

NUT ALLERGIES - A REVIEW ON THE PREVALENCE AND ON CURRENT CLINICAL ASPECTS

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Allergy to nuts is increasingly common in children and adults. Eleven types of nut are eaten regularly: hazelnut, walnut, almond, pistachio, cashew nut, pecan nut, Brazil nut, Macadamia nut, pine nut, coconut, and chestnut. Frequency of consumption may depend on export/import trade: hazelnut and cashew nut in France, cashew nut in Australia, walnut and cashew nut in the US, Brazil nut in the UK. Onset of these allergies is early and evolution to multiple sensitization and multiple allergies has been demonstrated. Severity is identical to that of peanut allergy. Nut allergy is the second most common cause of fatal anaphylaxis. Assay of specific IgEs is insufficient to indicate allergy or tolerance. Prick-tests are more helpful and can rule out allergy if they are negative (high negative predictive value). Conversely, positive values, between 3 and 8 mm, are not conclusive proof of allergy. Allergy is particularly severe with cashew nuts, Brazil nuts, and pecan nuts. Allergy to coconut is rare. Major recombinant nut allergens to identify specific IgEs will soon be available and an improvement of the diagnosis of allergy may be expected.

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Nut allergy is increasing, and is currently more common than peanut allergy in adults. However, peanut allergy continues to predominate in children.

Eleven different types of nut are eaten regularly: hazelnut, walnut, almond, pistachio, cashew nut, pecan nut, Brazil nut, Macadamia nut, pine nut, coconut and chestnut. Taxonomy is highly varied. Pistachio and cashew nut belong to the family of Anacardiaceae (Table 1).

■ **The frequency of allergies to different nuts** varies in different countries (Table 2). Hazelnut allergy predominates in France: 58.8% of cases of nut allergens (CICBAA¹ data), Brazil nut allergy is a specificity of UK (1, 2). 30% of nut allergies in the US are to walnut and another 30% to cashew nut (3). Cashew nut is responsible for 74% of nut allergies in Australia (4). These disparities probably reflect different importation circuits which result in different eating habits. According to a major North American study (5), the mean age of onset of nut allergy in children is two years later than that of peanut allergy, i.e. at the mean age of 36 months. In 1999, Pumphrey in the UK showed

that out of 731 sera of patients with nut allergy, 61% contained IgE specific to two different nuts and 44.9% to three different nuts (6). Clark confirmed that the problem increased with age: 19% of two-year olds allergic to nuts were polysensitized and 86% of children between 5 and 14 years. The increase in multiple allergies is similar: 2% at the age of two years, 47% of children over five years (7).

Data on nut allergy in the CICBAA data base report 141 cases 87 cases in children and 54 in adults. It is clear from these data, that allergy to Anacardiaceae (cashew nuts and pistachio) predominate in children (fig. 1).

■ **The clinical feature** of nut allergy is its severity (8-13). A German study reported that 20% of severe food allergy-induced anaphylaxis cases are caused by pea-

- Hazelnut: *Corylus avellana*
- Walnut: *Juglans regia*
- Almond: *Prunus dulcis* (Rosaceae)
- Pistachio: *Pistacia vera* (Anacardiaceae)
- Chestnut: *Castanea sativa*
- Brazil nut: *Bertholletia excelsia*
- Cashew nut: *Anacardium occidentale*
- Pecan nut: *Carya illinoensis*
- Macadamia nut: *Macadamia integrifolia*
- Pine nut: *Pinus halepensis*
- Coconut: *Cocos nucifera*

Table 1: Taxonomy of edible nuts.

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nut, with other nuts accounting for a further 20% (9). Moreover, many patients react to either peanut or nuts (10). North American data for fatal anaphylaxis show that nuts rank second, and data for fatal cases in the UK between 1999 and 2006 showed the same (11, 12). In France, the data of the Allergy Vigilance Network show that nuts were responsible for 12.8% to 17.6% of severe anaphylaxis between 2003 and 2005, with a drop to 4.9% in 2006 followed by an increase to 22% during the first six months of 2007. Cashew nut was mostly incriminated (13).

■ **The natural history** of nut allergy shows that it is just as serious as peanut allergy, and is often persistent. According to Fleischer, 68% of people who are allergic to nuts are also allergic to peanut. Recovery from peanut allergy, or the fact that a patient is allergic to not more than two types of nut, are favourable predictors of recovery. Conversely, if the patient presents with multiple food allergies, it is likely that food allergy will not resolve. Fleischer observed 13% of multiple food allergies in tolerant subjects, and 44% in subjects with positive oral challenge (3).

■ **Diagnosing nut allergy** has been particularly well studied. Fleischer showed that in patients with negative search for specific IgEs, 25% had a food allergy.

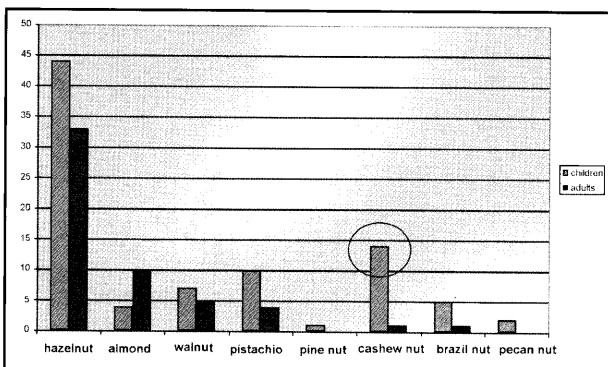


Figure 1: Nut allergies in 87 children and 54 adults (CICBAA data).

