Allergen Data Collection:
Peanut *(Arachis hypogaea)*

Authors in alphabetical order [contact information]

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Abstract

Among food allergy, peanut allergy is common and severe. Epidemiologic studies of the general population estimate a prevalence rate of 0.5%, and peanut allergy accounts for 10-47% of food-induced anaphylactic reactions. Symptoms may vary in severity from mild urticaria or localized oral symptoms, to severe systemic reactions that can be fatal. Reactions typically occur within a few minutes following ingestion. Peanut hypersensitivity usually begins in early childhood and usually persists throughout life, with only a small percentage of young children achieving tolerance.

Diagnosis rests upon a clear history of severe reaction with laboratory evidence of peanut-specific IgE antibody. Reactions could be confirmed by oral challenge procedures, when anaphylactic reactions are not expected. Diagnostic skin prick tests and determination of specific IgE are sensitive and have an excellent negative predictive value. Since very small amounts of peanut protein can elicit an allergic response, and the food is ubiquitous in most food supplies, accidental ingestion with reaction is common. Hidden peanut proteins have been reported as causes of adverse reactions to confectionary products, pastry, and Asian food. While crude peanut oil can induce allergic reactions, the allergenicity of refined peanut oils is controversial. Although peanut shares cross-reacting proteins with other legumes (e.g. - soybean, pea), clinical cross reactivity is not common, except for possibly lupine. Allergy to peanut most commonly occurs in atopic individuals who may have other food allergies (e.g. - egg, tree nut), but there are no known clinically relevant cross reacting proteins with tree nuts (e.g. - walnut). Peanuts and its products should always be declared according to a list of the Codex Alimentarius Commission on mandatory labelling of prepackaged foods. Although there are some promising advances in immunotherapy of peanut allergy, the only currently available treatment consists of strict avoidance with immediate availability of epinephrine for self-injection in the event of an accidental ingestion.

Three major peanut allergens are recognized by more than 50% of peanut allergic individuals: Ara h 1 (vicilin), Ara h 2 (conglutin- homologue protein), and Ara h 3 / Ara h 4 (glycinin). These allergens are seed storage proteins and their primary structure and major IgE-binding epitopes have been characterized. More recently three additional minor allergens Ara h 6 and Ara h 7 (both conglutin-homologue proteins) as well as the plant pan- allergen profilin (Ara h 5) were described.
The present review summarizes data on prevalence, symptoms, diagnostic features, immunotherapy, allergen stability, and allergen sources as well as molecular biological and allergenic properties of the major peanut allergens in tabular form.
(Internet Symposium on Food Allergens 2000, 2(2):87-122)

Contents

1 Prevalence of Peanut Allergy

1.1 General Population

Prevalences within the author's selected populations are listed. Those that are assigned randomly selected ("unselected") with numbers more than 500 may be regarded as representative of the "general population". Inclusion criteria may involve circumstances not related to atopic predisposition according to current knowledge.

Country / Subjects	Allergy / Sensitivity to	References
Sweden *(Göteborg, Uppsala, Västerbotten)* 1397 unselected adults, age of 20-44 years (study period 1991-92)	peanut 3% (RAST)	Björnsson et al. 1996
UK a) 16420 randomly selected adults (age of >15 years) b) based on 124 interview confirmed peanut allergic individuals (all ages) (questionniare)	a) peanut 0.4% b) peanut 0.5%	Emmett et al. 1999
UK, Isle of Wight 1218 unselected children (birth cohort study: born in 1989-1990, reviewed at 1, 2, and 4 years of age)	peanut 1.1% (SPT, RAST) peanut 0.5% (allergic reactions)	Tariq et al. 1996
USA 12032 randomly selected individuals (questionnaire): a) children (age of <18 years) b) adults (age of >18years) c) children and adults	a) peanut 0.4% (self-reported) b) peanut 0.7% (self-reported) c) peanut or tree nut 1.1% (corrected for typical IgE-mediated symptoms)	Sicherer et al. 1999b

1.2 Subjects with Atopic or Other Diseases

Country / Subjects	Allergy / Sensitivity to	References
Australia, Parkville 42 children with cow's milk allergy (followed for 2 years)	peanut 55% (SPT)	Hill et al. 1994
Australia, Victoria 100 cow's milk allergic children	peanut 34% (parents reported)	Bishop et al. 1990
France 81 cases of anaphylactic shock to food (from 1991-92)	peanut and other legumes 3%	Moneret-Vautrin & Kanny 1995
France 80 cases of food- related anaphylaxis (from 1993-97)	peanut 11% (reported to CICBAA databank)	European Commission 1998
France, Pierre Benite a) 580 patients with adverse reactions to food b) 60 cases of anaphylaxis (study period 1984-92)	a) peanut 37% (RAST) b) peanut 12%	Andre et al. 1994
France, Toulouse a) 142 food allergic children b) 378 food allergic children	a) peanut 42% (labial food challenge) b) peanut 34% (food challenge)	a) Rance & Dutau 1997 b) Rance et al. 1999a
Germany, Bonn 150 children allergic to egg white, milk, cod fish, wheat, peanut and/or soybean	peanut 59% (RAST)	Liappis & Starke 1999

Italy, Florence 102 children with grass pollen allergy	peanut 22.5% (epicutaneous skin test)	de Martino et al. 1988
Italy, Florence 54 episodes of food-dependent anaphylaxis in 44 children (age of 1 month to 16 years) (from 1994-1996)	peanut 1.9%	Novembre et al. 1998
Italy, Genua 132 pollen and food sensitive patients	peanut 6.6% (self-reported)	Troise et al. 1992
Italy, Milan 262 fruit and/or vegetable allergic patients	peanut 36% (clinical history, SPT, RAST)	Ortolani et al. 1988
Netherlands 131 cases of food- induced anaphylaxis (from 1993-1997)	peanut 23% (survey, reported to the TNO Nutrition and Food Research Institute)	European Commission 1998
Netherlands, Rotterdam 91 patients with atopic dermatitis (<5 years of age)	peanut 34% (SAFT)	Oranje et al. 1992
Poland 163 food allergic infants	peanut 29% (RAST)	Hofman 1994
Singapore 124 children with food- induced anaphylaxis (study period 1992-96)	no severe reactions to peanut (clinical history)	Goh et al. 1999
Spain, Barcelona 102 patients allergic to dried fruits	peanut 80%, 73%, and 68% (SPT, HR, and RAST)	Amat Par et al. 1990
Spain, Madrid 355 food allergic children	legumes 19% (of patients, SPT, RAST) peanut 3.9% (of 608 positiv results, SPT, RAST)	Crespo et al. 1995
Spain, Madrid 29 plant-derived food allergic patients	peanut 10% (SPT, RAST)	Diez-Gomez et al. 1999
Spain, Salamanca 84 mugwort sensitive patients without other pollen sensitizations	peanut 1.2% (RAST)	Garcia-Ortiz et al. 1996
South Africa, Cape Town 112 children with atopic dermatitis (age of 5 months to 13 years)	peanut 14% (questionnaire)	Steinman & Potter 1994
Sweden 61 cases of food- induced anaphylaxis (from 1994-1996)	peanut 21% (reported to the National Food Administration)	European Commission 1998
Sweden 55 cases of food- induced anaphylaxis (from 1994-1996)	peanut 36% (Hospital Reports)	European Commission 1998
Sweden, Halmstad / Malmö a) 380 birch pollen allergic patients b) 103 patients without birch pollen allergy	a) peanut 14% b) peanut 4% (questionnaire)	Eriksson et al. 1982
Switzerland, Zurich a) 402 food allergic adults (study period 1978-87) b) 383 food allergic patients (study period 1990-94)	a) peanut 1.5% b) peanut 13% (anamnesis, clinical relevance, diagnostic tests)	a) Wüthrich 1993 b) Etesamifar & Wüthrich 1998
UK, London 100 patients with food intolerance	nuts/peanut 22% (repeated challenge)	Lessof et al. 1980

UK, Manchester 90 patients experienced anaphylactic reactions to foods (from 1994-1996)	peanut 47% legumes (excluding peanut) 4.6% (suspected cause of patients' worst reaction)	Pumphrey & Stanworth 1996
USA, Baltimore, MD 196 food-allergic patients with atopic dermatitis	peanut 49% (DBPCFC, n=41)	Sampson & Ho 1997
USA, Denver, CO a) 74 food allergic children (age of <3 years) b) 111 food allergic children (age of 3-19 years)	a) peanut 18% (DBPCFC) b) peanut 41% (DBPCFC)	Bock & Atkins 1990
USA, Little Rock, AR 165 patients with atopic dermatitis	peanut 33% (SPT) from which 27/44 were DBPCFC-positive	Burks et al. 1998a
USA, Memphis, TN 266 patients with anaphylaxis (age of 12-75 years, study period 1978-92)	peanut 22% (from 89 food induced cases)	Kemp et al. 1995
USA, Providence, RI 248 atopic patients evaluated for allergy	peanut 3.2% (skin scratch test), from which 5/8 presented clinical relevance	Kalliel et al. 1989
USA, Rochester, MN 18 patients with food- related anaphylaxis	peanut in 4 cases	Yocum & Khan 1994

1.3 Prevalence of Associated Allergies

Country / Subjects	Allergy / Sensitivity to	References
Spain, Barcelona 65 patients sensitive to peanuts	tree pollen 49% weed pollen 32% grass pollen 23% (2 out of 3 tests positive: SPT, HR, RAST)	Amat Par et al. 1990
South Africa, Cape Town 25 peanut-sensitized children (age of 0-3 years)	egg 64% milk 64% soybean 52% wheat 28% codfish 24% (RAST)	Frank et al. 1999
UK, Birmingham 96 children with peanut and/or nut allergy (age of 18 months to 18 years) a) history of peanut allergy b) history of tree nut allergy	a) tree nuts 18% (direct challenge) a) tree nuts 47% (RAST) b) peanut 21% (direct challenge)	Armstrong & Rylance 1999
UK, Cambridge 62 patients with peanut and/or nut allergy (age of 11 months to 53 years)	peanut 65% brazil nut 29% almond 23% hazelnut 21% walnut 13% cashew nut 4.8% (clinical history, SPT)	Ewan 1996
UK, Cambridge 55 patients with peanut and/or nut allergy (age of 11 months to 53 years)	house dust mites 69% grass pollen 36% tree pollen 3.6% cat 35% dog 15% egg 18% milk 7.3% other legumes 7.3% sesame 7.3% (SPT)	Ewan 1996

