

Letter to the Editor

Tolerance to wheat in whole-grain cereal biscuit in wheat-allergic children

To the Editor:

The proteins implicated in IgE-mediated wheat allergy are not well defined¹⁻³ but are not thought to be significantly affected by heating and processing.^{1,2} Thus, wheat-allergic individuals generally avoid all foods containing wheat and may demonstrate clinical cross-reactivity to other grains.^{2,3} Wheat allergy typically presents in early childhood, and in most cases resolves by 3 to 5 years of age.⁴ Resolution is generally confirmed by oral food challenge (OFC) performed under medical supervision. A number of foods can be used for OFC, including bread, pasta, wheat flour in a paste, or whole-grain wheat cereal biscuits (WWCBs), for example, Weetabix (Weetabix Limited, Kettering, United Kingdom) and Weet-Bix (Sanitarium Co, New South Wales, Australia), which contain whole-grain wheat (with malted barley extract) but no other potential allergens. The use of the latter for diagnostic OFC in younger children is common in many countries. We report 2 children with confirmed wheat allergy who passed an OFC to WWCBs but continued to exhibit IgE-mediated symptoms to other wheat-containing products.

Both children were boys with a history of multiple food allergies and atopic dermatitis. The first child presented in infancy with moderate atopic eczema with exacerbation following exposure to wheat and cow's milk. At age 2 years, his eczema was well controlled and the family attempted introduction of wheat in the

form of WWCBs, but the child developed generalized urticaria with facial angioedema within 10 minutes. One year later, OFC to wheat was performed in the context of a decreasing skin prick test (SPT) wheal diameter (from 9 mm to 6 mm) to commercial wheat extract. The child tolerated the equivalent of 45 g of WWCBs at OFC but subsequently developed vomiting and urticaria after ingesting 100% wheat pasta and bread at home. The bread also contained soy and yeast, both of which were tolerated by the child in other foods. Nonetheless, he continued to tolerate 30 g of the WWCBs on a daily basis. Repeat SPT demonstrated a 9 mm reaction to wheat, homogenized bread mixture, and homogenized wheat pasta. Serum-specific IgE level to wheat was 55 kU_A/L. Under medical supervision, a formal OFC to bread (containing wheat) was performed, and he developed abdominal discomfort and significant vomiting 30 minutes after eating 15 g of bread. He continues to tolerate WWCBs but avoids all other wheat products.

The second child had known food allergies to cow's milk, soy, oats, wheat, and barley, with evidence of sensitization to egg, peanut, and tree nuts. He developed contact urticaria to WWCBs as an infant. He presented for review at age 5 years with a history of recent accidental exposure to a small amount of wheat noodles and soy. The SPT result was positive to wheat (7 mm), soy (5 mm), cow's milk (14 mm), egg (10 mm), and peanut (5 mm). OFC was performed under medical supervision on separate occasions to soy and WWCBs (45 g), and both were tolerated. However, over the following 3 weeks, he developed oral

