

# Sensitization to Rabbit Allergens in Italy – A Multicentre Study in Atopic Subjects without Occupational Exposure

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## Key Words

Respiratory allergy · Rabbit allergens · Rhinitis · Asthma

## Abstract

**Background:** Rabbits as pets are becoming popular in Italy, but few data are available on sensitization to rabbits in patients without occupational exposure. In a multicentre study, we assessed the prevalence of rabbit sensitization in atopic subjects and their modality of exposure. **Methods:** Allergists from the whole country were required to assess the presence of skin prick test positivity to rabbits in about 100 consecutive patients with allergic rhinitis and/or asthma. In the rabbit-positive patients, clinical history, pet ownership and modality of exposure were assessed. **Results:** Skin tests were performed on 2,329 outpatients, of whom 1,602 had at least one positivity. Among them, 39 (2.43%) were sensitized to rabbit dander (4 monosensitized). The prevalence of sensitization ranged between 0.65 and 4.72%. Nineteen patients reported direct rabbit contact (10 for ownership and 9 for occasional contact) and 5 patients only indirect exposure through the contact with rabbit owners. Fifteen subjects denied any direct or indirect exposure. All the monosensitized patients were rabbit owners and had persistent (moderate-severe) respiratory symptoms. **Con-**

**clusions:** Sensitization to rabbit in Italy is not to be neglected. In atopic subjects without occupational exposure, contact and indirect exposure to rabbits may induce sensitization. A progressive increase in rabbit sensitization is expected in the future as consequence of the increased rabbit ownership.

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## Introduction

Exposure to rabbits (*Oryctolagus cuniculus*) is well recognized as an occupational hazard for people who are in regular contact with these animals (laboratories, pet shops, farms) [1, 2]. The major allergen of rabbit (Ory c 1) has been characterized as an 18-kDa lipocalin, and several other allergenic proteins have been identified [3]. Commercial skin prick tests (SPTs) are available for diagnosis. In recent years, rabbits have become more and more popular as pets in European countries, but in Italy, there are no quantitative data on rabbit ownership. Indeed, some indirect indices suggest an increasing rate of rabbit ownership as commercial sources indicate an expanding business in rabbit breeding and rabbit-related materials (i.e. pet accessories). Nevertheless, the preva-

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**Table 1.** Classification of rabbit exposure in rabbit-sensitized patients

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<i>Rabbit at home:</i> patients with rabbits at home for at least 6–8 months. Rabbits are usually kept in cages, but in some cases, rabbits are free to enter all rooms, including sleeping rooms.
<i>Occasional contact:</i> patients without rabbits at home, but in some cases, in close contact with rabbits outside the home.
<i>Indirect exposure:</i> patients with no direct exposure to rabbits but in contact with rabbit owners.
<i>No contact:</i> patients who denied any apparent direct or indirect exposure to rabbits.

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lence of sensitization to rabbits, its clinical characteristics and the modality of exposure are poorly known, and only sporadic reports concerning allergic sensitization to rabbit due to domestic exposure are available [4–6]. Finally, it can be supposed that sensitization to rabbits may also occur in consequence of indirect exposure, as it happens with cats [7–9], but the role of direct or indirect exposure to rabbit allergens has not been studied.

With the cooperation of the Allergy Study Group of the Italian Society of Respiratory Medicine, we aimed at investigating the characteristics of allergic sensitization to rabbits assessed by SPTs in different areas of Italy, in patients suffering from respiratory allergy but without occupational exposure. Another objective was to evaluate the role of the different modalities of exposure to rabbits in the development of allergic sensitization.

