

Laboratory Animal Bite Anaphylaxis: A National Survey

Part 1: Case Series and Review of the Literature

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Objective: This study documents previously unreported cases of laboratory animal bite anaphylaxis in animal laboratory facilities in the United States.

Methods: An online survey was e-mailed to designated institutional officials at laboratory animal facilities identified by the National Institutes of Health Office of Laboratory Animal Welfare. **Results:** One hundred ninety eight organizations responded and 15 organizations indicated that workers had experienced anaphylaxis following an animal bite. Case report forms were completed by nine of these institutions for 14 cases, 13 for rodent bites, and one involving a needlestick from a horse. In half of the cases involving rodents, there was no prior history of animal allergy. All workers had uncomplicated recoveries. Treatment, testing, and work restrictions varied across cases. **Conclusions:** While uncommon, anaphylaxis from laboratory animal bites occurs more frequently than suggested by the literature.

Anaphylaxis is a systemic allergic reaction that can have a variable course, but may progress rapidly and is potentially life threatening.^{1,2} An estimated 100,000 cases occur annually in the United States.² While most cases are associated with medications, many are related to occupational exposures, including insect stings, non-rubber latex, chemicals, and bites from mammals.¹

Anaphylaxis following laboratory animal bites has been reported rarely in the literature, with only eight cases described in the English language world literature from 1983 to 2016.^{3–8} An additional nine non-occupational cases of anaphylaxis following rodent bites appear in the literature.^{9–16}

This study sought to identify previously unreported cases of anaphylaxis following laboratory animal bites in the United States and to determine whether this phenomenon occurs as infrequently as suggested by the literature. In addition, history of allergy, clinical characteristics, treatment, testing, and follow-up of newly identified cases was compared with occupational and non-occupational cases described in the literature.

METHODS

An online survey (Qualtrics) was e-mailed to the designated institutional official at all laboratory animal care facilities identified by the National Institutes of Health Office of Laboratory Animal Welfare (1272 facilities across the country). Supplemental requests to encourage completion of the survey were sent to occupational medicine physicians at medical centers.

Survey responses were collected and analyzed. The survey included questions on:

- (1) Whether and how many workers developed anaphylaxis following an animal bite
- (2) For workers who developed anaphylaxis following an animal bite, clinical information was requested regarding prior history

of allergy to animals, symptoms, treatment, outcome, and follow-up.

Cases of anaphylaxis following rodent bites in the occupational and non-occupational setting were identified by an English language literature search using PubMed, Google Scholar, and Google, with an iterative search for additional cases identified in references.

The study was conducted under a waiver from the Duke Institutional Review Board.

RESULTS

Of the 198 institutions responding to the survey, 183 answered the question about whether at least one employee had experienced anaphylaxis following a bite from a laboratory animal with 15 (8%) responding yes. Of those responding to a subsequent question asking how many cases they had experienced, seven indicated that they had experienced one case, three had two cases, one had three cases, and two had four cases (24 cases). Case report forms were completed by nine institutions for 14 previously unpublished cases of anaphylaxis. Eleven of these cases occurred between 2010 and 2016. While 13 of these reports involved rodents (10 due to mice and three caused by rats), there was also one report of anaphylaxis in a veterinarian drawing blood from the jugular vein of a horse who experienced a needle stick (Table 1).

Newly Identified Cases of Anaphylaxis Involving Rodents

All episodes of anaphylaxis involving rodents were preceded by bites to the hand or finger and all workers had uncomplicated recoveries (Table 1). Workers ranged in age from 23 to 56 years. One of the cases involved a graduate student. Of these 13 cases, six involved a worker with no prior known history of respiratory or dermal allergy to animals. Among those with a prior history of respiratory and/or dermal allergy, the interval between initial allergy symptoms and the episode of anaphylaxis ranged from less than 1 year to 12 years. Nine of the 13 workers were treated with epinephrine, usually in combination with other treatments. Nine workers underwent allergen testing. Of the four for whom results were provided, three had positive tests and one had negative skin and radioallergen sorbent tests (RAST). Work restrictions were instituted for all but two workers, and varied widely. Work restrictions ranged from use of personal protective equipment (PPE) to no longer working with the animal species involved in the episode. All workers were advised to carry injectable epinephrine and the four workers who continued to be at risk for bites were required by the employer to keep injectable epinephrine with them.

