Allergen Data Collection:

Sheep's Milk *(Ovis spp.)*

Authors in alphabetical order [contact information]

Matthias BESLER (Hamburg, Germany)
Philippe EIGENMANN (Genève, Switzerland)
Robert H. SCHWARTZ (Rochester, NY, USA)

Abstract

The true prevalence of goat's milk and sheep's milk allergy is not known. However, because IgE sensitization to sheep and goat casein has been found to be as high as 93% to 98% in children with IgE-mediated cow's milk allergy, it is to be expected that children who are allergic to cow's milk are also allergic to sheep's and goat's milks. Several case reports indicate that IgE-mediated sensitization and allergic reactions to sheep's and goat's milks can occur in children and adults who are tolerant of and not significantly sensitized to cow's milk. Because such sensitization and reactions have occurred with certain types of cheese and there are hundreds of different types of cheese, it is helpful to know the animal from which the cheeses are derived. Feta cheese can be made from cow, ewe, or goat; pecorino and Roquefort from ewe; ricotta from cow or ewe; mozzarella from cow, ewe, or buffalo. Other less common sources of milk used in cheese production include camel, mare, reindeer, and yak.
Symptoms of goat's milk and sheep's milk allergy may vary in severity from mild urticaria or localized oral pruritis to severe anaphylactic reactions.
The diagnosis of goat's and sheep's milk allergy is based on a thorough history supported by positive skin prick tests and high levels of specific serum IgE to goat's and sheep's milk allergens, especially casein, respectively. Because of both the high association with cow's milk allergy and the sometimes isolated occurrence of sheep's and goat's milk allergy, testing with cow's milk can be informative. Oral challenge procedures can be performed when acute anaphylactic reactions are not expected, when the diagnosis is in doubt, or to determine if tolerance is present or has developed.
This review presents data on prevalence, symptoms, cross-reacting allergens, and sources in tabular form.
(Internet Symposium on Food Allergens 2002, 4(1):125-30)

Contents

Disclaimer

The reference lists of the Allergen Data Collections are based mainly on searches of Medline and FSTA (Food Science & Technology Abstracts) databases up to the related dates of publication. The scientific rigor of the studies listed is variable and not subject of critique or evaluation by the authors or the editor of the Allergen Data Collections. The reader should be aware of considerable problems in comparing data from different studies (eg. patient cohorts, diagnostic performances, possible flaws in allergen preparations and methodologies for allergen characterization) and is encouraged to review the original publications.

The information provided by the Internet Symposium on Food Allergens is for educational, communication and information purposes only and is not intended to replace or constitute medical advice or treatments. Neither the authors nor the editorial board of the Internet Symposium on Food Allergens is responsible for the use which might be made of the information.

1 Prevalence of Sheep' s Milk Allergy

1.1 Subjects with Atopic or Other Diseases

Country / Subjects	Sensitivity / Allergy to	References
France, Gif Sur Yvette / Paris 58 patients with CMA and specific IgE to bovine CAS	sheep's milk: ovine CAS 98% (RAST) goat's milk: caprine CAS 93% (RAST) rat's milk CAS 59% (RAST) rabbit's milk CAS 57% (RAST)	Bernard et al. 1999
France, Pierre Benite a) 580 patients with adverse reactions to food b) 60 cases of anaphylaxis (study period 1984-92)	a) cow's milk 18% b) ewe's milk (sheep's milk) 1.7%, cow's milk 3.3%	Andre et al. 1994
Italy, Palermo 21 hydrolysed protein formula intolerant infants with CMA (median age at diagnosis 2 months) treated with an ass' milk-based diet	goat's milk in 5/6 (DBPCFC) sheep's milk in 4/7 (DBPCFC)	Carroccio et al. 2000

2 Symptoms of Sheep' s Milk Allergy

Symptoms & Case Reports	References
systemic reactions anaphylaxis (1, 3), anaphylactoid reaction (6) cutaneous symptoms angioedema (2), swelling of eyelids (2), rhinoconjunctivitis (2), urticaria (2, 4), contact urticaria (5), generalized urticaria (2) gastrointestinal symptoms oral pruritus (6) respiratory symptoms asthma (2, 4), dyspnea (2), allergic rhinitis (4)	(1) Andre et al. 1994 (2) Wüthrich & Johansson 1995 (3) Calvani & Alessandri 1998 (4) Fiocchi et al. 1999 (5) Umpierrez et al. 1999 (6) Orlando et al. 2000

