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Anaphylaxis to Horses and Epinephrine Use-Increasing Awareness Among Pediatric Patients and Families

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To the Editor:

Pet allergens follow aeroallergens as a common cause of asthma and rhinitis in children (1, 2). Specifically, cat and dog dander are typical triggers of these symptoms (1). However, high percent of patients with severe asthma can be sensitized to other mammals, such as horses and mice (3). This is not limited to occupational or rural areas where exposure to this animal is more prevalent. A high rate of sensitization to horses in people with no known direct exposure who live in urban areas is well documented (4). However, reports of anaphylaxis to furry animals is extremely rare, with only few cases reported in the literature. Despite the limited experience or reports with horse allergy and anaphylaxis, we have observed an increasing number of patients with the diagnosis of horse anaphylaxis in our hospital-based clinical practice (1). Unfortunately, anaphylaxis is often misdiagnosed by patients and health providers due to lack of recognition of its signs and symptoms. This can carry serious consequences. Furthermore, the etiology of the anaphylaxis episode is often unknown, making prevention difficult. Herein we report four male patients with an age range of 3 to 18 years who presented at our hospital with symptoms compatible with anaphylaxis to horses.

The first case, a previously healthy 3-year-old male, with history of peanut and cashew anaphylaxis and dog allergy, was in a horse drawn sleigh ride. Within minutes, he developed cough, wheezing and started to drool. He was treated with antihistamine and intramuscular

steroid with resolution of symptoms. He had not eaten peanuts or tree nuts at least 2 hours prior the episode. Injectable epinephrine was not used during this event. His IgE/ImmunoCAP test results were strongly positive for horse dander, dog epithelium, and several tree nuts (Table 1).

The second case, an 8-year-old male with history of allergy to dog and cat dander came to our clinic for initial evaluation. The patient visited a circus-type spectacle that involved horses. Within minutes of starting the show, he developed eye itchiness, facial urticaria and swelling associated with shortness of breath and cough. He did not have an epinephrine autoinjector available. History was not indicative of anaphylaxis secondary to any kind of ingestion. IgE/ImmunoCAP was positive to horse dander (Table 1).

The third case, a 9-year-old male with history of allergy to cats, chicken feathers, and shrimp anaphylaxis visited a farm for the first time. Within minutes of visiting the horse barn, he developed generalized urticaria, angioedema, and difficulty breathing. The patient did not have autoinjectable epinephrine with him at the time of this event, although it had been previously prescribed. IgE/ImmunoCAP to horse dander was positive (Table 1).

The fourth case, an 18- year-old male with history of cerebral palsy, perennial allergic rhinitis, and dog anaphylaxis, was exposed to horses on several occasions. The first exposure was at the age of 5 years when he visited a farm. He presented with cough when he approached the horses. At the age of 16 years, he started pet therapy. He developed cough the first time he rode a horse. At the time of the next exposure, he presented with angioedema and wheezing. Epinephrine was not used to treat his reaction. His IgE/ImmunoCAP results were strongly positive for horse, cat, and dog dander (Table 1).

Since we spend most of our time indoors, sensitization to allergens found in this environment contributes to an increased risk of allergic rhinitis and asthma (5). The most common indoor allergens causing sensitization and contributing to atopic diseases are dust mites, cockroaches, molds, pet dander and mice (3). Sensitization to pet dander, especially cat and dog dander, has frequently been described in atopic patients (6). In addition, a recent report has also associated mouse sensitization with asthma severity (7). In the United States, inner city children with asthma showed 41% and 22% sensitization to cats and dogs, respectively (3). In Europe, dog and cat sensitization rates were 27.2% and 26.3%, respectively, as determined by skin prick test (8). Furthermore, the prevalence of exposure and sensitization to dogs and cats is increasing with time, not only in North America but also in Europe (6, 9). For example, in a study done in North Sweden, the prevalence of sensitization to cat and dogs increased from 13.4% to 19.1% and 8.7% to 15.7%, respectively, in a 10-year period (9). In addition, these allergens have been found not only in the patient's home environment, but also in daycare centers and schools, places where these animals do not reside (10).

Horse dander is usually not taken into consideration as a possible culprit of atopic diseases, especially in an urban environment. While one might expect horse allergy to be a rare problem in urban environments, a previous report and our clinical experience shows that horse dander is an important and possibly overlooked allergen in children. A study which assessed the importance of furry animals in hypersensitivity reactions, found that 31 % of the 100 people examined had sensitization to horses (11). Many of the patients had no known contact with horses (11). Moreover, severe asthma in children was associated with higher levels of IgE antibodies against horse, besides cat and dog, compared to children with controlled asthma (6).

In three cases, the reaction occurred during the first known exposure. The sensitization to horses in people with no known contact could be due to cross-reactivity of some of their allergens with cats, mice, dogs, and the high prevalence of sensitization to these animals. The lipocalins are part of the major inhalant allergens causing symptoms in sensitized individuals among most of the animals discussed above (12). With a high molecular similarity across different species, this group of proteins constitute the most important allergen in dogs (Can f 1-2), mice (Mus m1) and horses (Equ c 1). Likewise, another group of allergens with high conserved structural properties across different species, the albumins, are important minor allergens in cats (Fel d 2), horses (Equ c 3) and dogs (Can f 3) (12). Another possible explanation for the anaphylaxis occurring at the first known exposure may be the passive carriage of horse allergen on the clothes or hair of individuals in contact with horses and children. These could lead to possible sensitization to horse allergens, resulting in anaphylaxis without previous known exposure.

