

Short communication

Siberian hamster: a new indoor source of allergic sensitization and respiratory disease

Background: The identification of 'unknown' allergic sensitizations may determine the prognosis and treatment of patients with respiratory airway disease. Currently, the presence in homes of 'exotic' animals as pets is increasing. In this article the Siberian hamster or dwarf hamster (*Phodopus sungorus*) was identified as a new indoor source of aeroallergens and respiratory disease.

Methods: The subjects were six outpatients who were treated for asthma and rhinitis. Siberian hamster hair extract was prepared with a standard wt/vol method, and patients were skin-prick tested with the extract. Serum-specific immunoglobulin (Ig)E against the Siberian hamster, common hamster (*Cricetus cricetus*) and golden hamster (*Mesocricetus auratus*) was determined. IgE-immunoblotting was also performed for all six sera. Specific bronchial challenge was carried out with the Siberian hamster extract.

Results: Skin prick tests (SPT) with the Siberian hamster extract, and specific IgE-antibodies against Siberian hamster, were strongly positive in all six patients. Determinations of specific IgE-antibodies against *C. cricetus* and *M. auratus* were negative in all patients. IgE-immunoblotting of the sera revealed two IgE-binding fractions (MW 18 and 32 kDa) in five of the six sera. Specific bronchial provocation tests resulted in early asthmatic responses in the two patients who were challenged.

Conclusions: The present study reveals the Siberian hamster to be able to induce both sensitization and disease, and this species of hamster should be taken into consideration as a cause of respiratory disease in exposed subjects. A noteworthy finding was the lack of sensitization in our patients to common hamster allergens (*M. auratus* and *C. cricetus*) that are usually tested when hamster allergy is suspected.

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In patients with respiratory airway disease, the recognition of the factors that cause allergy may determine the prognosis and treatment of asthma and rhinitis. Some patients may be sensitized to unknown allergens not included in skin test batteries of common aeroallergens. The detection of new removable allergenic sources such as 'uncommon' domesticated animals and pets is of particular significance.

Domestic animals currently represent the second most frequent source of indoor aeroallergens after house dust mites (1). Cats and dogs are the pets found most frequently in dwellings, and allergic sensitization to these animals is the most prevalent (2), but other domestic animals can also induce allergic sensitization and respiratory disease. Respiratory allergic diseases owing to rodents are well recognized (3). Both domestic and occupational exposure to these mammals play a significant role in the development of immunologic

sensitization to animal-derived antigens. The rodents involved in this type of reaction are rats, mice, guinea-pigs (4), common hamsters (5) and gerbils (6).

Currently, 'exotic' animals are being acquired with increasing frequency as pets. The Siberian hamster (SH) or dwarf hamster, *Phodopus sungorus*, is one of the latest rodents to have become a popular household pet. We report evidence that identifies SH as the cause of allergic asthma and rhinitis. We are not aware of other reports of this sensitization.

Material and methods

Patients

The subjects were six nonsmoking outpatients who were seen at the allergy clinic of the University Hospital and Clinics during a period of 19 months. All patients consulted for respiratory symptoms. The patients' characteristics and demographic data are summarized in Table 1.

The patients ranged in age from 19 to 44 years, and four of them were women. All six patients were taking inhaled corticosteroids on a regular basis and short-acting beta agonists as needed at the time of consultation. Five patients had attended the emergency room for asthma and two of them had required hospitalization. All six patients had acquired a SH in the preceding 1 to 13 months. The six patients lived in urban dwellings and none clearly related their symptoms with exposure to or handling of the animals.

SH extract

SH hair was obtained from two of the patient's hamsters, and the extract was prepared with a standard wt/vol method. The collected hair was extracted by magnetic stirring in phosphate-buffered saline (PBS) at a 10% (wt/vol) ratio for 24 h at room temperature (500 g). After centrifugation, the extract was dialyzed against distilled water and stored in aliquots at -20°C until use. The protein content of the extract was assayed according to the method of Lowry (7).

Aliquots of the same extract were used for all *in vitro* and *in vivo* tests performed in all six patients and in 10 atopic and nonatopic control subjects.

Skin tests

Skin prick tests (SPTs) were performed according to the Subcommittee on Skin Tests of the European Academy of Allergology and Clinical Immunology. Histamine hydrochloride at 10 mg/ml and 0.9% saline solution were used as positive and negative controls, respectively. Standardized lancets (Dome-Hollister-Stier, Berkshire, UK) were used for prick tests.