UK, Manchester 731 patients with at least one positive RAST result to peanut, brazil nut or hazelnut (age 7 months to 65 years, median 6.6 years) (study period 1994-98)	one nut 39% two nuts 18% all three nuts 44% similar pattern in all age groups (RAST >0.35 kU/L)	Pumphrey et al. 1999
UK, Southampton 60 adults with proven peanut allergy	(reported) (SPT) soybean 5% 53% tree nuts 56% 83% milk 3% 20% egg 13% 16% grass pollen 81% house dust mites 70% cat (n=44) 77%	Hourihane et al. 1997a
USA, New York, NY 68 peanut-, 20 tree nut-, and 34 peanut and tree nut reactive children (age of 6 months to 9 years), (tested sera from 111 children of these)	Correlation of peanut specific IgE to: hazelnut 0.60 almond 0.58 brazil nut 0.56 sesame 0.50 pine nut 0.37 pistachio 0.26 walnut 0.24 pecan nut 0.23 (RAST)	Sicherer et al. 1998

2 Outgrowing / Persistence of Peanut Allergy

Country / Subjects	Allergy / Sensitivity	References
France, Nancy and Toulouse 192 children with peanut allergy	Sensitivity to peanut according to age groups: 0-1 year in 11% 1-3 years in 44% 3-6 years in 26% 6-15 years in 19% (SPT and/or RAST, food challenge)	Rance et al. 1999b
UK, Manchester, Southampton 120 children evaluated of suspected peanut allergy (median age of resolvers 5 years, range 2-9 years)	18% resolved peanut allergy (criteria: clear history of peanut allergy and negative oral challenge with peanut or peanut butter)	Hourihane et al. 1998b
USA Food allergic patients	soy, egg, milk, wheat, and peanut: 26% loss (after 1 year of onset, DBPCFC)	Sampson & Scanlon 1989
USA, Denver, CO 32 children with peanut allergy (DBPCFC positive)	2 to 14 years after first positive DBPCFC none of the patients lost clinical sensitivity to peanut	Bock & Atkins 1989

3 Symptoms of Peanut Allergy

Symptoms & Case Reports	References
systemic reactions anaphylaxis (4, 6, 10, 14, 15, 16), excercise induced anaphylaxis (12), fatal reactions (5, 7, 9, 10, 15) cutaneous symptoms angioedema (2, 3, 7, 11, 14), atopic dermatitis (6, 14, 16), contact urticaria (2, 13, 14), eczema (1), erythema (11), pruritus (14), urticaria (1, 3, 16) gastrointestinal symptoms abdominal pain (1), burning mouth (8), diarrhea (1), nausea (1), oral allergy syndrome (14), vomiting (1, 3), general (14) respiratory symptoms allergic rhinitis (1, 14), asthma (7), choking (3, 11), conjunctivitis (1), dyspnea (14), laryngeal oedema (11), rhinorrhoea (3), sneezing (1), wheeze (1, 3, 16) other symptoms collapse (14), loss of consciousness (11)	(1) Bock et al. 1978b (2) Mathias 1983 (3) Kemp et al. 1985 (4) Ortolani et al. 1988 (5) Yunginger et al. 1988 (6) Burks et al. 1989 (7) Settipane 1989 (8) Whitley et al. 1991 (9) Sampson et al. 1992 (10) Malmheden Yman et al. 1994 (11) Ewan 1996 (12) Guinnepain et al. 1996 (13) Cantani 1997 (14) de Jong et al. 1998 (15) Foucard & Malmheden Yman 1999 (16) Szabo & Eigenmann 2000

Percentage of Reactions

Symptoms / Ref.	(1)	(2)	(3)	(4)	(5)	(6)
Anaphylaxis			6%		6%	4.7%
Collapse / fainting	7%					
Cyanosis	14%					
Cutaneous		95%		94%		
Angio-oedema			37%			
Atopic dermatitis			40%		43%	46%
Facial swelling	72%					
Itch	55%					
Rash	65%					
Urticaria / Angio-oedema						32%
Gastrointestinal		65%	1.4%	34%	1.5%	2%
Abdominal pain / cramp	21%					
Oral allergy syndrome					0.7%	0.5%
Vomiting	38%					
Respiratory		35%		42%		
Asthma			14%		14%	15%
Breathing difficulty	37%					
Wheeze	38%					
Hoarseness					35%	
No. of patients	406	20	142	102	132	192

(1) first reaction (questionnaire)
(2) children, symptoms after DBPCFC
(3) age of 6 months to 27 years
(4) median age of 7.4 years (questionnaire)
(5) age of 6 months to 15 years
(6) age of 0-15 years

(1) Hourihane et al. 1997b
(2) Sampson & Ho 1997
(3) Moneret-Vautrin et al. 1998
(4) Sicherer et al. 1998
(5) Rance & Dutau 1999
(6) Rance et al. 1999b

Onset of Symptoms

52% of patients reported immediate type reactions, onset of symptoms after exposure to peanut within 5 min in 76% and within 30 min in 93% of 622 self- reported peanut allergic subjects (questionnaire) (1)
Onset of symptoms after ingestion of peanut proteins within 3 min (median, range 0.3 to 45 min) in 102 peanut allergic children (2)

(1) Hourihane et al. 1997b
(2) Sicherer et al. 1998

Age at Onset of Peanut Allergy

Onset of peanut allergy in 55 children with peanut and/or nut allergy at age of:
<1 year in 20%, <2 years in 42%, <3 years in 49%, <5 years in 71%, and <7 years in 75% (cumulative percentage) (1)
Onset of peanut allergy in 142 children with peanut allergy at age of:
<1 year in 46%, <3 years in 80%, and <15 years in 93% (cumulative percentage) (2)
Median age at first reaction 24 months (range 6 to 108 months) in 102 peanut allergic children (3)

(1) Ewan 1996
(2) Moneret-Vautrin et al. 1998
(3) Sicherer et al. 1998

Threshold for Elicitation of Symptoms Amounts of peanut inducing symptoms: 100 mg - 8 g dry weight (DBPCFC, 14 peanut allergic children) (1) Amounts of peanut protein inducing objective symptoms: 5 mg (systemic reaction), 2 and 50 mg (mild reactions); subjective symptoms: 1-5 mg and 4-50 mg; short- lived subjective symptoms to preceeding doses of 100 µg in 2 cases (DBPCFC with peanut flour, 14 peanut allergic patients) (2) Amounts of peanut inducing symptoms: <100 mg in 25%, 100-1000 mg in 62.5%, and 1-7 g in 12.5% (DBPCFC, 50 peanut allergic patients) (3) Amounts of peanut inducing symptoms: </= 500 mg in 26%, 500 mg to 2.7 g in 43.5%, 2.7 to 4.3 g in 13%, 4.3 to 8 g in 8.7%, and >8 g in 8.7% (DBPCFC, 24 peanut allergic children with atopic dermatitis) (4)	(1) Bock et al. 1978b (2) Hourihane et al. 1997c (3) Moneret-Vautrin et al. 1998 (4) Sicherer et al. 2000b
Allergen Contact Route 90% of patients reported reactions after ingestion of less than 1 peanut and 50% reported reactions after skin contact (622 patients with self-reported peanut allergy, questionnaire) (1) Symptoms occurred in 40% after ingestion, in 20% after skin contact, and in 40% after inhalation of peanut allergens (35 individuals experiencing self- reported allergic reactions to peanut on airliners, questionnaire) (2)	(1) Hourihane et al. 1997b (2) Sicherer et al. 1999a

4 Diagnostic Features of Peanut Allergy

Family History

Family History

Relatives	Reported Peanut Allergy	Ref.
monozygotic twins (n=14)	in 64% (concordance)	(2)
dizygotic twins (n=44)	in 7% (concordance)	(2)
Siblings (n=610)	in 7%	(1)
Mothers (n=609)	in 2.3%	(1)
Fathers (n=609)	in 0.8%	(1)
Aunts / uncles (n=1213)	in 0.6%	(1)
Grandparents (n=2409)	in 0.1%	(1)

(1) Questionnaire: 622 adults and children with reported, suspected, or known peanut allergy: Atopy significantly more common in successive generations and more common in maternal than paternal relatives
(2) Questionnaire: 58 twin pairs with at least one member with convincing history of peanut allergy

References

(1) Hourihane et al. 1996

(2) Sicherer et al. 2000a

Parameters / Subjects	Outcome	References
Predictors of Peanut Allergy 1218 unselected children (birth cohort study: born in 1989-1990, reviewed at 1, 2, and 4 years of age)	Family history (92% in peanut allergic vs. 58% in non-peanut allergic children), allergy to egg (23% vs. 2.2% in SPT), and eczema (at age of 4 years) were important predictors for peanut allergy (all predictors have poor positive predictive values)	Tariq et al. 1996
Maternal Peanut Consumption 15 nut-sensitized children including 13 peanut- sensitized children (SPT, RAST)	Maternal peanut and/or tree nut ingestion during pregnancy and/or lactation did not increase sensitization to nuts in children	Tariq et al. 1996

