

The Obama dilemma: Allergic rhinitis (animal dander allergy)—The great burden of illness

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ABSTRACT

Allergic rhinitis is one of the most common chronic diseases with over 600 million people affected worldwide. More than 200 million of them also suffer from concomitant asthma. Allergic rhinitis is generally under-diagnosed and under-treated. A significant burden of allergic rhinitis is due to pet allergies. In 2008 two major evidence-based documents on the management of allergic rhinitis were published, namely the US Rhinitis Practice Parameters and the ARIA/WHO Guidelines that stress the burden of allergic rhinitis due to animal allergens and the comorbidities of allergic rhinitis. We need a new approach targeting individual disease control in rhinitis due to animal allergens emphasizing avoidance and active treatment. The goals of the avoidance-treatment are to first improve patient care by recognizing each individual patient's burden of disease and expectations of therapy, and then to target and adjust the appropriate therapies to meet these expectations. Achieving these goals will, ultimately, help the patient to better self-manage his or her disease, thereby improving overall quality of life.

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THE BURDEN OF ALLERGIC RHINITIS DUE TO ANIMAL DANDER

Allergic rhinitis due to animal dander received new media attention when President Obama united his dog-allergic child with a dog in the White House. Interest has been renewed in animal dander-induced perennial allergic rhinitis. Mounting evidence describing the burden of perennial and seasonal allergic rhinitis on a patient's physical, social, and emotional functioning and, in turn, on society as a whole has led to a new appreciation of the disease. Indeed, research shows that allergic rhinitis ranks as the sixth most common chronic illness in the United States¹ and affects more individuals than other common chronic conditions including hypertension, asthma, eczema, and diabetes.²

The Allergies in America survey, the largest and most comprehensive national survey of patients (2500) with allergic rhinitis, found the majority of participants (66%) indicated that nasal allergies affected their daily

lives, of which 40% classified as having moderate or more substantial effects.³ The most troubling physical symptoms reported by individuals with allergic rhinitis included a stuffed up nose, a runny nose, postnasal drip, red and itchy eyes, watering eyes, repeated sneezing, headache, itching, facial pain or pressure, and ear pain. Not surprisingly, patients also reported that their nasal allergies produced a substantial detrimental effect on their emotional health and quality of life, often causing tiredness, misery, irritability, and depression.⁴ Other research has shown that quality-of-life scores across multiple health dimensions are significantly lower in individuals with perennial allergic rhinitis compared with healthy individuals, and quality of life inversely correlates with the inflammatory response to allergens and the severity of allergic rhinitis symptoms.⁵ Allergic rhinitis has been associated with loss of productivity and sleep disturbances as well as various psychomotor abnormalities, which result in decreased cognitive performance in children and adults.⁶

There are large economic costs generated by animal dander allergy. Direct costs for allergic rhinitis are estimated between \$5 and 8 billion in 2008 and indirect costs as high as \$11 billion.⁷ Additionally, there are common comorbidities with rhinitis. The most common comorbidities were sinusitis and asthma. The presence of comorbid conditions generally increased rhinitis cost burden. Asthma, chronic obstructive pul-

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monary disease, sinusitis, migraine, depression, conjunctivitis, and nasal polyps all increased rhinitis-related medical costs, pharmacy, and total costs. Asthma had the greatest affect on predicted rhinitis-related pharmacy costs, and nasal polyps had the greatest affect on total medical costs. Sleep disorder, hypertension, diabetes, and otitis media had a less profound affect on rhinitis-related medical, pharmacy and total costs. Because of its prevalence and health care effects, rhinitis due to animal dander allergy is associated with considerable direct and indirect costs. Across studies, the annual direct costs of allergic rhinitis in the United States are estimated at \$1.6 to 4.9 billion.⁸ Estimates of annual indirect costs range from \$0.1 to 9.7 billion. The variability is caused by heterogeneous methods of ascertaining worker productivity and difficulty in estimating lost cost of working with symptoms. Allergic rhinitis is estimated to be responsible for at least 3–4 million workdays lost and >2–3 million missed school days per year. These estimated costs do not reflect the effect of chronic rhinitis for which similar statistics are not available. Although the national direct costs of allergic rhinitis have been estimated previously, little is known about specific direct and indirect costs of allergic rhinitis due to animal dander allergy.