Patients were skin tested by prick with a 1:10 wt/vol extract of SH and a commercially available hamster (*Cricetus cricetus*) dander extract (ALK-Abelló, Madrid, Spain).

Routine prick tests were also performed with a battery of 18 commercially available inhalants: two house dust mites (*Dermatophagoides pteroyissinus* and *D. Farinae*), two animal danders (dog and cat), five common molds (*Alternaria alternata*, *Cladosporium herbarum*, *Penicillium notatum*, *Aspergillus* spp., and *Mucor* spp.), and nine prevalent pollens (*Platanus orientalis*, *Olea europea*, *Phleum pratense*, *Cynodon dactylon*, *Chenopodium* spp., *Plantago lanceolata*, *Taraxacum officinale* and *Parietaria judaica*). Extracts were provided by ALK-Abelló and Dome-Hollister-Stier.

The mean wheal diameter was measured after 15 min. A wheal with a mean diameter of 3 mm or greater with erythema was defined as a positive reaction.

Serum-specific IgE assays

Specific IgE against SH and common hamster (*C. cricetus*) antigens was determined by RAST. Paper disks were activated with BrCN and coupled with SH hair and hamster dander extracts according to the method of Ceska and Lundqvist (8). Siberian hamster disks were incubated overnight with the patients' sera, then washed and incubated with 100,000 c.p.m. of (125) I-labelled mouse antihuman IgE monoclonal antibodies (mAb) (9). Lolium disks and four dilutions of a grass-specific serum pool which had been calibrated against the Pharmacia Phadebas RAST system were used as a reference. The results were reported as Phadebas RAST classes 0–4.

Specific IgE to golden hamster dander (*Mesocricetus auratus*), house dust mites, pollen, fungus spores, and cat and dog dander was determined by the CAP system (Pharmacia, Uppsala, Sweden) according to the manufacturer's instructions.

SDS-PAGE and IgE immunoblotting

SDS-PAGE was carried out according to Laemmli (10) under nonreducing conditions with a 15% polyacrylamide running gel. The SH extract proteins separated by SDS-PAGE were transferred

onto nitrocellulose membranes (0.4×5 cm) as described by Towbin et al. (11). After the reaction was blocked with 5% bovine serum albumin (BSA) in PBS, immunodetection of IgE-binding proteins was performed by incubating a 1:10 dilution of patients' sera in 1% BSA, 0.05% Tween 20 in PBS, and then a 1:3000 dilution of the sera in mouse antihuman IgE mAb HE-2 ascitic fluid. Finally, the IgE-binding protein bands were detected by enhanced chemiluminescence (ECL, Amersham, UK) according to the instructions of the manufacturer. One blot was incubated with dilution buffer instead of the patient's serum as a negative control.

Bronchial provocation test

Specific bronchial challenge was done with the water-soluble SH extract according to a previously described method (12). The patient inhaled the aerosolized allergen in progressive concentrations at tidal breathing for 2 min. A control challenge with PBS was done before antigen provocation. Increasing concentrations of SH extract were given by inhalation, starting with a concentration that induced a 2–3 mm wheal on skin prick testing. The dose was increased in five-fold increments at intervals of 10 min, and FEV₁ and FVC were measured 5 and 10 min after each concentration was inhaled. The bronchial challenge test was discontinued when there was a decrease in FEV₁ of 20% or greater from the lowest postsaline value, or when the highest concentration had been given. At the end of the inhalation challenge test, spirometric values were obtained 20, 30 and 60 min after challenge, and again on the following day. Peak expiratory flow rate (PEF) was measured before and every hour after bronchial challenge until bedtime, and again on the following day. A decrease in FEV₁ of 20% or more from the lowest postsaline value within 60 min of the challenge was considered a positive immediate reaction, whereas a decrease in PEF greater than 25% between 2 and 24 h after challenge was considered a positive late reaction.

Results

The results of SPTS with the SH extract were strongly positive, with the allergen wheal areas being larger than the wheal areas seen with 10 mg/ml histamine in most patients (Table 2). Prick tests with SH extract in 10 atopic and nonatopic control subjects were all negative. SPTs with commercially available hamster extract were negative in all six patients.

Three patients were sensitized exclusively to SH. The three other patients were also sensitized to common aeroallergens such as dust mites, cat dander and olive pollen. The latent interval from first contact with the SH to the development of symptoms in the three patients sensitized exclusively to this species (patients number 1, 2, and 5) was 1 month, 3 months and 1 month, respectively.