Maternal Peanut Consumption a) 25 peanut-sensitized children (age of 0-3 years) b) 18 controls (milk and/or egg sensitive, not to peanut)	Consumption of peanuts during pregnancy (and lactation): a) 48% of mothers consumed peanuts more than once a week (during lactation: 30%), b) 19% of mothers consumed peanuts more than once a week (during lactation: 17%) (p=0.063 and p=0.47)	Frank et al. 1999
Reactions to First Exposure (1) 8 infants with immediate hypersensitivity reactions to foods (milk, egg, or peanut) (2) 622 adults and children with reported, suspected, or known peanut allergy (questionnaire) (3) 102 peanut allergic children (questionnaire)	Symptoms occurring at the first- known exposure: irritability, erythematous rash, urticaria, angio-oedema, vomiting, rhinorrhoea, and cough (positive SPT in every case) (1) Reactions to first obvious exposure reported in 81% (2) and 72% (3) of patients	(1) van Asperen et al. 1983 (2) Hourihane et al. 1997b (3) Sicherer et al. 1998
Resolved, Persistent Allergy a) 15 children with persistent peanut allergy b) 15 children with resolved peanut allergy (both age of 5-38 months)	Allergy to other foods: a) in 60%, b) 13% (p=0.02) Wheal size of <6 mm (SPT): a) in 21%, b) in 100% (p<0.0001) No difference in total and peanut- specific serum IgE; some children will be tolerant to peanut despite a history of reactions and positive SPT (open challenge, SPT, PRIST, RAST)	Hourihane et al. 1998b
Puncture Skin Test, DBPCFC 26 peanut sensitive children (5 months to 15 years of age)	46% of skin test positive patients were positive in DBPCFC	Bock et al. 1978a
SPT, Extracts 104 children tested for evaluation of allergic disease	Raw, roasted (145°C, 1 h) and commercial peanut extracts tested: roasted extract had best specificity in SPT (8 children with peanut allergy after ingestion of peanut or peanut products)	Kemp et al. 1985
SPT, Extracts peanut allergic patients	Comparison of 6 commercial SPT extracts: Differences in contents of major allergens Ara h 1 and Ara h 2, protein pattern was the same in extracts from roasted peanuts but varied in extracts from raw peanuts, all extracts reactive in SPT (RAST inhibition, SDS-PAGE immunoblot)	Hefle et al. 1995
SPT, Extracts peanut allergic patients	SPT results with a) commercial extracts and b) fresh peanuts as compared to labial food challenge: Positive SPT a) 50%, b) 80% Sensitivity a) 66%, b) 90% Specificity a) 69%, b) 30%	Rance et al. 1997
a) ***RAST and Clinical Relevance*** **b)** ***SPT and Clinical Relevance*** 24 patients with clinical history of peanut allergy (oral allergy syndrome)	a) RAST (specific IgE > 0.7 kU/L): positive results in 42% positive preditive value 48% negative preditive value 55% b) SPT with commercial extracts and fresh food: positive results in 67% and 13% positive preditive value 51% and 59% negative preditive value 62% and 55%	Ortolani et al. 1989
SPT and DBPCFC peanut allergic patients a) <3 years, b) 3-19 years of age	SPT (> 3 mm) positive predictive value a) 72%, b) 45% negative predictive value a) and b) 100%	Bock & Atkins 1990
SPT and DBPCFC Children suspected of IgE- mediated symptoms of peanut allergy	Significant differences in SPT (wheal sizes) between peanut allergic or tolerant individuals (DBPCFC) (P < 0.05); SPT cut-off values mean diameter 6 mm / surface area of wheal 40 mm2	Eigenmann & Sampson 1998

<table>
<tr><td>a) RAST and DBPCFC
b) SPT and DBPCFC
food-allergic children with atopic dermatitis</td><td>a) predictive values Phadebas RAST score >/= 3
positive preditive value 44%
negative preditive value 100%
b) predictive values of SPT (> 3 mm)
positive preditive value 44%
negative preditive value 100%</td><td>Sampson & Albergo 1984</td></tr>
<tr><td>SPT and DBPCFC
60 children with positive prick test to peanuts</td><td>52% true positive, 48% false positive as compared to DBPCFC; wheal diameter significantly greater in DBPCFC positive children (median 25 mm vs. 5 mm, p<0.001)</td><td>Bernhisel-Broadbent & Sampson 1989</td></tr>
<tr><td>a) RAST and DBPCFC
b) SPT and DBPCFC
food-allergic children with atopic dermatitis</td><td>a) predictive values of specific IgE > 0.35 kU/L
positive predictive value 78%
(>95% at IgE 15 kU/L)
negative predictive value 85%
b) predictive values of SPT (> 3 mm)
positive predictive value 55%
negative predictive value 75%</td><td>Sampson & Ho 1997</td></tr>
<tr><td>Negative Tests, Open Challenge
17 children with negative SPT or RAST perceived to be peanut or nut sensitive</td><td>Simple open challenge procedure:
2 positive challenges with peanuts; clinical sensitivity persisted in 2 children despite negative SPT and RAST tests</td><td>Baker et al. 1999</td></tr>
<tr><td>Clinical Severity, Immunoblot
89 peanut allergic patients</td><td>Sensitivity to 15 kDa allergen significantly associated with severe symptoms (wheeze, cyanosis) but not to skin or gut symptoms; patients with specific IgE to 15 kDa allergen presented with mild 30%, moderate 36%, and severe reactions 72% (p<0.005); no significant differences for 17 and 63 kDa allergens (SDS-PAGE immunoblot)</td><td>Clarke et al. 1998</td></tr>
<tr><td>Specific IgE, IgG, IgG4
10 peanut allergic patients (age of 3 months to 20 years)</td><td>Positivity of serum immunoglobulins in patients:
<table><tr><th>Specific</th><th>IgE</th><th>IgG</th><th>IgG4</th></tr><tr><td>Ara h 1*</td><td>60%</td><td>80%</td><td>50%</td></tr><tr><td>Ara h 2*</td><td>80%</td><td>90%</td><td>80%</td></tr><tr><td>Ara h 3*</td><td>70%</td><td>90%</td><td>80%</td></tr></table>* presumed according to Mr of appr. 60, 16, and 14 kDa (SDS-PAGE immunoblot)
Similar IgE and IgG binding patterns</td><td>Szabo & Eigenmann 2000</td></tr>
<tr><td>Levels of Specific IgE
a) 70 peanut allergic children (age of 1-16 years)
b) 21 peanut allergic adults (age of 17-38 years)</td><td>Peanut specific IgE levels (RAST):
a) 49 kU/L (median)
b) 20 kU/L (median)</td><td>Clarke et al. 1998</td></tr>
<tr><td>Levels of Specific IgE
a) 91 peanut reactive children
b) 13 non-reactive children</td><td>Peanut specific IgE levels (RAST):
a) 52 (mean), 46 (median) kU/L
b) 2.8 (mean), 0.5 (median) kU/L
(p<0.0001)</td><td>Sicherer et al. 1998</td></tr>
<tr><td>Spontaneous Histamine Release
Children sensitive to peanut or other foods (3-16 years)</td><td>High spontaneous histamine release of basophils in vitro only in sensitized persons (predominantly to food antigens)</td><td>May & Remigio 1981</td></tr>
<tr><td>Heavy Chain Variable Region of IgE
2 patients with peanut allergy</td><td>Heavy chain variable region (VH) sequences of IgE from blood lymphocytes: predominantly VH1 family use; IgE VH sequences highly somatically mutated; in only 6/17 cases clear evidence for clustering of amino acids indicative of antigen selection (PCR amplification)</td><td>Janezic et al. 1998</td></tr>
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<tr><th>Cellular Parameters</th><th>References</th></tr>
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HLA Class II Genotypes

<table>
<tr><th>HLA Class II</th><th>Frequency</th><th>Ref.</th></tr>
<tr><td>DRB1*08</td><td>a vs. b (NS), b > c *</td><td>(1)</td></tr>
<tr><td>DRB1*08</td><td>a > c *, b > c *</td><td>(2)</td></tr>
<tr><td>DRB1*08/12 tyr 16</td><td>a > c *, b > c *</td><td>(2)</td></tr>
<tr><td>DQB1*04</td><td>a > c *, b > c *</td><td>(2)</td></tr>
<tr><td>DPB1*0101</td><td>a < c *</td><td>(2)</td></tr>
<tr><td>DPB1*0201</td><td>a < c *</td><td>(2)</td></tr>
<tr><td>DPB1*0301</td><td>a > c *</td><td>(2)</td></tr>
</table>

* significant, (NS) no significant difference

(1) a) grass pollen allergic, b) peanut allergic individuals, c) controls (80 patients with pollen- associated food allergy and 120 patients with pollinosis)
(2) a) 152 individuals from families containing at least 1 peanut allergic member and 9 unrelated patients, b) individuals from a) with peanut allergy, c) 293 unrelated controls

</td><td>(1) Boehncke et al. 1998
(2) Howell et al. 1998</td></tr>
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PBMC Proliferation, IFN-gamma, IL-4 *(Ara h 2)*
Stimulation of PBMC from peanut allergic patients, patients with asthma and nonatopic controls with Ara h 2 and *Candida albicans* allergens induced significantly higher levels of PBMC proliferation than ovalbumin, casein, and soy. Significantly lower IFN-gamma levels produced by PBMC from peanut allergic group after stimulation with Ara h 2. Inverse correlation between Ara h 2- specific serum IgE and IFN-gamma production in peanut allergic group. IL-4 expression in Ara h 2- stimulated PBMCs from peanut allergic group and control group (detection by PCR).

</td><td>Dorion et al. 1994</td></tr>
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PBMC Proliferation, IFN-gamma, IL-4, IL-5 *(Peanut Extract)*
Stimulation of PBMC from peanut allergic patients with crude peanut extract: significantly higher dose- dependent proliferation as compared to controls, peanut-specific T-cell clones from 1 selected patient were all CD4+/CD8- T helper cells with Th2 cytokine profile (high levels of IL-4 and IL-5, low or no IFN-gamma secretion)

</td><td>de Jong et al. 1996</td></tr>
<tr><td>

PBMC Proliferation, IFN-gamma, IL-4 *(Peanut Extract)*
Significantly higher proliferation of PBMCs in peanut allergic patients with atopic dermatits as compared to controls with and without atopic dermatitis. 80-100% of cells were CD4+, proliferative responses correlated significantly with increased IL-4 mRNA expression after peanut- specific stimulation. Polyclonal stimulation was preferentially associated with CD8+ cell proliferation.

</td><td>Laan et al. 1998</td></tr>
<tr><td>

PBMC Proliferation, Clinical Relevance, SPT, RAST *(Peanut Extract)*
Proliferation of PBMCs from peanut allergic patients stimulated with crude peanut extract was allergen-specific and dose- dependent, no correlation between PBMC proliferation and clinical severity, SPT reactions or peanut specific IgE levels (44 peanut allergic individuals, 13 non-peanut allergic controls)

</td><td>Hourihane et al. 1998a</td></tr>
<tr><td>

T-Cell Clones, HLA-Restriction
Peanut-reactive T-cell clones raised from a peanut- and Brazil nut-allergic individual without hazelnut allergy: T-cell clones were not cross- reactive to Brazil nut or hazelnut extracts (with the exception of 1 clone); peanut antigen recognition was associated with HLA-DR and HLA-DP but not with HLA-DQ MHC class II molecules; Th2-like profile of peanut specific clones (high levels of IL-4, low levels of IFN-gamma)

</td><td>Higgins et al. 1995</td></tr>
<tr><td>

T-Cell Receptor
Stimulation of T-cells from peanut allergic patients resulted in selective expansion of V beta 2+ T-cells (T-cell receptor variable beta regions)

</td><td>Dorion & Leung 1995</td></tr>
<tr><td>

T-Cells Preceeding Humoral IgE
Detection of peanut (Ara h 1) specific T-cell reactivity 3 months before peanut- specific IgE was detectable (1 child with initial cow's milk allergy and atopic dermatitis)