Several allergens have been isolated from horses with Equ c 1 being the most important for anaphylaxis (13). This protein is reported to account for most of the skin-prick test reactivity of horsehair and dandruff extract. Besides its presence in horsehair and dandruff, it can also be found in submandibular salivary glands of horses (13).

As stated above, anaphylaxis to furry animals is extremely rare, however identification is necessary due to its severe nature. Obtaining an accurate and complete history was crucial for identifying the causative allergen in each of our patients. All the children in this report were known to have food or cat/dog allergies. Children with previous history of atopy, or those who are sensitized to other pet dander, may be at an increased risk of having anaphylaxis to horses (14). Careful evaluation of these children should be completed since sensitization to horse could be associated with severe allergic reactions, such as anaphylaxis, as described in

this case series. Health care providers, patients, and parents should be aware of this possibility.

Interestingly, three out of our four patients had previously been prescribed injectable epinephrine for their history of other food or dog anaphylaxis. Despite education regarding the signs and symptoms of anaphylaxis, as well as the need to carry the epinephrine at all times, it was not used in any of the patients with anaphylaxis to horses. This is important to note because, after avoidance of exposure to allergens, the use of epinephrine is the most important step in preventing death from anaphylaxis.

Recognition of anaphylaxis to horses is necessary among the pediatric population. Testing to horse dander in patients who report exposure appears important for proper diagnosis.

Furthermore, increased patient education regarding identification of the signs and symptoms of anaphylaxis, as well as increased awareness about the importance of carrying and utilizing epinephrine, should be a priority.

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1. Roberts G, Lack G. Horse allergy in children. *Bmj*. 2000;321(7256):286-7.
2. Chapman MD, Wood RA. The role and remediation of animal allergens in allergic diseases. *The Journal of allergy and clinical immunology*. 2001;107(3 Supl):S414-21.
3. Gruchalla RS, Pongracic J, Plaut M, Evans R, 3rd, Visness CM, Walter M, et al. Inner City Asthma Study: relationships among sensitivity, allergen exposure, and asthma morbidity. *The Journal of allergy and clinical immunology*. 2005;115(3):478-85.
4. Liccardi G, Salzillo A, Dente B, Piccolo A, Lobefalo G, Noschese P, et al. Horse allergens: An underestimated risk for allergic sensitization in an urban atopic population without occupational exposure. *Respiratory medicine*. 2009;103(3):414-20.
5. Platts-Mills TA, Vervloet D, Thomas WR, Aalberse RC, Chapman MD. Indoor allergens and asthma: report of the Third International Workshop. *The Journal of allergy and clinical immunology*. 1997;100(6 Pt 1):S2-24.
6. Konradsen JR, Nordlund B, Onell A, Borres MP, Gronlund H, Hedlin G. Severe childhood asthma and allergy to furry animals: refined assessment using molecular-based allergy diagnostics. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology*. 2014;25(2):187-92.
7. Grant T, Aloe C, Perzanowski M, Phipatanakul W, Bollinger ME, Miller R, et al. Mouse Sensitization and Exposure Are Associated with Asthma Severity in Urban Children. *The journal of allergy and clinical immunology In practice*. 2016.
8. Heinzerling LM, Burbach GJ, Edenharter G, Bachert C, Bindslev-Jensen C, Bonini S, et al. GA(2)LEN skin test study I: GA(2)LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. *Allergy*. 2009;64(10):1498-506.

9. Ronmark E, Bjerg A, Perzanowski M, Platts-Mills T, Lundback B. Major increase in allergic sensitization in schoolchildren from 1996 to 2006 in northern Sweden. *The Journal of allergy and clinical immunology*. 2009;124(2):357-63, 63 e1-15.
10. Salo PM, Sever ML, Zeldin DC. Indoor allergens in school and day care environments. *The Journal of allergy and clinical immunology*. 2009;124(2):185-92, 92 e1-9; quiz 93-4.
11. Guinnepain MT, Laurent J, Brunet-Moret MJ, Eloit C, Herpin-Richard N, Colas Des Francs V, et al. Allergy to animal integument : natural history and frequency of latent associations. *Rev Fr Allergol Immunol Clin*. 1996;36(7):759-64.
12. Liccardi G, Triggiani M, Piccolo A, Salzillo A, Parente R, Manzi F, et al. Sensitization to Common and Uncommon Pets or Other Furry Animals: Which May Be Common Mechanisms? *Translational medicine @ UniSa*. 2016;14:9-14.
13. Loowenstein H, Markussen B, Weeke B. Isolation and partial characterization of three major allergens of horse hair and dandruff. *International archives of allergy and applied immunology*. 1976;51(1):48-67.
14. Mullins RJ. Anaphylaxis: risk factors for recurrence. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology*. 2003;33(8):1033-40.

Table 1. Patient Characteristics			
Age (years)	Symptoms	Location of exposure to horses	Specific IgE (Immunocap) to horse dander (kUnits/Liter)
3	Cough, drooling, wheezing, and itching	Horse drawn sleigh hayride	19.8
8	Eye itchiness, shortness of breath, facial urticaria, and cough	Circus-type spectacle	2.04
9	Angioedema, shortness of breath	Visit to a farm	1.24
18	Angioedema and wheezing	Pet/horse therapy	30.3