3 Diagnostic Features of Sheep' s Milk Allergy

Parameters / Subjects	Outcome	References
SPT, RAST, Clinical Reactivity without Sensitization to Cow's Milk 2-year old girl with allergy to goat' s and sheep' s cheese	Positive SPT to: goat casein, sheep' s milk, and sheep casein Positive prick-to-prick test to: goat' s milk and cheese, sheep' s milk and cheese Negative SPT and prick-to-prick test to cow' s milk Positive RAST to: goat' s milk and casein, and sheep' s milk and casein Negative RAST to: cow' s milk and casein Clinical reactivity to goat' s cheese and sheep' s cheese with tolerance of cow' s milk and cheese	Umpierrez et al. 1999

4 Composition of Sheep' s Milk

4.1 Distribution of Nutrients (Whole Milk)

For other sheep' s milk products seeUSDA Nutrient Database

Nutrients: Content per 100 g		
Energy 409 kJ (97 kcal) Water 82.7 g Protein 5.3 g Lipids 6.3 g Carbohydrate 4.6 g Organic Acids 0.1 g Minerals 0.9 g **Minerals** Sodium 30 mg Potassium 180 mg Magnesium 12 mg Calcium 185 mg Manganese 13 µg Iron 100 µg Copper 90 µg Zinc 470 µg Phosphorus 125 mg Chloride 75 µg Fluoride 20 µg Iodine 10 µg	**Vitamins** Vitamin A 60 µg Carotin 8 µg Vitamin D 160 ng Vitamin E 200 µg Vitamin B1 65 µg Vitamin B2 290 µg Nicotinamide 465 µg Pantothenic acid 395 µg Vitamin B6 80 µg Biotin 9µg Folic acid 6 µg Vitamin B12 550 ng Vitamin C 4 mg **Amino Acids** Arg 180 mg His 130 mg Ile 310 mg Leu 540 mg Lys 440 mg	Met 140 mg Phe 260 mg Thr 250 mg Trp 70 mg Tyr 260 mg Val 320 mg **Carbohydrates** Lactose 4550 mg **Lipids** Palmitic acid 1440 mg Stearic acid 800 mg Oleic acid 1390 mg Linolic acid 90 mg Linoleic acid 160 mg Cholesterol 11 mg **Others** Citric acid 120 mg

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

5 Allergens of Sheep' s Milk

Proteins / Glycoproteins	aa Sequence	Allergen Nomenclature	References
alpha-Lactalbumin [14 kDa]	Swiss-Prot: P09462		Docena et al. 2002
beta-Lactoglobulin [18 kDa]	Swiss-Prot: P02757		Docena et al. 2002
Serum Albumin [67 kDa]	Swiss-Prot: P14639		Fiocchi et al. 1995, Docena et al. 2002
Caseins [22-31 kDa]	Swiss-Prot: P04653 (alpha-S1) P04654 (alpha-S2) P11839 (beta) P02669 (kappa)		Umpierrez et al. 1999, Docena et al. 2002

6 Cross-Reactivities

Cross-Reacting Allergens	Subjects / Methods	References
Sheep's Milk cow' s and goat' s milk, and modified cow' s milk formulas	16 children with CMA: high inhibition of IgE- binding to cow' s milk by goat' s and sheep' s milk, modified cows' milk formula and CAS formula (RAST inhibition)	Dean et al. 1993
Sheep's Milk cow' s, goat' s, and buffalo milk	6 children with CMA: IgE- binding to milk allergens from cow, ewe, goat, and buffalo, but not from camel (SDS-PAGE immunoblot, inhibition)	Restani et al. 1999
Sheep's Caseins goat' s, sheep' s, and cow' s milk	Inhibition of IgE- binding to goat' s and sheep' s CAS by cow' s milk CAS in 1 adult (RAST inhibition)	Wüthrich & Johansson 1995
Sheep's Caseins whole casein fractions from cow, goat, ewe, rabbit and rat milk *	Sera from 58 patients with CMA and specific IgE to bovine CAS: specific IgE titers: bovine > ovine > caprine CAS; 79% and 66% of sera showed IgE-binding to rabbit-CAS and rat-CAS of <10% intensity as compared to bovine CAS (ELISA)	Bernard et al. 1999
Sheep's Caseins goat' s and sheep' s milk	1 cow' s milk tolerant child with goat' s and sheep' s milk allergy: high degree of cross-reactivity between goat' s and sheep' s milk CAS (RAST inhibition); IgE binding to allergens in goat' s milk at 22, 27, and 31 kDa and sheep' s milk at 31 kDa (SDS-PAGE immunoblot)	Umpierrez et al. 1999
Sheep's alpha Caseins goat' s, sheep' s, and cow' s milk	17 children with CMA (immediate type): Inhibition of IgE binding to bovine alpha-CAS by alpha-CAS from cow, goat, and sheep (RAST inhibition), lower specific IgE levels to goat- and sheep alpha-CAS (RAST)	Spuergin et al. 1997

