or clinical non-responsiveness, particularly in interventional studies. We aimed to characterize food-specific antibody responses in a more general pediatric food allergy population.

Methods: We measured serum specific IgA (sIgA), sIgG4, and sIgE to whole peanut, egg white, and wheat, along with total IgE, from 57 children (31 with peanut +/- egg allergy, 6 with natural tolerance, and 20 without any history of food allergy) using the Phadia ImmunoCAP system.

Results: As expected, total IgE was highest in children with food allergy compared to children without food allergy or naturally tolerant children ($p < 0.001$). sIgE and sIgG4 levels to peanut were highest in children with peanut allergy compared to naturally tolerant and control children ($p < 0.002$, $p < 0.001$, respectively). However, the specific IgG4/IgE ratio was lower in children with food allergies compared to control and naturally tolerant children ($p < 0.002$). Interestingly, children with only peanut allergy had comparable egg sIgE and wheat sIgE levels to children with both peanut and egg or peanut and wheat allergy. Children with only peanut allergy also had higher levels of egg and wheat sIgE compared to naturally tolerant or control children ($p < 0.02$, $p < 0.01$ respectively). sIgA levels were undetectable in 89% of participants.

Conclusions: Our findings indicate that children with peanut allergy have elevated sIgE to bystander foods that they are eating, suggesting that the mechanisms regulating production of IgE to foods is dysregulated in these children.

Introduction / Methods

Introduction:

Food allergy results from a loss of oral tolerance to ingested proteins and development of food-specific Immunoglobulin E (sIgE). sIgE levels are widely used in clinical practice for diagnosis and longitudinal follow up of patients to monitor development of natural tolerance. However, the value of sIgE in patients without clinical history of reaction is limited and sIgE levels to tolerated foods remain unknown. Data from oral immunotherapy trials (OIT) have shown changes in immunoglobulin isotypes with development of tolerance, particularly increased levels of IgG4^{1,2}. However, it remains unclear whether elevated food-specific IgG4 levels are associated with the development of natural tolerance. We sought to better understand the role of food specific immunoglobulins in the development of food allergy and natural tolerance.

Methods:

This cross-sectional study was approved by the Institutional Review Board (IRB) at Lurie Children's Hospital, Chicago, IL. Informed consent was obtained from one legal guardian. Assent was obtained from children between ages 12 to 18 years old. Our study included subjects 6 months to 18 years old who had a) allergist-diagnosed food allergy to egg, wheat, and/or peanut, or b) had previously diagnosed food allergy that was subsequently outgrown (natural tolerance), or c) were non-allergic. Food sensitization was evaluated by measurement of serum levels of food-specific IgA, IgE, and IgG4 to peanut, wheat and egg, as well as total IgE levels, using the Phadia ImmunoCAP system (Thermo Fisher Scientific, Waltham, MA).

Table 1. Patient Demographics

	Allergics (n=31)	Controls (n=20)	Naturally Tolerants (n=6)
Age, years (range)			
Mean	4.7 (0.8-12.3)	9.9 (0.5-18.3)	5.5 (0.7 - 10.6)
Median	4.2	10.6	5.1
Sex, Female, n (%)	14 (45)	5 (25)	3 (50)
Ethnicity, n (%)			
Caucasian	24 (77)	7/20 (35)	4/6 (66)
AA	2 (6)	3/20 (15)	NA
Hispanic	4 (13)	10/20 (50)	2/6 (33)
Asian	1 (3)	NA	NA
Atopic profile, n (%)			
Asthma	8 (26)	3 (15)	1 (17)
AD	20 (65)	4 (20)	3 (50)
AR	12 (39)	3 (15)	3 (50)
Food allergy, n (%)			
Egg	11 (35)	NA	1 (17)
Peanut	12 (39)	NA	4 (66)
Egg and peanut	8 (26)	NA	NA
Milk	NA	NA	1 (17)

Figure 4. Wheat sIgE(A) and sIgG4(B) were higher in peanut allergic, wheat nonallergic subjects compared to subjects with no food allergies

