Divezzamento ed allergia

Alessandro Fiocchi, Melloni Pediatria, Milano

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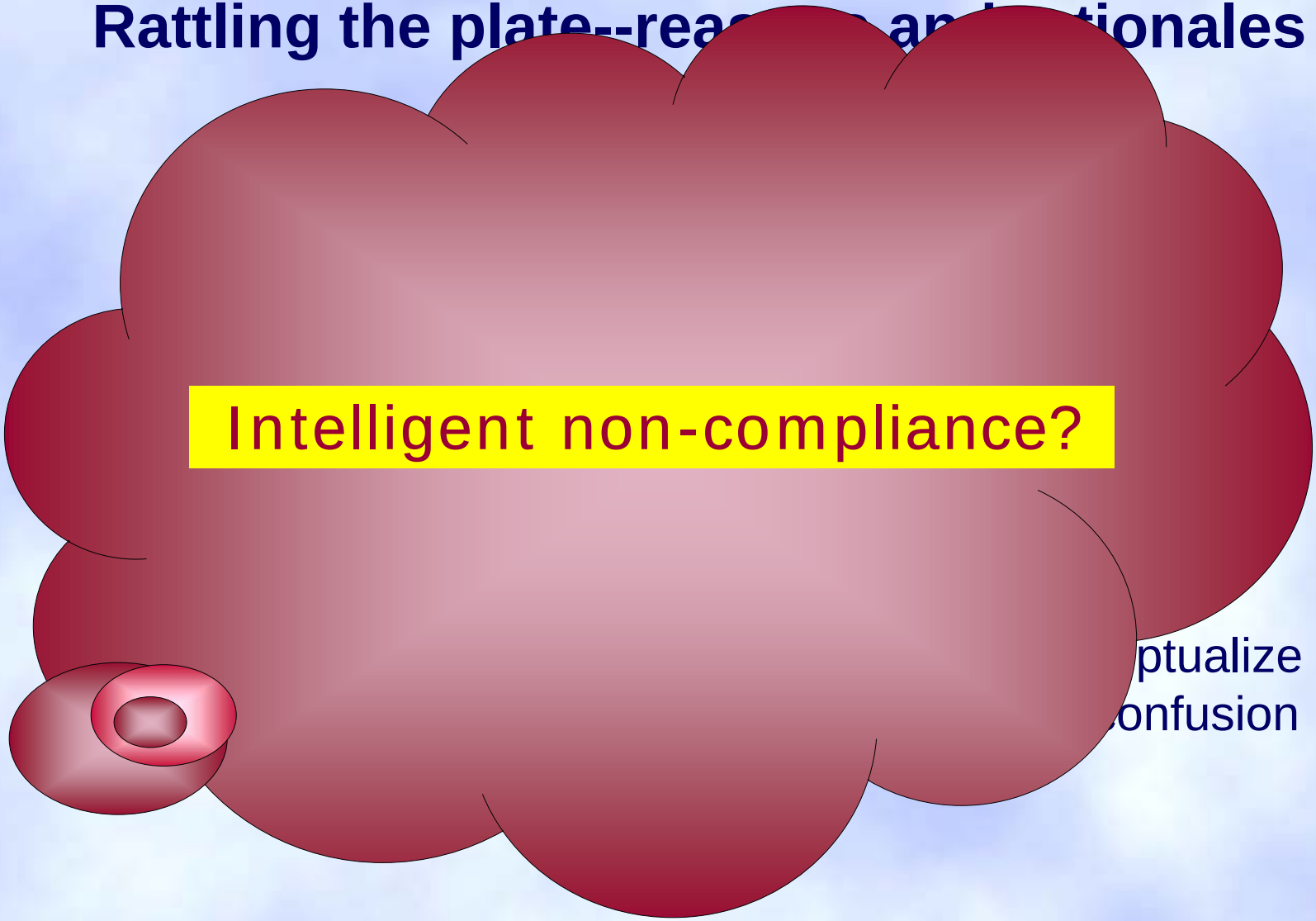

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Health Educ Res. 2001; 16:471-9

Factors affecting the introduction of complementary feeding

Further studies are necessary to see if weaning practices affect long-term growth and morbidity and to provide a basis for the development of appropriate recommendations.

Further studies are necessary to see if weaning practices affect long-term growth and morbidity and to provide a basis for the development of appropriate recommendations.

Eur J Clin Nutr. 2002; 56:448-54

Basi del divezzamento come scienza

- 1. La evizione dei cibi solidi può influenzare lo sviluppo di allergia alimentare?
- 2. Quali gli alimenti più allergizzanti?
- 3. Si può stabilire una scala temporale di introduzione degli alimenti solidi?

1. La evizione dei cibi solidi può influenzare lo sviluppo di allergia alimentare?

- 135 bambini con familiarità allergica, alimentati al seno fino a 6 mesi
- **gruppo a (70) -** a 6 mesi: verdure cotte, mela, pera, cereali
  a 8 mesi: carne, pesce
  a 10 mesi: uovo
- **gruppo b (65) -** a 3 mesi: patata, carota cotta, cereali, carne
  a 4 mesi: uovo, pesce
  a 5 mesi: frutti diversi, "commercial foods"
  a 6 mesi: dieta libera ed estesa

→ **sia eczema che allergia alimentare vennero riscontrati in misura maggiore nel gruppo b rispetto al gruppo a**

Saarinen UM, Kajosaari M Prophylaxis of atopic disease: role of infant feeding. Lancet i: 166-167, 1980
Kajosaari M, Saarinen UM Prophylaxis of atopic disease by six months' total solid foods elimination. Acta Paed Scand 72:411, 1983

