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Review

Cracking the egg: An insight into egg hypersensitivity

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ABSTRACT

Hypersensitivity to the chicken egg is a widespread disorder mainly affecting 1–2% of children worldwide. It is the second most common food allergy in children, next to cow's milk allergy. Egg allergy is mainly caused by hypersensitivity to four allergens found in the egg white; ovomucoid, ovalbumin, ovotransferrin and lysozyme. However, some research suggests the involvement of allergens exclusively found in the egg yolk such as chicken serum albumin and YGP42, which may play a crucial role in the overall reaction. In egg allergic individuals, these allergens cause conditions such as itching, atopic dermatitis, bronchial asthma, vomiting, rhinitis, conjunctivitis, laryngeal oedema and chronic urticaria, and anaphylaxis. Currently there is no permanent cure for egg allergy. Upon positive diagnosis for egg allergy, strict dietary avoidance of eggs and products containing traces of eggs is the most effecting way of avoiding future hypersensitivity reactions. However, it is difficult to fully avoid eggs since they are found in a rage of processed food products. An understanding of the mechanisms of allergic reactions, egg allergens and their prevalence, egg allergy diagnosis and current treatment strategies are important for future studies. This review addresses these topics and discusses both egg white and egg yolk allergy as a whole.

1. Allergy

Allergy is a symptomatic and an abnormal overreaction by the immune system to innocuous environmental substances, such as grass pollen and eggs, known as allergens. Allergens are a type of antigen, which trigger a complex immune response upon contact with the immune system. Allergy is classified as a *type 1* hypersensitivity reaction because of the immediate and inflammatory immune response that is characterised by the excessive production of the antibody Immunoglobulin E (IgE). An allergic response involves two reaction phases based on the contact of the allergen with the immune system; primary and secondary response. The primary response (upon initial contact with allergen), stimulates the generation of IgE by T-lymphocytes. The secondary response (upon secondary contact with the same allergen) results in the degranulation of mast cells (mastocytes) and basophils (basophil granulocytes). The mediators (e.g. histamine) released by the degranulation process elicit clinical allergic symptoms such as bronchoconstriction, sneezing, rashes, itching or life threatening conditions such as anaphylaxis, just to name a few (Janeway and Traverse, 1994; Kay, 2001).

2. Allergic response

2.1. Allergic sensitisation

Upon contact with the immune system, an allergen is engulfed and processed by antigen presenting cells (APCs) and presented to naïve T-helper cells (Th0). This causes Th0 cells to differentiate into T-helper type 2 (Th2) cells in the presence of cytokines including Interleukin-4 (IL-4). Th2 cells then further secrete IL-4, IL-5 and IL-13, which induce B-cell differentiation into plasma cells secreting IgE. The IgE antibodies subsequently bind to the high affinity FcεRI receptors on mast cells and basophils, thus sensitizing the immune system to the allergen (Kay, 2001) (Fig. 1).

Abbreviations: OIT, oral immunotherapy; SIT, specific immunotherapy; SPT, skin prick test.

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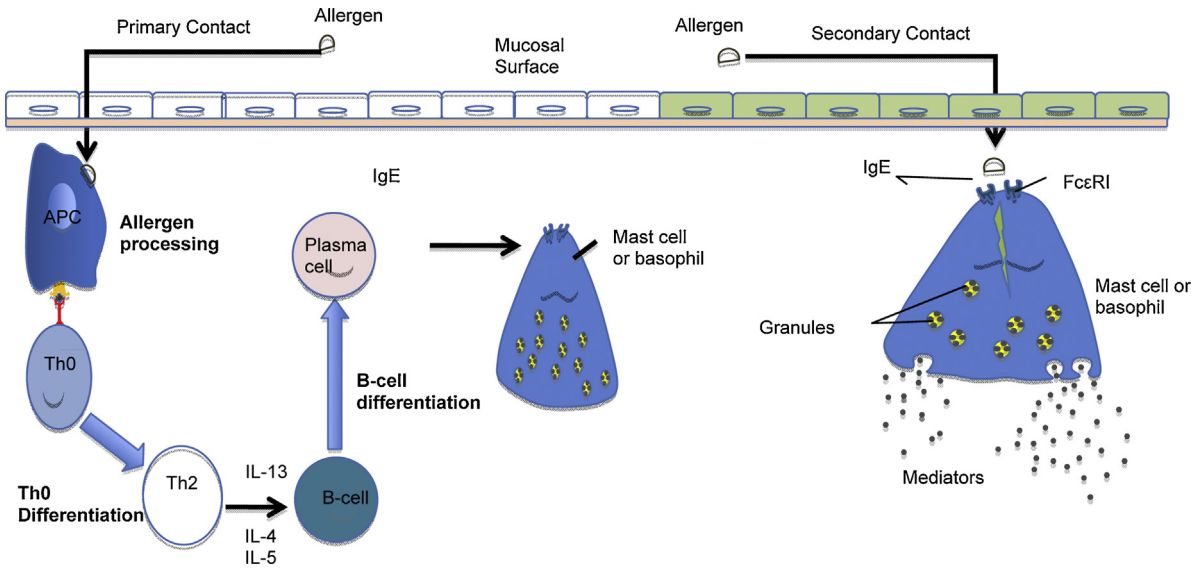