Occupational Cases of Anaphylaxis Involving Rodents in the Literature

Three of the eight cases previously reported in the literature are from the United States (Table 2).^{4,5,7} Five cases involved rats^{3–5,8} and three were caused by mouse bites.^{6–8} The workers ranged in age from 23 to 55 years. When work history was reported, the workers had between 6 to more than 20 years of experience with animal work. Only two had no history of any form of allergy or asthma.^{3,5} Four had histories of previous animal bites that did not result in an anaphylactic

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TABLE 1. New Occupational Cases of Anaphylaxis

Case	Year of Event	Species	Age	Sex	Years of Animal Work	Prior History of Allergy	Symptoms	Site of Treatment	Treatment	Testing	Work Restrictions after Anaphylaxis
1	2001	Mouse	56	M	13	None	Hives, swollen throat, chest tightness, shortness of breath	Urgent care center	Epinephrine, corticosteroids, antihistamines, H2 antagonists, oxygen	Skin and RAST by allergist	Injectable epinephrine at worksite, education, immunotherapy, PPE
2	2005	Rat	27	F	5	None	Hives, swollen throat, wheezing, chest tightness, shortness of breath, nausea	Emergency dept.	Epinephrine, antihistamines, oxygen	“don't recall”	Not given any work restrictions upon leaving the emergency room. Occupational health recommended restrictions (that were refused) and work with rodents continued. Provided with injectable epinephrine and coworkers were trained and present when she worked with rodents
3	2010	Mouse	43	F	17	None	Chest tightness, shortness of breath, swelling at the bite site and up her arm and a red streak up the arm	Worksite, workplace clinic	Epinephrine, antihistamines, H2 antagonists, oxygen	RAST testing and skin testing both negative for mice	Kidskin gloves to be used for mouse work
4	2011	Mouse	41	F	11	None	Hives, swelling of finger, streaking	Urgent care center	Antihistamines	RAST, skin test	None
5	2013	Rat		M	12	Mouse, rat, guinea pig—respiratory and dermal	Chest tightness, swelling of the hand, red streaking up into the axilla, flushing over chest, swelling over eyelids, cough	Workplace clinic	Antihistamines	Not tested	Kevlar gloves, Benadryl and injectable epinephrine at the worksite
6	2014	Mouse	25	F	3	None	Hives, shortness of breath	Physician office outside workplace, emergency dept.	Epinephrine	Tested, results not available	Employee reviewed proper handling techniques—hold by tail not scruff of neck. Worker must carry injectable epinephrine at all times
7	2014	Mouse	36	F	3	None	Hives, finger swelling, cellulitis	Urgent care center	Antihistamines, antibiotics	RAST, skin test	No direct handling of mice, immunotherapy
8	2014	Mouse	28	F	6	Mouse	Hives, wheezing, chest tightness, shortness of breath, nausea	Workplace clinic, emergency dept.	Epinephrine, corticosteroids, antihistamines, oxygen	Markedly elevated IgE to mouse epithelium and urine. Low level response to rat. Pulmonary function tests have remained stable. No asthma exacerbations. Stable follow up IgE	Limit allergen exposure through administrative controls. Use of N95 when in animal room. No handling of rodents

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TABLE 1. (Continued)