</td><td>van Reijsen et al. 1998</td></tr>
</table>

5 Therapy of Peanut Allergy

Treatment*	Outcome	References
Rush Immunotherapy 3 peanut allergic patients completed therapy	Subcutaneous injection therapy with increasing doses of peanut extract (4 per day for 5 days), 67-100% decrease in symptoms (DBPCPC), reduction in end point SPT reactivity to peanut extract, all peanut- treated subjects were able to reach maintenance dose, incidence of systemic reactions during immunotherapy was 13% in a total of 120 injections (no anaphylactic reaction occurred)	Oppenheimer et al. 1992
Immunotherapy 6 peanut allergic patients underwent therapy, 6 peanut allergic controls	Rush protocol with injections of increasing doses of aqueous peanut extracts maintained with weekly injections > 1 year. All treated patients experienced increased dose tolerance in DBPCFC. 3 patients remained tolerant of the full maintenance dose of injections and maintained increased oral tolerance. Part ial or complete loss of protection in 2 and 1 patient who required dose reduction because of systemic reactions. Systemic reactions common in treated group both during rush immunotherapy and maintenance injections. Unmodified peanut extracts not suitable for immunotherapy.	Nelson et al. 1997
Gene Immunization in Mice Immunization of different mice strains with plasmid DNA encoding peanut allergen Ara h 2	After pDNA immunization mice were challenged with Ara h 2 or peanut protein injections: immunized C3H mice strain expierienced anaphylactic reactions, while AKR/J and BALB/c mice had no reactions	Li et al. 1999
Oral Gene Immunization in Mice Immunization of mice by oral administration of nanoparticles (plasmid DNA encoding peanut allergen Ara h 2 complexed with chitosan)	Transduced gene expression in the intestinal epithelium in mice (strain AKR/J). Mice receiving nanoparticles produced secretory IgA and serum IgG2a (with low levels of IgE) and showed substantial reduction in allergen- induced anaphylaxis as compared with non- immunized mice or mice treated with 'naked' DNA	Roy et al. 1999

* Studies may be experimental, unproved, or controversial. Please notice the disclaimer !

6 Composition of Peanuts

6.1 Distribution of Nutrients (raw seeds)

For other peanut products see: USDA Nutrient Database

Nutrients: Content per 100 g		
Energy 2464 kJ (583 kcal)	Iodine 13 µg	Met 310 mg
Water 5.2 g	Selenium 2 µg	Phe 1540 mg
Protein 25.3 g		Thr 850 mg
Lipid 48.1g	**Vitamins**	Trp 320 mg
Carbohydrate 12.1 g	Carotin 10µg	Tyr 1190 mg
Fiber 7.1 g	Vitamin E 9100 µg	Val 1450 mg
Minerals 2.2 g	Vitamin B1 900 µg	
	Vitamin B2 150 µg	**Carbohydrates**
Minerals	Nicotinamide 15 mg	Starch 5500 mg
Sodium 5 mg	Pantothenic acid 2600 µg	
Potassium 750 mg	Vitamin B6 300 µg	**Lipids**
Magnesium 165 mg	Biotin 35 µg	Palmitic acid 5100 mg
Calcium 60 mg	Folic acid 55 µg	Stearic acid 1300 mg
Manganese 1 mg		Oleic acid 22.1 g
Iron 2110 µg	**Amino Acids**	Linolic acid 13.9 g
Copper 550 µg	Arg 3460 mg	Linoleic acid 530 mg
Zinc 3070 µg	His 710 mg	
Phosphorus 370 mg	Ile 1230 mg	**Others**
Chloride 7 mg	Leu 2030 mg	Salicylic acid 1120 µg
Fluoride 130 µg	Lys 1100 mg	Purines 90 mg

Reference: Deutsche Forschungsanstalt für Lebensmittelchemie, Garching bei München (ed), **Der kleine "Souci-Fachmann-Kraut" Lebensmitteltabelle für die Praxis**, WVG, Stuttgart 1991

6.2 Proteinfraction

Proteins / Glycoproteins	**Amount**
Soluble fractions	
albumines (water-soluble) globulines (salt-soluble)	15% 70%
65 kDa Allergen	1 % of crude peanut meal (1)
Ara h 2	6 % of crude protein extract (2)
Insoluble fraction	
glutelines	10%

References: (1) Barnett & Howden 1986, (2) Burks et al. 1992a

7 Allergens of Peanut

Proteins / Glycoproteins	Allergen Nomenclature	References
Vicilin [63.5 kDa]	Ara h 1	Burks et al. 1991, Burks et al. 1995c
Conglutin [17 kDa]	Ara h 2	Burks et al. 1992a, Stanley et al. 1997
Glycinin [14, 36, 57 kDa]	Ara h 3 / Ara h 4	Eigenmann et al. 1996, Kleber-Janke et al. 1999, Rabjohn et al. 1999
Profilin [14 kDa]	Ara h 5	Kleber-Janke et al. 1999
Conglutin-homologous protein [14.5 kDa]	Ara h 6	Kleber-Janke et al. 1999
Conglutin-homologous protein [16 kDa]	Ara h 7	Kleber-Janke et al. 1999
Peanut agglutinin [31 kDa]		Burks et al. 1994a
Peanut I: 20 and 30 kDa allergens		Sachs et al. 1981
65 kDa Allergen		Barnett & Howden 1986

7.1 Sensitization to Peanut Allergens

<table>
<tr><th>Country / Subjects</th><th>Sensitivity</th><th>References</th></tr>
<tr><td>Australia, North Ryde
a) 10 patients with peanut allergy
b) 8 peanut with peanut allergy</td><td>a) alpha-arachin, conarachin I, and concanavalin A-reactive glycoprotein gave significant RAST results; peanut lectin and phospholipase D gave poor RAST responses
b) peanut lectin: agglutinin (30 kDa) in all patients (RAST)</td><td>a) Barnett et al. 1983
b) Barnett & Howden 1987</td></tr>
<tr><td>France, Nancy
2 peanut allergic patients</td><td>a) Allergens from peanut kernels:
15, 18, 28, 41, and 67 kDa
b) Allergens from peanut shells:
18 and 41 kDa</td><td>Moutete et al. 1995</td></tr>
<tr><td>Germany, Borstel
9 peanut allergic patients</td><td>>50% to 17, 30, 48-66, and 116 kDa allergens (SDS-PAGE immunoblot)</td><td>Uhlemann et al. 1993</td></tr>
<tr><td>Germany, Borstel
40 peanut allergic patients</td><td><table><tr><th>6 Recombinant Allergens</th><th></th></tr><tr><td>Ara h 1</td><td>65%</td></tr><tr><td>Ara h 2</td><td>85%</td></tr><tr><td>Ara h 4 (Ara h 3)</td><td>53%</td></tr><tr><td>Ara h 5</td><td>13%</td></tr><tr><td>Ara h 6</td><td>38%</td></tr><tr><td>Ara h 7</td><td>43%</td></tr></table>(SDS-PAGE immunoblot)</td><td>Kleber-Janke et al. 1999</td></tr>
<tr><td>Netherlands, Zeist
14 peanut allergic patients</td><td><table><tr><th>13 Allergens from raw peanuts</th><th></th></tr><tr><td>18 kDa (Ara h 2)</td><td>80%</td></tr><tr><td>20 and 21 kDa</td><td>70%</td></tr><tr><td>40 kDa</td><td>60%</td></tr><tr><td>33 and 44 kDa</td><td>50%</td></tr><tr><td>14, 60, and 71 kDa</td><td>35%</td></tr><tr><td>36 kDa</td><td>30%</td></tr><tr><td>16, 28, 29 kDa</td><td></= 20%</td></tr></table>(SDS-PAGE immunoblot)</td><td>de Jong et al. 1998</td></tr>
</table>

UK, Southampton 91 peanut allergic patients	**19 Allergens from peanut powder**	
	63 kDa (Ara h 1)	73%
	17 kDa (Ara h 2)	71%
	15 kDa	54%
	10, 18, 27, 28, 30, and 51 kDa	30-45%
	7, 20, 21, 25, 33, 38, 44, 71, 96 and kDa	<30%
	(SDS-PAGE immunoblot)	
		Clarke et al. 1998
USA, Little Rock, AR 6 (a, b), 12 (c), and 18 (d) peanut allergic patients with atopic dermatitis	a) Ara h 1 in 100% b) Ara h 2 in 100% c) Agglutinin in 50% d) Ara h 3 in 44% (IgE specific ELISA) Weak IgE- binding inhibition by agglutinin	a) Burks et al. 1991 b) Burks et al. 1992a c) Burks et al. 1994a c) Rabjohn et al. 1999
USA, Madison, WI peanut allergic patients	38, 44, and 65 kDa allergens (SDS-PAGE immunoblot)	Hefle et al. 1990

7.2 Properties of Vicilin (Ara h 1)

7.2.1 Molecular Biological Properties

Vicilin			References
Allergen Nomenclature Ara h 1			(1) Larsen & Lowenstein 1999
Isoallergens and Variants 2 isoallergens in SDS-PAGE (1)			(1) Burks et al. 1991
Molecular Mass SDS-PAGE: 63.5 kDa (1), rAra h 1: 68 kDa (2)			(1) Burks et al. 1991 (2) Burks et al. 1995c
Isoelectric Point pI 4.55 (1)			(1) Burks et al. 1991
Amino Acid Sequence, mRNA, and cDNA			(1) Burks et al. 1995b, 1995c (2) de Jong et al. 1998
Ara h 1 (precursor)*	**Clone P17**	**Clone P41B**	
SWISS-PROT:	P43237	P43238	
GenBank:	L38853	L34402	
Amino acids	614 residues (1)	626 residues (1)	
mRNA	1949 bp, 2.3 kb (1)	2032 bp	
cDNA			
Gene			
* N-terminus of native protein (deduced from 2): aa 79 (P17) and aa 85 (P41B)			
Recombinant Protein cDNA expression library: Isolation of Ara h 1 mRNA by PCR (1, 2) expression in *Escherichia coli*: Expression of recombinant Ara h 1 selected from cDNA library (1) Subcloning into pDS56/RBSII vector and expression of recombinant Ara h 1 in E.coli M15 cells (2)			(1) Burks et al. 1995b, 1995c (2) Kleber-Janke et al. 1999
Formation of Oligomers Formation of stable trimeric structures of Ara h 1 measured by fluorescence polarization followed by SDS-PAGE of cross- linked Ara h 1 (1)			(1) Shin et al. 1998

