

Table 1. Thirteen cases of severe anaphylactic reaction caused by silkworm pupa consumption in China

Reference	No. of cases Sex: age (years)	History of previous allergy	History of previous allergic shock	First time SP consumed	Symptoms after SP ingestion	Reported time of onset of symptoms (h)	Diagnosis of reported case(s)	Treatment in emergency department
(2)	1 case 1 male: 21	–	None	Yes	P, U, FA, H, F, UC	0.5	Anaphylactic shock	Supplemental oxygen; Epinephrine 1 mg (HDI); hexadecadrol 10 mg (IVI).
(3)	3 cases 1 male, 19 2 females: 37,54	–	None	Yes	U, FA, HA, H, AP, V, D	2–3	Anaphylactic shock	Supplemental oxygen; Epinephrine 1 mg (HDI); hexadecadrol 10 mg (IMI); Chlorphenamine Maleate 10 mg (IMI); Cetacort 300 mg (IVI).
(4)	1 case 1 male: 20	–	None	Yes	P, U, FA, H, F, N, UC	0.5	Anaphylactic shock	Supplemental oxygen; Epinephrine 1 mg (HDI); hexadecadrol 10 mg (IVI).
(5)	8 cases 5 males: 9–46 3 females: 9–46	None	None	Yes	P, U, FA, A, AP, V, N, D	0.5–4	Severe anaphylactic reaction	Supplemental oxygen; Diprazine 25 mg (IMI) plus hexadecadrol 5 mg (IMI). After 2 h, hexadecadrol 10 mg (IVI) plus VtC 3 g (IVI) and VtB6 0.2 g (IVI) (only for 2 cases).

A, angioedema; AP, abdominal pain; D, dyspnoea; F, fainting; FA, flushed appearance; H, hypotension; HA, headache; N, nausea; P, pruritus; U, urticaria; UC, unconsciousness; V, vomiting; IMI, intramuscular injection; IVI, intravenous injection; HDI, hypodermic injection; SP, silkworm pupa.

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References

- Zhang J, Liu ZG, Lin G, Ye XF, Liu RT. Identification and purification of protein allergens from pupa of *Bombyx mori*. J Trop Med 2006;6:496–498 (article in Chinese).
- Cheng XL, Lin HZ, Zhang SY. Successful curative treatment of a patient with anaphylactic shock caused by ingestion of silkworm pupa. Guangzhou Med 1987; 3:36–36 (article in Chinese).
- Wang YL, Niu CX, Liu Y. Three cases of anaphylactic shock caused by ingestion of silkworm pupa. China J Lepr Skin Dis 1999;15:56–57 (article in Chinese).
- Zhang H. A case of anaphylactic shock caused by ingestion of silkworm pupa. Lit inf prev med 2002;8:458–459 (article in Chinese).
- Wang DJ, Zhang DL, Yang FX, Chen YZ, Wei L, Yang HX et al. Eight cases of severe type-I allergic reaction caused by consumption of silkworm pupa. Henan J Prev Med 2005;16:148–148 (article in Chinese).

- Hugh AS. Anaphylaxis and emergency treatment. Pediatrics 2003;111:1601–1608.

Dissociation between biological and clinical response to oral challenge in children with food allergy

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Key words: food allergy; food challenge; inflammatory markers; pediatrics.

Controlled oral food challenges are considered as the golden standard for the diagnosis of food-related symptoms (1), the diagnosis being carried out based on the symptoms after a challenge.

In children with food allergy, a biological response to food ingestion persists even when the clinical tolerance is acquired.

The retrieval of stable mediator metabolites from urine provides a valuable indication of the synthesis or release of mediators such as leukotrienes (LT) and prostaglandins (PG). LTE₄ is a stable urinary product considered as an integrated measure of overall LT production in the body, while 9 α ,11 β -PGF₂ is one of the major urinary metabolites of PGD₂, the main cyclo-oxygenase product released on mast-cell activation (2).

