



Letter

Work-related asthma secondary to IgE-mediated reactions to rodents successfully treated with immunotherapy

Work-related asthma (WRA) can lead to detrimental consequences, including progressive lung disease and economic distress. WRA includes occupational asthma (OA) and work-exacerbated asthma (WEA). OA refers to de novo or recurrence of previously quiescent asthma induced by the work environment, whereas WEA refers to preexisting or concurrent asthma that worsens at work. Laboratory workers and veterinarians can become sensitized to mouse and rat dander. Asthma and allergic rhinitis (AR) secondary to rodents can interfere with an employee's daily tasks and may force job termination.¹ Work withdrawal is the best treatment option for patients with WRA; but when not possible, allergen immunotherapy (AIT) can be considered. Mouse allergen is also known to be a major contributor to asthma morbidity in urban children.² AIT can be an effective treatment for AR, asthma, and venom-induced anaphylaxis³ by inducing immune tolerance and sustained therapeutic benefits, achieved by shifts to regulatory T-cell responses, decreased specific IgE levels, and increased IgG4 levels.⁴

We describe one of the first case series, to our knowledge, of 4 patients with symptoms of WRA who improved with AIT specific to mouse and rat allergens (Table 1). Because of the retrospective nature, most of the clinical outcomes were assessed by observing medication reduction or elimination rather than objective improvements in variable airflow obstruction. Patients were selected to receive AIT if occupation included rodent contact, exposure was unavoidable, and they developed respiratory symptoms (wheezing, cough, dyspnea) around these animals. All patients were seen in our allergy/immunology clinic from 2010 to 2015. Immunologic responses to laboratory animal desensitization were described in 23 patients with OA or AR; immunotherapy induced blocking antibodies to laboratory animals 12 times higher than control.⁵ Hansen et al⁶ described a patient who underwent rush AIT with rat epithelium for severe rhinoconjunctivitis and asthma and, after 18 months, returned to work without restraints. Another study described AIT for mouse bite anaphylaxis and AR and briefly discussed 2 cases of asthma induced by mouse exposure but without details regarding the clinical picture or outcome.⁷

Our first patient is a 53-year-old female veterinary technician who developed WRA and AR. When around mice or rats, she developed wheezing, dyspnea, and ocular pruritus. Peak flows were 475 L/min off work, which decreased by 50% to 79% at work. Her pulmonologist diagnosed severe occupational asthma. Inhaled corticosteroids, salmeterol, montelukast, antihistamines, intermittent oral corticosteroids, and powered air-purifying respirators (PAPRs) were no longer effective. Occupational medicine specialists recommended she avoid the workplace.

Because of her strong desire to return to work, she underwent AIT to mouse and rat epithelia. Glycerinated extracts of *Mus*

musculus and *Rattus norvegicus* (Greer Labs, Lenoir, North Carolina) were obtained in a 1:20 (wt/vol) concentration. Extract was diluted 5 times to 1:100 (wt/vol); 0.5 mL of this solution was used for maintenance therapy. AIT was started at 1:1,000 (vol/vol) dilution.⁸ Four months later, she returned to work wearing an N-95 respirator and PAPR when handling rodents. After 18 months of AIT, she discontinued use of all maintenance asthma medications, and after 3 years, skin test results converted to negative to mouse and rat. She is now asymptomatic while handling rodents and performs surgical procedures wearing a high-efficiency particular air (HEPA) filter respirator and gloves. After 5 years of AIT, peak flows were 520 L/min at home and work.

The second patient is a 36-year-old female veterinarian who developed cough, wheezing, and dyspnea around rats and mice despite wearing an N-95 mask and gloves. On the basis of symptoms and spirometry, she was diagnosed as having intermittent asthma. She began AIT to rat and mouse and after 4 years no longer has symptoms around rodents and rarely requires albuterol. She continues wearing an N-95 respiratory mask and gloves.

The third patient is a 35-year-old male pharmacology researcher with a history of dyspnea, wheezing, pruritus, and facial swelling around rats and mice and 1 episode of anaphylaxis after a rat bite. He wore gloves but not a face mask around rodents. Although he had a prior diagnosis of asthma before starting his occupation, it is difficult to distinguish OA from WEA.^{9,10} While he was working with rodents, asthma exacerbations became more frequent, requiring emergency department visits and oral corticosteroids. Pulmonary function test results remained stable but were only tested after 12 hours off work. He started AIT to rat and mouse and 9 months later had substantial reduction in albuterol use and improvement in cutaneous and respiratory symptoms, despite not wearing a face mask around rodents.

The fourth patient is a 31-year-old male student who developed wheezing, rhinorrhea, itchy throat, watery eyes, and localized rash while working with mice. Daily montelukast, cetirizine, and a face mask improved his respiratory symptoms, but cutaneous symptoms continued when he was around mice. Fourteen months after starting AIT, he no longer wore a mask, cutaneous symptoms resolved, and his respiratory symptoms drastically improved. This patient discontinued AIT after 14 months because of time commitments but restarted after a 15-month break.

This is one of the only case series of rodent-induced WRA in which patients significantly improved after AIT to mouse and rat allergens. The first patient exemplifies the most significant response and was able to fully return to work after AIT. Symptoms improved in all patients within 9 to 24 months of AIT, and further improvement is anticipated with completion of their course.

