Food allergies affect as many as 6% of young children and mostly present with atopic dermatitis or gastrointestinal symptoms (1). Sensitization to ingested allergens can also lead to severe immunoglobulin E (IgE)-mediated systemic reactions including anaphylaxis (2). Cow’s milk, egg, cereals, peanut, soy, fish and shellfish are the most common food allergens (1–3). Peanut has recently received much attention as an important cause of anaphylaxis and its major allergens are well-characterized (4). In contrast, wheat is rarely reported to have caused anaphylaxis in children and the knowledge of ingested cereal allergens at the molecular level is scanty (5–7). Previously, we showed that wheat \(\omega-5\) gliadin is a major allergen in adults with food-dependent, exercise-induced anaphylaxis (8). Recently, we found that this water/salt-insoluble allergen is also a potentially important sensitizer in atopic children who react with urticaria or other immediate symptoms to oral wheat challenge (9).

In the present study, we investigated seven children experiencing anaphylactic reactions after ingesting wheat-containing food and show that they all had IgE antibodies against wheat \(\omega-5\) gliadin.

**Material and methods**

**Patients**

Seven children (five boys, two girls) with an anaphylactic reaction after ingesting wheat-containing food were examined in the Department of Pediatrics, Siriraj Hospital in Bangkok (Table 1). The study was retrospective and the children were examined from 2 weeks to 8 months after the last anaphylactic reaction. This was defined as angioedema on the face, severe bronchospasm and collapse. Vomitus and generalized urticaria were also common symptoms during the attack. All children had experienced from 2 to 10 anaphylactic reactions in a year. For example, one child (patient number 4, Table 1) ate at the age of 7 months a 1 cm long wheat rusk immediately after which he developed swelling in the face, dyspnea and cyanosis. In the emergency room he was resuscitated and his condition started to improve after the third dose of epinephrine. Four of the seven anaphylactic children were atopics; one...
child had atopic eczema/dermatitis syndrome and three had positive skin prick tests (SPT) to common inhalant or food allergens. Blood was drawn and serum stored at 20°C for IgE enzyme-linked immunosorbent assay (ELISA) and radioallergosorbent test (RAST) examinations. Informed consent was obtained from the parents.

Control sera were obtained from nine Thai children (mean age 8.4 years, eight examined for systemic illnesses) and six young adults (mean age 25 years) who had no history of wheat allergy.

x-5-Gliadin IgE ELISA and skin prick tests

Wheat x-5 gliadin was extracted from wheat grains (Triticum aestivum) and purified with reversed phase chromatography as previously described (8). For IgE ELISA microtiter plates (100 μl/well) were coated with x-5 gliadin (2 μg/ml), then 100 μl of patient or control serum (diluted 1:10) was added followed by biotinylated goat antihuman IgE (Vector, Burlingame, CA, USA; diluted 1:1000), streptavidin-conjugated alkaline phosphatase (Zymed, San Francisco, CA, USA; diluted 1:3000) and color substrate (Bio-Rad, Hercules, CA, USA). The color formed was read at 405 nm with an automated ELISA reader (Titertek Multiscan, Eflab, Turku, Finland) as previously described (9). All seven sera from the anaphylactic children were examined in the same run which included a positive and negative control. The CAP RAST (Pharmacia, Uppsala, Sweden) was used to measure IgE antibody levels to crude wheat.

Results

All seven children with anaphylaxis showed in ELISA IgE antibodies to x-5 gliadin (Table 2, Fig. 1). Five of the six tested children showed a positive SPT to crude and x-5 gliadin, and all seven children had positive wheat RAST and SPT (Table 2). All 15 controls were negative in x-5 gliadin IgE ELISA (Fig. 1) but one had positive wheat RAST (1.8 kU/l).

Open egg and wheat challenges were performed in one child (patient number 2, Table 1). A challenge with 4 g of egg white was negative. The wheat challenge was started by rubbing the patient's lips with pure spaghetti. Thereafter, the child ate 0.5 g and then 2 g of spaghetti. 30 min later she developed anaphylactic reaction (abdominal pain, vomiting, generalized urticaria, severe bronchospasm and hypotension), which was successfully treated with epinephrine.

All seven children with anaphylaxis adhered to a wheat-free diet. The parents received written instructions

### Table 1. Clinical findings in seven children with wheat-induced anaphylaxis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age*</th>
<th>Atopy</th>
<th>Causative food</th>
<th>Attacks in a year</th>
<th>Systemic symptoms</th>
<th>Treatment with epinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/13 (14) years</td>
<td>–</td>
<td>Bun, noodle</td>
<td>3</td>
<td>ANA, URT</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>F/6 months (4 years)</td>
<td>SPT+</td>
<td>Cake, macaroni</td>
<td>3</td>
<td>ANA</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>M/4 (8) years</td>
<td>–</td>
<td>Pizza, bun</td>
<td>3</td>
<td>ANA, URT</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>M/7 (20) months</td>
<td>–</td>
<td>Bread, noodle</td>
<td>4</td>
<td>ANA, URT</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>F/3 (14) years</td>
<td>SPT+</td>
<td>Bread</td>
<td>2</td>
<td>ANA</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>M/7 (24) months</td>
<td>AE</td>
<td>Bread</td>
<td>2</td>
<td>ANA, URT</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>M/7 (12) years</td>
<td>SPT+</td>
<td>Cracker</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Onset of symptoms, in parenthesis age at diagnosis.

