

Hazelnut allergy: from pollen-associated mild allergy to severe anaphylactic reactions

Annebeth E. Flinterman^a, Jaap H. Akkerdaas^b, André C. Knulst^a,
Ronald van Ree^b and Suzanne G. Pasmans^a

^aDepartment of Dermatology, University Medical Centre Utrecht, Utrecht and ^bDepartment of Experimental Immunology, Academic Medical Centre, Amsterdam, The Netherlands

Correspondence to Annebeth Flinterman, MD, PhD, Department of Dermatology, G02.124, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands
Tel: +31 88 755 7388;
e-mail: a.e.flinterman@umcutrecht.nl

Current Opinion in Allergy and Clinical Immunology 2008, 8:261–265

Purpose of review

Hazelnut allergy can vary between mild oral symptoms and potentially dangerous anaphylaxis. There is a need to predict which subjects are at risk for severe reactions. In this study, possibilities for 'component-resolved diagnosis', based on sensitization to different allergens in hazelnut, are discussed.

Recent findings

One type of hazelnut allergy can be associated with sensitization to homologues of pollen allergens, predominantly birch, in hazelnut: Cor a 1 (Bet v 1) and Cor a 2 (profilin). These allergens account for relatively mild symptoms. However, subjects can also be sensitized to several other allergens in hazelnut that are related to more severe symptoms. These allergens are homologues of allergens in other nuts and peanut: Cor a 8 (lipid transfer protein) and Cor a 9 (11S globulin) and perhaps Cor a 11 (7S globulin). The clinical relevance of these and other potential hazelnut allergens has to be further defined. The diagnosis of hazelnut has to be confirmed by oral double-blind placebo-controlled food challenge.

Summary

Sensitization to hazelnut can either be associated with mild oral symptoms, depending on sensitization to pollen, or with more serious allergic symptoms, related to sensitization to homologues of nut and peanut allergens.

Keywords

challenge, component-resolved diagnosis, hazelnut allergens, hazelnut allergy, pollen

Curr Opin Allergy Clin Immunol 8:261–265
© 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins
1528-4050

Introduction

Hazelnut, *Corylus avellana*, is commonly used in the food industry. The worldwide production of hazelnuts in the last few years is approximately 600 000 tons of shelled hazelnuts per year (www.fao.org). In the Netherlands, consumption of hazelnuts is relatively high, with an average of 2 kg of unshelled hazelnut kernels per person per year. In comparison, peanut consumption in this country is twice as much. Products in which hazelnut can be 'hidden' as an ingredient are mostly pastries and chocolate [1,2]. Allergy to hazelnut has been listed as the top five serious food allergies, as it can cause serious and life-threatening symptoms in sensitive subjects [3,4]. However, most allergic subjects will develop milder symptoms [5]. In this paper, the different features of hazelnut allergy are presented in relation to sensitization to hazelnut allergens.

Pollen-related type of hazelnut allergy causing oral allergy syndrome

Pollen allergy is very common; up to 25% of the northern European population suffers from allergic rhinitis [6]. Typically, affected subjects display seasonal symptoms. Pollen-related food allergy has been reported by more than half of subjects with seasonal rhinoconjunctivitis, in whom the symptoms may aggravate during the pollen season [7].

The most notorious example is the 'birch-fruit-vegetable syndrome'. In addition to allergy to stone-fruits and several vegetables, allergy to nuts, such as hazelnut and almond, can be related to birch pollen allergy. Symptoms are mostly restricted to the oral cavity, consisting of itch and mucosal swelling [oral allergy syndrome (OAS)]. Although these symptoms are generally

mild, swelling of the laryngeal mucosa may cause significant distress. OAS after ingestion of hazelnut has mainly been documented for adults sensitized to birch pollen [8–10]. The prevalence of sensitization to pollen increases significantly in children 1–5 years old [11]. OAS to hazelnut has been reported accordingly in children, the youngest being 4 years [12–14].

