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ORIGINAL ARTICLE

# Allergy to goat and sheep cheese with tolerance to cow's milk and its derivatives

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**Abstract**
*Objective:* We present two adult and three paediatric patients who had allergic reactions after cheese ingestion and subsequently tolerated cow's milk derivatives. The objective of this study was to determine possible cross-reactivity between different types of cheese.
*Methods:* Skin tests were performed to cow's milk fractions, and prick–prick tests for goat, sheep and cow cheese. Specific IgE to the fractions of cow's milk and cow, sheep and goat cheese was analysed. The protein profile of cow, sheep and goat cheese extracts was determined by SDS-PAGE and the allergenic profile by immunoblot. Cross-reactivity was investigated by immunoblot inhibition.
*Results:* Skin tests were positive for casein in the patients. The prick–prick tests were positive for the three cheeses in patients 1 and 4, for goat and sheep cheese in patients 2 and 3, and for sheep cheese in patient 5. The specific IgE test was positive in patients 1, 3 and 4 for goat and sheep cheese, and negative in patients 2 and 5. Serum 3 and 4 clearly recognised goat and sheep cheese extracts. Goat casein was almost completely inhibited with sheep casein and partially inhibited with goat and sheep serum proteins, while there was no inhibition with cow cheese. Sheep casein was totally inhibited with sheep serum proteins. Sheep casein was inhibited with goat and cow caseins, suggesting cross-reactivity among the three types of cheese.
*Conclusions:* We showed sensitisation to goat and sheep cheese in two patients, and only to sheep cheese in another two of the studied patients.


## Introduction

Allergy to cow's milk proteins is one of the most common food allergies in children and caseins are probably the primary allergens involved.[1] A high degree of

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cross-reactivity between the milk caseins of different mammals has previously been described.[2–5] Allergy to goat's milk showing cross-reactivity between sheep and goat casein, without reactivity with cow casein, was published in 1995 by Wüthrich and Johanson.[3] Since then, several cases have been reported of anaphylaxis and other allergic reactions related to goat's and sheep's milk and their derivatives, with good tolerance to cow's milk and its derivatives.[4–7]

## Case reports

Patient 1: A 54-year-old male who presented anaphylaxis after the ingestion of cured cheese made from a mixture of goat's, sheep's and cow's milk. He subsequently tolerated cow's milk and its derivatives.

Patient 2: A 61-year-old woman who reported repeated episodes of angio-oedema of the lips, eyelids, tongue and glottis, which she occasionally related to eating cured cheese.

Patient 3: A nine-year-old boy diagnosed with allergy to nuts and seafood, who presented anaphylaxis after eating a portion of cheese. He subsequently tolerated cow's milk and its derivatives.

Patient 4: A six-year-old boy with a history of allergy to egg, which ceased at the age of five, who presented anaphylaxis after eating meat with Roquefort sauce. He subsequently tolerated cow's milk and its derivatives.

Patient 5: A nine-year-old boy allergic to nuts, egg, seafood and honey, who presented anaphylaxis after eating a mixture of cow's, sheep's and goat's cheese. He tolerated cow's milk without a problem.

## Material and methods

### Skin tests

Patients were skin prick tested with commercial casein, alpha-lactalbumin and beta-lactoglobulin extracts (Laboratorios Diater, Madrid, Spain). Prick-by-prick tests with goat, sheep and cow cheese were also performed.

### Extracts manufacturing

Cow's, sheep's and goat's cheese was purchased at a local market. Serum proteins and casein of different cheeses were separated and extracts prepared. The protein content was measured by the Lowry-Biuret method (Sigma, St. Louis, Mo., USA).

### Determination of total and specific IgE

Total and specific IgE, to cow's milk, cow's milk serum, casein alpha-lactalbumin, beta-lactoglobulin, sheep's milk and serum, goat's milk and serum, Cheddar cheese and a mixture of cheeses were quantitated by the ImmunoCAP® (Phadia, Uppsala, Sweden) technique.

Direct ELISA was used to determine specific IgE to the different cheese extracts in all patients.

### Oral provocation tests

We performed oral provocation test with two different cheeses (cow's, sheep's and goat's mixture cheeses) only in patient 2 and they were all negative. In the rest of the patients we did not perform oral challenges with cheeses because they presented anaphylaxis with their ingestion and had positive skin prick tests. As all five patients tolerated cow's milk at home we considered that it was not necessary to perform oral provocation test with cow's milk.

### SDS-PAGE and immunoblotting

A total of 40 μg of protein from each extract were loaded in a gel, run and stained with Biosafe Coomassie (Bio-Rad, Laboratories, Hercules, CA, USA.

Allergenic profile was studied by immunoblot. A total of 50 μg of protein from each extract were separated and electrotransferred to a PVDF and hybridised with the serum samples from different individuals (dilution 1/2).

### Cross-reactivity studies

Immunoblot inhibition assays were performed to determine the possible cross-reactivity among different extracts. A serum pool from patients 3 and 4 was prepared (50%–50%). The goat and sheep cheese casein extracts were used in solid phase. The serum pool was inhibited with all the extracts (500 μg) used in the study.

## Results

### Skin tests

The skin prick tests with the commercial extracts were only positive to casein in the fourth patient. The prick-by-prick tests with the different types of cheese were positive for the three cheeses in patients 1 and 4, for goat and sheep cheese in patients 2 and 3, and for sheep cheese in patient 5.

### Determination of total and specific IgE

Total and specific IgE values obtained by CAP are shown in Table 1. Specific IgE values obtained by direct ELISA are shown in Fig. 1. Patients 2 and 5 were negative for all extracts.

## SDS-page

The protein profile of casein extracts showed two bands at 15 and 32 kDa approximately, being more prominent in sheep and cow casein extracts. In the whey protein extracts, the most abundant proteins corresponded to the 14 and 18 kDa bands The albumin band with 69.2 kDa was also observed in all cases (Fig. 2).