

# Food Induced Urticaria in Children

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**SUMMARY** We conducted a prospective study at King Chulalongkorn Memorial Hospital, from June 2001 to November 2003, to identify the contribution of food allergy to urticaria in children. During the study period, 100 children with urticaria were enrolled, 36 of whom had a history suspicious of food allergy. Fifteen of 100 patients had fever (9 from upper respiratory tract infections, 4 from diarrhea and 2 from skin infections). A skin prick test (SPT) was positive in 15 of the 36 children who were suspected of having food allergy; 5 patients out of the positive SPT group had anaphylaxis due to food (2 from cow milk, 2 from wheat and 1 from egg). Six patients in the positive SPT group had a negative food challenge test (4 from open challenges and 2 from double-blind placebo-controlled food challenges [DBPCFC]). The other 4 patients of the positive SPT group refused the food challenge test. The parents of a patient who had urticaria from egg refused the skin prick test; an oral challenge test confirmed the diagnosis of egg allergy. One of the 21 patients that had a negative SPT had shrimp allergy proven by DBPCFC. Of the 64 patients who had no history related to food, SPT was done in 27 patients and revealed a positive result in 7 patients, all of whom had a negative food challenge test (4 with open challenge and 3 with DBPCFC). Urticaria from food was found in 7% and was suspected in another 4% of the patients. Severe reactions to food like anaphylaxis may occur. SPT alone is not adequate in making the diagnosis of food allergy; it must be confirmed by a food challenge test. Thirty percent of patients that did not have a history related to food had false positive SPT. Without a history suspicious of food allergy, SPT yields only minimal benefit.

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Urticaria is a common disease in children with a prevalence of 5% to 25% in the general population.<sup>1-3</sup> It is characterized by the appearance of transient intensely pruritic, well circumscribed wheals and flares of the skin or mucous membranes. The etiology of urticaria is often not well understood and may be related to many factors such as foods, drugs, blood products, infections, physical factors and many diseases. The occurrence of urticaria due to an IgE-mediated reaction to food is not known.<sup>4</sup> Parents of children suspected of food-induced urticaria tend to remove the suspicious food from their children's diet which can lead to anxiety and malnutrition. Skin prick test (SPT) and double-blind placebo-controlled food challenge (DBPCFC) test help with the diagno-

sis of food allergy.<sup>5,6</sup> The purpose of this study was to identify the contribution of food allergy to urticaria in children.

## MATERIALS AND METHODS

All patients who presented with urticaria at the Department of Pediatrics, King Chulalongkorn Memorial Hospital from May 2001 to October 2003, were prospectively recruited after informed consents

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**Table 1** Cases of food allergy and suspected food allergy

No.	Age (years)	Sex	No. of episodes*	Type of urticaria	Food
<b>Food allergy</b>					
1**	1/12	F	1	Acute	Cow milk
2**	1/12	F	2	Acute	Cow milk
3	5/12	F	1	Acute	Egg
4**	1	F	5	Acute	Egg
5	3	M	2	Acute	Shrimp
6**	4	M	2	Acute	Wheat
7**	14	F	4	Acute	Wheat
<b>Suspected food allergy***</b>					
8	1/12	M	1	Acute	Cow milk
9	5/12	M	1	Acute	Egg
10	2	M	2	Acute	Cow milk
11	8	F	2	Acute	Fish

\*Number of episodes of urticaria at the time of the study

\*\*Anaphylaxis and SPT positive to the suspected food.

\*\*\*History of food allergy and skin prick test positive to suspected food.

were obtained from their parents (Table 1). Urticaria was defined by the appearance of wheals and flare lesions varying from moment to moment, and disappearing within 24 hours without hyperpigmentation.<sup>6</sup>

Acute urticaria was defined as urticaria with less than 6 weeks of continuous activity. For chronic urticaria, the duration of continuous activity was 6 weeks or more.<sup>7</sup> The initial evaluation included a careful history of the food intake, drugs, infections, timing of onset and the number and duration of the urticaria lesions. A complete physical examination was done including description of swollen joints and hyperpigmentation at previous urticaria sites. All children were treated with oral antihistamine: chlorpheniramine 2 mg/kg/day and hydroxyzine 1 mg/kg/day except for anaphylaxis and angioedema which were treated according to the severity of the clinical presentation. All patients were invited to do SPT and DBPCFC test during the follow-up visit.