* multiple sensitization (not proved by inhibition-tests)

Unique Allergens	Subjects / Methods	References
Sheep's Caseins goat' s and sheep' s vs cow' s milk CAS	No inhibition of IgE- binding to goat' s and sheep' s CAS by cow' s milk CAS in 1 adult (RAST inhibition)	Wüthrich & Johansson 1995
Sheep's Caseins goat' s and sheep' s vs cow' s milk CAS	1 cow' s milk tolerant child with goat' s and sheep' s milk allergy: Decreased inhibition of IgE- binding to goat' s milk and CAS by cow' s milk and CAS, but not by goat' s and sheep' s milk and CAS (RAST inhibition); IgE binding to allergens in goat' s milk at 22, 27, and 31 kDa, in sheep' s milk at 31 kDa and cow' s milk at 34 kDa (SDS-PAGE immunoblot)	Umpierrez et al. 1999

7 Allergen Sources

Reported Adverse Reactions	References
Inhalation of Proteins A young man with IgE-mediated allergy to milk, caseins, and beta-lactoglobulin experienced respiratory crisis every time he milked his sheep (1)	(1) Vargiu et al. 1994
Goat' s and Sheep' s Cheese Several allergic reactions after ingestion of feta (cheese made from sheep' s milk) in a 15-year-old boy, after ingestion of sheep' s or goat' s cheese in a 25-year old patient, both tolerated ingestion of diary procucts from cow' s milk (1) Allergic reactions after eating goat' s cheese and after touching of goat' s and sheep' s cheese in a 2-year-old girl with tolerance to dairy products from cow' s milk (2) A young adult male had severe a anaphylactoid reaction after eating goat' s cheese; goat' s and sheep' s milk elicited mainly oral pruritus while cow' s milk and cheese was well tolerated (3)	(1) Wüthrich & Johansson 1995 (2) Umpierrez et al. 1999 (3) Orlando et al. 2000
Sheep' s Cheese Several anaphylactic reactions after ingestion of food containing "pecorino" cheese made from sheep' s milk in a 5-year-old atopic boy unaffected by cow' s milk protein allergy (1)	(1) Calvani & Alessandri 1998
Mozarella / Ricotta / Parmesan Cheese Asthma, urticaria and rhinitis in a boy with atopic dermatitis after ingestion of mozarella cheese made from ewe' s and cow' s milk; several allergic reactions after ingestion of ricotta cheese containing ewe' s milk and parmesan cheese made from cow' s milk, respectively (1)	(1) Fiocchi et al. 1999

8 Food Allergen Labelling

Food Allergen	Labelling / Regulation Status	References
International Regulations Sheep' s milk and products of these	labelling not recommended (1)	(1) Codex Alimentarius Commission 1999
European Regulations Sheep' s milk and products of these	labelling not recommended (1)	(1) Bousquet et al. 1998