Case	Year of Event	Species	Age	Sex	Years of Animal Work	Prior History of Allergy	Symptoms	Site of Treatment	Treatment	Testing	Work Restrictions after Anaphylaxis
9	2014	Horse	55	M	30	None	While drawing blood from jugular vein of horse, accidentally stuck himself with used needle. Finger swelled within minutes of needle stick. Within an hour, hand was swollen. At ER within 2 hours of event reported tightness in chest and light headedness. Treated by ER and observed for 6 hours until all swelling and symptoms had dissipated	Emergency dept.	Unknown	None by occupational health	Declined occupational medical assessment. Still working with animals. Advised to carry injectable epinephrine
10	2015	Rat	34	M	12	Mouse, rat—respiratory and dermal	Chest tightness, shortness of breath, localized swelling and redness	Workplace clinic, emergency dept.	Epinephrine, antihistamines	Not tested	PAPR, puncture resistant gloves
11	2016	Mouse	23	F	<1	Allergy to rodents, type not specified. Previously, 30 minutes after a mouse bite a rash appeared on arm	Hives, rash	Physician office outside workplace	Antihistamines	Not tested	None
12	2016	Mouse	32	F	10	Mouse—respiratory and dermal	Wheezing, chest tightness	Emergency dept.	Epinephrine, corticosteroids	Tested, results not available	No further work with the type of animal that caused anaphylaxis
13	2016	Mouse	35	M	13	None	Hives, swollen throat, wheezing, chest tightness, shortness of breath	Workplace clinic, emergency dept.	Epinephrine, corticosteroids, antihistamines, oxygen	Test “positive”	No further work with the type of animal that caused anaphylaxis
14	2016	Mouse	39	F	8	Mouse—dermal	Swollen throat, wheezing, chest tightness, shortness of breath, red swollen hand at site of bite	Worksite (received epinephrine injection), emergency dept.	Epinephrine, corticosteroids	RAST positive for mouse and negative for latex	Provided employee with leather gloves and N95 respiratory protection. No cage changing permitted. Accommodations to enable safe work (not specified). Follow up with allergist

IgE, Immunoglobulin E; PAPR, powered air purifying respirator; PPE, personal protective equipment; RAST, radioallergen sorbent tests.

TABLE 2. Previously Reported Occupational Cases of Anaphylaxis Following Animal Bites

Case	Species	Age	Sex	Years of Animal Work	Prior History of Allergy	Symptoms	Treatment	Testing	Comments	Country	Reference
1	Rat	23	M	6	Sneezing, itching, irritation of nasal passages, severe rhinorrhea when working with animals	Within a few minutes felt tightness in chest; skin became bright red and complained of "tingling"; eyes became bloodshot, nasal passages congested, and expectorated mucus	Not specified	Pronounced increase in reactivity, principally to rat and mouse allergens but also to guinea pig serum, over 8 months; the latter tests were carried out 9 months before the anaphylactic reaction. Specific IgE antibodies to these allergens were also increased	Stopped work with animals	UK	Teadale et al ³
2	Rat	30	M	8	No history of allergy or atopy	Within 5 minutes felt a warm flush in hand, which gradually spread to arm and body over the next 10 minutes; 20 minutes after the bite eyes and nose began to run profusely and developed tightness of the chest	Clorpheniramine malate 10 mg IV and salbutamol by inhaler	High concentration of IgE antibody to mouse urine		UK	Teadale et al ³
3	Rat	35	F	10	Rhinitis, conjunctivitis, and mild asthma after exposure to molds and house dust as a child. Increasing symptoms of rhinitis and conjunctivitis after exposure to rats, rat urine that progressed to development of bronchospasm, for at least 9 yrs prior to anaphylaxis	Approximately 2 minutes after the bite, noted facial erythema and periorbital swelling, then had shortness of breath. While walking to the medical center, which was located approximately 200 yards from her laboratory, experienced increasing difficulty breathing. Upon arrival in the emergency department 5 minutes after the bite, was dyspneic, cyanotic, and exhibited stridorous respirations. Then lost consciousness, with no palpable pulse	Cardiopulmonary resuscitation started immediately and was intubated. Aqueous epinephrine 1:1000 (0.5 mg) administered subcutaneously. Ten minutes later, given a rapid intravenous infusion of 100mcg of epinephrine at a rate of 4 mcg/min. Hydrocortisone (100mg) was administered IV. Within 10 minutes, cardiorespiratory function was normal as well as a normal level of consciousness. Extubated after 4 hours. During next 20 hours, methylprednisolone and diphenhydramine administered IV. Discharged from hospital 24 hours after admission with an epinephrine-containing emergency kit	Skin tests demonstrated strong and immediate reactions to a 1:10,000 weight-to-volume dilution of rat urine and to a 1:1,000 dilution of guinea pig dander and horse dander	USA	Hesford et al ⁴	

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TABLE 2. (Continued)