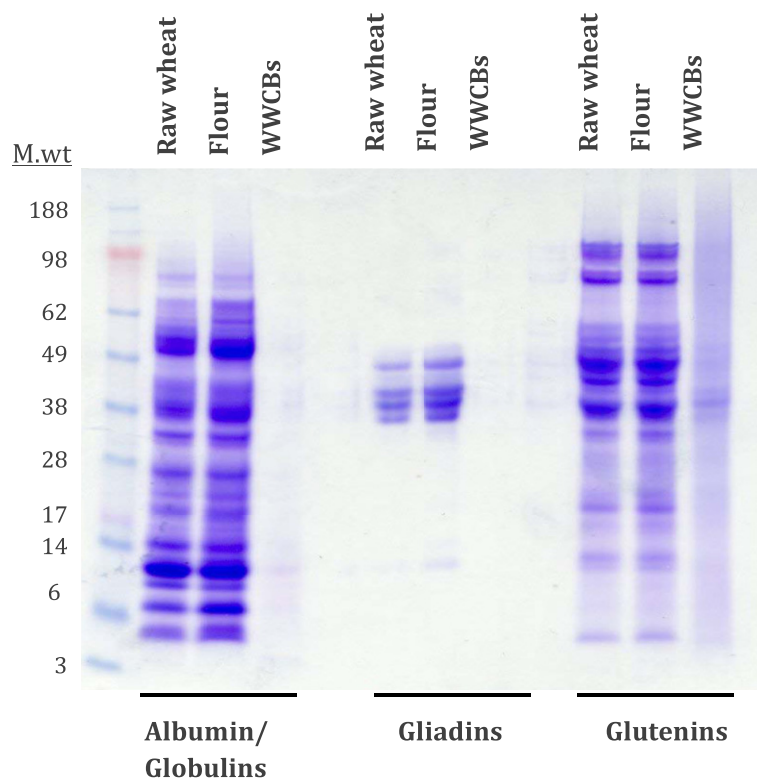
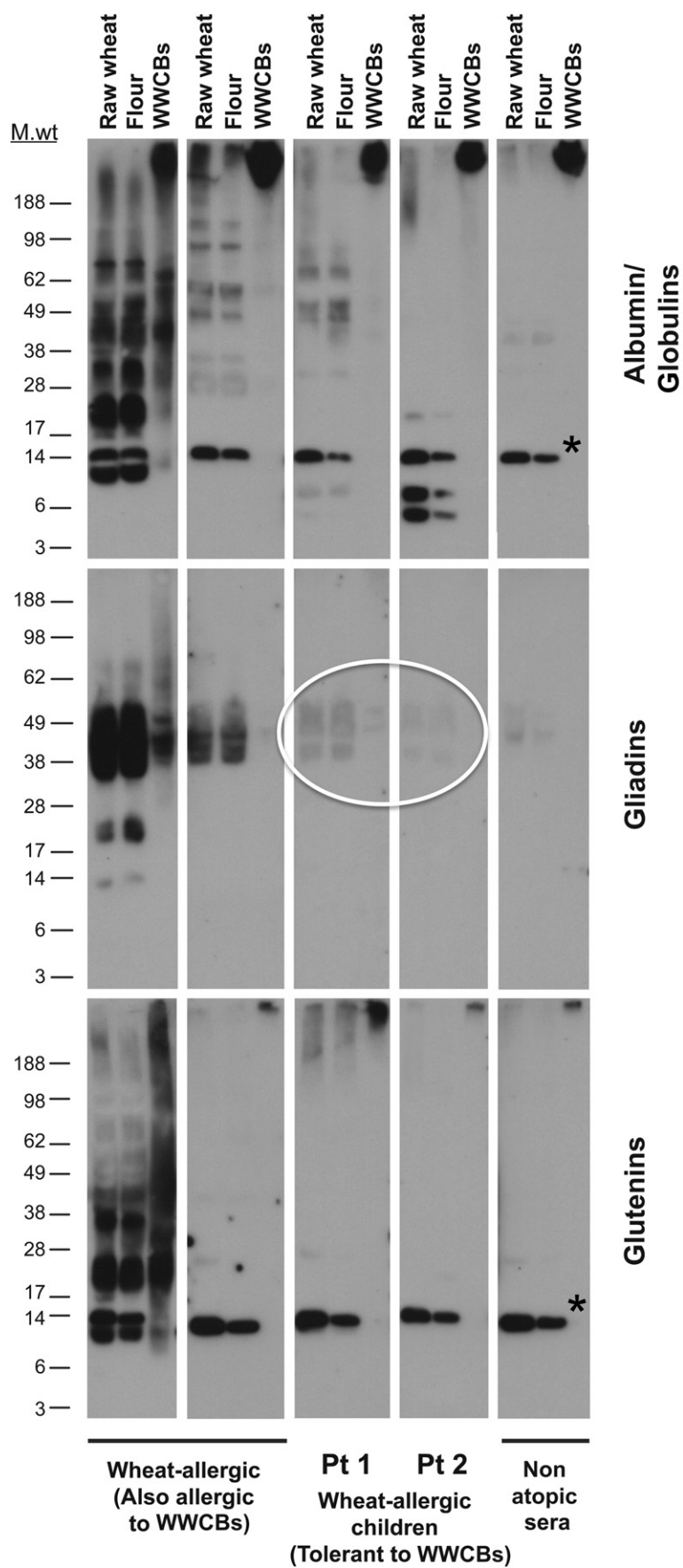