9 References

- Andre F, Andre C, Colin L, Cacaraci F, Cavagna S (1994) **Role of new allergens and of allergens consumption in the increased incidence of food sensitizations in France** *Toxicology 93(1):77-83*
- Bellioni-Businco B, Paganelli R, Lucenti P, Giampietro PG, Perborn H, Businco L (1999) **Allergenicity of goat' s milk in children with cow' s milk allergy** *J Allergy Clin Immunol 103:1191-4*
- Bernard H, Creminon C, Negroni L, Peltre G, Wal JM (1999) **IgE Cross- reactivity with caseins from different species in humans allergic to cow' s milk** *Food Agric Immunol 11:101-11*
- Bousquet J, Björkstén B, Bruijnzeel-Koomen CAFM, Huggett A, Ortolani C, Warner JO, Smith M (1998) **Scientific criteria and the selection of allergenic foods for product labelling** *Allergy 53:3-21*
- Calvani M Jr, Alessandri C (1998) **Anaphylaxis to sheep' s milk cheese in a child unaffected by cow' s milk protein allergy** *Eur J Pediatr 157:17-9*
- Carroccio A, Cavataio F, Montalto G, D' Amico D, Alabrese L, Iacono G (2000) **Intolerance to hydrolysed cow' s milk proteins in infants: clinical characteristics and dietary treatment** *Clin Exp Allergy 30:1597-603*
- Codex Alimentarius Commission (1999) **Food labelling - complete texts** *Joint FAO/WHO Food Standards Programme, FAO/WHO, Rome*
- Dean TP, Adler BR, Ruge F, Warner JO (1993) **In vitro allergenicity of cows' milk substitutes** *Clin Exp Allergy 23:205-10*
- Docena G, Rozenfeld P, Fernandez R, Fossati CA (2002) **Evaluation of the residual antigenicity and allergenicity of cow' s milk substitutes by in vitro tests** *Allergy 57:83-91*
- Fiocchi A, Restani P, Riva E, Qualizza R, Bruni P, Restelli AR, Galli CL (1995) **Meat allergy: I - Specific IgE to BSA and OSA in atopic, beef sensitive children** *J Am Coll Nutr 14:239-44*

- Fiocchi A, Restani P, Decet E, Travaini M, Mirri GP, Bernardo L, Riva E (1999) **Evolution from ewe' s milk to cow' s milk allergy** *Allergy 54:401-2*
- Gjesing B, Osterballe O, Schwartz B, Wahn U, Lowenstein H (1986) **Allergen- specific IgE antibodies against antigenic components in cow milk and milk substitutes** *Allergy 41:51-6*
- Novembre E, Cianferoni A, Bernardini R, Mugnaini L, Caffarelli C, Cavagna G, Giovane A, Vierucci A (1998) **Anaphylaxis in children: clinical and allergological features** *Pediatrics 101(4):e8*
- Orlando JP, Breton-Bouveyron A (2000) **Anaphylactoid reaction to goat' s milk** *Allerg Immunol (Paris) 32:231-2* (in French)
- Rance F, Kanny G, Dutau G, Moneret-Vautrin DA (1999b) **Food hypersensitivity in children: Clinical aspects and distribution of allergens** *Pediatr Allergy Immunol 10:33-8*
- Restani P, Gaiaschi A, Plebani A, Beretta B, Cavagni G, Fiocchi A, Poiesi C, Velona T, Ugazio AG, Galli CL (1999) **Cross- reactivity between milk proteins from different animal species** *Clin Exp Allergy 29:997-1004*
- Sabbah A, Drouet M, Lauret MG (1996) **Western blotting or immunoblotting: application of the Alastat-Alablot to the study of cross reactions between cow' s milk and goat' s milk** *Allerg Immunol (Paris) 28:335-9* (in French)
- Spuergin P, Walter M, Schiltz E, Deichmann K, Forster J, Mueller H (1997) **Allergenicity of alpha- caseins from cow, sheep, and goat** *Allergy 52:293-8*
- Umpierrez A, Quirce S, Maranon F, Cuesta J, Garcia-Villamuza Y, Lahoz C, Sastre J (1999) **Allergy to goat and sheep cheese with good tolerance to cow cheese** *Clin Exp Allergy 29:1064-8*
- Vargiu A, Vargiu G, Locci F, Del Giacco S, Del Giacco GS (1994) **Hypersensitivity reactions from inhalation of milk proteins** *Allergy 49:386-7*
- Wüthrich B, Johansson SGO (1995) **Allergy to cheese produced from sheep' s and goat' s milk but not to cheese produced from cow' s milk** *J Allergy Clin Immunol 96:270-3*