1. La evizione dei cibi solidi può influenzare lo sviluppo di allergia alimentare?

- 279 lattanti ad alto rischio atopico *vs.* 80 lattanti con lo stesso rischio (non-intervention group)
- Incidenza di sintomi allergici : 1 anno (11.5 *vs.* 54.4%,) a 2 anni (14.9 *vs.* 65.6%) a 3 anni (20.6 *vs.* 74.1%).
- Fattori più importanti nella patogenesi dei sintomi: (i) formula somministrata nella prima settimana di vita; (ii) divezzamento precoce (< 4 mesi); (iii) assunzione di manzo (< 6 mesi); (iv) introduzione precoce di latte vaccino (< 6 mesi); (v) fumo passivo e socializzazione precoce (< 2 anni di vita).

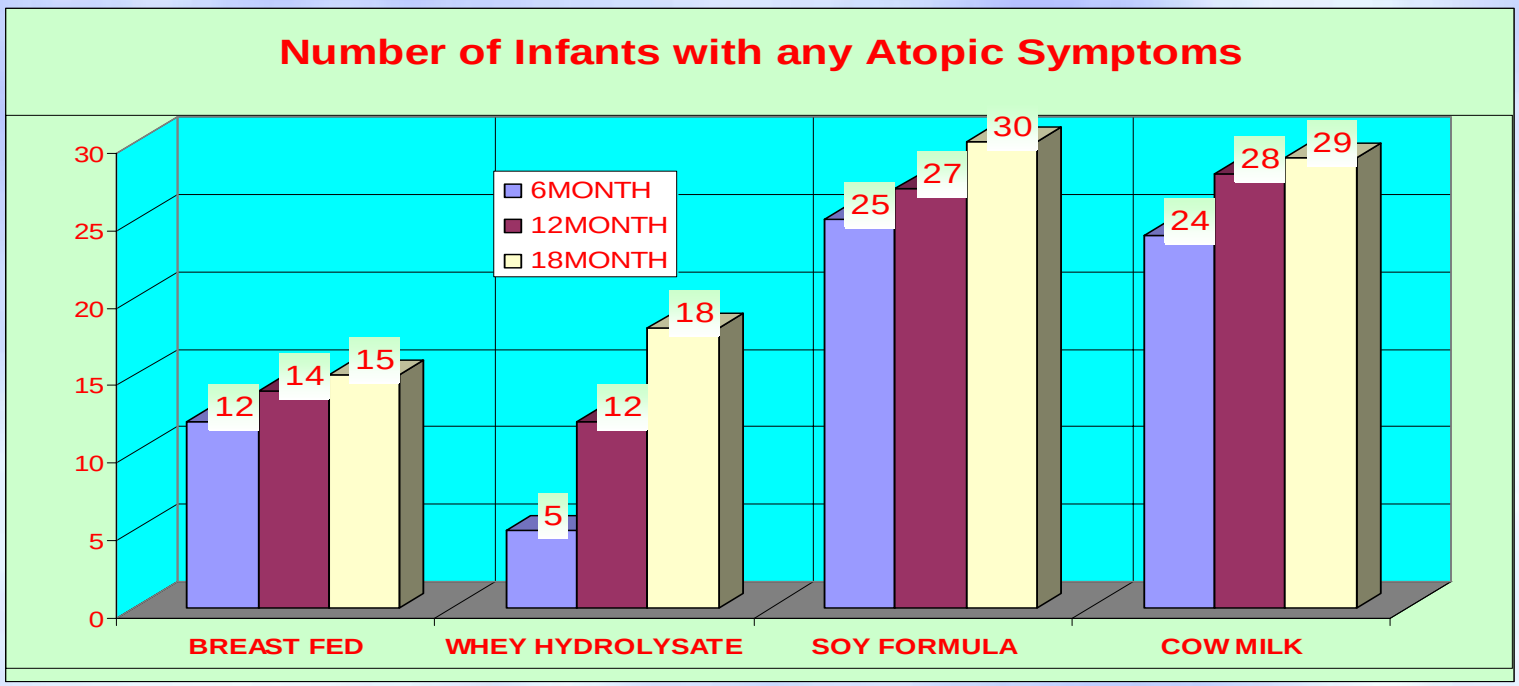
Marini A, *Acta Paediatr Suppl* 1996 May;414:1-21

2. Quali gli alimenti più allergizzanti?

- Italia: uovo, latte, grano, pesce,
- USA: ++ Arachidi,
- Scandinavia : ++ Pesce,
- Giappone : ++ Soya, riso.

- La frequenza di sensibilizzazione varia con la cultura gastronomica, e riflette di regola la intensità e precocità dell'esposizione allergenica

2. Quali gli alimenti più allergizzanti?



Chandra RK, Hamed A. Cumulative incidence of atopic disorders in high risk infants fed whey hydrolysate,soy and conventional cow milk formulas. *Ann Allergy* 1991; 67:129-32

Allergenicità

- frequenza relativa con cui un alimeno determina sensibilizzazione ed allergia in un gruppo di bambini atopici

.

- Fattori proponibili per calcolare un "indice di allergenicita`" di ciascun alimento per ciascun bambino.