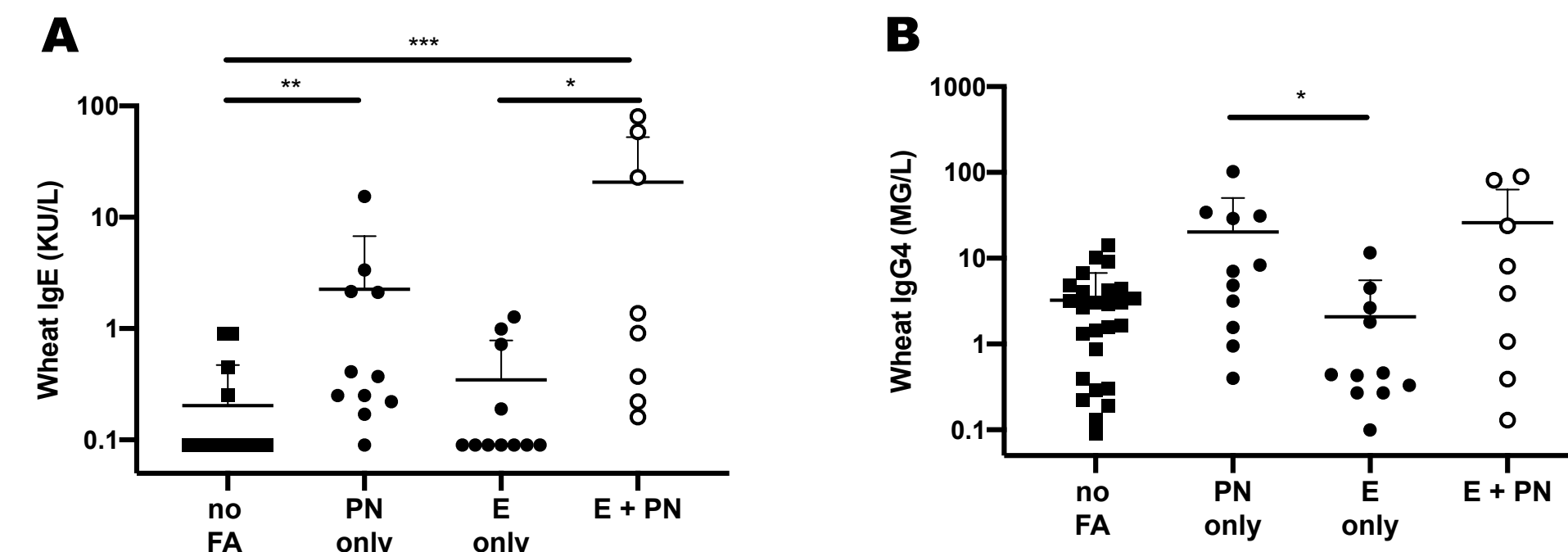
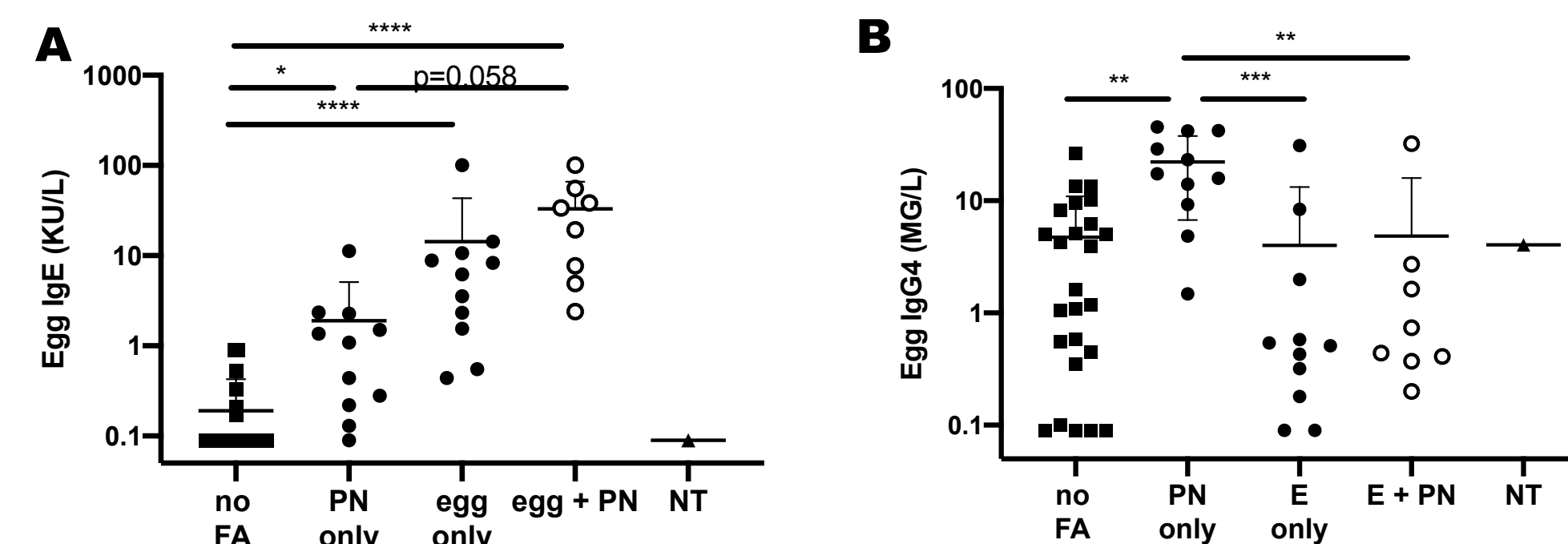