FIG 1. Analysis of wheat extracts. Wheat fractions were prepared from ground raw wheat, unbleached flour, and WWCBs. Extracts were resolved under reducing conditions with 4% to 12% SDS-PAGE and stained with Coomassie brilliant blue. *M.wt*, Molecular mass markers.



irritation, nausea, and vomiting shortly after consuming other wheat-containing products, such as noodles and bread, but continued to tolerate the WWCBs. He developed nausea, abdominal discomfort, and wheeze after consuming 5 g of homemade bread (containing unbleached, wholemeal flour) at subsequent in-hospital OFC. SPT prior to challenge demonstrated a 9-mm response to wholemeal flour and the bread and a 3.5-mm response to a slurry of WWCBs. Serum-specific IgE level to wheat was more than 100 kU_A/L.

To investigate possible explanations for these observations, we prepared extracts of raw wheat, unbleached wheat flour, and WWCBs as previously described^{2,5} and analyzed the extracts by using SDS-PAGE. Successful extraction of wheat fractions (water-soluble albumin/globulins, gliadins, and glutenins) was observed by electrophoresis and staining with Coomassie brilliant blue (Fig 1) with confirmatory staining using silver stain. Immunoblotting was then performed to investigate serum IgE binding to extracts by using patient sera, together with control sera (from other wheat-allergic patients with demonstrated clinical reactivity to WWCBs) and nonatopic sera. Compared with wheat-allergic controls, the immunoblot of sera from the wheat-allergic children tolerant to WWCBs (patients 1 and 2) demonstrated reduced IgE binding to wheat extracts, with minimal binding to extracts from the WWCBs, in particular to proteins in the gliadin fraction (highlighted by a white circle, Fig 2).

The production of WWCBs involves a pressure-cooking step. Pressure cooking has been demonstrated to alter the structure of lupin proteins, with a resulting decrease in overall clinical reactivity in allergic patients.⁷ We hypothesize that the pressure-cooking step during the production of WWCBs alters or removes some wheat proteins, resulting in clinical tolerance in otherwise wheat-allergic children. This may be due to deamidation of gliadin proteins, resulting in increased solubility *in vitro* (resulting in removal of the proteins during the production of WWCBs) and digestibility *in vivo*.^{1,8} Alternatively, it is possible that these children have a predominance of IgE production to a novel wheat allergen removed during the production of WWCBs. Whether wheat-allergic children are often able to tolerate WWCBs, and whether this represents a stage of intermediate “outgrowing” of wheat allergy, remains to be determined.

We have demonstrated that some wheat-allergic children are able to tolerate WWCBs. We therefore caution against using WWCBs alone for diagnostic OFC in wheat allergy, as this may

cause false-negative results. There may be a role, however, for specific challenge to identify WWCB tolerance in otherwise wheat-allergic individuals, allowing some liberalization of the diet.

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FIG 2. IgE Immunoblotting of wheat extracts from raw ground wheat, unbleached flour, and WWCBs. *Top panel:* Albumin/globulin fraction; *middle panel:* gliadins; *bottom panel:* glutenins. Extracts were transferred to nitrocellulose and probed with patient sera at 1:50 dilution followed by rabbit antihuman IgE and a goat antirabbit IgG-horseradish peroxidase antibody conjugate. *M.wt*, Molecular mass markers; *Pt*, patient. *Nonspecific binding of secondary antibody, an artifact reported elsewhere because of nonspecificity of the antibody to wheat proteins.⁶