Assessment and Treatment of Laboratory Animal Allergy

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Abstract

Laboratory animal allergy (LAA) is a form of occupational sensitivity affecting up to one third or more of exposed workers. Symptoms involve the eyes, nose, skin, and lower respiratory tract. Asthma may develop in 20 to 30% of sensitized individuals. An occupational medical history is the primary tool if a diagnosis of LAA is suspected. The diagnosis is confirmed by demonstrating the presence of immunoglobulin E antibodies to laboratory animal allergens by skin testing or in vitro assays. If laboratory animal allergen-induced asthma is suspected, measurements of lung function are necessary for confirmation and assessing the degree of impairment. One approach to the problem is presented in this article. For individuals with LAA, avoidance of exposure is the primary treatment. For individuals who continue to work in the environment, pharmacological treatment of their symptoms may be necessary. Methods to prevent the development of LAA are also discussed.

Key Words: IgE antibodies; immunotherapy; medical history; occupational asthma; preplacement screening; questionnaires; sensitization; skin testing

Introduction

Symptoms of laboratory animal allergy (LAA[1]) can involve the skin, eyes, nose, and lower respiratory tract. The most common symptoms are nasal congestion, runny nose, sneezing, skin rashes, and itchy, watery eyes. Asthmatic symptoms have been reported in 20 to 30% of sensitized individuals (Bush et al. 1998). The diagnosis of LAA requires a comprehensive occupational history, which can be facilitated by specifically designed questionnaires (Bernstein 1993; Seward 2001; Table 1). Important information to obtain from the worker includes onset and severity of symptoms and correlation of the symptoms to exposures in the laboratory facility (Bernstein 1993). Confirmation of the diagnosis requires appropriate testing to detect the presence of immunoglobulin E (IgE[1]) antibodies to laboratory animal allergens (specific sensitization). To confirm the suspicion that occupational asthma is due to sensitivity to laboratory animals, additional tests of lung function are required (Figure 1).

Skin testing to common seasonal and perennial allergens outside the workplace should also be performed to investigate the possibility of non-laboratory animal-induced disease (Bernstein et al. 1996). The presence of specific sensitization can be detected by skin testing or specific in vitro testing.

Assessment of the degree of impairment of lung function is measured by performing spirometry, which can be conducted before and after the administration of a bronchodilator. Evidence for nonspecific bronchial hyperresponsiveness (a marker for asthma) is determined by methacholine or histamine bronchoprovocation testing (Bernstein 1993; Bernstein et al. 1996). To establish whether specific exposures to laboratory animals are the cause of symptoms, assessment of lung function can be confirmed by performing spirometry or monitoring serial peak expiratory flow rate (PEFR[1]) while the individual is at work and away from the workplace. It is rarely necessary to perform a bronchoprovocation challenge with laboratory animal allergens.

Occupational History

Diagnosis of LAA requires a detailed and comprehensive medical history. Therefore, an experienced physician who is knowledgeable regarding allergic and occupational diseases is best qualified to make the diagnosis. Important elements of an occupational history are listed in Table 1. The information should include demographic data about the individual worker's present and past employment history; the nature, duration, and timing of the patterns of symptoms; and any potential risk factors for the development of LAA (Bernstein 1993).

Although questionnaires can be extremely sensitive, they are not specific and cannot be used to make a diagnosis of LAA without confirmatory objective testing. In the case of occupational asthma due to other causes, there has been a poor correlation between the history and the diagnosis as confirmed by specific challenge testing (Malo and Chan-Yeung 1993). It is important to note that there is no standardized questionnaire available for diagnosing LAA. However, one example is provided (Table 2), and a simplified version appears elsewhere in this volume (Seward 2001).

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[1]Abbreviations used in this article: FEF, forced expiratory flow rate; FEV_1, forced expiratory volume in 1 sec; IgE, immunoglobulin E; LAA, laboratory animal allergy; PEFR, peak expiratory flow rate; PPE, personal protective equipment; RAST, radioallergosorbent test.