Clark and Ewan found the same percentage (22.5%) in 1,000 patients allergic to nuts. Prick-tests were more effective, since only 0.5% of allergic patients had negative results to prick-tests. There is high probability of allergy where prick-test wheals exceed 8 mm for walnut, hazelnut and cashew nut (PPV: 95%) (14). Unfortunately, prick-test wheals between 3 and 7 mm, even with specific IgE exceeding 15 kU/l, are not completely conclusive since they may be found in people who tolerate these nuts (2).

■ Nuts have specific characteristics:

➤ **Cashew nut allergy** is the most common nut allergy in France. Data from the CICBAA data base confirm this, as does a study in 42 children (15, 16). In this study, mean age was two years, and there was often cross-reactivity between cashew nut and pistachio (another Anacardiaceae). Mean prick-test wheals were 7 mm, and specific IgE were 3.1 kU/l. Potential severity was confirmed by one death following liver transplant from a donor who died of anaphylaxis caused by peanut and whose serum also contained IgEs specific to cashew nut (17).

➤ **Brazil nut allergy** is rarer in France (5 cases out of 141 nut allergies in the CICBAA data base). However, it is the second most commonly implicated nut in UK and one death has just been reported to the Allergy Vigilance Network. Anaphylactic shock occurred following a prick-test (18). A recent case of allergy by proxy concerned a woman whose partner had eaten Brazil nut before sexual intercourse and whose sperm was tested positive to a prick-test (19). As for all nuts, prick-test results of just a few millimetres and specific IgE blood levels less than 3.5 kU per litre can correspond to serious allergy (20).

➤ **Pecan nut allergy** has caused at least two deaths (21, 22). It has been demonstrated that when pecan nuts are heated, neoallergens appear (23). There are lots of pecan tree plantations in Israel and there is marked sensitization to pecan tree pollen (24). It is not

	hazelnut	walnut	cashew	pistachio	Brazil	almond	pecan	pine nut
CICBAA France, 2007* (141 cases)	58.8%	6.5 %	10.3 %	9.3 %	4.6 %	7.4 %	1.8 %	0.9%
Fleischer USA 2005 (278 cases)	5%	30 %	30%	4%	3%	3%	14%	
Davoren 2005 Australia		-	74.1%	-	-	-	-	-
Clark 2003 UK	63 cases	-	29 cases	-	162 cases	-	-	-
Ewan, 1996, 2003 UK	16.1%	-	-	-	29%	22.5%	-	-

Table 2: Relative frequency of food allergy to different types of nuts according to country.

* CICBAA data bank: computerized data of 1137 patients with food allergy. 141 patients with nut allergy have been registered. Nut allergy has been demonstrated by prick-tests specific IgEs and positive double or simple blind placebo-controlled food challenges.

known whether this presents a particular risk of food allergy to this nut.

➤ **Hazelnut allergy** is the most common allergy in France. All clinical pictures are observed, with a predominance of oral syndrome in patients sensitized to Betulaceae pollen, but anaphylactic shocks and angioedema may occur, probably related to a different major allergen. In fact, Cor a 1, a Bet v 1 homologue, is incriminated in oral syndrome, and Cor a 8, a lipid transfer protein is involved in more serious reactions. Out of the 63 cases of hazelnut allergy recorded in the CICBAA data base, we observed a wide range of clinical profiles: 27% of subjects had isolated hazelnut allergy, 27% were also allergic to Prunoideae, 11% had an associated allergy to Apiaceae (celery, carrot), 25% had an associated allergy to peanut. Finally, 9.5% had other associated food allergies. Most of these French cases are probably related to Cor a 1, since clinical symptoms are mild and since in all these cases, prick-test to a chocolate cream with ground hazelnut (Nutella) is negative. In this food product, hazelnut has been heated up to 180°C.

➤ **Coconut allergy**, unlike the preceding allergies, is very rare, and is described as being cross-reactive to peanut and hazelnut (25, 26). The CICBAA data base has no cases out of more than 1,100 reported food allergies. In subjects allergic to peanut, screening for cross-sensitization showed that only 10% of the prick-tests were positive. This is a third of the rate with other nuts. Some cases have been published, including two recently; one was a case of severe anaphylaxis in a patient allergic to nuts. The study identified a 29 kDa allergen which is a 7S globulin crossing with a nut protein and destroyed by pepsin within 60 seconds (27). Allergists must therefore be increasingly vigilant, and test for the whole range of nuts when carrying out prick-tests. However, the size of prick-test wheals and the level of specific IgEs are currently no guarantee of allergy or tolerance, needing standardized oral challenges in patients requiring an assurance that they can safely consume these nuts. Which is why the possibility of detecting IgE specific to major recombinant nut allergens is eagerly awaited to help the diagnosis of clinical relevance of such sensitivities.

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