- **rischio di sensibilizzazione = % sensibilizzati/esposti**
- **rischio di allergia = % allergici/sensibilizzati**
- **rischio di persistenza allergia = % allergici dopo x anni**

- **rischio personale di allergia = familiarita`**


Fish
Seafood
Egg and poultry
Legumes
Tree nuts
Seeds
Cereal Grains
Fruits and vegetables
ARBP
“

Cross-reactivity between fish species

Isolated allergy to a single species of fish:

tropical sole

Asero R. True monosensitivity to a tropical sole. Allergy 1999;54:1228-9.

swordfish

Kelso JM. Monospecific allergy to swordfish. Ann Allergy Asthma Immunol 1996;77:227-8.

Positive skin test responses and clinical reactions to multiple fish in subjects with fish allergy

Bernhisel-Broadbent J. I. In vitro and oral challenge results in fish-allergic patients. J Allergy Clin Immunol 1992;89:730-7.

Helbling A. Fish allergy: is cross-reactivity among fish species relevant? Ann Allergy Asthma Immunol 1999;83:517-23.

Allergy to different fish species in cod-allergic children

Species	*SPT%*	*Clinical reaction% (history)*
Dogfish	10	0
Sole	55	55
Tuna	55	35
Wrasse	55	5
Mackerel	20	5
Anchovy	35	5
Sardine	20	5
Salmon	20	5

de Martino M.
Allergy to different fish species in cod-allergic children: in vivo and in vitro studies.
J Allergy Clin Immunol 1990;86:909-14.

Allergy to different fish species in cod-allergic adults

- **Eight adult patients**
- **History of reaction to codfish**

Species	Positive reaction	Tolerated	Never eaten
Plaice	6	0	2
Herring	5	0	3
Mackerel	6	0	2
Codfish	8	0	0

Hansen TK,.
Codfish allergy in adults: IgE cross-reactivity among fish species.
Ann Allergy Asthma Immunol 1997;78:187-94.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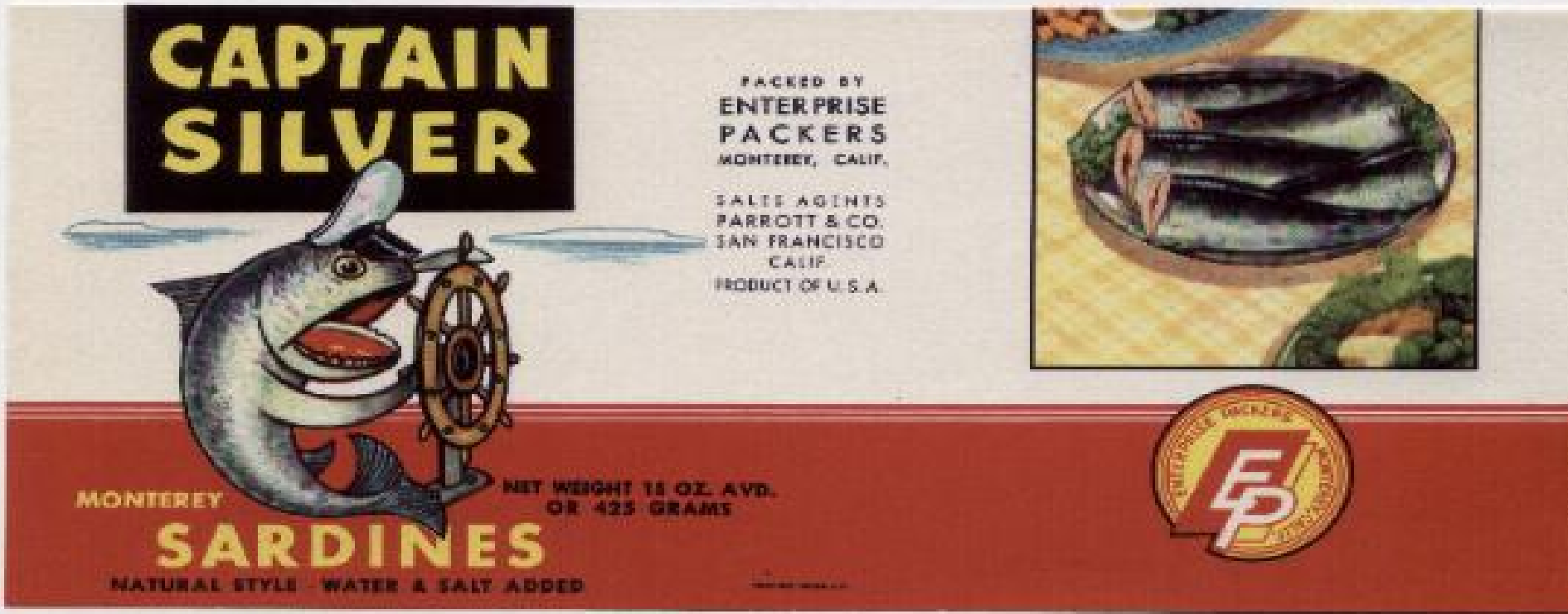
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Tree nuts
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Fruits and vegetables
Latex and fruits
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“Doctor, can I eat….”

Identification of tropomyosin

Shrimp

Daul CB. Identification of the major brown shrimp *(Penaeus aztecus)* allergen as the muscle protein tropomyosin.
Int Arch Allergy Immunol 1994;105:49-55.

Crab

Leung PS. Identification and molecular characterization of Charybdis feriatus tropomyosin, the major crab allergen.
J Allergy Clin Immunol 1998;102:847-52.

Lobster

Leung PS. Molecular identification of the lobster muscle protein tropomyosin as a seafood allergen.
Mol Mar Biol Biotechnol 1998;7:12-20.