Table 1 Key elements of occupational history in the evaluation of occupational asthma[a]

I. Demographic information
   A. Name and address
   B. Personal data including sex, race, and age
   C. Educational background with number of school years completed
II. Employment history
   A. Current department and job description including dates begun, interrupted, and ended
   B. All other work processes and substances used in the employee's work environment (a schematic diagram of the workplace is helpful to identify indirect exposure to substances emanating from adjacent work stations)
   C. Prior jobs at current workplace with description of job, duration, and identification of material used
   D. Employment preceding current workplace (including job descriptions and exposure history)
III. Symptoms
   A. Categories
      1. Chest tightness, wheezing, cough, shortness of breath
      2. Nasal rhinorrhea, sneezing, lacrimation, ocular itching
      3. Systemic symptoms such as fever, arthralgias, and myalgias
   B. Months or years of duration
   C. Months or years of employment duration at current job before onset of symptoms
   D. Temporal pattern of symptoms in relation to work
      1. Immediate onset beginning at work with resolution soon after coming home
      2. Delayed onset beginning 4-12 hr after starting work or after coming home
      3. Immediate onset followed by recovery with symptoms recurring 4-12 hr after initial exposure to suspect agent at work
   E. Improvement away from work
IV. Potential risk factors
   A. Smoking history (including current smoking status and number of pack years)
   B. Asthmatic symptoms preceding current work exposure
   C. Atopic status
      1. Consistent history of seasonal nasal or ocular symptoms
      2. Family history of atopic disease
      3. Confirmation by epicutaneous testing to a panel of common aeroallergens
   D. History of accidental exposures to substances such as heated fumes or chemical spills

[a]Adapted from Bernstein JA, Bernstein DI. 2001. Occupational asthma. Diagnostic approaches and treatment. In: Bush RK, ed. Environmental Asthma. New York: Marcel Dekker, p 265-284.

Basic components of the questionnaire include employment and medical history (Malo and Chan-Yeung 1993). Of particular importance is information regarding the task and jobs the employee performs that can be related to specific exposure levels. Previous employment, where the worker may have been exposed to laboratory animal allergens, is also important. From the medical history, it should also be possible to determine whether there is any relation between symptoms experienced before, during, or after a specific exposure in the workplace (Bernstein 1993; Malo and Chan-Yeung 1993). Also of importance is the duration of symptoms after leaving the laboratory environment. Improvement of symptoms on weekends or while away from the exposure, particularly, adds credence to the possibility that exposure to laboratory animal allergens is the etiological agent. Improvement in symptoms while away from exposure may be a more sensitive question for establishing a work-related etiology than worsening of symptoms while at work. The information should also include dermatological symptoms; the presence or absence of systemic symptoms such as chills and fever; smoking history; preexisting history of allergy or asthma; and a family history of allergic diseases.

The time from beginning exposure to the onset of symptoms due to LAA varies considerably, possibly from <30 days to >3 to 4 yr. A study by Cullinan (1994) revealed that the mean duration of employment before the onset of symptoms was approximately 1 yr for chest symptoms, 214 days for nose and eye symptoms, and approximately 1 yr for skin symptoms.

Classically, individuals with LAA will complain of symptoms that begin at work and resolve or improve shortly after leaving work at night, during weekends, or while on vacation. However, as symptoms become more severe, they may not improve when the individual is away from the workplace because of chronic inflammation of the tissues, which is a result of persistent exposure to the allergens (Park and Nahm 1997). Therefore, the diagnosis of LAA should not be overlooked because of the apparent lack of correlation between the symptoms and workplace exposure.