The aim of our study was to compare LTE₄ and 9 α ,11 β -PGF₂ urinary concentrations in children with food allergy and in healthy controls and to evaluate the change in these biological mediators before and after a controlled food challenge.

We recruited 31 children with food sensitization and a history of immediate reaction after food ingestion (mean age 3.6 years) and 16 healthy controls (mean age 3.3 years). All patients had been on an elimination diet and had serum positive for specific IgE (>0.35 kU/l) for the offending food. Thirty-one open food challenges with cow's milk ($n = 24$), egg ($n = 5$), wheat ($n = 1$)

and soy ($n = 1$) were performed following the international guidelines (1).

A urine sample was collected before and 1 h after ending the challenge. Leukotriene E_4 and $9\alpha,11\beta$ -PGF $_2$ were measured by commercially available competitive enzyme immunoassays (Chemical Company, Ann Arbor, MI, USA). Values are expressed per mg of creatinine. The reproducibility of urinary measurements was assessed in 10 children by collecting two urine samples 2 h apart.

Our hospital's ethical committee reviewed and approved the protocol and all parents gave their informed consent. The reaction to the oral food challenge was judged to be clinically positive in 16/31 children.

No significant difference emerged in the baseline urinary levels of LTE $_4$ and $9\alpha,11\beta$ -PGF $_2$ between patients who reacted to the challenge, patients who did not and healthy controls ($P = 0.15$ and 0.06 , respectively) (Fig. 1).

The mean urinary LTE $_4$ and $9\alpha,11\beta$ -PGF $_2$ concentrations rose significantly in patients with and without a positive reaction to the challenge (Fig. 1). In children allergic to cow's milk (the

majority of our patients) with a positive test, the severity of the reaction did not correlate with the increase in LTE $_4$ and $9\alpha,11\beta$ -PGF $_2$.

A good reproducibility was demonstrated with all individual points for LTE $_4$ and 9/10 points for $9\alpha,11\beta$ -PGF $_2$, falling on the Bland–Altman plot within the coefficient of reproducibility range. Our study shows that urinary LTE $_4$ and $9\alpha,11\beta$ -PGF $_2$ levels increase after oral food challenge in children with IgE-mediated food allergy, whether they have a positive or a negative test.

In adults with food allergy, it has been reported an intestinal release of PGD $_2$ after the intraluminal administration of food antigens (3) and an increase of urinary levels of LTE $_4$ after a food challenge (4).

In our study, most of the children challenged with a food responded with an increase in urinary levels of LT and PG whether they had or not a clinical reaction. The finding of increased levels of LT and PG after food challenge irrespective of the clinical reaction, suggests inflam-

matory cell activation with mediator release after exposure to the food.

Our results are in keeping with a previous study that demonstrates a similar increase in serum tryptase levels in both patients with positive and negative oral food challenge (5). Taken together, these findings suggest that a patient who clinically acquires tolerance to a food can still have an underlying biological response to its ingestion.

This observation highlights a new aspect of food allergy that may be worth further investigations to establish if the biological response persists even after the food is reintroduced in the patient's diet and if such biological response may have any long-term clinical rebound. In addition, it would be interesting to know whether this mechanism is present in children performing specific oral tolerance induction (6).

In conclusion, in children with food allergy, we demonstrated an increase in inflammatory mediators after a food challenge both in the presence and in the absence of a clinical reaction, suggesting that a biological response to the ingestion of a food allergen could