Case	Species	Age	Sex	Years of Animal Work	Prior History of Allergy	Symptoms	Treatment	Testing	Comments	Country	Reference
4	Rat	50	M	Not reported	No history of allergic reactions to contact with rat dander or that of any other mammal. Previously bitten on hand by a rat in a research laboratory with no sequelae	Three months later, working with a rat in the same experiment, was bitten on right hand. Within 5 minutes developed severe swelling at the site and a foreign body sensation in his throat. While being assessed developed a sensation of chest tightness	50 mg of diphenhydramine orally, diphenhydramine (25 mg) intramuscularly, albuterol (2.5 mg) nebulized. 0.3 mg of epinephrine intramuscularly, and 125 mg of intravenous methylprednisolone. Discharged home in good condition with a prescription for an epinephrine autoinjector, prednisone, diphenhydramine, and amoxicillin/clavulanate for his bite wound	Not reported		USA	Rankin et al ⁵
5	Mouse	40	F	26 years: 10 years work with rats, followed by 10 years without animal work, followed by 6 years work with mice	During work with rats, no allergic signs or symptoms. Several rat bites with no difficulties. Developed rhinoconjunctivitis 2 years after started working with mice. After 3 further years of work with mice was bitten without developing allergic symptoms	One year later (after a total of 6 years of work with mice) she was bitten again by a mouse through the glove in the left index finger. After 15 minutes, visible swelling developed. Subsequently her lips and then her entire face became swollen, while she was warm and dizzy. Hypotension (90/50 mmHg) and bradycardia (34/min) as well as nausea and vomiting developed. The swelling spread to the entire index finger	Observed as inpatient for 48 hours. Symptoms were significantly diminished after 250 mg prednisolone intravenously, one ampule clemastine and one ampule ranitidine. Further one ampule atropine was administered IV. Symptoms disappeared within 24 hours	Strongly positive reaction to rat epithelia and an even stronger one to mouse epithelia	For 9 years prior to episode of anaphylaxis, allergic symptoms reasonably well-controlled by cromolyn sodium and albuterol inhaler, terfenadine, and pseudoephedrine hydrochloride as needed, although the patient experienced intermittent nighttime bronchospasm	Germany	Leng et al ⁶

6	Mouse	55	M	22	Rummy nose and sneezing at work over past few years. Occupational mouse bite 10 years earlier that was uneventful	Ten minutes later, felt itchy throughout his body and noticed diffuse erythematous rash, starting on arms bilaterally. Five minutes later, chest felt tight and his throat felt "clogged." Lips became swollen, and rash resolved after 7 hours. Discharged where he was pale on presentation, with heart rate 85 beats per minute, blood pressure 94/59 mmHg, and oxygen saturation 95%. Examination was remarkable for distress, edematous lips, and urticaria	Received intramuscular diphenhydramine, intravenous steroids, ranitidine, and intravenous fluids; no epinephrine was given. Swelling improved within 2 hours, chest discomfort resolved after 6 hours, and rash resolved after 7 hours. Discharged after 8 hours with an epinephrine autoinjector, completed a 5-day course of prednisone and diphenhydramine	Sensitization to rat epithelium in addition to mouse epithelium (no history of rat exposure)	Changing employment not possible; patient elected immunotherapy with mouse antigen. Fourteen months after starting immunotherapy reported complete resolution of rhinitis symptoms when working with mice. No subsequent bites reported	USA	Bunyavanich et al ⁷
7	Rat	48	F	Not reported	History of asthma (not described further)	Within 5 minutes, developed a diffuse erythema followed by cough, chest tightness, and shortness of breath	Administration of oral antihistamine and bronchodilator. Epinephrine was not administered. Symptoms were gradually reduced after several hours	Skin prick testing—positive reaction for rat epithelium with wheal diameter of 7 mm. Radioallergen sorbent test (RAST) for specific IgE antibodies against rat epithelium was positive class 2 with a value of 0.99 KU/L	Continued to work with complete avoidance of direct exposure to laboratory rats	Canada	Kamptak and Betschel ⁸
8	Mouse	25	F	Not reported	Previous laboratory mouse bites had resulted in only self-remitting local reactions. History of allergic rhinitis (not described further)	Approximately 30 minutes after being bitten, reaction included facial erythema and swelling	Initially took antihistamine with little benefit, later received additional antihistamine, corticosteroid, and bronchodilator at emergency room. Epinephrine not administered. Symptoms resolved within an hour	RAST for specific IgE antibodies against mouse and rat epithelium were found positive class 4 with a value of 42.40 KU/L and positive class 3 with 10.50 KU/L, respectively	Later resumed laboratory animal handling; however, without any direct contact with laboratory mice and rats	Canada	Kamptak and Betschel ⁸