Although this type of hazelnut allergy, OAS, has been related to birch pollen, it has not been well documented whether other pollen allergens may also be crossreactive with hazelnut. Interestingly, sensitization to hazel pollen does not seem to play a significant role in the induction of sensitization to hazelnut [15,16].

In summary, both children and adults can suffer from the pollen-related type of hazelnut allergy mainly causing OAS, especially in northern parts of the world where birch trees are common.

Allergens involved in pollen-related type of hazelnut allergy

The major allergen in birch pollen is Bet v 1. Sensitization to Bet v 1 is related to symptoms of OAS to foods [17,18]. The allergen Cor a 1 in hazelnut is a homologue of Bet v 1. This allergen has been implicated in OAS to hazelnut, as an example of the birch fruit vegetable-syndrome [9]. From 50 subjects with sensitization to Bet v 1, 93% were also sensitized to Cor a 1 [19]. The association between pollen allergy and plant food allergy can be explained by shared IgE-binding sites, resulting in IgE crossreactivity. The IgE-binding sites on Bet v 1 homologues, such as Cor a 1, are rather unstable to heating and digestion [20]. Most symptoms, therefore, remain restricted to the oral cavity. We should, however, be aware of the case reports on Bet v 1 homologues in jackfruit and soy among others causing more serious allergic reactions [21,22].

Another protein capable of crossreactive IgE between pollen and plant foods is profilin, Bet v 2 in birch pollen. Approximately 10–20% of birch pollen-allergic subjects are sensitized to Bet v 2 [12,23]. Monosensitization to Bet v 2 in particular can be demonstrated not only in children with grass pollinosis but also in subjects with birch pollen allergy [12,14,18]. In hazelnut, this allergen is known as Cor a 2. Some subjects with pollen-related food allergy are only sensitized to Cor a 2 and not to Cor a 1 or Bet v 1 [24•]. The clinical relevance of sensitization to profilin, though remains questionable, seems limited [18].

The extent of sensitization to Cor a 1 and Cor a 2 in the general population is currently unknown, but may approach the prevalence of sensitization to birch pollen [9]. Detection of sensitization to Cor a 1 and Cor a 2 has

been difficult because these allergens were not detectable in all commercial extracts, probably because Cor a 1 is easily denatured in the extraction procedure [25]. A recent paper [26•] has shown that addition of recombinant Cor a 1 to the natural extract can enhance the IgE-detection capacity for Cor a 1.

Sensitization to Cor a 1, and to a lesser extent Cor a 2, is related to pollen sensitization, especially to Bet v 1 and Bet v 2, respectively. The prevalence of the pollen-related type of hazelnut allergy seems related to the prevalence of pollen allergy and may therefore be rather extensive.

More severe type of hazelnut allergy independent from pollen

Although pollen-related hazelnut allergy remains mainly restricted to the oral cavity, hazelnut can also elicit more severe symptoms such as generalized urticaria, gastrointestinal symptoms, dyspnoea and cardiovascular symptoms [10,13,27–29]. Hazelnut, together with peanut and other tree nuts, accounts for 90% of fatalities due to food allergy [3].

One study [28] describing more severe allergic reactions from hazelnut was conducted in adult subjects with a positive challenge or with a history of previous anaphylactic reactions to hazelnut. Interestingly, the group with a history of more severe reactions to hazelnut in this study was in general not sensitized to birch pollen. These were adult subjects from the Mediterranean area, where birch trees are absent. Another study [29] investigating more severe hazelnut allergy also preferentially studied Mediterranean subjects who were not sensitized to birch. Only few studies have performed oral hazelnut challenges, and these were predominantly performed with adults sensitized to birch [8]. Taking these studies together, it appears that the number of adult subjects with severe allergic reactions to hazelnut was small compared to the hazelnut-allergic group with only OAS.

The prevalence of more severe hazelnut allergy has not yet been documented, but the prevalence of tree nut allergy causing more severe symptoms, including hazelnut allergy, has been estimated between 0.4 and 0.7% [30].