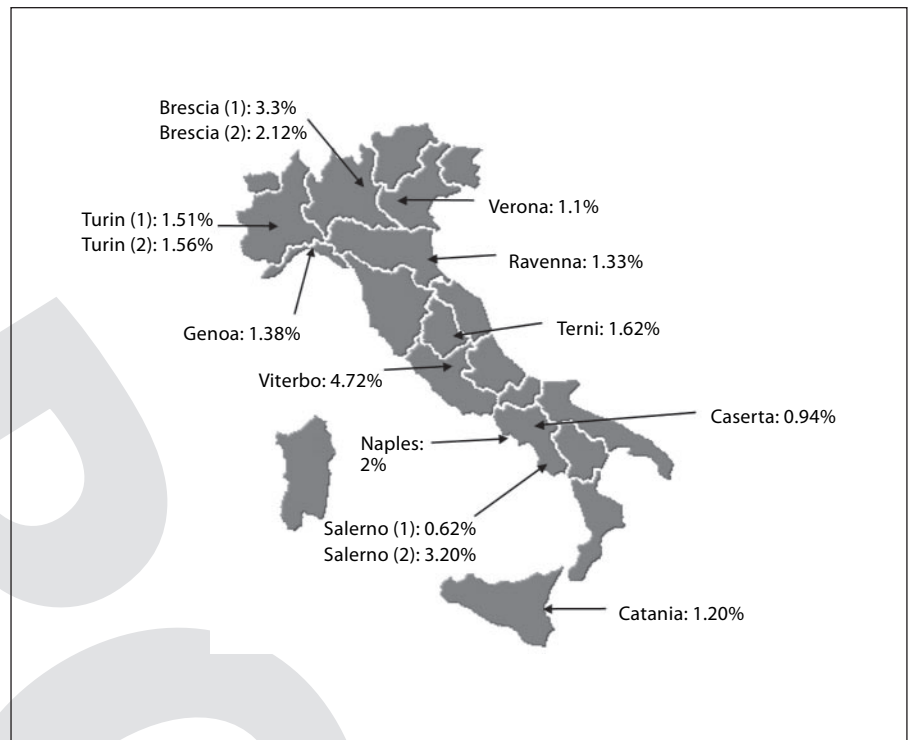
## Methods

Fourteen allergy units, distributed all over Italy, participated in this cross-sectional study. Each centre was required to collect the results of about 100 visits of consecutive outpatients diagnosed with respiratory allergy (asthma and/or rhinitis with positive skin test to one or more aeroallergens) from January until June 2004. All centres were required to use the same panel of allergens for SPTs and to include the rabbit extract. The panel of commercial extracts (ALK Abellò, Milan, Italy) included: *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, *Alternaria alternata*, *Cladosporium herbarum*, cat, dog and rabbit dander, *Parietaria*, grass mix, *Artemisia vulgaris*, *Olea europaea*, *Betula pendula*, *Cupressus sempervirens* and *Corylus avellana*. These represent the vast majority of causative allergens in Italy. Positive (10 mg/ml histamine HCl) and negative controls were used as well. SPTs were carried out according to international guidelines [10], and the result was expressed as the mean of the major wheal diameter plus its orthogonal. A skin reaction of 3 mm or greater was considered positive. SPTs were performed by the same opera-

tor at each centre. The diagnosis of respiratory allergy (asthma and/or rhinoconjunctivitis) was made according to the clinical history and following the ARIA and GINA criteria [11, 12]. Once the diagnosis of respiratory allergy was made, a standardized form for each patient was filled out, containing demographic data, type and duration of respiratory symptoms, pets and rabbit ownership, as well as results of the SPTs. Patients living in rural areas were excluded, as well as patients with severe cutaneous disorders, negative skin reaction to histamine, or using drugs interfering with SPTs [13, 14]. The absence of a pet at home does not exclude the possibility of a direct exposure to pets outside [12], and thus, we classified exposure into four categories (table 1).

## Results

The participating centres were homogeneously distributed across Italy, as shown in figure 1. In total, 2,329 patients were examined, and 1,602 (69%) were diagnosed as having respiratory allergy, with an SPT positivity for at least one of the allergens. The remaining 720 subjects (31%) had totally negative SPTs. The 1,602 subjects with respiratory allergy had a mean age of 29.2 years (range 2–76), and 890 (55%) were females. Thirty-nine were sensitized to rabbit dander, and thus, the overall prevalence of sensitization in subjects with respiratory allergy was 2.43%, ranging between 0.62 and 4.72% among centres (fig. 1). The main characteristics of the rabbit-sensitized patients are summarized in table 2. Only 4 of the 39 patients were monosensitized to rabbits. Nineteen patients reported direct rabbit contact (10 for rabbit ownership and 9 for occasional contact outside the home), whereas 5 patients excluded any direct exposure but were sometimes in contact with rabbit owners. Finally, 15 subjects denied any direct or indirect exposure to rabbits or rabbit allergens. The four (non-smoking) patients with single sensitization to rabbits had persistent moderate/severe rhinitis, moderate asthma and were rabbit owners. The time elapsed from the first contact with a rabbit to the development of symptoms was 3–5 months. Since 35 rabbit-sensitized patients showed multiple positivities to common allergens (mites, pollens and other pets), we could not quantify the clinical relevance of rabbit sensitization in these patients. The rate of skin positivity did not differ between rabbit-positive and rabbit-negative subjects for mites (53.8 vs. 48.2%;  $p = \text{NS}$ ) and dog dander (28.2 vs. 16.3%;  $p = \text{NS}$ ), whereas rabbit-positive subjects were more frequently sensitized to cats (43.5 vs. 23.1%;  $p = 0.05$ ). Since methods to measure rabbit allergens in indoor environments are not yet available, we have no information on the real level of exposure.