Oyster, Scallop, Squid

Leung PS.
IgE reactivity against a cross-reactive allergen in crustacea and mollusca: evidence for tropomyosin as the common allergen.
J Allergy Clin Immunol 1996;98:954-61.

Anisakis

Asturias JA. Is tropomyosin an allergen in Anisakis?
Allergy 2000;55:898-9.

Cockroach, grasshopper, dust mite

Santos AB. Cockroach allergens and asthma in Brazil: identification of tropomyosin as a major allergen with potential cross-reactivity with mite and shrimp allergens.
J Allergy Clin Immunol 1999;104:329-37.

van Ree R. Asthma after consumption of snails in house-dust-mite-allergic patients: a case of IgE cross-reactivity.
Allergy 1996;51:387-93.

Allergenicity of shellfish

16 patients with shrimp allergy: > 80% positive SPT to crab, crayfish, and lobster

Daul CB. Immunologic evaluation of shrimp-allergic individuals.
J Allergy Clin Immunol 1987;80:716-22.

11 patients with shrimp allergy: the reaction to lobster, crab, and crayfish - 50% to 100%

Waring NP. Hypersensitivity reactions to ingested crustacea: clinical evaluation and diagnostic studies in shrimp-sensitive individuals.
J Allergy Clin Immunol 1985;76:440-5

Allergy to shrimp without allergy to other species

Morgan JE. Species-specific shrimp allergens: RAST and RAST-inhibition studies.
J Allergy Clin Immunol 1989;83:1112-7.

Why seafood has not to be introduced early

1. High risk for reactions to crustaceans
2. Reactions can be severe
3. Less common allergy to mollusks
4. IT with dust mite may be an additional risk factor
5. Determination of the precise risks requires further investigation

Sicherer SH. Clinical implications of cross-reactive food allergens
J Allergy Clin Immunol 2001;108:881-90

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Bird-egg syndrome

alpha-livetin (feathers, egg, meat) indicated as sensitising protein

associated with reactions to chicken meat in 22% to 32%.

ausela BA. Peculiarities of egg allergy in children with bird protein sensitization.

nn Allergy Asthma Immunol 1997;78:213-6.

zepfalusi Z. Egg yolk a-livetin (chicken serum albumin) is a cross-reactive allergen in the bird-egg syndrome.

Allergy Clin Immunol 1994;93:932-42.

the majority of children with egg allery tolerate chicken

Cross-sensitisation between egg and meat from different avian species

- avian meat allergy uncommon
- cross-reaction to turkey, pheasant, and quail

Kelso JM. Common allergens in avian meats. J Allergy Clin Immunol 1999;104:202-4

- cross-sensitisation among various avian eggs common
- the clinical implications have not been systematically studied

Langland T.
Allergens in hen's egg white from turkey, duck, goose, seagull, and in hen egg yolk, and hen and chicken sera and flesh. Allergy 1983;38:399-412.

Anibarro B, Seoane FJ, Vila C, Lombardero M.
Allergy to eggs from duck and goose without sensitization to hen egg proteins. Allergy Clin Immunol 2000;105:834-6.


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The leguminosae family

Family	Subfamily	Genus	Species
Leguminosae	Mimosoideae	Acacia	Arabic gum
	Caesalpinoideae	Cassia	Senna
		Ceratonia	Carob bean
	Papillionoideae	Glycyrrhiza	Liquorice
		Arachis	Peanut
		Vicia	Broad bean
		Lens	Lentil
		Pisum	Pea
		Phaseolus	Beans
		Glycine	Soy bean

Sensitisation in the leguminosae botanical family

Allergen	Tested at SPT	Positive	% positive
Peanut	69	60	87
Soy	69	30	43
Pea	69	18	26
Lima bean	41	9	22
Green bean	32	13	41

Bernishel-Broadbent J, Sampson HA.
Cross-allergenicity in the leguminosae botanical family in children with food hypersensitivity.
J Allergy Clin Immunol 1989, 83:435-40

Soy allergy: fact or fiction?

Allergen	SPT- positive	DBPCFC+	% false- positive SPT
Peanut	60	31	48
Soy	30	10	67
Pea	18	2	89
Lima bean	9	0	100
Green bean	13	0	100

Bernishel-Broadbent J, Sampson HA.
Cross-allergenicity in the leguminosae botanical family in children with food hypersensitivity.
J Allergy Clin Immunol 1989, 83:435-40

Soy allergy : fiction!

Challenge-based studies

Source	Setting	SPT+	DBPCFC+	False+ SPTs
Giampietro	Food allergy	22%	3%	86%
Bock	Food allergy		3%	
Sampson	AD		5%	
Magnolfi	AD	21%	0,85%	94%

Giampietro PG. Soy hypersensitivity in children with food allergy. Ann Allergy 1992; 69:143-46

Bock SA. Patterns of food hypersensitivity during sixteen years of double-blind, placebo-controlled food challenges.J Pediatr 1990; 117:561-67

Sampson HA. The role of food allergy and mediators release in atopic dermatitis. J Allergy Clin Immunol 1988; 81:635-45