The previous findings suggest that severe hazelnut allergy will predominantly occur in subjects who are not necessarily sensitized to birch pollen. Similar findings have been described for apple allergy; apple-sensitized subjects living in birch-endemic areas merely reported OAS to apple, whereas apple-sensitized subjects from non-birch-endemic areas, mainly Mediterranean, may also develop more serious symptoms [31]. A recent study

from our group has shown that eight of the 12 (67%) hazelnut-allergic children from the Netherlands developed more severe symptoms, regardless of whether they were sensitized to birch pollen or not [24[•]].

Concluding, hazelnut allergy can cause severe allergic reactions both in children and adults. This type of hazelnut allergy is independent of birch pollen sensitization and occurs less frequently than the pollen-related type of hazelnut allergy.

Allergens involved in the more severe type of hazelnut allergy

Several allergens have been implicated in the more severe allergic reactions to hazelnut. First of all, sensitization to a LTP in hazelnut, Cor a 8, has been shown in eight children and at least 18 adults with more severe allergic reactions in two studies [24[•],32]. LTP has a compact tertiary structure that makes it resistant to heat and digestion, hence increasing its allergenicity [33]. Previously, sensitization to LTP was mainly confined to Mediterranean areas, but we showed that sensitization to LTP was also present in all children with more severe allergic symptoms from a birch-endemic area [24[•]]. The observation that a significant subset (34%) of all ($n = 191$) hazelnut-sensitized children from this study was sensitized to LTP, and in particular young children not always in combination with sensitization to Bet v 1, suggests that they became sensitized to hazelnut before pollen sensitization [24[•]].

Another allergen that has been related to more severe hazelnut allergy is Cor a 9, an 11S globulin of around 40 kDa. Cor a 9 was found to be recognized by IgE from 86% of hazelnut-allergic subjects with systemic reactions, mainly children [27]. In particular, sensitization to this allergen was observed in subject not sensitized to pollen. In another study [34], sensitization to Cor a 11 was demonstrated in less than half of the hazelnut-allergic subjects with more severe allergic reactions. The clinical relevance of this allergen remains questionable according to the limited capacity to induce histamine release in comparison with other hazelnut allergens.

Although the amino acid sequence has not been elucidated and purification is still under investigation, experiments have indicated the presence of 2S albumins in hazelnut [28]. Investigation of the clinical relevance of oleosin, also a hazelnut allergen, has been limited because this allergen is involved in the formation of fatty particles and is difficult to extract [35]. The first data on this allergen show that this allergen may in fact be important as well, because subjects sensitized to LTP also recognize oleosin.

Looking at the hazelnut immunoblots shown in literature, many allergic subjects recognize more than one allergen rather than just one. This is in concordance with previous studies [36,37] on peanut allergy, where the number of allergens/IgE epitopes per subject was related to the severity of the reaction.

So, several non-pollen-related hazelnut allergens, particularly Cor a 8 and Cor a 9, can be associated with more severe allergic reactions to hazelnut. These subjects generally recognize more than one allergen in hazelnut.

Does crossreactivity of hazelnut allergen with other nuts and peanut occur?

Cosensitization to hazelnut and other tree nuts, and also to peanut, has been reported extensively, especially in children [30,38,39]. Of all children sensitized to hazelnut, 60% are also sensitized to at least one other tree nut [38]. In one earlier study [39], it was shown that more than 90% of children with sensitization to hazelnut are sensitized to peanut and Brazil nut. We showed that children with more severe reactions were sensitized to significantly more tree nuts and to a lesser extent peanut than hazelnut-sensitized children with only OAS or no symptoms at all [13]. In this group [24[•]], sensitization to multiple other tree nuts was associated with sensitization to multiple hazelnut allergens on immunoblot.