The Dean Clinic Allergy Department has attempted to estimate an extrapolated cost for perennial animal dander allergy using data from two large managed-care plan databases, 44 children, aged 4–17 years, with allergist-documented animal allergies (23 cat only, 9 dog only, and 12 both dog and cat). Thirty-four had continued exposure, all of whom agreed to keep the animal out of their bedroom; 10 removed the animal completely from their home. Allergy/comorbidity cost was 2.4 times higher in the continued exposure group compared with the animal removal group over a 6-month (winter) evaluation period. Twenty-one patients who had pet dander allergy and concomitant asthma had costs 2.8 times higher with continued exposure.⁹ Extrapolated annualized national cost estimates (Dean Clinic data) indicate total costs due to animal dander allergy of \$1–3 billion a year, which could be reduced by up to 50% if animals were removed or there was no animal in the home. The bulk of this cost reduction (80%) is caused by decreased costs associated with the comorbidities associated with allergic rhinitis.⁹ Although the number of patients evaluated is small, it illustrates that many of the direct and indirect costs of pet dander allergy are associated with its difficult-to-control comorbidity and with continued daily exposure.

LET'S TAKE A CLOSER LOOK AT SOME OF THESE COMORBIDITIES

One of the most common complaints from patients with allergic rhinitis due to animal dander is sleep

disturbance caused by sleep-disordered breathing, sleep apnea, snoring, and frequent arousal.¹⁰ This can be caused by the overt symptoms of allergic rhinitis *per se*, such as nasal congestion, sneezing, and a runny nose, and contributes to systemic effects resulting from the inflammatory response, such as fatigue, somnolence, and malaise.¹¹ Sleep disturbance impinges on both mental health and cognitive function to affect quality of life. Sleep disturbance has the potential to increase the risk for psychiatric disorders, depression, anxiety, and alcohol abuse.¹² Decreased cognitive ability has the potential to interfere with performance at work or school, to cause missed work or school days, and to increase the risk for accidents.^{11,13} A well-controlled study showed that untreated patients with allergic rhinitis, who were exposed to allergens, showed decreased vigilance, longer response times, and decreased efficiency on measures of psychomotor speed, working memory, and reasoning, and computation in comparison with nonexposed individuals.¹⁴ In a large national survey of >2000 individuals with allergic rhinitis suffering from nasal congestion, roughly 60% of respondents indicated that this bothersome symptom affected them at work or at school, primarily by disrupting their concentration or by leading to poor productivity.

Such losses in work and school productivity, in conjunction with the high prevalence of allergic rhinitis due to animal dander,¹⁵ contribute to the staggering population-based economic burden of the condition. Although the direct costs of allergic rhinitis for medical visits, laboratory tests, medications, immunotherapy, and hospitalization are estimated to tally between \$2.4 and 4.9 billion, the indirect costs of job absenteeism and presenteeism (reduced productivity while at work) contribute an additional \$5.5–9.7 billion, bringing the total economic burden of the disease to \$7.9–14.6 billion.¹⁶ More than 13 million workers in the United States are affected by allergic rhinitis, and estimates indicate that 3.5 million workdays and 2 million school days are lost each year in the United States because of the condition.^{17,18} There are also additional “hidden costs” of allergic rhinitis attributable to respiratory complications caused or worsened by the disease and to the adverse effects of sedating over-the-counter medications used in self-treatment. Although the percent contribution of pet dander allergy (compared with rhinitis associated with other allergens) to this economic figure is uncertain; estimates run as high as one-half to \$1 billion based on the percent of patients with pet dander allergy that live with their allergen and remain symptomatic.

The effect of allergic rhinitis in causing complications or worsening comorbidities is highly burdensome both clinically and economically. These typically involve the upper and lower respiratory tract.¹⁹ Although the

prevalence of asthma in the general population is 3–5%, research indicates that 38% of patients with allergic rhinitis also have asthma, and up to 78% of patients with asthma also have allergic rhinitis, suggesting a link between these upper and lower airway diseases.²⁰ Similar links have been observed between allergic rhinitis and chronic sinusitis,²¹ otitis media,²² eustachian tube problems,²³ and nasal polyps.²⁴ These correlations suggest that successful treatment and control of allergic rhinitis has the potential to decrease the risk of the development and severity of comorbidity, thereby averting additional negative impact on quality of life and medical resource utilization. This conclusion is supported by research showing that among patients with both allergic rhinitis and asthma, those who received allergic rhinitis treatment were roughly half as likely to require hospitalization or a visit to the emergency department because of an asthma-related event when compared with patients who received no treatment for their nasal allergies.²⁵

AVOIDANCE AND TREATMENT OF ANIMAL DANDER ALLERGY

Because of the rising prevalence of pet ownership, the rising prevalence of allergic sensitivity to animal dander and its association with the costly burden of perennial allergic rhinitis in the United States, specific strategies are necessary to address animal dander allergy as it relates to perennial allergic rhinitis. Allergists are in an ideal position to educate patients, caregivers, and payers with regard to the burden of perennial allergic rhinitis to pet dander and to develop and use cost-effective therapies. It is important that there be early recognition and cost-effective treatment of allergic rhinitis due to pet dander and, when possible, greater use of practical preventative strategies. The value equation needs to be the focus of treatment of allergic rhinitis with regard to pet dander allergy.