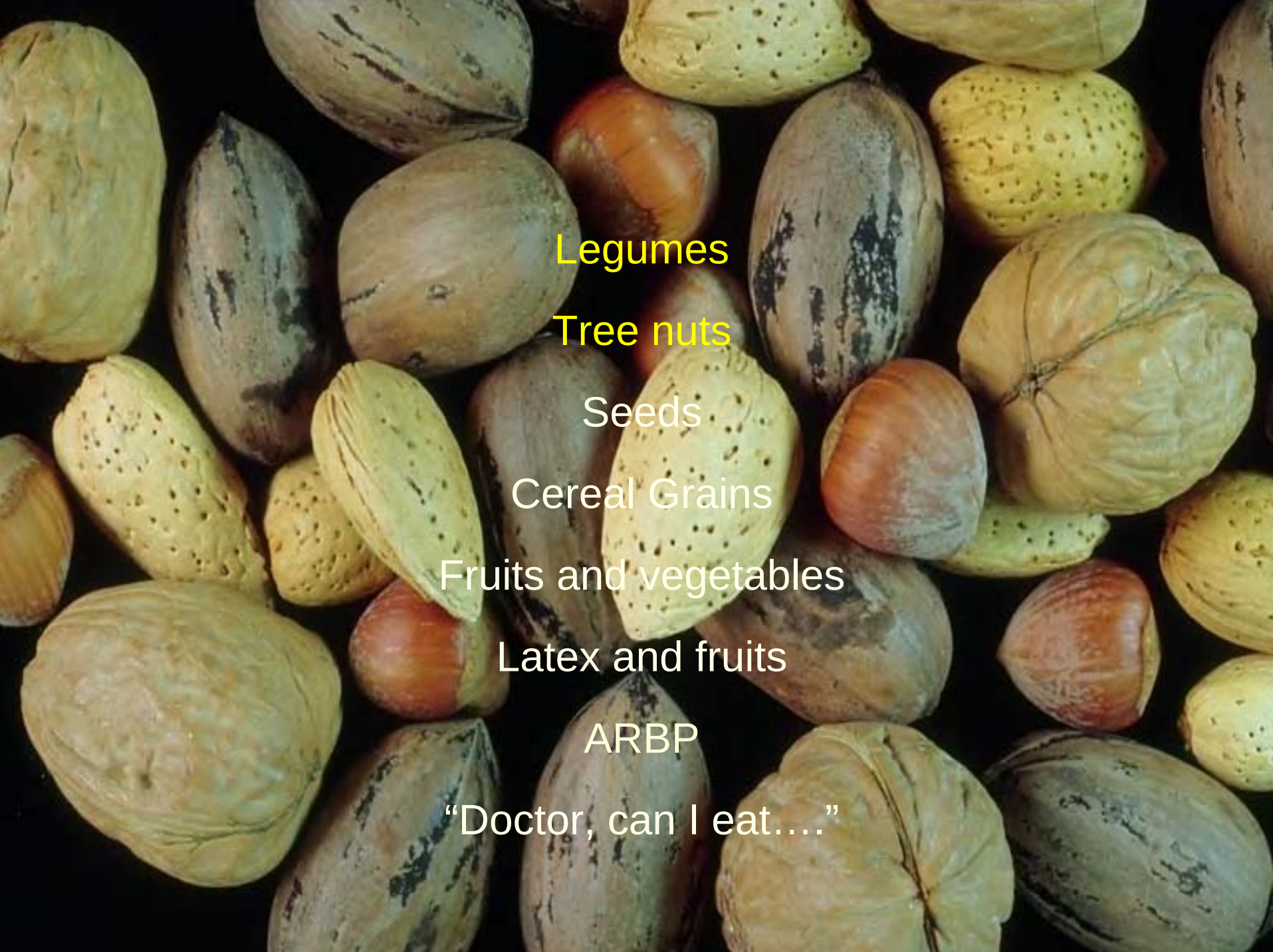
Magnolfi CF. Soy allergy in atopic children. Ann Allergy Asthma Immunol 1996;77:197-201

Allergy to other legumes among children allergic to peanut

Reference	Legume	Number	SPT	RAST	Immunoblot	DBPCFC+
Moneret-Vautrin	Lupine	24	11 (44%)	ND	ND	7/8 (87.5%)
Fiocchi	Carob	12	6 (50%)	3 (25%)	12 (100%)	None

Moneret-Vautrin DA.
Cross-allergenicity of peanut and lupine: the risk of lupine allergy in patients allergic to peanuts.
J Allergy Clin Immunol 1999;104:883-8.

Fiocchi A. Carob is not allergenic in peanut-allergic subjects.
Clin Exper Allergy 1999;29:402-6


Legumes
Tree nuts
Seeds
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Latex and fruits
ARBP
“Doctor, can I eat….”

Tree nuts

Severe clinical l reactions to tree nuts

Ewan PW.
Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations.
BMJ 1996;312:1074-8.

Fatal or near-fatal reactions to tree nuts – also from a first exposure

Bock SA.
Fatalities due to anaphylactic reactions to foods.
J Allergy Clin Immunol 2001;107:191-3.

High degree of IgE binding to multiple tree nuts

Pumphrey RS.
Specific immunoglobulin E to peanut, hazelnut and brazil nut in 731 patients: similar patterns found at all ages.
Clin Exp Allergy 1999;29:1256-9.
Vocks E.
Common allergenic structures in hazelnut, rye grain, sesame seeds, kiwi, and poppy seeds.
Allergy 1993;48:168-72.

92% of 111 patients with peanut allergy, tree nut allergy, or both had IgE antibody to, and 37% had convincing reactions to more than one nut

Sicherer SH.
Clinical implications of cross-reactive food allergens
J Allergy Clin Immunol 2001;108:881-90

Allergenicity of tree nuts

No comprehensive studies

Extensive cross-reactions found:

Peanut – Nut – Brazil nut – Almond

Bock SA. The natural history of peanut allergy. J Allergy Clin Immunol 1989;83:900-4.