ANA, anaphylaxis (angioedema on the lips and face, bronchospasm and collapse); URT, generalized urticaria; AE, atopic eczema/dermatitis syndrome; SPT+, skin prick test-positive (patient number 2, egg, fish, shrimp, peanut, house-dust mite; patient number 5 cockroach; patient number 7 egg).

### Table 2. Skin prick test, RAST and IgE ELISA results in seven children with wheat-induced anaphylaxis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Histamine (10 mg/ml)</th>
<th>Wheat (1:10, w/v)</th>
<th>Gliadin (1 mg/ml)</th>
<th>x-5 Gliadin (50 μg/ml)</th>
<th>Wheat RAST (KU/l)</th>
<th>x-5 Gliadin IgE ELISA†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>10</td>
<td>ND</td>
<td>ND</td>
<td>0.9</td>
<td>0.45</td>
</tr>
<tr>
<td>2‡</td>
<td>6</td>
<td>16</td>
<td>4</td>
<td>3</td>
<td>&gt;100</td>
<td>3.36</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>0.50</td>
<td>1.71</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>12</td>
<td>15</td>
<td>7</td>
<td>35</td>
<td>1.86</td>
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<tr>
<td>5</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>9</td>
<td>2.14</td>
<td>1.31</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>10</td>
<td>6</td>
<td>3</td>
<td>10.4</td>
<td>0.31</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>3</td>
<td>1.51</td>
<td>0.36</td>
</tr>
</tbody>
</table>

* Wheat diameter in mm.
† 2 μg/ml; absorbance units at 405 nm.
‡ Oral challenge with wheat caused anaphylaxis.
ND, not done; RAST, radioallergosorbent test; IgE, immunoglobulin E; ELISA, enzyme-linked immunosorbent assay.

IgE antibodies to x-5 gliadin
Discussion

The results of this study show that all seven children suspected for anaphylaxis from wheat-containing food had IgE antibodies to \( \omega-5 \) gliadin in ELISA. In addition, five of the six children tested had a positive SPT to \( \omega-5 \) gliadin further supporting that this water/salt-insoluble gliadin is a major allergen in the children with wheat-induced anaphylaxis. A previous immunoblotting study in seven Japanese children with wheat-induced anaphylaxis showed IgE binding to water/salt-insoluble gliadins (16, 38 and 70 kDa wheat proteins (6). These IgE-binding proteins were not characterized but it is quite possible that the 70 kDa allergen could correspond to \( \omega-5 \) gliadin (8). Water/salt-soluble albumins and globulins appear to be the most important wheat allergens contributing to Baker’s asthma (10) whereas information regarding wheat proteins responsible for allergic reactions after ingestion is limited (7, 11, 12). A few studies have presented evidence that water/salt-insoluble gliadins seem to be important IgE-binding proteins in wheat-allergic children (13, 14). A recent study using highly purified wheat protein fractions in immunoblotting and RAST confirmed that gliadins bind frequently IgE from the sera of wheat-allergic patients (15). The same study showed also that 48% of the 28 wheat-allergic children and adults had IgE antibodies against \( \omega-5 \)-gliadins. This finding in agreement with the present and our previous study showing that \( \omega-5 \)-gliadin is a major IgE-binding allergen in children with wheat-induced anaphylaxis or other immediate symptoms (9).

Oral food challenges carry the risk of provoking serious, even life-threatening reactions in children with immediate hypersensitivity (23). In the present study, we observed an anaphylactic wheat challenge reaction in one child. In our previous study, oral wheat challenge caused anaphylaxis in one child although she had no previous history of wheat-induced anaphylaxis (9). Instead of performing potentially dangerous oral wheat challenges, measurement of IgE antibodies to \( \omega-5 \)-gliadin by IgE ELISA seems to be a good method to confirm the diagnosis. The \( \omega-5 \)-gliadin IgE ELISA was positive in all seven children with wheat-induced anaphylaxis but negative in all 15 control subjects. The specificity of \( \omega-5 \)-gliadin IgE ELISA cannot be evaluated in the present study because of the small number (\( n = 7 \)) of children with wheat anaphylaxis. However, in our previous study (9) where outcome was positive or negative wheat...
challenge, the sensitivity of the ω-5 gliadin IgE ELISA for detecting immediate allergy to ingested wheat was 84% and the specificity, 100%. The corresponding values for wheat RAST were 95 and 67%.

After diagnosis all children adhered to wheat-free diet and as in our previous study in adults with wheat-dependent, exercise-induced anaphylaxis (8), this markedly reduced recurrences of anaphylaxis. Mistakes following a wheat-free diet can occur especially when eating outside the home. Children with wheat-induced anaphylaxis, like other children at high risk for food-induced anaphylaxis, should receive epinephrine autoinjector for emergency treatment (24). A follow up study is needed to show whether children with wheat-induced anaphylaxis can outgrow their allergy like children who are allergic to cow’s milk (25).

In conclusion, ω-5 gliadin was shown to be a major allergen in the seven children with wheat-induced anaphylaxis.

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