It seems reasonable to assume that an allergic patient who is sensitized to dog or cat allergen should not live with a pet in their home. Furthermore, because the risk of sensitization is great in atopic patients, it seems intuitive that a patient with allergic airway disease should not bring a pet into their home. These general principles are rarely adhered to in practice. At the present time, there seems to be no other clinical advice that is supported. The only clinical trial testing removal of cats and dogs from the home of a sensitized individual explores primarily asthma and not allergic rhinitis outcomes.²⁶ Furthermore, the second recommendation—not adding a pet to the environment of an already sensitized person—should not be confused with the recently published data from the Childhood Origins of Asthma study suggesting that growing up in an environment with a dog (the data does not sug-

gest a similar effect with cats) where the dog has been present since birth (presensitization) decreases the risk of allergic asthma.

Once the cat or dog has been removed from the home, it is important to recognize that the clinical benefit may not be seen for a period of several months because allergen levels fall quite slowly after cat removal. In most homes, dander levels fall to those seen in homes without cats within 4–6 months after cat removal. Levels may fall much more quickly if extensive environmental control measures are undertaken: these include removal of carpets, upholstered furniture, and other reservoirs from the home. Thorough and repeated cleaning will be required once the animal has been removed. Because cat and dog allergen may persist in mattresses for years after the animal removal from the home, the purchase of new bedding and impermeable mattress encasement should be recommended.

Because so many patients are unwilling to remove their pet, even if they themselves are sensitized, many compromise measures have been suggested. Blaiss⁶ showed significant reductions in airborne Fel d 1 with a combination of air filtration, cat washing, thorough vacuum cleaning, and removal of some furnishings, but these findings could not be confirmed and in other studies these measures were shown to produce only a transient decrease in airborne allergen levels. Although tannic acid has been shown to reduce cat allergen levels in carpets, the effects are modest and short lived when the cat is present, so the treatment should not be routinely recommended. The notion of creating a clean room from which the cat is excluded and vigorous environmental controls such as vacuuming, mattress and pillow covers, carpet removal, and room air filters was tested recently. In one study, adults with asthma or allergic rhinitis and cat sensitivity were asked to keep their bedroom doors closed, and a bedroom air cleaner and covers for mattresses and pillows were provided. The control group was provided with non-active air cleaners. Airborne cat allergen was reduced in the group with active filters but there was no significant difference detected in the group with placebo filters. In a second study in children with asthma, in which the sensitivity to either dogs or cats was treated with either active or placebo air cleaners, investigators found the active treatment group in the study had significant reduction in airway responsiveness but no change in any clinical outcome measure. Therefore, it does not appear that it is possible to produce a clinical effect without removing the pet from the home. Although additional research is necessary, current data suggest that “halfway” or partial environmental control is not sufficient and that this should not be looked at as a “reasonable compromise.”²⁷

There is evidence that there is significant animal dander exposure in public places such as schools.²⁸ There is only very preliminary data from Scandinavia about the effect of an environmental control measure in school environments. This becomes an important issue when animal-allergic patients do not improve with elimination of animals from the home or patients without any animals at home are symptomatic. This raises an important question as to the appropriate therapy of animal dander sensitivity, because it is likely that significant dander exposure may be unavoidable for many.

Aside from avoiding known allergic triggers, allergic rhinitis is typically managed with pharmacotherapy to alleviate disease symptoms and control comorbid conditions. Such pharmacologic treatments include oral and intranasal antihistamines, intranasal corticosteroids, decongestants, and, less frequently, intranasal anticholinergic agents, and parenteral corticosteroids. The Allergies in America survey showed that 53% of patients used over-the-counter medications to relieve their allergy symptoms within the prior 4 weeks, while 45% used a prescription medicine; 31% used no medication at all.^{3,29–30} Specific immunotherapy, in which relevant allergens are administered over a prolonged period to desensitize patients to specific allergens, is generally reserved for patients with severe disease or those with a poor response to other management approaches.

The primary goal of pharmacotherapy is to reduce or eliminate allergic rhinitis symptoms and comorbidities. Key facets of this goal entail alleviating nasal discomfort and restoring good nasal airflow to eliminate sleep-related abnormalities and fatigue. Monotherapy is often inadequate, so multiple medications are often used concurrently to provide relief from different disease symptoms as well as decrease the incidence of comorbidities.