Specific IgE antibodies against SH hair extract were also strongly positive in all six patients (Table 2). RAST class 3 or 4 was found in five sera. Determinations of specific IgE antibodies against *C. cricetus* were negative in all patients, as were tests for *M. auratus*.

The results of IgE immunoblotting of sera from all six patients are reported in Fig. 1. Two IgE-binding fractions (estimated MW of 18 and 32 kDa) were

Table 1 Characteristics of 6 patients sensitized to Siberian hamster (SH)

Patient No.	Age (years)	Sex	Symptoms (Asthma severity)	Duration of symptoms	Baseline FEV1 (% predicted)	Treatment on a regular basis	Admissions in emergency room
1	43	Female	A,R (Severe)	10 m	71	IC, LABA	3 (one hospital admission)
2	44	Female	A,R,C (Moderate)	7 m	77	IC, LABA	2
3	32	Male	A (Severe)	3 y	84	IC, LABA	2 (one hospital admission)
4	30	Male	A,R (Moderate)	7 y	82	IC	1
5	43	Female	A,R,C (Moderate)	8 m	84	IC	1
6	19	Female	A,R,C (Moderate)	11 y	93	IC	—

A, Asthma; R, Rhinitis; C, Conjunctivitis; IC, Inhaled corticosteroids; LABA, Long-acting beta 2 agonist.

detected in five of the six sera. Serum from patient 5 showed a different pattern of IgE-binding proteins: IgE from this serum reacted to only one band at 20 kDa.

Specific bronchial challenge with SH extract was done in only two patients. The test resulted in early asthmatic responses in both patients. No late asthmatic responses were detected. The concentration of the extract that caused a decrease in FEV₁ of 20% or greater was 1:10 wt/vol in patient 4, and 1:1000 wt/vol in patient 5. The results of the bronchial provocation tests are shown in Table 2.

Discussion

An exhaustive search for causative allergic factors in patients with respiratory airway disease is imperative. The recognition of allergic sensitizations may determine the prognosis and treatment of asthma and rhinitis. As described previously (13), some patients diagnosed as having 'Nonallergic asthma or rhinitis' may, in fact, be sensitized to unknown allergens not included in skin test batteries of common aeroallergens. Of particular significance is the detection of removable allergenic sources such as pets. In this report, SH were established as the cause of allergic

asthma and rhinoconjunctivitis in six patients, on the basis of the clinical course, skin tests, serum-specific IgE, IgE-binding fractions in immunoblotting, and bronchial challenge (in two of them).

The SH, dwarf hamster or Djungarian hamster, *Phodopus sungorus*, is a member of the *Cricetinae* subfamily of rodents which has recently become a popular household pet. This hamster can also be present in laboratories as an experimental animal (14). The *Cricetinae* subfamily also comprises the *Cricetus* and *Mesocricetus* genera, including the species *C. cricetus* (common hamster) and *M. auratus* (golden hamster). The lack of sensitization to these hamsters in our patients is noteworthy, as these are currently the most prevalent species of hamster as pets or laboratory animals. Thus, *M. auratus* and *C. cricetus* dander-derived antigens are the allergens usually tested in skin tests, and specific IgE determines when hamster allergy is suspected. Therefore, it is clinically relevant to determine exactly which species each patient is exposed to at home or at the workplace, in order to test the appropriate allergens and avoid false negative diagnoses.

When the six patients in this report were asked about the presence of pets in their homes, only two

Table 2. Results of skin-prick tests, specific IgE determinations and specific bronchial challenge tests

Prick tests BPT fall in FEV1 Total IgE Other RAST (Class) (kU/l) sensitizations** CAP (Class)									
Patient No.	Siberian hamster* (<i>P. sungorus</i>)	Golden hamster* (<i>M. Auratus</i>)	Common hamster* (<i>C. cricetus</i>)	Histamine*	Siberian hamster* (<i>P. sungorus</i>)	Golden hamster* (<i>M. Auratus</i>)	Common hamster* (<i>C. cricetus</i>)		Histamine*
1	9	0	7	4	0	0	—	218	ND
2	12	1	10	3	0	0	—	57	ND
3	11	0	8	3	0	0	Dust mites	264	ND
4	14	0	8	3	0	0	Dust mites, Cat dander, <i>Alternaria</i>	186	35%
5	8	0	7	1	0	0	—	45	26%
6	8	1	8	3	0	0	Dust mites, Cat dander, Olive	211	ND

*Mean orthogonal diameter of largest wheal in mm, **By prick tests, CAP or both.