Posttranslational Modifications Glycosylation: Carbohydrate content: 2.4% (1)* Carbohydrate composition: Xyl, Man, Glu (2:1:1), and GlcNAc (1)* Concanavalin A reactive (1)* Periodic acid-Schiff staining positive (SDS-PAGE), ConA binding negativ (2)	(1) Barnett & Howden 1986 (2) Burks et al. 1991
Biological Function Seed storage protein (1)	(1) Burks et al. 1998
Sequence Homology ConA-binding peanut allergen (65 kDa, pI 4.6, N-terminal aa: GSAPGERQRGCYPGN) (1) may be identical to Ara h 1: aa composition score 6 and 8, and 66.7% and 64.3% aa identity (of 15 N-terminal aa) to Ara h 1 clones (2) Vicilins from broad beans and peas: 60-65% DNA homology to Ara h 1 (3)	(1) Barnett & Howden 1986 (2) Amino Acid Composition Search and Similarity Search (SIM) at ExPASy (3) Burks et al. 1995c

* Results obtained for 65 kDa allergen with similarity to Ara h 1 (see Sequence Homology)

7.2.2 Allergenic Properties

<table>
<tr><th>Vicilin</th><th>References</th></tr>
<tr><td>Frequency of Sensitization
IgE-binding to Ara h 1 in 65-100% of patients (1)</td><td>(1) see 7.1 Sensitization to Peanut Allergens</td></tr>
<tr><td>Allergenic Potencies
3-48% inhibition of IgE binding to raw peanut extract (8 peanut allergic patients, RAST inhibition) (1)*</td><td>(1) Barnett & Howden 1986</td></tr>
<tr><td>Allergenicity of recombinant Ara h 1
95% of peanut allergic patients reacted to recombinant Ara h 1 (18 peanut-allergic patients with positive IgE-binding to native Ara h 1, SDS-PAGE immunoblot) (1)</td><td>(1) Burks et al. 1995c</td></tr>
<tr><td>IgE binding
3 different IgE binding sites indicated by RAST inhibition with mAb vs patients' IgE (1)</td><td>(1) Burks et al. 1994b</td></tr>
<tr><td>B-Cell Epitopes
IgE binding sites located on Ara h 1 (precursor sequence):
<table>
<tr><th>Peptides</th><th>Positivity in Patients</th></tr>
<tr><td>aa 25-34 (synthetic peptide)</td><td>80% (1)*</td></tr>
<tr><td>aa 65-74 (synthetic peptide)</td><td>80% (1)*</td></tr>
<tr><td>aa 89-98 (synthetic peptide)</td><td>80% (1)*</td></tr>
<tr><td>aa 344-353 (synthetic peptide)</td><td>80% (1)</td></tr>
<tr><td>aa 498-507 (synthetic peptide)</td><td>80% (1)*</td></tr>
<tr><td>aa 578-587 (synthetic peptide)</td><td>80% (1)</td></tr>
</table>
dot / immunoblot (SPOTs membrane technique)
* bound more IgE from individual sera than any other epitopes

(1) In total 23 IgE-binding epitopes were identified (10 patients with peanut allergy)</td><td>(1) Burks et al. 1997</td></tr>
</table>

Mutational Analysis of B-Cell Epitopes

Critical aa residues for IgE binding identified by single site aa substitution:

Peptides	aa Substitution*	IgE binding
aa 25-34 (synthetic peptide)	a) S28 b) P29 c) Y30 d) K32	a) - (1, 2) b) - (1, 2) c) - (1, 2) d) - (1, 2)
aa 65-74 (synthetic peptide)	a) Y67 b) D68 c) P69 d) V72 e) Y73	a) - (1, 2) b) - (1, 2) c) - (1, 2) d) - (1, 2) e) - (1, 2)
aa 89-98 (synthetic peptide)	a) R91 b) R93 c) G94 d) R95 e) Q96	a) - (1, 2) b) - (1) c) - (1, 2) d) - (1, 2) e) - (1, 2)
aa 344-353 (synthetic peptide)	a) G349	a) - (2)
aa 498-507 (synthetic peptide)	a) R498 b) R499 c) Y500	a) - (1, 2) b) - (1, 2) c) - (1, 2)
aa 578-587 (synthetic peptide)	a) S585	a) - (2)

dot / immunoblot (SPOTs membrane technique)
* aa substitution with A (1) and A or M (2), respectively

(1, 2) Pooled serum from 15 patients with peanut allergy
(2) In total 21 epitopes analyzed with similar results

(1) Burks et al. 1997
(2) Shin et al. 1998

Sequence Homology of B-Cell Epitopes

Epitope 498-507 shares significant sequence homology to other vicilins from legumes, epitopes 25-34, 65-74, and 89-98 do not share significant homologies to other vicilins (1)

(1) Burks et al. 1997

Types of Critical Amino Acids

In 21 epitopes studied by single mutational aa substitution contained 45% charged aa, 36% hydrohopic aa, and 18% polar aa; 35% of mutated hydrophobic residues, 25% of polar, and 17% of charged aa resulted in loss of IgE binding (1)

(1) Shin et al. 1998

Location of B-Cell Epitopes on 3D-Structure

IgE-binding sites clustered into 2 main regions, despite their even distribution throughout the primary sequence; 10 IgE-binding residues buried beneath the surface and 25 residues exposed on the surface of Ara h 1 (homology based 3D-model of Ara h 1: alignment to x-ray crystal structure of phaseolin) (1)
IgE-binding epitopes 311-320 and 325-334 as well as epitopes 551-560 and 559-568 of one monomer contact one another in trimeric formation of Ara h 1 (2)

(1) Shin et al. 1998
(2) Maleki et al. 2000

Alteration of Allergenicity

Deglycosylation:
IgE binding potency reduced about 25-50% after chemical deglycosylation (pooled sera from 5 peanut allergic patients, RAST inhibition) (1)*

(1) Barnett & Howden 1986

see also 10 Stability of Peanut Allergens

* Results obtained for 65 kDa allergen with similarity to Ara h 1 (see Sequence Homology)

7.3 Properties of Conglutin-like Protein (Ara h 2)

7.3.1 Molecular Biological Properties

Conglutin-like Protein	References
Allergen Nomenclature Ara h 2	(1) Larsen & Lowenstein 1999
Isoallergens and Variants 4 isoallergens in IEF/SDS-PAGE (1)	(1) Burks et al. 1992a
Molecular Mass SDS-PAGE: 17 kDa (1)	(1) Burks et al. 1992a
Isoelectric Point pI 5.2 (1)	(1) Burks et al. 1992a
Amino Acid Sequence, mRNA, and cDNA **Ara h 2 (precursor)** **SWISS-PROT:** **GenBank:** L77197 **PIR:** **Amino acids** 157 residues (1) **mRNA** 0.7 kb (1) **cDNA** 717 bp (1) **Gene** * signal peptide 1-18, native protein 19-157 (1)	(1) Stanley et al. 1997
recombinant Protein cDNA expression library: Isolation of Ara h 2 mRNA by PCR (1, 2) expression in *Escherichia coli*: Subcloning into pDS56/RBSII vector and expression of recombinant Ara h 2 in E.coli M15 cells (2) Expression in bacterial cells: Expression of recombinant Ara h 2 and mutated Ara h 2 by using procaryotic expression vector pET24 plasmid (2)	(1) Stanley et al. 1997 (2) Burks et al. 1998, 1999 (3) Kleber-Janke et al. 1999
Posttranslational Modifications Glycosylation: Carbohydrate content: 20% (1) Carbohydrate composition: Galacturonic Acid, Ara, Xyl, Glu, Gal, Rha, Man, Fuc (1)	(1) Burks et al. 1992a
Biological Function Seed storage protein (1)	(1) Stanley et al. 1997
Sequence Homology Conglutin-gamma from lupin: 39% aa similarity (1) Mabinlin I (chain B) from caper: 32-35% aa similarity (1) 2S-albumins from sunflower and castor bean: 34% and 30% aa similarity (1)	(1) Stanley et al. 1997

7.3.2 Allergenic Properties

<table>
<tr><th>Conglutin-like Protein</th><th>References</th></tr>
<tr><td>Frequency of Sensitization
IgE-binding to Ara h 2 in 71-100% of patients (1)</td><td>(1) see 7.1 Sensitization to Peanut Allergens</td></tr>
<tr><td>IgE binding
2 different IgE binding sites indicated by RAST inhibition with mAb vs patients' IgE (1)</td><td>(1) Burks et al. 1995a</td></tr>
<tr><td>B-Cell Epitopes
IgE binding sites located on Ara h 2 (precursor sequence):
<table>
<tr><th>Peptides</th><th>Positivity in Patients</th></tr>
<tr><td>aa 15-24 (synthetic peptide)</td><td>50% (1)</td></tr>
<tr><td>aa 27-36 (synthetic peptide)</td><td>100% (1)*</td></tr>
<tr><td>aa 57-66 (synthetic peptide)</td><td>100% (1)*</td></tr>
<tr><td>aa 65-74 (synthetic peptide)</td><td>100% (1)*</td></tr>
</table>
dot / immunoblot (SPOTs membrane technique),
* bound more IgE from individual sera than any other epitopes (densitometry)

(1) In total 10 IgE-binding epitopes were identified (10 patients with peanut allergy)</td><td>(1) Stanley et al. 1997</td></tr>
<tr><td>Sequence Homology of B-Cell Epitopes
Epitopes 57-66 and 65-74 both contain the sequence DPYSP (1)</td><td>(1) Stanley et al. 1997</td></tr>
<tr><td>Mutational Analysis of B-Cell Epitopes
Critical aa residues for IgE binding identified by single site aa substitution:
<table>
<tr><th>Peptides</th><th>aa Substitution</th><th>Positivity in Patients</th></tr>
<tr><td>aa 15-24 (synthetic peptide)</td><td>a) Q20A
b) W22A</td><td>a) - (1)
b) - (1)</td></tr>
<tr><td>aa 27-36 (synthetic peptide)</td><td>a) R28A
b) R29A
c) Q31A
d) E35A
e) R36A</td><td>a) - (1)
b) - (1)
c) - (1)
d) - (1)
e) - (1)</td></tr>
<tr><td>aa 57-66 (synthetic peptide)</td><td>a) D60A
b) P61A
c) Y62A</td><td>a) - (1)
b) - (1)
c) - (1)</td></tr>
<tr><td>aa 65-74 (synthetic peptide)</td><td>a) D67A
b) P68A
c) Y69A</td><td>a) - (1)
b) - (1)
c) - (1)</td></tr>
</table>
dot / immunoblot (SPOTs membrane technique)