The hazelnut allergens that have been suggested as major allergens for severe hazelnut allergy are homologous to allergens in peanut and other tree nuts (Table 1). Using inhibition assays, hazelnut was crossreactive with either walnut and pecan or cashew, Brazil nut, pistachio and almond [40]. Especially Cor a 9 is suggested as a possible crossreactive allergen. In a recent study [41[•]], linear IgE-binding epitopes identified in Ara h 3 from peanut were shown to exhibit structural homology with not only Cor a 9 in hazelnut but also other allergenic tree nuts. Furthermore, histamine release assays showed that walnut-specific IgE placed on basophils can be crosslinked by hazelnut and degranulate basophils [42].

In summary, there are indications that hazelnut allergens related to more severe hazelnut allergy are crossreactive with allergens in other tree nuts and peanut. Further research is recommended in order to better understand the development of sensitization to different nuts and peanut.

Diagnosis of hazelnut allergy

So far, two types of hazelnut allergy have been identified: a pollen-associated type of hazelnut allergy causing OAS

Table 1 Hazelnut allergens, their homologues in peanut, tree nuts and pollen, and their presumed clinical relevance

Hazelnut allergen	Allergen	Homologues ^a	Molecular weight (kDa)	Clinical relevance	References
Cor a 1	Bet v 1	Bet v 1	17	OAS, none	Flinterman <i>et al.</i> [24 [•]], Hirschwehr <i>et al.</i> [15], Wensing <i>et al.</i> [18]
Cor a 2	Profilin	Bet v 2, grass pollen	14	OAS? none	Flinterman <i>et al.</i> [24 [•]], Ricci <i>et al.</i> [14], Wensing <i>et al.</i> [18]
Cor a 8	Lipid Transfer Protein	Jug r 3	8–10	More severe symptoms	Schocker <i>et al.</i> [32], Flinterman <i>et al.</i> [24 [•]]
Cor a 9	11S globulin	Ara h 3, Ana o 2, Jug r 4, Ber e 2	40	More severe symptoms	Beyer <i>et al.</i> [27]
Cor a 11	7S vicilin	Ara h 1, Jug r 2, Ana o 1	48	More severe symptoms?	Lauer <i>et al.</i> [34]
2 S albumins	2S albumins	Ara h 2, Ara h 6, Jug r 1, Ber e 1	12	More severe symptoms?	Pastorello <i>et al.</i> [28]
Oleosin	Oleosin	Peanut	15–18	Unknown	Akkerdaas <i>et al.</i> [35]

^a Ana o, cashew; Ara h, peanut; Ber e, Brazil nut; Bet v, birch; Jug r, walnut.

and more severe hazelnut allergy independent from pollen sensitization. A combination of both can also occur.

It may be important to differentiate these two types in order to give appropriate advice on risk management, dietary restrictions and rescue medication. When in doubt, it should be advocated to perform a food challenge, preferably double-blind placebo controlled. This is especially the case in children, as many of them are not aware of previous ingestion of hazelnut [43,44]. When taking into account that OAS during challenge can either be pollen-associated OAS or the first sign of more severe allergy, it may be suggested to proceed with the challenge until objective symptoms occur. Objective symptoms are an indication that the patient has a more severe type of hazelnut allergy. However, it cannot be excluded that patients with birch pollen-related hazelnut allergy will not develop objective symptoms at high doses. Studies so far have reported objective symptoms to doses of hazelnut up to 10 g [9,18,24[•]].

Interestingly, mild and severe hazelnut allergy appeared to be associated with sensitization to different allergens. Recently, this has also been described for apple and peach allergy. Sensitization to Bet v 1 or Bet v 2 homologues in apple and peach has been associated with pollen sensitization and relatively mild OAS, whereas sensitization to LTP was observed in all subjects with more severe allergic reactions [31,45].

That means that if a hazelnut-sensitized subject is only sensitized to Cor a 1 and/or Cor a 2, it can be expected that this subject will develop OAS to hazelnut. Perhaps in these cases, a food challenge is not necessary in the future, bearing in mind that some subjects may experience more serious mucosal swelling of the laryngeal area. On the contrary, if a subject is sensitized to multiple

allergens in hazelnut other than Cor a 1 and Cor a 2, there is a significant chance that this subject will develop more severe allergic symptoms. More studies performing challenges are needed to prospectively demonstrate the clinical relevance of each of these allergens. As this type of hazelnut allergy is not likely to resolve, it is advocated to challenge this group before advising a lifelong elimination of hazelnut. This concept is known as 'component-resolved diagnosis' and has the potential to discriminate different types of hazelnut allergy in the future.