Peanut – Nut

Ewan PW.
Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations.
BMJ 1996;312:1074-8.

Pistachio-Cashew

Garcia F.
Allergy to Anacardiaceae: description of cashew and pistachio nut allergens.
J Investig Allergol Clin Immunol 2000;10:173-7

→ caution is prudent! Total elimination of the nut family (perhaps with the exception of previously tolerated nuts eaten in isolation)

Hourihane JO.
Peanut allergy in relation to heredity, maternal diet, and other atopic diseases: results of a questionnaire survey, skin prick testing, and food challenges.
BMJ 1996;313:518-21


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Cross-reactivity between legumes, tree nuts, and seeds

Allergen	Co-sensitisation	%	Reference
Peanut	Hazelnut and Brazil nut	59	Hourihane 1996
Peanut	Tree nut	23-50 (sensitisation)	Hourihane 1997, Sicherer 2001
Peanut	Tree nut	2.5 (self-report)	Sicherer 1999
Nuts	Sesame, poppy, mustard seed	Occasional reports	Rance, Asero

Hourihane JO. Peanut allergy in relation to heredity, maternal diet, and other atopic diseases: results of a questionnaire survey, skin prick testing, and food challenges. BMJ 1996;313:518-21.

Hourihane JO'B. Clinical characteristics of peanut allergy. Clin Exp Allergy 1997;27:634-9.

Sicherer SH. A voluntary registry for peanut and tree nut allergy: characteristics of the first 5,149 registrants. J Allergy Clin Immunol 2001;108:128-32.

Sicherer SH. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. J Allergy Clin Immunol 1999;103:559-62.

Rance F. Mustard allergy in children. Allergy 2000;55:496-500.

Asero R. A case of sesame seed-induced anaphylaxis. Allergy 1999;54:526-7.


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Allergenicity of cereal grains

- Wheat, rye, barley, and oat share homologous proteins
- Cross-sensitisation with grass pollens
- High rate of cosensitization to these foods
- Low rate of clinical cross-reactivity at challenges
- Children with reactions to one grain are tolerant of all other grains in 80% of cases

Jones SM,.
Immunologic cross-reactivity among cereal grains and grasses in children with food hypersensitivity.
J Allergy Clin Immunol 1995;96:341-51.

Donovan GR.
Crossreactivity of IgE antibodies from sera of subjects allergic to both ryegrass pollen and wheat endosperm proteins:evidence for common allergenic determinants.
Clin Exp Allergy 1990;20:501-9.


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The molecular basis of allergenicity

Pathogenesis-related proteins (PRs) - Glucanases, Chitinases, Thaumatin-like proteins, Bet v 1–homologous proteins, Lipid transfer proteins.

Inhibitors of proteases and amylases

2S albumins

Vicillins

Conglutinins

Thyol-proteases

Lectins

Breiteneder H, Ebner C. Molecular and biochemical classification of plant-derived food allergens. J Allergy Clin Immunol 2000;106:27-36

Oral allergy syndrome

isolated oral symptoms
labile proteins in fresh fruits and vegetables
homology with proteins in pollens

Kazemi-Shirazi L.
Quantitative IgE inhibition experiments with purified recombinant allergens indicate pollen-derived allergens as the sensitizing agents responsible for many forms of plant food allergy.
J Allergy Clin Immunol 2000;105:116-25.

Valenta R.
Type 1 allergic reactions to plant-derived food:
a consequence of primary sensitization to pollen allergens.
J Allergy Clin Immunol 1996;97:893-5

Allergenicity of fruits and vegetables

All fruits and vegetables can be allergenic

Jensen-Jarolim E. Characterization of allergens in Apiaceae spices: anise, fennel, coriander and cumin. Clin Exp Allergy 1997;27:1299-306.

Figueredo E. Allergy to pumpkin and cross-reactivity to other Cucurbitaceae fruits. J Allergy Clin Immunol 2000;106:402-3.

Reindl J. Allergy caused by ingestion of zucchini *(Cucurbita pepo)*. J Allergy Clin Immunol 2000;106:379-85

Clinical reactivity determined by DBPCFCs varies with the fruit (10% for pear and up to 90% for peach). Multiple fruit allergy common.

Pastorello E. Allergenic cross-reactivity among peach, apricot, plum, and cherry in patients with oral allergy syndrome: an in vivo and in vitro study. J Allergy Clin Immunol 1994;94:699-707.

Cross-reactions between fruits and vegetables

Cross-reactivity between families - *e.g.* Rosaceae (peach, apple, apricot, almond, plum, pear, and strawberry).

Rodriguez J. Clinical cross-reactivity among foods of the Rosaceae family. J Allergy Clin Immunol 2000;106:183-9.

Cross-reactivity across families: *e.g.* melon – watermelon – avocado – kiwi – chestnut – banana - peach

Rodriguez J. Randomized, double-blind, crossover challenge study in 53 subjects reporting adverse reactions to melon *(Cucumis melo)*. J Allergy Clin Immunol 2000;106:968-72

.