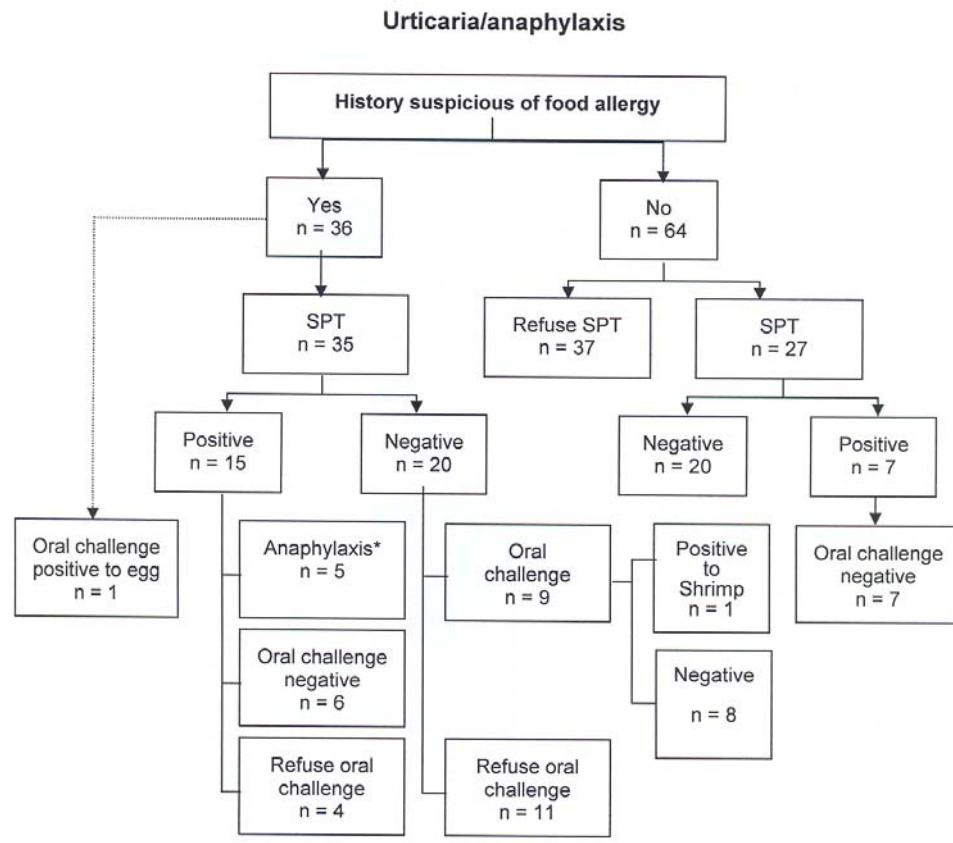
SPT was performed after the urticaria had subsided and the antihistamine had been discontinued for at least one week. SPT was performed by using the following commercial extracts (Greer laboratories, Inc, Lenoir, USA): cow milk, casein, egg (whole), egg (white), soybean, peanut, wheal, yeast, cocoa; the positive control consisted of histamine,

the negative control of normal saline. A positive SPT was defined by a wheal diameter of at least 3 millimeters larger than the negative control.<sup>8,9</sup>

Food allergy was diagnosed by means of DBPCFC. The challenge material was extracted from the suspected food or placebo at 1% of the total amount (10 g). The challenge dose was increased to 2%, 5%, 10%, 20%, 25% and then the remaining amount at 15-minute intervals. If no immediate reaction occurred within 3 hours, the challenge with the other sample (placebo or suspected food) was performed.<sup>10</sup> If the parents denied to do DBPCFC, an open challenge test was performed with the suspected food in the same way as DBPCFC, but without placebo.

## RESULTS

One hundred patients with urticaria were included in the study. The mean age of the patients was 4.33 years (range of 1 month to 14 years) and the male:female ratio was 1.7:1. Thirty-six patients (36%) had a history suspicious of food allergy. SPT was done in 35 of these 36 patients (see Fig. 1) and revealed a positive result in 15 patients. Five of the 15 patients had anaphylaxis from food (2 from cow



\*Presented with anaphylaxis and SPT positive to cow milk (n = 2), wheat (n = 2), egg (n = 1)  
SPT; skin prick test

**Fig. 1** Results of skin prick test and food challenge test in patients with urticaria/anaphylaxis

milk, 2 from wheat, and 1 from egg). Of the remaining 10 patients, six had a negative food challenge test (4 with DBPCFC and 2 with open challenge). The other 4 patients refused to do a food challenge test. The parents of one patient that had urticaria from egg refused to allow a skin test but an open challenge test confirmed the diagnosis of egg allergy. One of the 20 patients with a negative SPT had a shrimp allergy proven by DBPCFC. The false negativity rate in the patients that had a history of food-related urticaria was 2.8% (1 in 35 patients).

Of the 64 patients that had no history related to food, SPT was done in 27 patients, 7 of whom had a positive SPT result and a negative food challenge test (4 open challenge tests and 3 DBPEFCs). The

false positive SPTs in the patients that had no history related to food accounted for 30%. Urticaria from infection was found in 15% (9% from upper respiratory tract infection, 4 from diarrhea and 2 from skin infection).

#### First episodes and recurrent urticaria

Sixty-nine patients had their first episode of urticaria and 31 patients had recurrent episodes. Of the 69 patients that had their first episode, 19 patients had a history suspicious of food allergy. Urticaria from food allergy accounted for 3% (2 patients), which were confirmed by oral challenge tests. One patient (age 1 month) had cow milk allergy, the other patient (age 5 month) had allergy to egg. From 50

patients with their first episode of urticaria not suspected of food allergy, SPT was done in 23 patients (4 were SPT positive, but all had negative food challenge tests; 19 were SPT negative).