Conclusion

Hazelnut allergy among pollen-allergic subjects is supposed to be rather common, as is pollen allergy, and is based on crossreactivity between pollen and hazelnut allergens. This type of allergy is associated with mild oral symptoms because the involved allergens Cor a 1 and Cor a 2 are relatively instable to heat and digestion.

A small group of subjects with hazelnut allergy suffer from more severe and potentially life-threatening symptoms after ingestion of hazelnut. This type of allergy is independent of pollen sensitization. In childhood, before the increase in sensitization to pollen, this type of hazelnut allergy is more common than among adults. Sensitization is directed to different allergens such as LTPs (Cor a 8), 11S globulin (Cor a 9), and perhaps also Cor a 11, 2S albumins and oleosin. Interestingly, these allergens are homologues of major allergens in other tree nuts and peanut.

Differentiation of these types of hazelnut allergies should be based on history and oral double-blind placebo-controlled food challenge. In the future, screening for IgE directed against the different allergens in hazelnut, so-called component-resolved diagnosis, may facilitate the diagnosis of hazelnut allergy.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 282).

- 1 Hefle SL. Hidden food allergens. *Curr Opin Allergy Clin Immunol* 2001; 1:269–271.
- 2 Wensing M, Koppelman SJ, Penninks AH, *et al.* Hidden hazelnut is a threat to allergic patients. *Allergy* 2001; 56:191–192.
- 3 Bock SA, Munoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol* 2001; 107:191–193.
- 4 Mehl A, Wahn U, Niggemann B. Anaphylactic reactions in children: a questionnaire-based survey in Germany. *Allergy* 2005; 60:1440–1445.
- 5 Roehr CC, Edenharter G, Reimann S, *et al.* Food allergy and nonallergic food hypersensitivity in children and adolescents. *Clin Exp Allergy* 2004; 34:1534–1541.
- 6 Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J* 2004; 24:758–764.
- 7 Ma S, Sicherer SH, Nowak-Wegrzyn A. A survey on the management of pollen-food allergy syndrome in allergy practices. *J Allergy Clin Immunol* 2003; 112:784–788.
- 8 Wensing M, Penninks AH, Hefle SL, *et al.* The range of minimum provoking doses in hazelnut-allergic patients as determined by double-blind, placebo-controlled food challenges. *Clin Exp Allergy* 2002; 32:1757–1762.
- 9 Hansen KS, Ballmer-Weber BK, Luttkopf D, *et al.* Roasted hazelnuts: allergenic activity evaluated by double-blind, placebo-controlled food challenge. *Allergy* 2003; 58:132–138.
- 10 Ortolani C, Ballmer-Weber BK, Hansen KS, *et al.* Hazelnut allergy: a double-blind, placebo-controlled food challenge multicenter study. *J Allergy Clin Immunol* 2000; 105:577–581.
- 11 Julge K, Vasar M, Bjorksten B. Development of allergy and IgE antibodies during the first five years of life in Estonian children. *Clin Exp Allergy* 2001; 31:1854–1861.
- 12 Cudowska B, Kaczmarek M. Diagnostic value of birch recombinant allergens (rBet v 1, profilin rBet v 2) in children with pollen-related food allergy. *Rocz Akad Med Białymst* 2004; 49:111–115.
- 13 Flinterman AE, Hoekstra MO, Meijer Y, *et al.* Clinical reactivity to hazelnut in children: association with sensitization to birch pollen or nuts? *J Allergy Clin Immunol* 2006; 118:1186–1189.