TABLE 3. Reported Non-Occupational Cases of Anaphylaxis Following Bites by Rodents

Case	Species	Age	Sex	Prior History of Allergy	Symptoms	Treatment	Testing	Country	Reference
1	Mouse	9	F	Not reported	Within 30 minutes developed an exanthema with general pruritus. Thirty minutes later, experienced shortness of breath	Emergency treatment in hospital with high-dose corticosteroids and antihistamines. Recommended patient avoid playing with mice, provided an emergency set consisting of corticosteroids, antihistamines, and adrenaline	Prick tests inducing seasonal and perennial aeroallergens showed a type 1 sensitization to dog hair, cat hair, horse hair, and mouse epithelia, and antibodies against egg (RAST class 2) and mouse epithelia (RAST class 3) were found	UK	Thewes et al ⁹
2	Hamster	36	F	History of atopic dermatitis and bronchial asthma in childhood. Raised three hamsters and, though bitten on the hands several times, had no symptoms	Within a few minutes felt a warm flush in left hand, which gradually spread. Generalized urticaria accompanied by pruritus of her eyes. She began to sneeze and feel itchy 20 minutes later, and breathing became difficult. On admission, she was pale, and her blood pressure was low (95/36 mmHg). After a few minutes, she fainted	Emergency treatment with IV hydrocortisone, sodium succinate (500 mg), and antihistamines	Specific IgE antibodies (CAP RAST FEIA) against Dermatophagoides pteronyssinus and house dust were class 5 but specific IgE antibodies against mouse epithelium, mouse urine, rat epithelium, rat urine, rat serum proteins and hamster epithelium were all negative. On prick testing, showed positive reactions to their saliva with 4, 5, and 4 mm diameters of wheals, but negative results with their urine	Japan	Tomitaka et al ¹⁰
3	Dwarf hamster	23	F	Not reported	The hand with which she usually handled the hamster became itchy, as did her face. After 5 minutes, the bitten finger became warm, red, and swollen. The swelling and redness spread to the arm, and she felt sick. After several minutes, she began to feel dizzy, and the redness spread over the entire body	Emergency treatment with IV aminophylline and hydrocortisone	Reaction to common hamster epithelium was class 2 on testing with CAP-RAST	Japan	Niisuma et al ¹¹

4	Dwarf hamster	45	F	Atopic bronchial asthma had been diagnosed at age 16. For prior 3 years had two dwarf hamsters as pets. Had been bitten previously on hands 3 times without symptoms. Cough and dyspnea worsened when cleaned the hamster cage	After several minutes, the bitten thumb became warm, red, and swollen. Palpitations and malaise occurred. After 20 minutes, the patient had an asthmatic attack and took inhaled salbutamol. A few minutes later, she fainted at home. On admission she was somnolent	Emergency treatment with inhaled salbutamol sulfate solution and IV hydrocortisone	Reaction to specific IgE antibody against dwarf Djungarian hamsters (<i>Phodopus sungorus</i>) epithelium, examined by CAP-RAST was class 4	Japan	Niitsuma et al ¹¹
5	Dwarf hamster	13	F	History of asthma, allergic rhinitis and Dermatophagoides pteronyssinus (Der p) allergy. Bitten on three previous occasions and did not develop symptoms after the bites	Within 5 minutes, she developed generalized urticaria associated with angioedema	Symptoms resolved within 24 hours with IV hydrocortisone and antihistamines	Negative reactions to the skin tests and specific IgE to the commercially available hamster epithelium extract. IgE-mediated reaction to a novel 21 kD protein found in the saliva which has cross-reactivity with Der p	China	Lim et al ¹²
6	Dwarf hamster	11	M	History of asthma and Der p allergy. Previously bitten on numerous occasions with no symptoms	Within minutes began sneezing and developed generalized urticaria and angioedema. In the emergency room, he also was noted to be wheezing but his blood pressure was normal	Received subcutaneous epinephrine, nebulized salbutamol, intravenous hydrocortisone and antihistamines. Symptoms resolved within 24 hours	Negative reactions to the skin tests and specific IgE to the commercially available hamster epithelium extract. IgE-mediated reaction to a novel 21 kD protein found in the saliva which has cross-reactivity with Der p	Japan	Lim et al ¹²
7	Gerbil	25	F	No respiratory problems when handling pet. Occasionally was bitten when playing with the animal, with no adverse reactions	5 minutes later felt pruritus in right hand and wrist. Wheals then appeared on right arm, head and back accompanied by swelling of eyelids. After another 5 minutes developed dyspnea	Took antihistamines and called doctor. At arrival, blood pressure was 90/50 mmHg with pulse 96 beats/min. Treated with IV antihistamines (dimetindene maleate 4 mg) and IV corticosteroids (187 mg prednisolone)	Skin-prick testing with commercial test solutions (mouse, rat, golden hamster) revealed sensitization to the pollen allergens birch, timothy grass and rye grass, and to dander from cat, rat, mouse, and hamster, but negative results to dog and rabbit epithelia. Specific IgE antibodies against mice were class 3, cat class 2, hamster class 3, rat class 4, and negative against rabbit. A skin provocation test with soaked hairs was positive	Austria	Trummer et al ¹³