(1) Pooled serum from 15 patients with peanut allergy, in total 10 epitopes analyzed with similar results</td><td>(1) Stanley et al. 1997</td></tr>
<tr><td>Allergenicity of mutated rAra h 2
Amino acids critical for IgE- binding of 4 epitopes (27-36, 39-48, 57-66, and 65-74) of Ara h 2 gene were mutated to encode alanine; recombinant mutated protein showed decreased IgE- binding from 12 of 16 sera from peanut allergic patients as compared to recombinant wild-type Ara h 2, while 3 showed similar and 1 increased IgE- binding. No difference in IgG binding to mutated and wild-type Ara h 2 (1)</td><td>(1) Burks et al. 1998b, Burks et al. 1999</td></tr>
</table>

T-Cell Proliferation No difference in proliferative response of Ara h 2- specific T-cell lines from peanut sensitive patients after stimulation with mutated and wild-type Ara h 2 (1)	(1) Burks et al. 1999
T-Cell Epitopes Specific T-cell proliferation after stimulation with (synthetic peptides): aa 19-28, 45-53, 96-114, and 131-139 (1)	(1) Burks et al. 1998b

7.4 Properties of Glycinin (Ara h 3 / Ara h 4)

7.4.1 Molecular Biological Properties

Glycinin	References
Allergen Nomenclature Ara h 3 / Ara h 4	(1) Larsen & Lowenstein 1999
Isoallergens and Variants At least 2 isoallergens designated Ara h 3 and Ara h 4 sharing 91.3% aa sequence identity (not known at the time of approval of names by the IUIS Allergen Nomenclature Sub- Committee) (1)	(1) Kleber-Janke et al. 1999
Molecular Mass SDS-PAGE: 14 kDa (1)*, 57 kDa (rAra h 3) (2) calculated 35.9 kDa (3), 61.0 kDa (full length clone, 3) *N-terminal breakdown product (?)	(1) Burks et al. 1998b (2) Rabjohn et al. 1999 (3) Kleber-Janke et al. 1999
Isoelectric Point Calculated pI 5.5 (1)	(1) Kleber-Janke et al. 1999
Amino Acid Sequence, mRNA, and cDNA	(1) Rabjohn et al. 1999 (2) Kleber-Janke et al. 1999

	Ara h 3 (1)	**Ara h 4** (2)
SWISS-PROT:		
GenBank:	AF093541	AF086821
PIR:		
Amino acids	510 residues (1)	315 residues (2)*
mRNA	1524 bp	1853 bp
cDNA	1530 bp (1)	1170 bp (2)*
Gene		

*full lenght cDNA clone 1872 bp, 530 aa, 61.0 kDa (2)

Recombinant Protein cDNA expression library: Isolation of Ara h 3 mRNA by PCR (1) Phage surface display of functional cDNA expression products, selection of cDNA clones on microtiter wells coated with serum IgE from peanut sensitive patients (pJuFo cloning system) (2) Expression in *Escherichia coli*: Subcloning into pDS56/RBSII vector and expression of recombinant Ara h 4 in E.coli M15 cells (2) Expression in bacterial cells: Expression of recombinant Ara h 3 by using procaryotic expression vector pET24 plasmid (1)	(1) Rabjohn et al. 1999 (2) Kleber-Janke et al. 1999
Biological Function 11S seed storage protein (1)	(1) Rabjohn et al. 1999

Sequence Homology Glycinins (11S-storage proteins) from soybean and pea: aa 62-72% identity with Ara h 3 (1) Glycinin (11S-storage proteins) from soybean: aa 56% identity with Ara h 4 (2)	(1) Rabjohn et al. 1999 (2) Kleber-Janke et al. 1999

7.4.2 Allergenic Properties

<table>
<tr><th>Glycinin</th><th>References</th></tr>
<tr><td>Frequency of Sensitization
IgE-binding to Ara h 3 in 44-53% of patients (1)</td><td>(1) see 7.1 Sensitization to Peanut Allergens</td></tr>
<tr><td>IgE binding to rAra h 3
44% of 18 peanut allergic patients showed IgE- binding to recombinant Ara h 3 (SDS-PAGE immunoblot) (1)</td><td>(1) Rabjohn et al. 1999</td></tr>
<tr><td>B-Cell Epitopes
IgE binding sites located on Ara h 3:
<table>
<tr><th>Peptides</th><th>Positivity in Patients</th></tr>
<tr><td>aa 33-47 (synthetic peptide)</td><td>25% (1)</td></tr>
<tr><td>aa 240-254 (synthetic peptide)</td><td>38% (1)</td></tr>
<tr><td>aa 279-293 (synthetic peptide)</td><td>100% (1)</td></tr>
<tr><td>aa 303-317 (synthetic peptide)</td><td>38% (1)</td></tr>
</table>
dot / immunoblot (SPOTs membrane technique)
(1) Sera with Ara h 3 specific IgE from 8 patients with peanut allergy</td><td>(1) Rabjohn et al. 1999</td></tr>
<tr><td>Mutational Analysis of B-Cell Epitopes
Critical aa residues for IgE binding identified by single site aa substitution:
<table>
<tr><th>Peptides</th><th>aa Substitution</th><th>Positivity in Patients</th></tr>
<tr><td>aa 33-47 (synthetic peptide)</td><td>a) P38A
b) N39A</td><td>- (1)</td></tr>
<tr><td>aa 240-254 (synthetic peptide)</td><td>a) F244A
b) F247A
c) F250A
d) L251A</td><td>- (1)</td></tr>
<tr><td>aa 279-293 (synthetic peptide)</td><td>a) L285A
b) I287A
c) L288A
d) P290A</td><td>- (1)</td></tr>
<tr><td>aa 303-317 (synthetic peptide)</td><td>a) E308A
b) Y309A
c) D310A
d) E311A</td><td>- (1)</td></tr>
</table>
dot / immunoblot (SPOTs membrane technique)
(1) Serum pooled from 8 patients with peanut allergy</td><td>(1) Rabjohn et al. 1999</td></tr>
<tr><td>Types of Critical Amino Acids
68% of amino acids from 4 epitopes were either polar uncharged or apolar residues (1)</td><td>(1) Rabjohn et al. 1999</td></tr>
</table>

7.5 Properties of Profilin (Ara h 5)

7.5.1 Molecular Biological Properties

Profilin	References
Allergen Nomenclature Ara h 5	(1) Larsen & Lowenstein 1999
Molecular Mass Calculated 14.0 kDa (1)	(1) Kleber-Janke et al. 1999
Isoelectric Point Calculated pI 4.6 (1)	(1) Kleber-Janke et al. 1999
Amino Acid Sequence, mRNA, and cDNA **Ara h 5** **SWISS-PROT:** **GenBank:** AF059616 **PIR:** **Amino acids** 131 residues (1) **mRNA** 743 bp **cDNA** 743 bp (1) **Gene**	(1) Kleber-Janke et al. 1999
recombinant Protein cDNA expression library: Phage surface display of functional cDNA expression products, selection of cDNA clones on microtiter wells coated with serum IgE from peanut sensitive patients (pJuFo cloning system) (1) Expression in *Escherichia coli*: Subcloning into pDS56/RBSII vector and expression of recombinant Ara h 5 in E.coli M15 cells (1)	(1) Kleber-Janke et al. 1999
Sequence Homology Profilin from soybean (Gly m 3): aa 83% identity (1)	(1) Kleber-Janke et al. 1999

7.5.2 Allergenic Properties

Profilin	References
Frequency of Sensitization IgE-binding to Ara h 5 in 13% of patients (1)	(1) see 7.1 Sensitization to Peanut Allergens

7.6 Properties of Conglutin-homologue Protein (Ara h 6)

7.6.1 Molecular Biological Properties

Conglutin-homologue Protein	References
Allergen Nomenclature Ara h 6	(1) Larsen & Lowenstein 1999
Molecular Mass Calculated 14.5 kDa (1)	(1) Kleber-Janke et al. 1999
Isoelectric Point Calculated pI 5.2 (1)	(1) Kleber-Janke et al. 1999
Amino Acid Sequence, mRNA, and cDNA **Ara h 6** **SWISS-PROT:** **GenBank:** AF092846 **PIR:** **Amino acids** 124 residues (1) **mRNA** **cDNA** 627 bp (1) **Gene**	(1) Kleber-Janke et al. 1999
Recombinant Protein cDNA expression library: Phage surface display of functional cDNA expression products, selection of cDNA clones on microtiter wells coated with serum IgE from peanut sensitive patients (pJuFo cloning system) (1) Expression in *Escherichia coli*: Subcloning into pDS56/RBSII vector and expression of recombinant Ara h 6 in E.coli M15 cells (1)	(1) Kleber-Janke et al. 1999
Sequence Homology Ara h 2 peanut allergen: aa 59% identity (1) Ara h 7 peanut allergen: aa 35% identity (1) Conglutin (2S-storage protein) from lupine: aa 39% identity (1)	(1) Kleber-Janke et al. 1999

7.6.2 Allergenic Properties

Conglutin-homologue Protein	References
Frequency of Sensitization IgE-binding to Ara h 6 in 38% of patients (1)	(1) see 7.1 Sensitization to Peanut Allergens

7.7 Properties of Conglutin-homologue Protein (Ara h 7)

7.7.1 Molecular Biological Properties

Conglutin-homologue Protein	References
Allergen Nomenclature Ara h 7	(1) Larsen & Lowenstein 1999
Molecular Mass Calculated: 15.8 kDa (1)	(1) Kleber-Janke et al. 1999
Isoelectric Point Calculated pI 5.6 (1)	(1) Kleber-Janke et al. 1999
Amino Acid Sequence, mRNA, and cDNA **Ara h 7** **SWISS-PROT:** **GenBank:** AF091737 **PIR:** **Amino acids** 135 residues (1) **mRNA** 712 bp **cDNA** 637 bp (1) **Gene**	(1) Kleber-Janke et al. 1999
recombinant Protein cDNA expression library: Phage surface display of functional cDNA expression products, selection of cDNA clones on microtiter wells coated with serum IgE from peanut sensitive patients (pJuFo cloning system) (1) Expression in *Escherichia coli*: Subcloning into pDS56/RBSII vector and expression of recombinant Ara h 7 in E.coli M15 cells (1)	(1) Kleber-Janke et al. 1999
Sequence Homology Ara h 2 peanut allergen: aa 35% identity (1) Ara h 6 peanut allergen: aa 35% identity (1) Conglutin (2S-storage protein) from lupine: aa 39% identity (1)	(1) Kleber-Janke et al. 1999

7.7.2 Allergenic Properties

Conglutin-homologue Protein	References
Frequency of Sensitization IgE-binding to Ara h 7 in 43% of patients (1)	(1) see 7.1 Sensitization to Peanut Allergens