Pollen-fruit syndrome

Birch pollen - Rosaceae fruits
Ragweed – melon
Mugwort – celery

In general, low severity

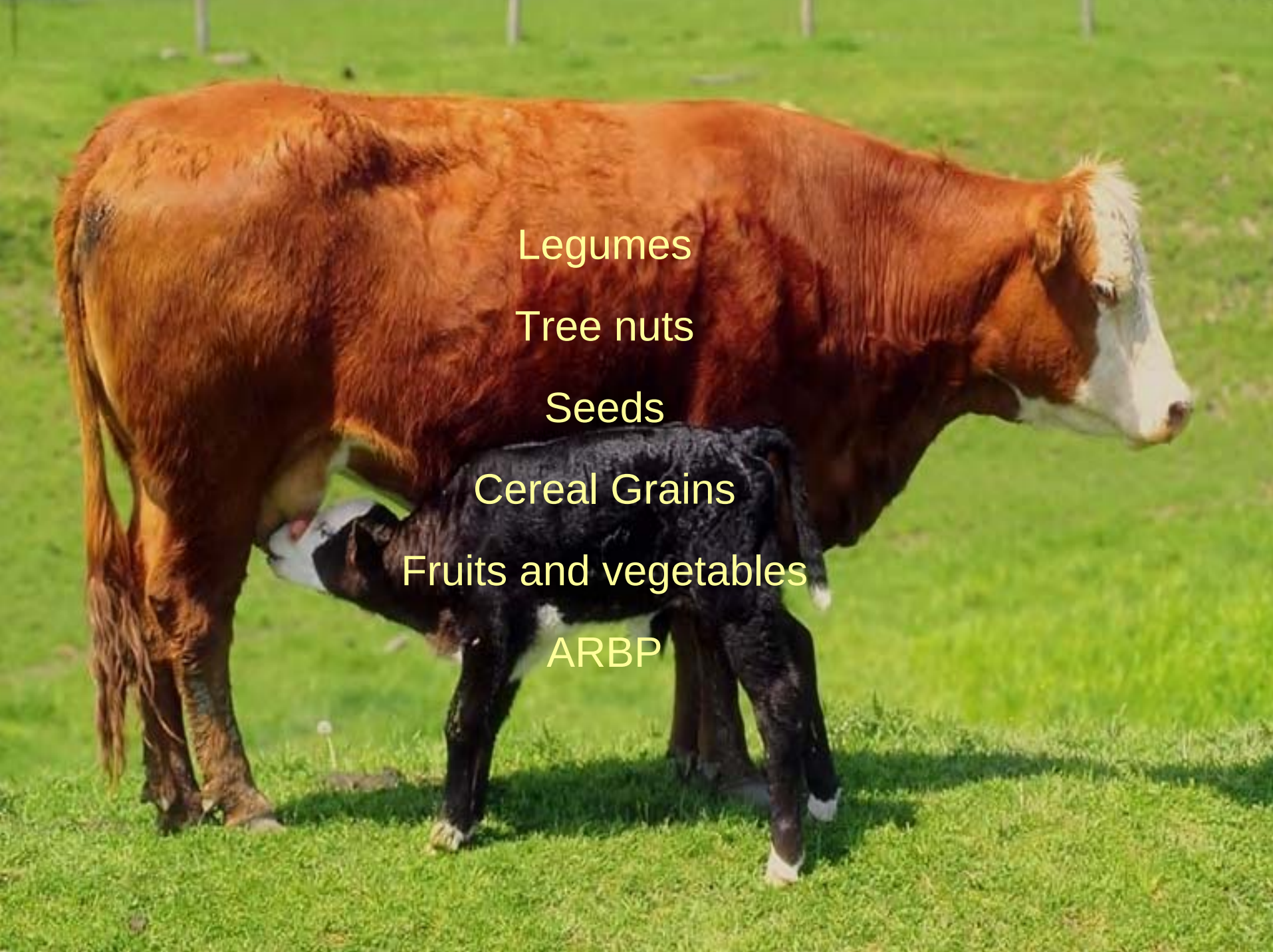
Risk for severe reactions:

- fruit allergy develops without pollen allergy
- sensitisation to lipid transfer proteins (LTPs).
- systemic reactions occurred in 82% without compared with 45% with pollinosis

Cuesta-Herranz J.
Pollen allergy in peach-allergic patients: sensitization and cross- reactivity to taxonomically unrelated pollens.
J Allergy Clin Immunol 1999;104:688-94.

Fernandez-Rivas M. Allergy to Rosaceae fruits without related pollinosis.
J Allergy Clin Immunol 1997;100:728-33.

Schocker F. IgE binding to unique hazelnut allergens: identification of non pollen- related and heat-stable hazelnut allergens eliciting severe allergic reactions. Eur J Nutr 2000;39:172-80.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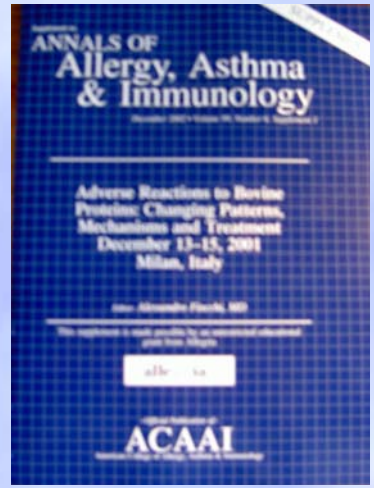

Adverse Reactions to Bovine Proteins

Annals of Allergy Asthma Immunology
December 2002; 89:6, Suppl 1

Goat's and sheep's milk

100% reactions at challenge in children with CMA

100% sensitisation at blotting in children with CMA

Spuergin P Allergenicity of alpha-caseins from cow, sheep, and goat. Allergy 1997;52:293-8.

Bellioni-Businco B. Allergenicity of goat's milk in children with cow's milk allergy. J Allergy Clin Immunol 1999;103:1191-4 .