Occasionally, the diagnosis of LAA is made incorrectly

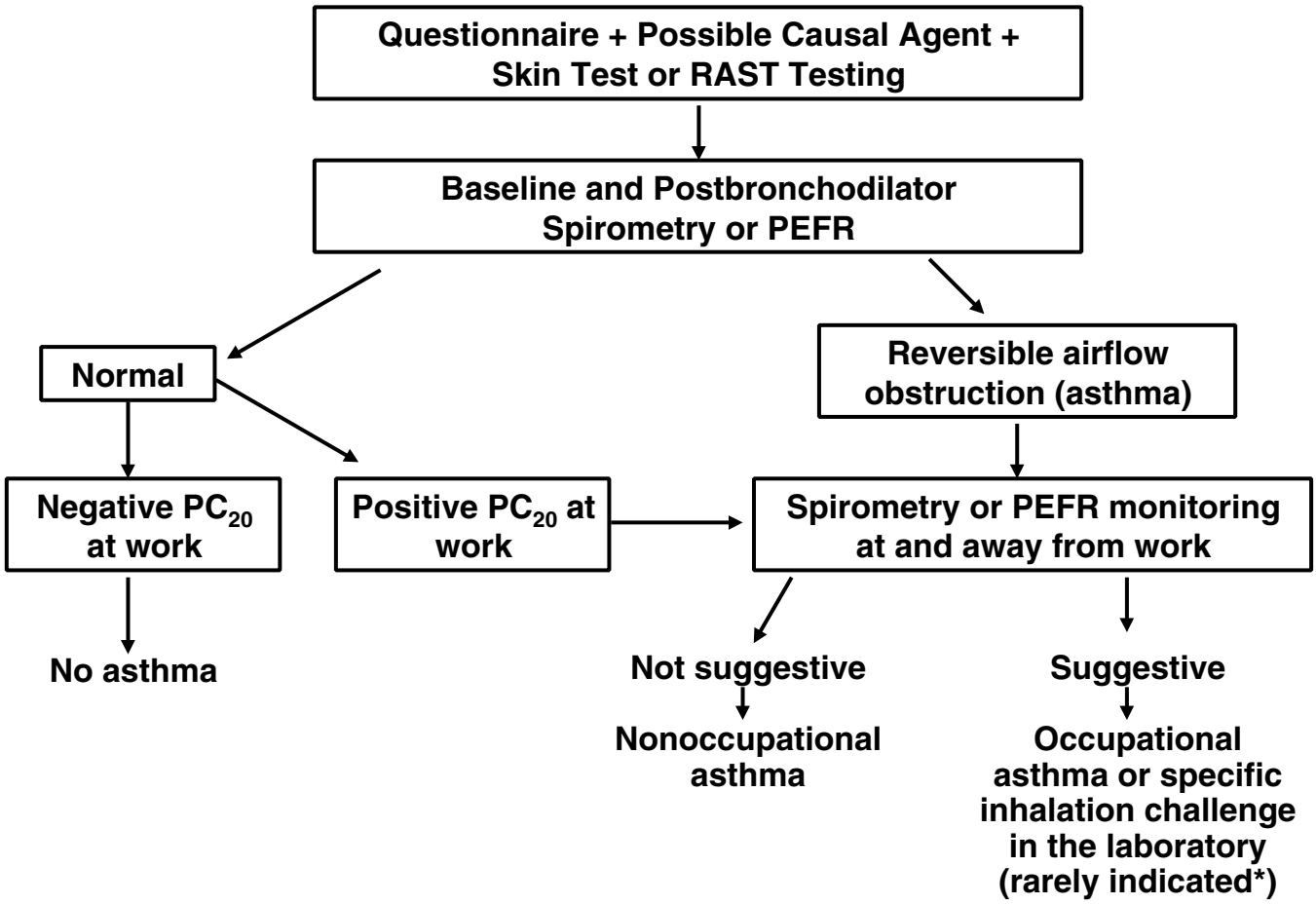

Figure 1 An algorithmic approach for the assessment and diagnosis of occupational asthma. Provocative concentration causes a 20% decrease (negative PC_{20}) in forced expiratory volume in 1 sec. PC, provocative concentration; PEFR, peak expiratory flow rate; RAST, radioallergosorbent test. *If diagnosis remains in doubt, to establish etiology of newly identified laboratory animal allergen, or for medico-legal purposes.