BPT, bronchial provocation test with Siberian hamster extract (maximum decrease in FEV1 observed during the EAR). ND, not done.

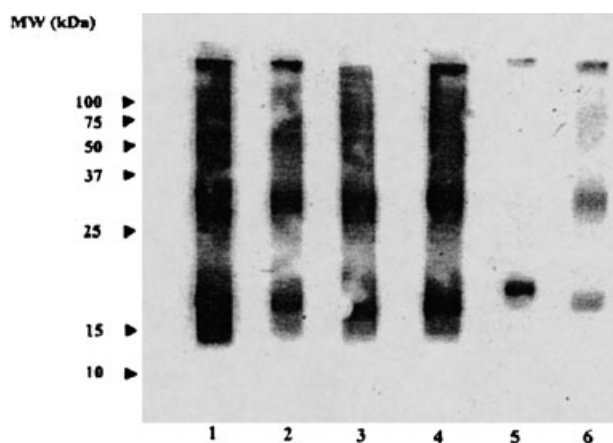


Figure 1. Immunoblotting results for Siberian hamster in sera from different patients (lanes 1–6).

specified the type of hamster as the dwarf or SH. Therefore, careful clinical questioning should aim to determine the actual hamster species the patient is exposed to.

The short duration of SH exposure before symptoms appeared in the three patients sensitized exclusively to this species suggests that the allergenic power of these antigens is high.

The other three patients also presented sensitizations to common aeroallergens, including cats in two patients. In these patients, cat sensitization seems to be compatible with multiple sensitizations in atopic patients. However, crossreactivity between SH and cat allergens is a possibility worth investigating, as several studies have demonstrated crossreactivity between a variety of rodents and other mammals (15, 16).

The pattern of IgE-binding proteins indicates the presence of two main groups of allergenic proteins: one band at 18 kDa and the other at 32 kDa. These components, which react with five of the six individual sera included in this study, can be considered clinically relevant allergens of SH. The molecular weight of the 18-kDa component coincides with that of lipocalin proteins. The components of the lipocalin family are low-molecular-weight (typically 17–20 kDa) proteins which are generally accepted as an important cause of crossreactivity between furred animals (17). It would be worthwhile to conduct further studies with this SH fraction (MW 18 kDa) to establish the possible lipocalin nature of this protein.

Atopic status seems to be a risk factor for sensitization to SH, as is assumed for other domestic or laboratory animals (18). Thus, although there is some controversy about the development of allergy in children (19), early preventive measures to avoid SH sensitization are advisable for atopic subjects, including children known to have atopic characteristics.

With respect to the clinical course, all six of our patients presented moderate to severe asthma requiring continuous anti-inflammatory therapy. Clinical improvement was observed in all the patients a few weeks after the animals were removed from the homes. Two of the three patients sensitized exclusively to SH remained asymptomatic, and the other patient presented intermittent mild asthma requiring short acting beta-agonist as needed, 14 months after the animals were removed.

The maintenance of 'hidden' allergenic exposure could explain why the removal of pets from the home sometimes does not lead to the anticipated decrease in respiratory symptoms in subjects sensitized to common pets (20). Cat and dog allergens can be detected in public places and homes with no pets (21, 22), although it is unlikely that SH allergens are present in public places. However, Fel d 1 is known to persist for several months after the removal of cats from apartments (23). SH allergens can probably also persist in homes for several months after the animal is removed.

No patient was occupationally exposed to SH, but the increasing use of this species as a laboratory animal should be taken into consideration. Sensitization to laboratory animals has a high prevalence among laboratory workers (24, 25), and home transportation of laboratory animal allergens on clothing has been demonstrated (26). Thus, sensitization to SH is a possibility in laboratory workers exposed to SH and in people living with such employees.

The present study shows that SH is able to induce IgE-mediated asthma, rhinitis and conjunctivitis (27); we therefore conclude that this species of hamster should be taken into consideration as a cause of respiratory disease in exposed subjects. A progressive increase in SH sensitizations should be expected because of the increase in domestic and occupational exposure to this rodent. Crossreactivity between SH and other hamsters seems unlikely in view of the lack of sensitization to other hamster species in our patients. Further immunological studies are needed to identify and characterize the allergens of *P. sungorus*, and to determine the degree of cross-reactivity between SH, other rodents, and other mammals.

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