8 Isolation & Preparation

Extract / Purified Allergens	Methods	References
Peanut I: 20 and 30 kDa allergens	Extraction of dry defatted peanut powder with 0.1-M NH_4HCO_3 (pH 8.75), centrifugation, supernatant lyophilized, dissolved in phosphate buffer, centrifugation and dialysis followed by two steps of IEC-chromatography (DEAE column), purification by preparative PAGE	Sachs et al. 1981
65 kDa Allergen	Extraction of ground defatted peanut meal with Tris-HCl / NaCl (pH 8.0), isolation with affinity chromatography (ConA-Sepharose) and purification by SEC and IEC	Barnett & Howden 1986
a) Ara h 1 b) Ara h 2	Extraction of defatted, powdered peanuts with phosphate / NaCl buffer (pH 7.0), centrifugation, dialysis, anion exchange chromatography (a: Mono Q column, b: PL-SAX column), fractions dialyzed and lyophilized	a) Burks et al. 1991 b) Burks et al. 1992a
Ara h 1	Immunoaffinity chromatography: Ara h 1 specific mAb bound to cynogen bromide- activated Sepharose beads; isolation of Ara h 1 from crude peanut extract	Burks et al. 1994b
a) Ara h 1 b) Ara h 2	Lyophilized crude peanut extract dissolved in TRIS- bis-propane buffer (pH 7.2), centrifugation, anion exchange chromatography (Source Q column); Ara h 2 containing fractions were dialyzed and further purified by IEC (Source S column)	de Jong et al. 1998
Agglutinin	Isolation by IEC and further purification by SDS-PAGE electroelution	Burks et al. 1994a

9 Cross-Reactivities

Cross-Reacting Allergens	Subjects / Methods	References
Peanut: *(Nuts)* almond, brazil nut, black walnut, pecan	Positiv inhibition of IgE-binding: to peanut by brazil nut and pecan (1 patient each), by peanut to almond, brazil nut, and pecan (1 patient each) (5 patients, RAST inhibition)	Gillespie et al. 1976
Peanut: *(Nuts)* coconut and walnut	Almost complete inhibition of IgE binding to 35, 36.5, and 55 kDa allergens from coconut and 35, 36, and 50 kDa allergens from walnut by peanut extract (2 tree nut allergic patients, SDS-PAGE immunoblot inhibition) (1) Minimal or no cross- reactivity between walnut and peanut proteins (4 walnut sensitive patients, immunoblot inhibition) (2)	(1) Teuber & Peterson 1999 (2) Teuber et al. 1999
Peanut: *(Legumes)* peanut (sensitivity in 90% of patients), soybean (90%), green pea (80%), lima bean (53%), string bean (43%)*	30 atopic children with suspected soybean allergy (Skin test)	Fries 1971
Peanut: *(Legumes)* soybean, garden pea, and chick pea	15 peanut-sensitive patients (RAST-inhibition)	Barnett et al. 1987

Peanut: *(Legumes)* peanut (sensitivity in 87% of patients), soybean (43%), green bean (22%), pea (26%), and lima bean (41%) (SPT)*	69 legume-sensitive patients (SPT) (1) frequency of multiple sensitization: 4.9%; 43 patients DBPCFC positive: peanut 72%, soybean 23%, pea 5% (1) In vitro cross-reactivity did not correlate with clinical hypersensitivity, most prominent 20 kDa allergen in all legumes except green beans (SDS-PAGE and dot / immunoblot) (2)	(1) Bernhisel-Broadbent & Sampson 1989 (2) Bernhisel-Broadbent et al. 1989
Peanut: *(Legumes)* soybean	patient allergic to peanut and soy: 73% reduction of IgE-binding to peanut after adsorption of cross-reacting antibodies (ELISA)	Eigenmann et al. 1996
Peanut: *(Legumes)* soybeans and peas	4 peanut allergic and 2 pea allergic adults (RAST-inhibition)	Hagner et al. 1998
Peanut: *(Legumes)* lupine flour *	Lupine allergens with 21 kDa and 35-55 kDa, positive SPT with extract from lupine-flour containing pasta in 5 patients (7 peanut allergic patients, RAST, SDS-PAGE immunoblot)	Hefle et al. 1994
Peanut: *(Legumes)* lupine flour and pollen	Positive SPT with lupine flour in 44% patients, positive DBPCFC with lupine flour in 7/8 patients, cross-reactivity between peanut and lupine flour / pollen extracts in RAST and immunoblot inhibition, major lupine flour allergen: 43 kDa (24 peanut allergic patients)	Moneret-Vautrin et al. 1999
Peanut: *(Legumes)* carob bean *	Carob allergens with 17.5, 48, and 66 kDa; positive SPT with raw carob bean in 50%, with carob pulp in 25%, and with cooked carob in none of 12 peanut sensitive patients; carob specific RAST positive in 25%; no clinical reactivity to raw and cooked carob (RAST, SDS-PAGE immunoblot)	Fiocchi et al. 1999
Peanut: *(Legumes)* lupine	A case of lupine- induced anaphylaxis with positive SPT and in vitro cross- reactivity with other legumes (peanut), positive open challenge with pea, but negative open challenge to peanut and green bean	Matheu et al. 1999
Peanut: *(Gramineae, Legumes)* corn, rice, and soybean	123 soybean, corn, rice, and/or peanut allergic patients: significant inhibition of IgE- binding to peanut by soybean, but not by corn and rice; significant inhibition to soybean, corn, and rice by peanut; significant correlation between soybean and peanut specific RAST (r=0.76) (RAST, RAST inhibition)	Lehrer et al. 1999
Peanut: *(Grass Pollen)* grass pollen and tomato	Inhibition of IgE-binding: peanut, grass pollen, and tomato (grass pollen allergic children, RAST inhibition)	de Martino et al. 1988
Peanut: *(Grass Pollen)* cross-reactive carbohydrate determinants (CCD) from grass pollen	a) 11 patients with grass pollen allergy and positive RAST to peanut without clinical relevant peanut sensitivity b) 4 controls with clincal relevant peanut allergy Results: a) 94% inhibition of IgE-binding to peanut allergens by CCD, b) only partial inhibition (59%) in 1 patient	van der Veen et al. 1997

* multiple sensitization (not proven by inhibition-tests)

Unique Allergens	Subjects / Methods	References
Peanut / Soybean 46, 29, 25, 19, 17, 14, and 5 kDa allergens from peanut did not cross-react with soybean allergens; 46 and 21 kDa allergens from soybean did not cross-react with peanut allergens	3 patients allergic to peanut 2 patients allergic to peanut and soy a) removal of cross-reacting antibodies from serum by soy- and peanut-affinity chromatography, respectively b) detection of unique IgE-binding proteins in SDS-PAGE immunoblot	Eigenmann et al. 1996

10 Stability of Peanut Allergens

Treatment	Effects	References
Peanuts *(Heat)* raw and roasted peanuts (140°C, 45 min)	IgE binding proteins were heat stable (SDS-PAGE immunoblot, pooled serum from 3 peanut allergic patients)	Vieths et al. 1998
Crude Peanut Protein *(Heat)* heat RT to 100°C, 5 to 60 min	No change in IgE and IgG binding (10 peanut allergic patients, EAST inhibition)	Burks et al. 1992b
65 kDa Allergen *(Heat, pH-Range)* heated in solution (20-100°C, 30 min), pH 2.8-10.0	Stable in-vitro allergenicity over the whole temperature and pH range (RAST inhibition)	Barnett & Howden 1986
Ara h 1 *(Heat)* heating of ground peanuts (20-140°C, 15 min)	No difference of IgE binding inhibition between purified Ara h 1 from raw and heated peanuts (EAST inhibition, 8 peanut allergic patients)	Koppelman et al. 1999
Crude Peanut Protein *(Chewing)* a) 10 min chewing of peanuts in the mouth b) successive treatment with artificial gastric fluid (pH 1.3, 10-80 min)	a) No detectable degradation of peanut allergens b) No detectable degradation of Ara h 1 (SDS-PAGE immunoblot, 10 patients with peanut allergy)	Becker 1997
Crude Peanut Protein *(Hydrolysis)* 2 step enzyme digestion a) pepsin and b) trypsin, chymotrypsin and intestinal mucosal peptidase digestion	50%-inhibition concentration: 100 fold increased for digested peanut proteins (10 peanut allergic patients, EAST inhibition)	Burks et al. 1992b
Peanuts *(Hydrolysis)* Digestion of crude peanut extract with pepsin (immobilized to agarose) at pH 1.8 (24 or 48 h)	Complete loss of IgE binding from sera of 5 peanut allergic patients (SDS-PAGE immunoblot); Positive T-cell response after stimulation with pepsin- digested peanut extract in 7 peanut allergic patients (PBMC proliferation)	Hong et al. 1999
Peanuts *(Hydrolysis)* 2 step digestion with a) pepsin (2 h) and b) pancreatic enzymes (45 min) (extract from roasted peanuts)	Various IgE binding fragments after peptic digestion, IgE binding decreased strongly after subsequent pancreatic digestion; inhibition of IgE binding to peanut proteins persisted after both digestions at values of about 50% (SDS-PAGE immunoblot, peanut allergic patients)	Vieths et al. 1999
Ara h 1 *(Hydrolysis)* Digestion with pepsin, trypsin, or chymotrypsin (up to 3 h)	After hydrolysis with each enzyme 5-8 IgE binding fragments of Ara h 1 detected in the range of 16-60 kDa (SDS-PAGE immunoblot, pooled serum from 12-15 peanut allergic patients)	Maleki et al. 2000

