

ABC OF ALLERGOLOGY

DIAGNOSING WHEAT HYPERSENSITIVITY

Adrian Morris, MB ChB, DCH, MFPG, Dip Allergy (SA)

Wheat is a widely cultivated cereal and very important staple food source. Despite the myriad of non-specific symptoms attributed to wheat allergy or intolerance, and the intense media interest therein, wheat hypersensitivity is a relatively uncommon condition. If wheat hypersensitivity does occur, it presents in a clearly defined manner, while sensitisation takes place via inhalation (baker's asthma) or ingestion (presenting as true food allergy or coeliac disease in children and adults). Wheat allergy may manifest as classic food allergy affecting the skin, gut or respiratory tract; or food-dependent exercise-induced anaphylaxis; or occupational asthma and rhinitis; or occasionally with contact urticaria. Wheat ingestion may also result in coeliac disease (gluten intolerance), an enteropathy mediated via T-cell intestinal inflammation which may be associated with dermatitis herpetiformis.

Cereal grains of the grass family (Graminae) provide edible kernels which contain 15% protein. Osborne¹ categorised cereal grain proteins into four fractions on the basis of their solubility in solvents: water soluble (albumins), dilute-salt soluble (globulins), aqueous-alcohol soluble (gliadins) and dilute-alkali or -acid soluble (glutenins) (Fig. 1). Recent studies reveal that wheat-derived lipid transfer proteins (LTP) found in the albumin/globulin fraction play an increasingly important allergenic role.²

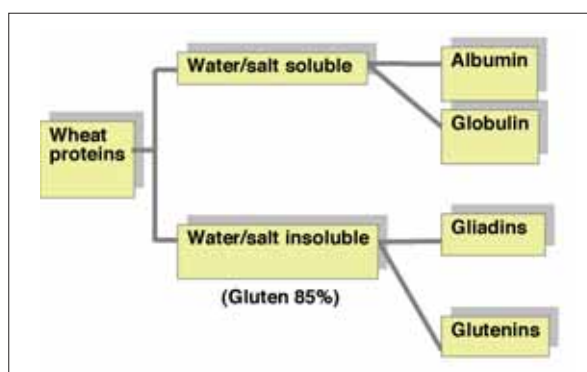


Fig. 1. Classification of wheat proteins.

Common wheat hypersensitivity manifestations

Baker's asthma

Baker's asthma is an IgE-mediated occupational hypersensitivity reaction to inhaled raw wheat flour that affects up to 30% of individuals in the baking industry. It usually presents with rhinitis, asthma, conjunctivitis and even contact urticaria. However, most people with baker's asthma are able to tolerate eating wheat products in their diet. About 60% of bakers with work-related respiratory symptoms have IgE antibodies to water-soluble specific wheat and rye proteins, mainly the alpha-amylases.

Childhood wheat allergy

Wheat is usually introduced into the child's diet around the age of 5 months. Sensitisation may however take place prior to this during breastfeeding and casual skin contact. Wheat-related food allergy may affect the skin, gastrointestinal tract and respiratory system. Most wheat-allergic children will present with moderate to severe eczema and many are also transiently sensitised to cow's milk and hen's egg, but in many instances outgrow their food allergies by age 7 years.

Ingested wheat in sensitised individuals elicits the immediate onset of urticaria, angio-oedema, wheezing, nausea and abdominal pain. Delayed reactions are reported to occur about 24 hours after ingestion with gastrointestinal symptoms and deteriorating eczema. Ingestion of wheat is unlikely to trigger classic immediate IgE-mediated food allergy symptoms presenting for the very first time in adulthood.

Recent evidence suggests that the water-insoluble gliadin fraction contains many clinically relevant allergens responsible for wheat allergy in children. Omega-5 gliadin IgE antibodies are strongly associated with immediate oral wheat-challenge reactions. Skin-prick testing solution panels for suspected food anaphylaxis might thus include gluten/gliadin solutions for better wheat-specific diagnostic reliability.

Wheat-dependent exercise-induced anaphylaxis (WDEIA)

In adults, wheat accounts for 60% of all cases of food-dependent exercise-induced anaphylaxis (FDEIA); other triggers include shellfish, vegetables and nuts.³ In this unique form of allergy, the ingestion of a specific food in combination with exercise triggers anaphylaxis, urticaria or asthma. The severity of the reaction varies from localised reactions to generalised anaphylaxis, and the severity is unpredictable because the amount of food allergen consumed and degree of exercise needed to trigger a reaction varies from individual to individual. The timing of wheat ingestion and the latent period that follows before exercise ranges from 10 minutes to 4 hours. Typically all WDEIA patients are adult, usually female, and there is no history of associated childhood wheat or food allergy. All respond well to a gluten-free diet and WDEIA allergic reactions may be enhanced by concomitant ingestion of aspirin. Current evidence again implicates the water-insoluble gliadin proteins, specifically omega-5 gliadin, and most



WDEIA patients will have specific IgE antibodies to this protein.