In addition to the burden of allergic rhinitis symptoms, there is an additional burden associated with the therapeutic management of the condition. This burden of therapy stems from the cost of treatment, as well as from its side effects, which can sometimes be profound. Oral antihistamines are one of the most commonly used medications among patients with allergic rhinitis; however, many of these agents suffer from powerful sedating and anticholinergic effects. Because first-generation antihistamines easily cross the blood-brain barrier, they can affect the central nervous system to elicit sedation, vertigo, ataxia, altered mood, and impaired cognition, as well as dry mouth, blurred vision, and constipation.³¹ The sedating effects of first-generation antihistamines can seriously jeopardize patient safety. Diphenhydramine has been shown to cause worse driving performance than a blood alcohol level of 0.1%.³² Use of sedating antihistamines in-

creases the risk of on-the-job injuries nearly threefold, causing an estimated \$143 million in direct medical costs.³³ Second-generation antihistamines are purported to have less severe sedating effects than their predecessors because they are less readily able to cross the blood-brain barrier. However, some of these agents still produce varying degrees of sedation, and some are associated with clinically important drug-drug interactions and have been associated with cardiotoxicity.³⁴ The other classes of allergic rhinitis therapies suffer from their own unique sets of side effects.

In the Allergies in America survey, many individuals identified several moderately or extremely bothersome side effects of allergic rhinitis pharmacotherapy that they felt significantly and negatively affected their daily lives.³ The most common and troublesome side effects reported included a drying sensation (34%), dripping down the throat (33%), drowsiness (33%), headaches (25%), bad taste (22%), and a burning sensation (18%). Although some of these side effects of treatment are difficult to disentangle from the symptoms of allergic rhinitis *per se*, it remains clear that many of the current therapies for allergic rhinitis can negatively impact patient quality of life and the patients' willingness to adhere to the medication regimen.

Perhaps more important than patients' annoyance at the side effects of allergic rhinitis treatment is their dissatisfaction with the effectiveness of treatment. In the Allergies in America survey, 54% of participants reported that they had changed their medication at least once because of lack of efficacy.³ Among the 760 individuals who had used an intranasal steroid, 48% were disappointed by the fact that the agent lacked 24-hour coverage; most reported that efficacy diminished after 7–11 hours.

THE VALUE OF ALLERGIC RHINITIS THERAPY

The value of a given therapy can be determined by how well the medication leads to the desired change in health status and how satisfied patients are with the therapy versus the direct and indirect cost of the disease being treated. This is represented by the following equation:

$$\text{value} = \frac{\text{change in health status} + \text{patient satisfaction}}{\text{cost}}.$$

As described previously, pet dander allergic rhinitis is associated with a large economic burden that includes the direct costs of disease diagnosis and management, the indirect costs of lost productivity at work and school, and the hidden direct costs of comorbidity management. Several pharmacotherapies exist to help offset the burden of allergic rhinitis symptoms and effects on quality of life; however, it is clear that pa-

tients frequently are not satisfied with the available pharmacotherapeutic options, either because of lack of perceived long-term efficacy (*e.g.*, nasal corticosteroids), bothersome side effects (*e.g.*, sedating antihistamines), or other factors. These other factors include their desire to continue to live with their animal or to live with a more normal lifestyle that permits tolerable intermittent contact with dander-containing environments including friends' and family homes and public places including schools. Clearly, there is a need to develop more effective allergic rhinitis therapies with improved side effect profiles to improve patient satisfaction. It is also clear that avoidance of animal dander is not an option for most patients or their families!

THE QUESTION OF THE VALUE OF IMMUNOTHERAPY FOR ALLERGIC RHINITIS SECONDARY TO ANIMAL DANDER

Antihistamines, nasal steroids, and nasal antihistamines are the mainstay of pharmacotherapy for allergic rhinitis, but these agents are generally minimally effective at preventing or controlling nasal symptoms and comorbidities of perennial allergic rhinitis due to animal dander, presumably because of constant allergenic exposure in the vast majority of patients who are unable or unwilling to eliminate pets from their environment and the almost ubiquitous nature of animal dander in our daily lives.³⁵

There is currently considerable room for improvement in the management of perennial allergic rhinitis due to pet dander and recognition of the fact that most patients will not eliminate their animals from their environment suggests that immunotherapy may well be able to fulfill these unmet treatment needs. Studies comparing the effectiveness and adherence of new-generation allergy pharmacotherapy to new forms of immunotherapy generally support the notion that immunotherapy is superior to other competitive agents. In addition, immunotherapy's superior ability to target inflammatory pathways has the potential to lead to a decrease in the expensive comorbidities of pet dander allergy making it a very cost-effective option.³⁶ Together, all of these factors indicate that, with the realization that our patients will not give up their pets or have unavoidable exposure to dander in their normal activities, we must strive for improved allergic rhinitis control than we usually achieve with pharmacotherapy and consider immunotherapy high therapeutic and cost-effective value for reducing the burden of allergic rhinitis disease and its management.

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