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TABLE 3. (Continued)

Case	Species	Age	Sex	Prior History of Allergy	Symptoms	Treatment	Testing	Country	Reference
8	Hamster	51	M	History of anaphylactic reaction to penicillin	Within minutes turned grey and began making a gurgling sound. Face went white and felt itchy all over. Within seconds began to wheeze. Treated with EpiPen, but did not respond. Paramedics arrived to find man unconscious and turning blue with “blocked” airway	Taken to hospital where improved with a “series of injections”	Allergic to proteins in hamster saliva	UK	Wilkes ^{14,15}
9	Dwarf hamster	23	F	No previous history of allergic diseases. When playing with hamster experienced slight itching and erythema on fingers	Generalized urticaria and facial angioedema a few minutes after bite. Patient’s condition later worsened, with general malaise, pharyngeal obstruction, hypotension (90/50 mmHg), tachypnea, profuse perspiration, shortness of breath and wheezing. Pulse oximetry reading in emergency room showed 79% oxygen saturation. Arterial blood gases revealed hypoxemia and respiratory acidosis. Chest x-ray showed air trapping	Received crystalloid fluids, 100% oxygen, subcutaneous epinephrine, IV corticosteroid and antihistamine, inhaled salbutamol, and antitietanus prophylaxis. Discharged 1 day after complete remission of symptoms	Analysis of 3 IgE-binding bands found in hair, urine, and salivary glands of the Siberian hamster showed a new allergenic protein belonging to the lipocalin family and lacking cross-reactivity with allergens from other rodents	Spain	Torres et al ¹⁶

response.^{5–8} Everyone had uneventful recoveries, although one required cardiopulmonary resuscitation and intubation,⁴ and only two were treated with epinephrine.^{4,5} Subsequent allergen testing with laboratory animal extracts (skin prick test and/or Immunoglobulin E [IgE]) was reported for seven workers and all had positive test results.^{3,4,6–8} Some workers stopped working with animals or with the species that caused their anaphylaxis.^{3,8} One worker received immunotherapy, which resulted in a reduction of rhinitis symptoms and no subsequent bites were reported.⁷ None of the workers were required to carry injectable epinephrine with them.

Non-Occupational Cases of Anaphylaxis Involving Rodents in the Literature

Of the nine non-occupational cases described in the world literature, seven involved hamsters^{10–12,14,16} (including five from dwarf hamster bites),^{11,12,16} while one involved a mouse,⁹ and another was due to a gerbil bite¹³ (Table 3). All case reports were from outside the United States. The patients ranged in age from 9 to 51 years. When prior history was provided, most had a history of some form of allergy or asthma. Five patients had a history of prior bites from the same animal without an anaphylactic reaction.^{10–13} For the eight patients whose treatments were described, all were treated with hydrocortisone or unspecified corticosteroids. Patients were treated with epinephrine in only two cases.^{12,16} All patients recovered. Subsequent allergen testing was positive in all cases, including an IgE-mediated reaction to a novel 21 kD protein found in the saliva of dwarf hamsters which has cross-reactivity with *Dermatophagoides pteronyssinus* (Der p) in two cases.¹²

DISCUSSION

Using a survey of laboratory animal research facilities in the United States, this study identified previously unpublished cases of anaphylaxis from laboratory animal bites. While it is not possible to calculate the incidence of anaphylaxis from bites from this study, it appears to be significantly higher than is suggested by the previous literature.