Out of the 31 patients that had recurrent episodes of urticaria, 17 patients were suspected of food allergy, whereas 14 patients were not. SPT was performed in all the patients suspected of food allergy. Seven of the 17 patients had a positive SPT, 5 patients had food allergy and 1 patient had suspected food allergy. From the other 14 patients that had no history of food allergy, SPT was positive in 3 of 13 patients (one patient refused to do skin test). None had food allergy.

### Acute and chronic urticaria

Eighty patients in this study had acute urticaria and twenty patients had chronic urticaria. Of the acute urticaria cases, food allergy caused 7.5 % of definite and 5% of suspected cases. Food allergy was not found to be associated with chronic urticaria in our study population.

In the group without history of food allergy, all of the patients with a positive SPT to food had negative oral challenge tests.

### DISCUSSION

Food-induced urticaria may be over-reported by the patients. Food challenges are the definite diagnosis of food-induced urticaria.<sup>11</sup> SPT may be helpful but it is not a definite method for confirming food allergy. The positive predictive accuracy of SPT in this study was about 50%. However the negative predictive accuracy was much higher as only one patient who had a negative SPT was found to have food allergy diagnosed by DBPCFC. The prevalence of food induced urticaria in this study was lower than that previously reported by Ligrain *et al.*<sup>1</sup> and Morturex *et al.*<sup>7</sup> who recruited patients in their infancy and early childhood. This study included patients from the age of 1 month to 14 years, which resulted in an older average age than the previous studies. The incidence of food allergy in younger age groups was higher because some of the patients that had food allergy may grow out of the disease. Patients with IgE-mediated clinical food

hypersensitivity in an early age may grow out of the disease especially patients with allergy to cow milk and soybean.<sup>12,13</sup> Of the seven patients that had definite food allergy in this study, only one patient who had wheat allergy was more than 4 years old. Another reason might be that some patients who had mild to moderate urticaria to known food might not have sought medical treatment at a tertiary care center. Some patients may be able to identify the causative food by themselves, especially when urticaria appears right after ingestion in repeated occasions and therefore did not search for medical advice. Moreover, the incidence of food allergy may vary from place to place. Lastly, since this study was performed in a tertiary care center, the results may not represent food-induced urticaria in the general population.

The foods that were found to induce urticaria in this study were cow milk, wheat and egg, similar to other studies. An accurate diagnosis of food allergy helps to minimize the number of restricted food items and also lessens the chance of subsequent nutritional deficiencies.<sup>12</sup> The positive predictive accuracy, even in a high prevalence population, is never more than about 70% for the most predictive skin test (egg) and is lower in other foods.<sup>10</sup> The prick test remains positive even after clinical tolerance to that food occurs.<sup>12</sup> A negative SPT has a negative predictive value of 95% for common food allergy such as egg, nuts, cow milk, wheat and soybean.<sup>14</sup> A negative SPT with a clinically suspected food allergy should be verified by food challenges. In this study one patient who had allergy to shrimp had a negative SPT. We did not calculate the positive and negative predictive value because we could not persuade all of our patients that had a history of food related urticaria to do SPT and DBPCFC. We did not perform food challenges in cases of food-induced anaphylaxis because SPT can be used to confirm the causes of anaphylaxis. The RAST test for the common childhood food allergens had no specific advantage over the skin test in predicting the reaction to DBPCFC.<sup>15</sup> DBPCFC is not necessary in patients with unequivocal history of anaphylaxis following an isolated ingestion of food.

In this study, SPT had no benefit for patients who were not suspected of food allergy. The false positive rate was 30%. In chronic urticaria, no

one in this study had food allergy, similar to a previous report showing that food is not a common cause of chronic urticaria.<sup>17</sup> In patients that had their first episode of urticaria, the prevalence of food allergy was 3%. Nineteen patients were suspected of having food allergy and 2 patients (aged 1 month and 5 months) had a definite diagnosis of food allergy by oral challenges. In the infancy period, food is mostly introduced one by one, so it is easier for parents to suspect any newly introduced food. In patients who were older than one year, food allergy usually had recurrent episodes.

Several problems were encountered in this study; SPT had to be done after the clinical symptoms had subsided and antihistamine had been discontinued for at least one week. The test was painful and some parents did not want to hurt their children with SPT. Food challenges are time consuming, and the patients had to be hospitalized.

In conclusion, the prevalence of food-induced urticaria in this study was 7% and suspected food allergy was 4%. A detailed history on a possible food allergy in children with urticaria is mandatory. SPT should be considered only as screening in patients who have recurrent food related urticaria. In patients that had no food related history the false positive rate was 30%. Food is more frequently associated with acute than with chronic urticaria.

### ACKNOWLEDGEMENT

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