11 Allergen Sources

Reported Adverse Reactions	References
Various Food Products 4 cases of fatal anaphylaxis after ingestion of cake and cookie containing peanuts, chili containing peanut butter, and a Vietnamese dish with slivered peanuts atop (1) 3 cases of fatal anaphylaxis after ingestion of candy, cake, and a sandwich containing peanuts in different forms; 1 case of severe anaphylaxis after ingestion cookies (2) Life-threatening allergic reactions after ingestion of peanut butter and peanut paste (3) Recurrent anaphylactic reactions after ingestion of Asian food, chocolate products, and bakery products containing hidden peanut protein in 3 peanut allergic patients (4)	(1) Yunginger et al. 1988 (2) Sampson et al. 1992 (3) Foucard & Malmheden Yman 1999 (4) Borelli et al. 1999
Almond Icing Fatal reaction to peanut antigen in almond icing (1)	(1) Evans et al. 1988
"Almond" Bun Fatal reaction after ingestion of an "almond bun" with peanut flakes (substituted for almond flakes) in a 15 year old boy (presumed co-factor: cold beverage) (1)	(1) Foucard & Malmheden Yman 1999
Cake Anaphylaxis after ingestion of cake containing undeclared peanut proteins (1)	(1) Malmheden Yman et al. 1994
Cookies Anaphylaxis after ingestion of gingersnap cookies containing undeclared peanut proteins (1)	(1) Kemp & Lockey 1996
Dry Soup Mixture Systemic allergic reaction after ingestion of a soup in a 33 year old peanut sensitive woman; the dry soup preparation contained undeclared peanut flour as a component of flavouring ingredient; appr. 45 mg peanut protein were ingested (1)	(1) McKenna & Klontz 1997
Pasta Urticaria and angioedema after ingestion of spaghetti-like pasta fortified with sweet lupine seed flour in a 5-year old peanut sensitive girl (1)	(1) Hefle et al. 1994
Pizza Sauce 2 cases of severe anaphylaxis after ingestion of pizza sauce containing peanut proteins (1)	(1) Hogendijk et al. 1998
Milk Formulas, Peanut Oil Adverse reactions in 4 children (4-13 months) with atopic dermatitis after ingestion of infant formula containing peanut oil; 2 children positive on labial challenge with peanut oil (1)	(1) Moneret-Vautrin et al. 1994
Crude Peanut Oil DBPCFC with doses of 1 to 10 mL of unrefined peanut oil: 6 positiv reactions (oral and throat itching, swelling of lips, wheeze) in 60 peanut allergic patients (1)	(1) Hourihane et al. 1997a
Refined Peanut Oil DBPCFC with doses of 5 - 15 mL refined peanut oil: 14 positiv reactions in 62 peanut allergic patients. Immediate reactions: facial erythema and pruritus (6 cases), bronchospasm (1 case). Delayed reactions: bronchospasm (1 case), labial oedema (1 case), abdominal pain with nausea (2 cases), eczema (3 cases), buccual itching and oral syndrome (2 cases) (1)	(1) Moneret-Vautrin et al. 1998
Peanut Oil Labial food challenge with peanut oil positive in 4% of 50 tested and 30% of 63 peanut allergic children tested by oral food challenge (1)	(1) Rance & Dutau 1999

Allergens in Food Products	Content / Products	References
Roasted Peanuts Dry and oil roasted peanuts (serum pool from 5 peanut allergic patients)	Roasted peanuts had almost the same inhibition of IgE-binding to raw peanut extract as compared to standard peanut inhibitor (RAST inhibition)	(1) Nordlee et al. 1981

Roasted Peanuts Roasted peanuts (serum pool from 10 peanut allergic patients)	No difference of raw and roasted peanuts in RAST inhibition; 16 IgE binding antigens in raw peanut and 7 in roasted peanut (CRIE)	(1) Barnett et al. 1983
Peanut Flour 8 commercially available peanut flours and 1 peanut hull flour (serum pool from 5 peanut allergic patients)	All peanut flour extracts showed high inhibition of IgE-binding to raw peanut extract, RAST slopes from 3 flours significantly different from raw peanut; the peanut hull flour was less allergenic (RAST inhibition)	(1) Nordlee et al. 1981
Hydrolyzed Peanut Protein Commercially available acid hydrolyzed peanut protein (serum pool from 5 peanut allergic patients)	No inhibition of IgE-binding by hydrolyzed peanut protein to raw peanut extract (RAST inhibition)	(1) Nordlee et al. 1981
Peanut Butter Products a) Peanut butter, b) Peanut butter powder (peanut butter, dried whey), c) Peanut butter syrup (ingredients: corn syrup, peanut butter, water, dried whey, cellulose, and lecithin), d) Peanut butter flavoured chips	All peanut butter product extracts showed high inhibition of IgE-binding to raw peanut extract (serum pool from 5 peanut allergic patients, RAST inhibition)	(1) Nordlee et al. 1981
Peanut Butter Products 3 allergens in peanut butter identified	Greatest reactivity to heat- stable, water-soluble, nonglycosylated protein >10 kDa (1 patient)	(1) Whitley et al. 1991
Peanut Oil Commercially available peanut oil (serum pool from 5 peanut allergic patients)	No inhibition of IgE-binding by peanut oil to raw peanut extract (RAST inhibition)	(1) Nordlee et al. 1981
Peanut Oil 4 Commercially available peanut oils (serum pool from 17 peanut and/or nut allergic patients)	IgE-binding potencies: unrefined oil (54°C max. processing temperature) > unrefined oil (65-93°C) >> refined, bleached, deodorized oils (230-260°C) (dot immunoblot) Protein contents of unrefined oils: 10-11 µg/mL and 2 refined oils: 3 and 5.7 µg/mL	Teuber et al. 1997
Peanut Oil Crude, neutralized and refined peanut oils	18-20 kDa allergen in protein extract of refined peanut oil (SDS-PAGE immunoblot, 2 peanut allergic patients), 9-52% inhibition of IgE-binding to peanut proteins by peanut oil protein extract in 7 of 11 peanut allergic patients (RAST inhibition) Protein contents of unrefined oil: 3.4 µg/g, neutralized oil: 0.2 µg/g, and 5 refined oils: 0.1 to 0.2 µg/g	Olszewskiet al. 1998
Crude Peanut Oil Protein extract from unrefined peanut oil (41 peanut sensitive children)	Positive SPT in 37% of peanut sensitive children	Kull et al. 1999
Used Vegetable Oils Vegetable oils used to roast peanuts (serum pool from 5 peanut allergic patients)	Detection of peanut allergens in used oils; 100-1000 fold reduction of peanut allergen contents after filtration and steam cleaning (RIA)	(1) Keating et al. 1990

Reported Safe Products	References
Refined Peanut Oil ***** 10 patients with clinical relevant peanut allergy: safe ingestion of 8 mL refined peanut oil (total dose) in DBPCFC (1) No reaction in 60 peanut allergic patients after ingestion of 16 mL of refined peanut oil (total dose) in DBPCFC (2) No reaction in 41 peanut sensitive children in SPT with protein extract from refined peanut oil (3)	(1) Taylor et al. 1981 (2) Hourihane et al. 1997a (3) Kull et al. 1999

* see also Reported Adverse Reactions

12 Food Allergen Labelling

Food Allergen	Labelling / Regulation Status	References
International Regulations Peanuts, soybeans and products of these	mandatory labelling of prepackaged food / advisary status (1)	(1) Codex Alimentarius Commission 1999
European Regulations Peanuts and peanut products	labelling appropriate / recommendation (1)	(1) Bousquet et al. 1998

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Common Abbreveations

2D	two-dimensional
3D	three-dimensional
aa	amino acid(s)
Ab	antibody
Act c 1, 2	nomenclature of kiwi fruit allergens *(Actinidia chinensis)*
Ara h 1-7	nomenclature of peanut allergens *(Arachis hypogaea)*
Bos d 4, 5, 6, 7, 8	nomenclature of cow's milk allergens *(Bos domesticus)*
C	concentration of N,N'-methylenbisacrylamide (crosslinker)
CAST	cellular antigen stimulation test
CCD	cross-reactive carbohydrate determinants
CICBAA	Cercle d'Investigations Cliniques et Biologiques en Allergologie Alimentaire (France)
CIE	crossed immunoelectrophoresis
CNBr	cyanogen bromide
cIEF	capillary isoelectric focussing
CLA	cutaneous lymphocyte antigen
CLIE	crossed line immunoelectrophoresis
CMA	cow's milk allergy
CRIE	crossed radioimmunoelectrophoresis
Cor a 1	nomenclature of hazel pollen allergens *(Corylus avellana)*
Cyn d 1	nomenclature of bermuda grass pollen allergens *(Cynodus dactylus)*
DBPCFC	double-blind, placebo-controlled food challenge
DEAE	diethylaminoethyl (cellulose) (anion exchanger)
DNA	deoxyribonucleic acid
EAST	enzyme allergosorbent test
EC	enzyme classification system
EDTA	ethylenediaminetetraacetic acid, disodium salt
ELISA	enzyme linked immunosorbent assay
EW	egg white
Fuc	fucose
Gad c 1	nomenclature of baltic cod allergen *(Gadus callarias)*
Gal	galactose
Gal d 1, 2, 3, 4	nomenclature of egg white allergens *(Gallus domesticus)*
GlcN	glucosamine
GlcNAc	N-acetylglucosamine
Gly m 1, 2, 3	nomenclature of soybean allergens *(Glycine max)*
HLA	human leucocyte antigen
HPLC	high performance liquid chromatography
HR	Histamine Release
IEC	ion exchange chromatography
IEF	isoelectric focussing
Ig	immunoglobulin
IL	interleukin
INF-gamma	interferon-gamma

Lol p 1	nomenclature of rye grass allergens *(Lolium perenne)*
LTA4	leukotriene A4
LTB4	leukotriene B4
LTC4	leukotriene C4
LY	lysozyme
Man	mannose
Mal d 1, 2, 3	nomenclature of apple fruit allergens *(Malus domestica)*
MALDI-MS	matrix-assisted laser-induced desorption/ionization mass spectrometry
MAST	multiple allergen sorbent test
MHC	major histocompatibility complex
Mr	molecular mass
NeuNAc	N-acetylneuraminic acid
NMR	nuclear magnetic resonance (spectroscopy)
OA	ovalbumin
OAS	oral allergy syndrome
OM	ovomucoid
Ory s 1	nomenclature of rice allergens *(Oryza sativa)*
OT	ovotransferrin
PAGE	polyacrylamide gel electrophoresis
PBMC	peripheral blood mononuclear cells
PBS	phosphate buffered saline
Phl p 1	nomenclature of timothy grass allergens *(Phleum pratense)*
pI	isoelectric point
PCA	passive cutaneous anaphylaxis (test)
PCR	polymerase chain reaction
PVDF	polyvinyliden difluoride
PVPP	polyvinyl polypyrrolidone
RAST	radioallergosorbent test
RBL cells	rat basophil leukaemia cells
RIEP	radioimmunoelectrophoresis
RNA	ribonucleic acid
RT	room temperature
SAFT	skin application food test
SDS	sodium dodecylsulfate
SEC	size exclusion chromatography
SPT	skin prick test
T	total acrylamide concentration
TCC	T-cell clone
TCL	T-cell line
TGF-beta-1	transforming growth factor beta-1
TNF-alpha	tumor necrosis factor alpha
TR	trypsin
Tris	tris-(hydroxymethyl)aminomethane
Xyl	xylose