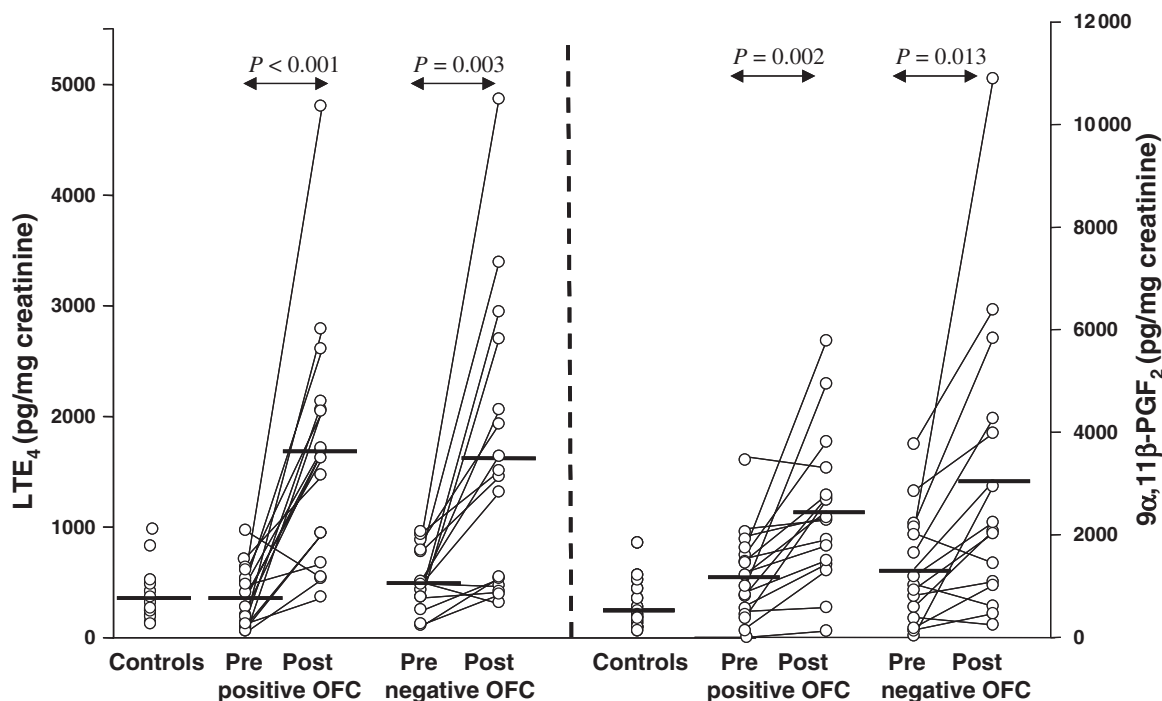


Figure 1. Urinary LTE $_4$ and $9\alpha,11\beta$ -PGF $_2$ concentrations before and after oral food challenge (OFC) in children with positive and negative challenge and in control subjects. Horizontal bars represent mean values.

persist even when clinical tolerance is acquired.

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References

1. Bindslev-Jensen C, Ballmer-Weber BK, Bengtsson U, Blanco C, Ebner C, Hourihane J et al. Standardization of food challenges in patients with immediate reactions to foods – position paper from the European Academy of Allergology and Clinical Immunology. *Allergy* 2004;**59**:690–697.
2. Liston TE, Roberts LJ 2nd. Metabolic fate of radiolabeled prostaglandin D₂ in a normal human male volunteer. *J Biol Chem* 1985;**260**:13172–13180.
3. Santos J, Bayarri C, Saperas E, Nogueiras C, Antolin M, Mourelle M et al. Characterisation of immune mediator release during the immediate response to segmental mucosal challenge in the jejunum of patients with food allergy. *Gut* 1999; **45**:553–558.
4. Van Odijk J, Peterson CGB, Ahlstedt S, Bengtsson U, Borres MP, Hulthén L et al. Measurements of eosinophil activation before and after food challenges in adults with food hypersensitivity. *Int Arch Allergy Immunol* 2006;**140**:334–341.
5. Vila L, Sanz L, Sanchez-Lopez G, Garcia-Alvies C, Dieguez I. Variations in serum eosinophil cationic protein and tryptase measured in serum and saliva, during the course of immediate allergic reactions to food. *Allergy* 2001;**56**:568–572.
6. Niggemann B, Staden U, Rolinck-Werninghaus C, Beyer K. Specific oral tolerance induction in food allergy. *Allergy* 2006;**61**:808–811.