Restani P. Cross-reactivity between milk proteins from different animal species. Clin Exp Allergy 1999;29:997-1004.

Goat's milk

26 children with CMA

SPT with goat's milk: 100% positive

Challenge with goat's milk: 24/26 positive

Blotting cross-inhibition: 100%

Bellioni-Businco B. Allergenicity of goat's milk in children with cow's milk allergy. J Allergy Clin Immunol 1999;103:1191-4

Donkey's milk

Tolerated by:

- children with severe gastrointestinal CMA
- children with "multiple food intolerance" allergic to eHF

Iacono G et al, J Pediatr Gastroenterol Nutr 1992; 14: 177
Carroccio A, et al, Clin Exp Allergy 2000; 30: 1597

Mare’s milk

17 children with CMA

SPT with mare’s milk: positive 1/17

Challenge with mare’s milk : positive 1/17

Blotting cross-inhibition: not relavant

Mare’s milk tolerated in 96% of children

Businco L. Allergenicity of mare’s milk in children with cow’s milk allergy.
J Allergy Clin Immunol 2000;105:1031-4.

Proteins in milk from different species

RAST in 28 children with BA

	Proteins %		
	Total	Albumin	Casein
Human milk	1.03	0.4	0.4
Donkey	2.0	0.7	0.6
Mare	2.2	1.2	0.3
Cow	3.3	2.5	0.2
Goat	3.7	3.1	0.6
Sheep	5.3	4.5	1.7

Prevalence (%) of adverse reaction to beef in children with CMA

	Gerrard	Sampson	Bishop	Høst	Werfel
N	150	15	96	21	25
Follow-up	>10y	Not specified	5y	36 mo	Not specified
ARB	7 (4,6%)	2 (13,3%)	14 (14.5%)	1 (4.7%)	5 (20%)
Notes		Open challenge	Parent report		DBPCFC +ve

Gerrard JW. Milk allergy:clinical picture and familial incidence. *CMAJ* 1967;97:780-5.

Sampson HA. Food hypersensitivity as a pathogenetic factor in atopic dermatitis. NER *Allergy Proc* 1986;7:511-9.

Bishop JM. Natural history of cow milk allergy: clinical outcome. *J Pediatr* 1990;116:862-7.

Høst A. A prospective study of cow milk allergy in Danish infants during the first three years of life. *Allergy* 1990;45:587-96.

Werfel SJ. Clinical reactivity to beef in children allergic to cow's milk. *J Allergy Clin Immunol* 1997;99:293-300.

SPT in 28 children with BA

	cBeef	fBeef	BSA	cMilk	fMilk	Casein
SPT+	28/28	28/28	26/28	26/28	26/28	10/28

Martelli A
Allergy to cow's milk in beef-allergic children.
Ann Allergy Asthma Immunol. 2002; 89S, 25-33

Specific IgE in 28 children with BA

	Beef	Milk
CAP +ve	26/28	23/28

Cut-off point: 5 kU/L (beef)
18 kU/L (milk)

Martelli A
Allergy to cow's milk in beef-allergic children.
Ann Allergy Asthma Immunol. 2002; 89S, 25-33

CMA in 28 children with BA

	Beef	Milk
DBPCFC	28/28	26/28

Martelli A
Allergy to cow's milk in beef-allergic children.
Ann Allergy Asthma Immunol. 2002; 89S, 25-33

Persistenza delle allergie alimentari

- La "sopravvivenza media" di una diagnosi di allergia alimentare e` del 71% a 3 anni, del 50% a 6 anni e del 28% a 9 anni.

- Uno stato di tolleranza viene raggiunto nella maggior parte dei bambini per il latte a 3 anni, per l'uovo a 7 anni, mentre molti altri alimenti possono determinare allergie di durata indefinita: e` il caso del pesce, della soia, dell'arachide e dei crostacei.

Kjellmann NJM, Natural history and prevention of food allergy. Food Allergy 325, 1991
Koletzko B. Complementary foods and the development of food allergy. Pediatrics 2000; 106: 1285.

Fattori negativi per l’acquisizione di tolleranza

- - alta età alla diagnosi
- - lunga durata dei sintomi
- - alto diametro del pomfo
- - presenza di più di una manifestazione allergica
- - noncompliance alla dieta di esclusione .
- - allergia a crostacei,frutta secca, arachidi,pesce,frutti di mare

Pastorello EA. Role of the elimination diet in adults with food allergy. J Allergy Clin Immunol, 1989; 84: 475-483

Raccomandazioni per il divezzamento bambino a rischio atopico

- Ritardare l'introduzione dei cibi solidi al 5°-6° mese
- Ritardare l'introduzione del latte vaccino al compimento del 1° anno
- Introdurre l'uovo al compimento del 2° anno di vita
- Introdurre pesce, arachidi e frutta secca al compimento del 3° anno di vita
- Preferire gli alimenti estremamente cotti

Sampson H.A Evaluation and Management of Patients with Adverse Food Reactions, in Bierman et al. Allergy, Asthma and Immunology from infancy to childhood, Saunders ed, 1997

Raccomandazioni per il divezzamento bambino normale

Evidence-based

oppure

Eminence-based?

Dal mito alla realtà

L'allergologia pediatrica
dall'arte alla scienza

Temi specifici di interesse
pratico alla luce
della letteratura scientifica

Dalla buona scienza al piccolo
paziente

"Allergy and Eczema"

Adverse reactions to food proteins. Changing Patterns, Mechanism and Treatment

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