Table 1
Characteristics of the 4 Patients Treated With AIT to Rodent Allergens

Age/sex	Occupation; OA or WEA	Prick allergy skin test positivity	Symptoms around mice and rats	Spirometry before AIT, % predicted	Management before AIT	AIT schedule ^a and allergens	Testing after AIT	Measures of improvement	Outcome after AIT	Adverse events during AIT	Duration of AIT thus far
53/F	Veterinary technician; OA	Rat, mouse Nonoccupational: rabbit, cattle, hog, guinea pig, horse, cat, weeds, grasses, trees and molds	Wheezing, dyspnea, tongue swelling, ocular pruritus	FEV ₁ : 91; FVC: 105; FEV ₁ /FVC: 0.69	Inhaled fluticasone and salmeterol, montelukast, albuterol as needed, prednisone, gloves, PAPR	Cluster immunotherapy: 2 injections 2 days each week during build-up phase; Allergens in AIT: mouse, rat, rabbit, grasses, molds, weeds	Prick skin test result negative to mouse and rat after 3 years; FEV ₁ : 99; FVC: 104; FEV ₁ /FVC: 0.75; spirometry performed when patient was not using controller inhaler; peak flow of 520 L/min at home and work	Improved spirometry and peak flow readings; negative skin prick test results to rodents	Returned to work after 6 months of AIT; able to perform surgery on rats and mice while wearing gloves and a HEPA filter respirator; rarely uses albuterol	During build-up: small local swelling at injection site	5 years; completed AIT
36/F	Veterinarian; OA	Rat, mouse Nonoccupational: cat, dog, horse, weeds, grasses, trees, dust mites	Cough, wheezing, dyspnea	FEV ₁ : 81; FVC: 88; FEV ₁ /FVC: 0.92	Inhaled fluticasone (during upper respiratory tract infection), albuterol as needed, gloves, N-95 respiratory mask	Conventional immunotherapy: single injection each visit during build-up phase; Allergens in AIT: mouse, rat, cat, dog, horse, dust mite, weeds, grasses and trees	Not done	Decrease in albuterol prescriptions	Able to work around mice and rats without cough, wheezing, dyspnea, or urticaria while wearing gloves and an N-95 respiratory mask; significantly decreased albuterol use; daily cetirizine.	During build-up: dizziness, flushing, sweating itching of the palms, mild tension in her throat after 1 injection	4 years; completed AIT
35/M	Pharmacology researcher; WEA; baseline FEV ₁ , 70%	Rat, mouse Nonoccupational: cat, dog, weeds, molds and dust mite	Wheezing, dyspnea, facial swelling, contact urticaria, pruritus	FEV ₁ : 76; FVC: 89; FEV ₁ /FVC: 0.82	Inhaled budesonide, montelukast, albuterol frequently, fluticasone nasal spray, gloves	Conventional immunotherapy: Allergens in AIT: mouse, rat, cat, dog, weeds, walnut, dust mite and molds	FEV ₁ : 71; FVC: 79; FEV ₁ /FVC: 0.90	FEV ₁ /FVC ratio improved	Able to work with rodents without respiratory or cutaneous symptoms; wears gloves without face mask; AR resolved; rare albuterol; discontinued use of montelukast; daily inhaled budesonide	During build-up: 1 occurrence of pale skin, dizziness, and hypotension (anaphylactic reaction); epinephrine given	2 years
31/M	Physiology graduate student; OA	Rat, mouse Nonoccupational: cat, dog, weeds, grass, trees and dust mites	Wheezing, rhinorrhea, itchy watery eyes, localized rash	FEV ₁ : 92; FVC: 91; FEV ₁ /FVC: 1.01	Montelukast, albuterol as needed, cetirizine, gloves, face mask	Conventional immunotherapy: Allergens in AIT: mouse, rat, cat, dog, weeds, grasses, trees, and dust mite	Spirometry performed after 14 months of AIT and after 15 months of not receiving AIT; FEV ₁ : 88; FVC: 91; FEV ₁ /FVC: 0.97	PFT results were stable despite only after completing 14 months of AIT	After 14 months of AIT, able to work around mice without a mask; still wearing gloves; AR resolved; daily montelukast; no albuterol use; seasonal cetirizine	None	14 months then stopped; restarted since for 15 months

Abbreviations: AIT, allergen immunotherapy; AR, allergic rhinitis; OA, occupational asthma; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; HEPA, high-efficiency particulate air; PAPR, powered air-purifying respirator; PFT, pulmonary function test; WEA, work-exacerbated asthma.

^aAll patients in this case series received AIT from glycerinated extracts of *Mus musculus* and/or *Rattus norvegicus* (Greer Labs, Lenoir, North Carolina) from a 1:20 (wt/vol) concentration. Extracts were diluted 5 times to 1:100 (wt/vol) (0.5 mL used for maintenance therapy). AIT started at 1:1,000 (vol/vol) dilution.⁸

In conclusion, specific AIT to laboratory animals should be considered as a potentially effective therapy in patients with WRA secondary to laboratory animal hypersensitivity. Immunotherapy could result in significant symptom improvement and return to the work environment. This report is limited by the small number of patients and retrospective nature, which limit the data available. Three patients did not have objective documentation of variable airflow obstruction, but their WRA diagnosis was based on a strongly suggestive clinical history. All had positive skin test results to rodents, wheezing, cough, and dyspnea triggered by rodent exposure, which resolved when physically removed from this environment. Further large-scale, double-blind studies in patients with objectively confirmed WRA are warranted to establish the effectiveness of AIT to rodents. In the meantime, AIT should be strongly considered for select patients with WRA induced by rodents, especially when other treatment options have been exhausted.

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