Figure 5. Egg sIgE(A) and sIgG4(B) were higher in Peanut allergic, egg nonallergic subjects compared to nonallergics and tolerants



Results

Figure 1. Total IgE was elevated in subjects with food allergy

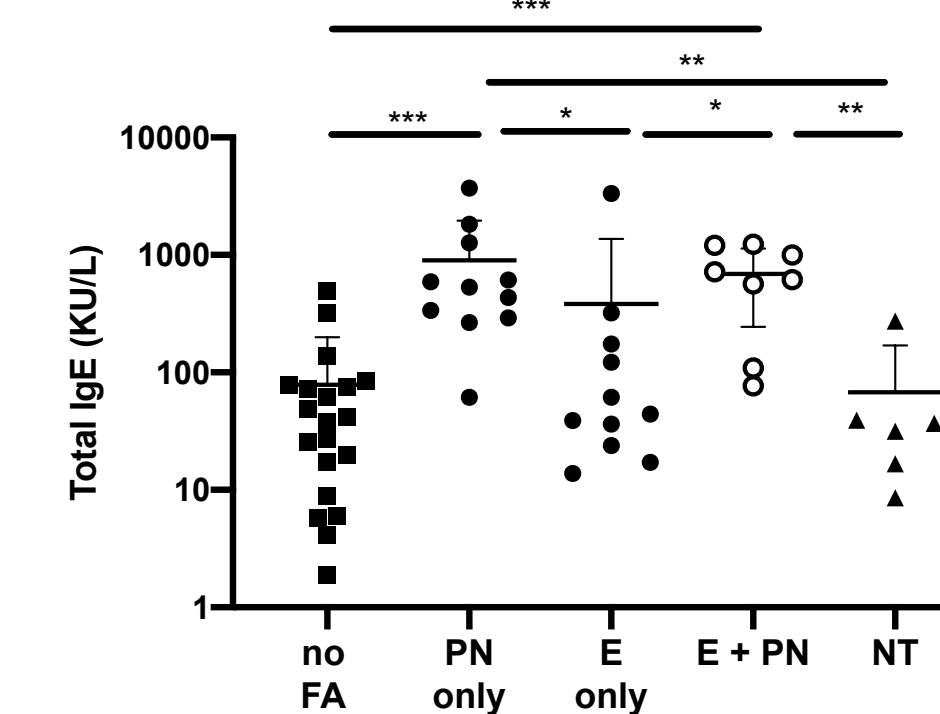


Figure 2. Food-specific IgA was undetectable in the serum

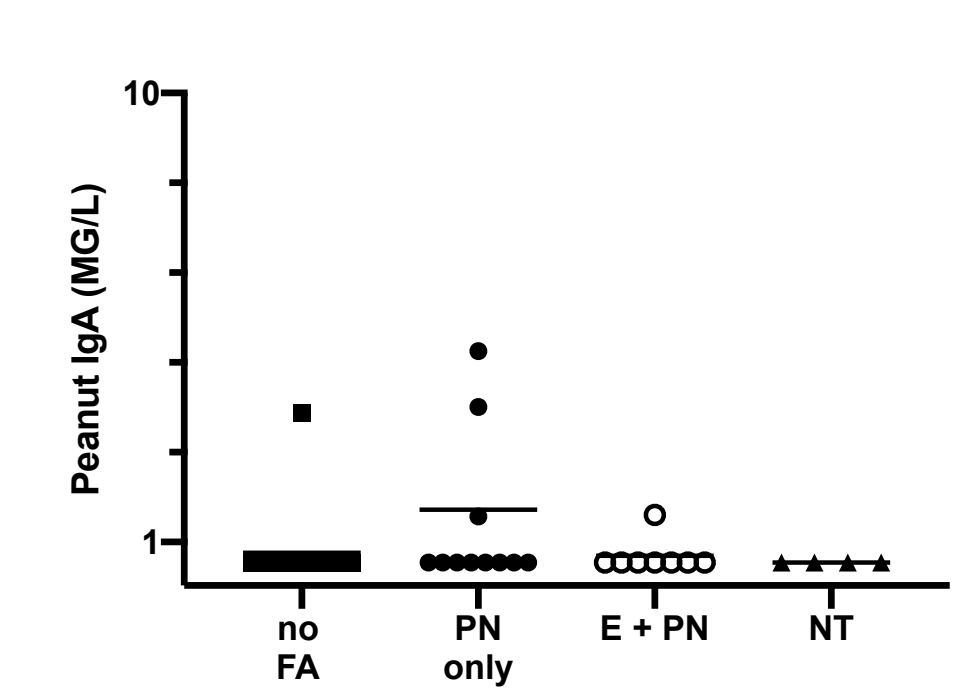
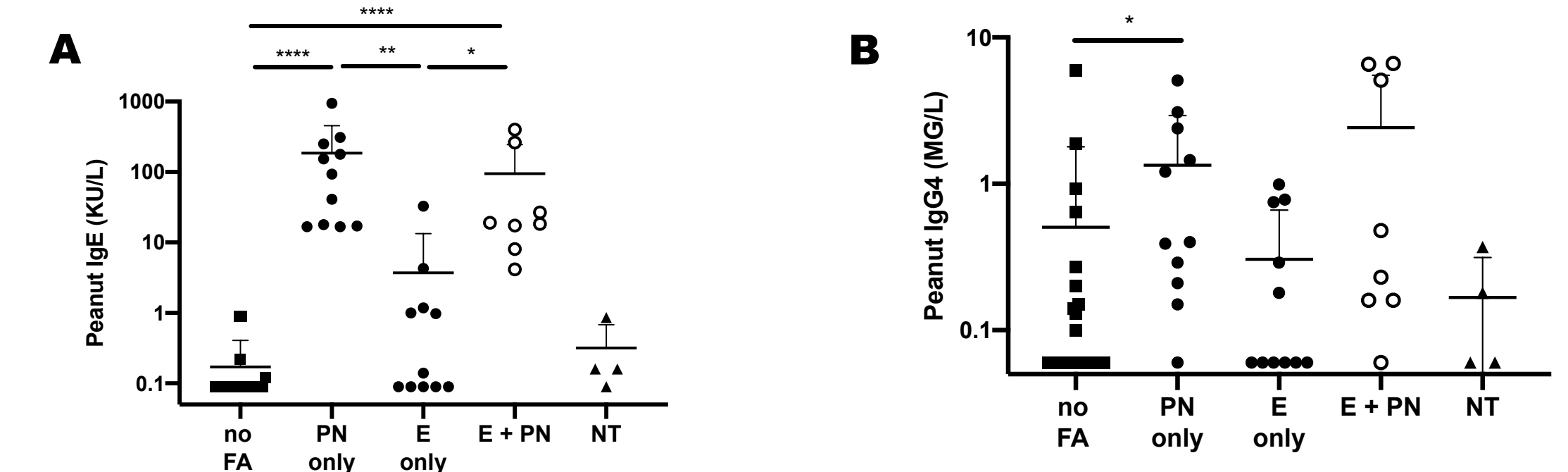


Figure 3. Peanut sIgE(A) and sIgG4(B) were higher in peanut allergic subjects compared to nonallergics and tolerants



Summary

- Subjects with food allergy have elevated levels of total serum IgE
- Food-specific IgA was not detectable in most patients
- Peanut allergic subjects have higher peanut sIgG4 compared to nonallergics and tolerants
- Subjects with peanut allergy, but not egg or wheat allergy, have elevated levels of egg- and wheat-specific IgE, even though they have been eating those foods.
- Subjects with egg allergy, but not peanut allergy, do not have elevated levels of peanut-specific IgE.
- Subjects with peanut allergy but not egg allergy have higher egg sIgG4 levels compared to nonallergic and egg allergics

Conclusion

- IgE production is dysregulated in patients with peanut allergy, who are much less likely to outgrow their allergy, and suggest that the mechanisms driving more persistent forms of food allergy may be distinct.
- Role of IgA may be better understood with local sampling in stool or intestinal mucosa.

References

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