Fig. 1. Illustration of the allergic reaction. This figure outlines the steps of an allergic reaction. Once the initially encountered allergen is processed and presented by APCs to the Th0 cells, the Th0 cells differentiate into Th2 cells in allergic individuals. These Th2 cells then further secrete IL-4, IL-5 and IL-13, triggering B-cell differentiation into plasma cells. Subsequently, these plasma cells proliferate and produce excessive amounts of allergen specific IgE, which bind to the FcεRI receptors on mast cells and basophils, thus sensitizing the immune system to the allergen. Upon secondary encounter of the immune system with the same allergen, the allergen binds to multiple IgE held on mast cells and basophils. Cross linking of the FcεRI receptors, as a result of interaction between a single allergen and multiple IgE molecules, triggers the release of mediators including histamine, causing an allergic inflammation.

2.2. Allergic reaction

Upon secondary exposure to the same allergen (unprocessed by APCs), the allergen binds to the membrane bound IgE molecules on mast cells and basophils. Cross-linking of FcεRI occurs when multiple IgE molecules interact with the same intact allergen, triggering degranulation of mast cells and basophils, consequently releasing granule-derived vasoactive chemicals such as histamine, serine protease tryptase, lipid mediators such as leukotrienes, prostaglandins and platelet activating factor, chemokines and cytokines IL-4, IL-5 and IL-13 (Fig. 1). These mediators cause allergic symptoms such as airway smooth muscle constriction (bronchoconstriction), mucus hypersecretion, mucus cell metaplasia, redness, rashes, sneezing and anaphylaxis (Kay, 2001).

3. Food allergy

Food allergy is one of the major allergies in today's society. In a double-blind placebo controlled food challenge study conducted by Allan Bock et al. (1988), 80% of the subject children were found to develop hypersensitivity symptoms to food allergens. In the developed world, 10% of children are affected by food allergies, while emerging or developing nations has a prevalence of 7% (Prescott et al., 2013). Occurrence of food allergy, like other atopic diseases, is rising and remains a problem throughout the world. It is a major cause of anaphylaxis, especially by nuts, and treated worldwide in emergency departments and hospitals, incurring a massive financial burden on the governments and the public (Bock et al., 2001; Hugh, 2004). Food hypersensitivities include abnormal overreactions caused by intolerance to food (non-allergic) and allergic responses caused by an antigen in the food. Intolerance to food is due to some physiological abnormality, such as the lack of lactase which causes intolerance to lactose, whereas the allergic food reactions are mediated by IgE or non-IgE immune responses (Hugh, 2004). Food allergies arise through the interaction between the intestinal immune system and food allergens present in the food that we consume on a daily basis. Allergenic foods include, but not limited to, eggs, peanuts, fish and milk. Antigens (allergens) present in these foods are responsible for IgE mediated hypersensitivity reactions. For example, people allergic to milk react to the milk whey protein allergen β-lactoglobulin (Jabed et al., 2012) and patients allergic to egg may be due to the egg white protein ovomucoid (Ando et al., 2008). Most of these allergens are glycoproteins that can withstand heat, acids and proteases (Hugh, 2004), this explains why most allergenic foods remain allergenic even after cooking or processing.

4. Egg allergy

Hypersensitivity to the chicken (*Gallus gallus*) egg is a widespread disorder mainly affecting children, with a recent meta-analysis suggesting a prevalence of 0.5–2.5% of children (Rona et al., 2007). It is the second most common food allergy next to cow's milk allergy and it is the most common allergy among children with atopic dermatitis (Caubet and Wang, 2011; Langeland, 1985; Sampson, 1983). According to an Australian study conducted by the Murdoch Children's Research Institute (MCRI), 8.9% of infants are allergic to eggs (Osborne et al., 2011). However, egg allergy is not limited to children, with cases that have been reported of adult onsets (Unsel et al., 2013). Children allergic to egg generally grow out of the condition by school age (Boyano-Martínez et al., 2002; Venter et al., 2008). Hypersensitivity to allergens present in the eggs causes conditions such as itching, atopic dermatitis, bronchial asthma, vomiting, angio-oedema, rhinitis, conjunctivitis, laryngeal oedema, chronic urticaria and allergic eosinophilic gastroenteritis (Eigenmann, 2000; Fremont et al., 1997; Jaffe et al., 1994; Quirce et al., 2001). Egg allergic patients produce IgE specific to sequential (linear) and conformational epitopes of egg allergens. However some sequential epitopes recognised by persistent egg allergic patients are not recognised by patients with transient egg allergy (Järvinen et al., 2007). This suggests a difference in severity of allergic reaction between persistent and transient egg allergic patients. Anaphylaxis may also occur in some individuals, however this depends on the processing of the egg. This may be due the reduction in IgE reactivity in heated egg, possibly due to the disruption of conformational IgE binding epitopes in the egg