- 14 Ricci G, Righetti F, Menna G, *et al.* Relationship between Bet v 1 and Bet v 2 specific IgE and food allergy in children with grass pollen respiratory allergy. *Mol Immunol* 2005; 42:1251–1257.
- 15 Hirschwehr R, Valenta R, Ebner C, *et al.* Identification of common allergenic structures in hazel pollen and hazelnuts: a possible explanation for sensitivity to hazelnuts in patients allergic to tree pollen. *J Allergy Clin Immunol* 1992; 90:927–936.
- 16 Luttkopf D, Muller U, Skov PS, *et al.* Comparison of four variants of a major allergen in hazelnut (*Corylus avellana*) Cor a 1.04 with the major hazel pollen allergen Cor a 1.01. *Mol Immunol* 2002; 38:515–525.
- 17 De Amici M, Mosca M, Vignini M, *et al.* Recombinant birch allergens (Bet v 1 and Bet v 2) and the oral allergy syndrome in patients allergic to birch pollen. *Ann Allergy Asthma Immunol* 2003; 91:490–492.
- 18 Wensing M, Akkerdaas JH, van Leeuwen WA, *et al.* IgE to Bet v 1 and profilin: cross-reactivity patterns and clinical relevance. *J Allergy Clin Immunol* 2002; 110:435–442.
- 19 Bohle B. The impact of pollen-related food allergens on pollen allergy. *Allergy* 2007; 62:3–10.
- 20 Schimek EM, Zwolfer B, Briza P, *et al.* Gastrointestinal digestion of Bet v 1-homologous food allergens destroys their mediator-releasing, but not T cell-activating, capacity. *J Allergy Clin Immunol* 2005; 116:1327–1333.
- 21 Bolhaar ST, Ree R, Bruijnzeel-Koomen CA, *et al.* Allergy to jackfruit: a novel example of Bet v 1-related food allergy. *Allergy* 2004; 59:1187–1192.
- 22 Kleine-Tebbe J, Vogel L, Crowell DN, *et al.* Severe oral allergy syndrome and anaphylactic reactions caused by a Bet v 1-related PR-10 protein in soybean, SAM22. *J Allergy Clin Immunol* 2002; 110:797–804.
- 23 Elfman L, Svensson M, Lidholm J, *et al.* Different profiles in specific IgE to rBet v 1 and rBet v 2 in patients allergic to birch pollen from six countries. *Int Arch Allergy Immunol* 1997; 113:249–251.
- 24 Flinterman AE, Akkerdaas JH, den Hartog Jager CF, *et al.* Lipid transfer protein-linked hazelnut allergy in children from a non-Mediterranean birch-endemic area. *J Allergy Clin Immunol* 2008 [Epub ahead of print].
This study describes the sensitization to different hazelnut allergens Cor a 1, Cor a 2, Cor a 8 in relation to clinical reactivity and the prevalence of sensitization of these allergens in a pediatric allergic population.
- 25 Akkerdaas JH, Wensing M, Knulst AC, *et al.* How accurate and safe is the diagnosis of hazelnut allergy by means of commercial skin prick test reagents? *Int Arch Allergy Immunol* 2003; 132:132–140.
- 26 Andersson K, Ballmer-Weber BK, Cistero-Bahima A, *et al.* Enhancement of hazelnut extract for IgE testing by recombinant allergen spiking. *Allergy* 2007; 62:897–904.
This study describes the necessity of good allergen extracts, including the important hazelnut allergens Cor a 1 and Cor a 8, for a correct diagnosis of hazelnut allergy.
- 27 Beyer K, Grishina G, Bardina L, *et al.* Identification of an 11S globulin as a major hazelnut food allergen in hazelnut-induced systemic reactions. *J Allergy Clin Immunol* 2002; 110:517–523.
- 28 Pastorello EA, Vieths S, Pravettoni V, *et al.* Identification of hazelnut major allergens in sensitive patients with positive double-blind, placebo-controlled food challenge results. *J Allergy Clin Immunol* 2002; 109:563–570.