**Fig. 1.** Geographic distribution of the centres, with the percentages of subjects having positive skin reactions to rabbit dander.

**Table 2.** Characteristics of the 39 subjects with positive SPT to rabbit

	Number	Percentage		Number	Percentage
Sex, M/F	14/25	36/64	Rhinitis severity		
Mean age, years	26.6		Mild	12	30.7
Age range			Moderate/severe	21	53.8
0–20 years	13	33.3	Clinical symptoms		
21–40 years	20	51.3	Rhinitis only	16	41
41–60 years	6	15.4	Asthma only	3	7.6
Positive family history of allergy	21	54	Rhinitis + asthma	20	51.2
Pet at home			Monosensitized	4	10.2
Cat	7	18	Other sensitizations		
Dog	10	25.6	<i>Parietaria</i>	11	28.2
Rabbit	10	25.6	House dust mites	21	53.8
None	12	30.8	Grasses	25	64.1
Other animals	0	0	Olive	13	33.3
Modality of exposure to rabbit			Mugwort	7	17.9
Direct (ownership)	10	25.6	<i>Alternaria</i>	5	12.8
Direct (occasional contact)	9	23	<i>Cladosporium</i>	2	5.1
Indirect (with rabbit owners)	5	12.8	Birch	5	12.8
No direct or indirect contact	15	38.4	Hazelnut	5	12.8
Asthma severity			Dog	11	28.2
Mild	11	28.2	Cat	17	43.5
Moderate/severe	12	30.7	Diameters of rabbit allergen induced wheals (SPTs)		
			≤ 6 × 6 mm (18)	18	46.1
			> 6 × 6 mm (21)	21	53.8

## Discussion

The results of our study show that the prevalence of sensitization to rabbits is not to be neglected, ranging from about 1 to 5% of the allergic individuals. Of course, our data provide information only for a selected population (subjects referred to allergy centres), but this kind of study is a mandatory step before a general population-based survey is planned. Of note, our results suggest that rabbit contact (ownership or occasional) may be a risk factor for the development of allergic sensitization to rabbit allergens. Nevertheless, also some indirectly or unexposed individuals showed a sensitization to rabbit dander. The finding that an indirect exposure to rabbit allergens might be responsible for allergic sensitization confirms the previous documented report of severe respiratory allergy induced by indirect exposure [16]. Indeed, it is not easy to explain allergic sensitization to rabbits in patients who denied any apparent exposure to rabbits allergens. A possible reason could be a cross-reactivity between rabbit allergens and lipocalins [17] of other animal species such as mouse, guinea pig, dog, cow, horse and cat [18–23]. In this regard, one of the major allergens in the saliva of rabbits was identified as an 18-kDa lipocalin [3, 24]. Nevertheless, in our population, about one third of the subjects had direct exposure to neither cats nor dogs (table 2).

In the 4 individuals monosensitized to rabbits, respiratory symptoms were persistent and of moderate-severe degree of intensity. This finding is in agreement with Yarnell et al. [25] who found that the ownership of small animals (rabbits, guinea pigs or gerbils), but not cats and dogs, was independently associated with both severe wheeze and asthma.

In conclusion, rabbits seem to represent a non-negligible cause of allergic sensitizations and, probably, of

clinical symptoms in susceptible individuals even in the absence of occupational exposure. Direct rabbit contact is a heavy risk factor, but also occasional direct/indirect exposure may induce allergic sensitization.

A progressive increase in rabbit sensitization (also by indirect exposure) is expected in the future as a consequence of increased rabbit ownership. Finally, as a consequence of our previous experience [16], we suggest to perform SPT assay for rabbit allergens in potentially susceptible (allergic) individuals before the introduction of a rabbit indoors, also in the absence of respiratory symptoms after previous occasional rabbit contact.

## Appendix

### *The Allergy Study Group of the Italian Society of Respiratory Medicine*

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