Anaphylaxis is a severe allergic reaction that involves IgE triggering release of mediators from basophils and mast cells. However, the precise pathway that differentiates a simple allergic reaction, such as rhinoconjunctivitis, from an anaphylactic reaction is not completely understood.² For animal allergies, the offending IgE usually targets a member of the lipocalin family.^{17,18} The lipocalins include odorants and pheromones and can be found in saliva, dander, hair, and urine, as well as places where animals are housed, such as bedding and cages. These proteins have been characterized in many animal species, including rodents, cats, dogs, horses, and cows.¹⁸ Members of the lipocalin family share some sequence homology, which may also allow for cross-reactivity.

Since anaphylaxis requires IgE to trigger a cascade, it seems reasonable to assume that all persons experiencing anaphylaxis following a bite would have been sensitized prior to the bite. While most of the patients previously described in the literature had a history of atopy, there was no history of animal allergy reported for half of the cases newly reported here. While it is possible that some of these workers had symptoms that they did not recognize as allergic, it appears that anaphylaxis can be the first presentation of allergy. It is also notable that in three of the occupational and two of the non-occupational cases in the literature, the patients had experienced prior animal bites without developing anaphylaxis. Therefore, prior bites without an anaphylactic reaction do not predict protection from a future episode.

It is encouraging that in all occupational and non-occupational cases reported, the injured persons had uncomplicated recoveries. However, there was great variation in treatment, particularly in the non-occupational cases. This is consistent with David Golden's observation that while "epinephrine has long been held to be the treatment of

choice, it is clearly underutilized and not always effective, whereas steroids are widely used despite the total lack of evidence to support this practice."² For the new occupational cases identified by this study, treatment with epinephrine was much more likely. Current recommendations include the advice that if epinephrine is available, it should be administered while awaiting emergency services.¹

Following recovery, many, but not all, of those experiencing anaphylaxis were tested for sensitization, usually by RAST. Except for one worker, all who were tested had positive results. A negative test in this setting should be interpreted cautiously and the possibility of a false negative result should be considered. Another possibility is that another antigen is involved, such as the novel antigen with cross-reactivity to Der p described by Lim et al.¹² In addition, it may be useful to test more broadly than just for the animal species involved with the bite, since workers can be sensitized to more than one species.¹⁹ This may be especially helpful information for those considering a return to animal work, for whom results of testing should be available as part of the return to work process.

Given the potentially life-threatening nature of anaphylaxis, workers experiencing anaphylaxis should be assigned to jobs that do not involve a risk of bites when possible. When this is not feasible, a review of work practices, administrative controls, engineering controls, and PPE should be performed, preferably including a worksite visit. Before returning to work, employees should also be asked about prior respiratory symptoms (allergy or asthma) or dermal allergy associated with animal work and, if present, these should be addressed. Workers identified as previously unreported cases in this study who returned to work with animals implicated in causing anaphylaxis were required to keep injectable epinephrine with them, which is a recommended practice.²⁰

Although the focus of this study was anaphylaxis associated with rodent bites, one respondent provided information on what appears to be a first report of anaphylaxis following a needlestick involving a horse. This case demonstrates that bites are not the only workplace injury in the research setting that carry a risk for anaphylaxis.^{20,21} For example, an anaphylactic reaction following a needle injury after use on rabbit tissue has been described.²¹ It is also a reminder that, in addition to rodents, a variety of animals used in research may pose a risk for anaphylaxis.

CONCLUSION

Anaphylaxis from laboratory animal bites occurs more frequently than suggested by the earlier literature. While atopy or respiratory allergy to animals may be risk factors, anaphylaxis following an animal bite may be the first indication of allergy. Anaphylaxis may also occur after a prior history of bites without an adverse reaction. After an episode of anaphylaxis, a review of allergy history and testing is helpful. Workers should be advised to carry injectable epinephrine. When possible, workers should be restricted from work where they would be at risk for a subsequent bite. If this is not feasible, precautions should be taken to reduce the risk of future bites and to ensure prompt treatment should a bite occur.

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