- 29 Schocker F, Luttkopf D, Muller U, *et al.* IgE binding to unique hazelnut allergens: identification of non pollen-related and heat-stable hazelnut allergens eliciting severe allergic reactions. *Eur J Nutr* 2000; 39:172–180.
- 30 Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: a 5-year follow-up study. *J Allergy Clin Immunol* 2003; 112:1203–1207.
- 31 Fernandez-Rivas M, Bolhaar S, Gonzalez-Mancebo E, *et al.* Apple allergy across Europe: how allergen sensitization profiles determine the clinical expression of allergies to plant foods. *J Allergy Clin Immunol* 2006; 118:481–488.
- 32 Schocker F, Luttkopf D, Scheurer S, *et al.* Recombinant lipid transfer protein Cor a 8 from hazelnut: a new tool for in vitro diagnosis of potentially severe hazelnut allergy. *J Allergy Clin Immunol* 2004; 113:141–147.
- 33 Pastorello EA, Pompei C, Pravettoni V, *et al.* Lipid transfer proteins and 2S albumins as allergens. *Allergy* 2001; 56 (Suppl 67):45–47.
- 34 Lauer I, Foetisch K, Kolarich D, *et al.* Hazelnut (*Corylus avellana*) vicilin Cor a 11: molecular characterization of a glycoprotein and its allergenic activity. *Biochem J* 2004; 383:327–334.
- 35 Akkerdaas JH, Schocker F, Vieths S, *et al.* Cloning of oleosin, a putative new hazelnut allergen, using a hazelnut cDNA library. *Mol Nutr Food Res* 2006; 50:18–23.
- 36 Beyer K, Ehlman-Grunther L, Jarvinen KM, *et al.* Measurement of peptide-specific IgE as an additional tool in identifying patients with clinical reactivity to peanuts. *J Allergy Clin Immunol* 2003; 112:202–207.
- 37 Lewis SA, Grimshaw KE, Warner JO, Hourihane JO. The promiscuity of immunoglobulin E binding to peanut allergens, as determined by Western blotting, correlates with the severity of clinical symptoms. *Clin Exp Allergy* 2005; 35:767–773.
- 38 Clark AT, Ewan PW. The development and progression of allergy to multiple nuts at different ages. *Pediatr Allergy Immunol* 2005; 16:507–511.
- 39 Pumphrey RS, Wilson PB, Faragher EB, Edwards SR. Specific immunoglobulin E to peanut, hazelnut and Brazil nut in 731 patients: similar patterns found at all ages. *Clin Exp Allergy* 1999; 29:1256–1259.
- 40 Goetz DW, Whisman BA, Goetz AD. Cross-reactivity among edible nuts: double immunodiffusion, crossed immunoelectrophoresis, and human specific IgE serologic surveys. *Ann Allergy Asthma Immunol* 2005; 95:45–52.
- 41 Barre A, Jacquet G, Sordet C, *et al.* Homology modelling and conformational analysis of IgE-binding epitopes of Ara h 3 and other legumin allergens with a cupin fold from tree nuts. *Mol Immunol* 2007; 44:3243–3255.
This study demonstrates a potential IgE-binding area on a peanut allergen, Ara h 3, that is similar to allergens in several tree nuts including hazelnut.
- 42 de Leon MP, Drew AC, Glaspole IN, *et al.* Functional analysis of cross-reactive immunoglobulin E antibodies: peanut-specific immunoglobulin E sensitizes basophils to tree nut allergens. *Clin Exp Allergy* 2005; 35:1056–1064.
- 43 Clark AT, Ewan PW. Interpretation of tests for nut allergy in one thousand patients, in relation to allergy or tolerance. *Clin Exp Allergy* 2003; 33:1041–1045.
- 44 Sicherer SH, Furlong TJ, Munoz-Furlong A, *et al.* A voluntary registry for peanut and tree nut allergy: characteristics of the first 5149 registrants. *J Allergy Clin Immunol* 2001; 108:128–132.
- 45 Gamboa PM, Caceres O, Antepara I, *et al.* Two different profiles of peach allergy in the north of Spain. *Allergy* 2007; 62:408–414.