Coeliac disease (CD)

Coeliac disease (CD), otherwise known as gluten sensitivity enteropathy, is non-IgE-mediated. It is a T-cell-mediated auto-immune enteropathy which occurs in a minority of genetically susceptible individuals and affects 1% of western populations. Ninety-five per cent of people with CD express the HLA antigen DR3-DQ2, which is also present in 30% of asymptomatic western populations.⁴ Gluten, the water-insoluble wheat-flour protein, actually includes two protein groups: the glutenins and gliadins. Individuals sensitive to gluten react to the gliadin fraction which is also found in rye and barley but they tend to be able to tolerate oats. Antibodies to gliadin are not specific and may be found in the blood of healthy individuals as well as those with CD.

Clinical presentation of CD is variable, with both intestinal and extra-intestinal manifestations (Tables I & II).

Table I. Classic GI signs of coeliac disease

Chronic diarrhoea
Abdominal distension
Poor weight gain, weight loss
Anorexia
Constipation
Abdominal pain
Vomiting

Table II. Extra-intestinal signs of coeliac disease

Elevated liver enzymes
Short stature
Puberty delay
Iron deficiency anaemia
Aphthous ulcers
Dermatitis herpetiformis
Osteopenia/osteoporosis
Dental enamel hypoplasia

Dermatitis herpetiformis consists of intensely pruritic papules with excoriation, presenting on the elbows, knees, scalp and buttocks of CD sufferers, and occurring in the 30-40-year age group.

Asymptomatic CD is the most common form of the disease, and will only be identified by screening of high-risk populations (Table III).

Screening for CD is most effectively done by measuring IgA antibodies to the enzyme tissue transglutaminase (tTG) and IgA endomysial antibodies which are both highly specific and sensitive for CD. However, CD may be associated with an IgA deficiency, and therefore total IgA levels should first be checked. If there is

Table III. Coeliac disease risk groups

First-degree relatives
Type 1 diabetes
Down syndrome
Auto-immune thyroid disease
Secretory IgA deficiency

an IgA deficiency, testing for IgG antibodies to endomysium, gliadin and tTG should be performed. A positive CD screen is usually followed with a confirmatory small-bowel intestinal biopsy as false-positive antibody results may occur. Twenty-five per cent of screen-positive individuals will have a normal intestinal biopsy, but whether this indicates a false-positive result or perhaps represents early or mild CD remains contentious. HLA DQ2 or DQ8 testing has an excellent negative predictive value, as CD does not occur in the absence of these genetic markers.

A single test for IgA antibodies to tissue transglutaminase or endomysium is sufficient for CD screening (except in IgA deficiency).

Making sense of the various diagnostic tests

Wheat allergy diagnosis has been historically hampered by the low positive predictive value of the available ImmunoCAP wheat IgE test (f4) and skin-prick test solutions. There is also a great deal of cross-reactivity between grass pollen and wheat albumin leading to a 20% likelihood of a false-positive result to the currently available wheat IgE test (f4) in grass-pollen allergic individuals. In previously available wheat-specific IgE tests, there was an under-representation of the allergenic water-insoluble proteins such as the gliadins. Fortunately this has recently been remedied by the development of recombinant wheat allergens such as the ImmunoCAP omega-5 gliadin test (f416), since omega-5 gliadin has been found to be a highly allergenic wheat protein.⁵

Wheat allergy specific ImmunoCAP IgE tests

- Alpha amylase (k87) relevant in baker's asthma
- Wheat (f4) water-soluble wheat albumins
- Gluten (f79) water-insoluble wheat protein
- Gliadin (f98) water-insoluble wheat protein
- Omega-5 gliadin (f416) recombinant allergen relevant to WDEIA and classic wheat anaphylaxis

Coeliac disease screen tests

- IgA endomysium
- IgA tissue transglutaminase (tTG)

Wheat is a ubiquitous protein in our diet and although an uncommon cause of true food allergy, is responsible for baker's asthma, childhood wheat allergy in association with eczema, wheat-dependent exercise-induced anaphylaxis (WDEIA) and coeliac disease (delayed enteropathy).

Declaration of conflict of interest

The author declares no conflict of interest.

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