in an individual with pre-existing asthma due to nonworkplace exposure. Other physical factors in the workplace, such as exposure to temperature extremes, irritant chemicals, or other allergens, could contribute to the individual's symptoms at the workplace. However, it should be recognized that individuals with pre-existing asthma (not due to their employment) may also develop symptoms due to LAA from their workplace exposure. Other diseases that may mimic LAA include conditions such as chronic obstructive lung disease, hypersensitivity pneumonitis, and other asthma-like syndromes (Bernstein1993; Bernstein et al. 1996). These conditions can usually be distinguished by the appropriate medical history and contributory laboratory tests.

Detection of Laboratory Animal Sensitivity

Ultimately, diagnosis of LAA is contingent on demonstration of specific IgE antibodies to laboratory animal allergens. Laboratory animal allergens are considered to be high molecular antigens and therefore complete antigens because they do not require structural modification to elicit a specific immune response (Bernstein et al. 1996; Grammar and Patterson 1993). The presence of specific IgE antibodies (in the absence of symptoms) as demonstrated by skin tests or in vitro tests may only reflect exposure (Zeiss et al. 1977). However, symptoms that correlate with the individual's exposure at work and positive tests suggest that the patient is indeed sensitized to the agent, which is causing the symptoms. Although positive skin tests to laboratory animal allergens indicate a high risk for the development of occupational asthma, the tests are not sufficient to make the diagnosis (Grammar and Patterson 1993).

Test reagents used in the diagnosis of laboratory animal allergens are not standardized. Standardization of an allergenic extract requires identification of the allergen source, details of the extraction procedure, and assessment of the biochemical composition (Grammar and Patterson 1993). Many of the reagents used for skin testing or in vitro testing, especially for rats and mice, are prepared from dander rather than from urinary proteins, and this preparation can result in falsely negative tests. Some of the in vitro tests use purified

Table 2 Laboratory animal allergy questionnaire[a]

Date_____

Name:_____
Supervisor:_____
Department:_____

Age:_____ Sex: ___Male ___Female

OCCUPATIONAL HISTORY

Answer these questions about your present job:

Job title:_____
Number of years employed at this facility:_____
How many months/years at your present position?_____
Brief description of duties _____
_____
_____
_____

Do you work with laboratory animals? ___Yes ___No
If yes, complete the following.

Animal	Yes	No	Approximate Contact Hours/Day
Rats	___	___	_____
Mice	___	___	_____
Rabbits	___	___	_____
Guinea Pigs	___	___	_____
Monkeys	___	___	_____
Cattle	___	___	_____
Dogs	___	___	_____
Cats	___	___	_____
Other	___	___	_____

Do you feel that you are allergic to any of these animals? ___ Yes ___ No

___ Rats ___ Mice ___ Rabbits ___ Dogs ___ Other
___ Cats ___ Monkeys ___ Cattle ___ Guinea Pigs

Did you work with laboratory animals before your employment at this facility?
___ Yes ___ No
If yes, how long?_____ years What type of animals? _____

Do you use or wear any of the following items when working with animals?

Protective Eye Glasses	___ Yes	___ No
Mask/Respirator	___ Yes	___ No
Lab Coat	___ Yes	___ No
Gloves	___ Yes	___ No

HOME ENVIRONMENT INFORMATION

Do you have any indoor pets? ___ Yes ___ No If yes, which animals and for how long?

Animal	1-2 Years	2-3 Years	3-4 Years	Over 4 Years
Dogs	___	___	___	___
Cats	___	___	___	___
Other (Type)_____	___	___	___	___
_____	___	___	___	___

continued

Do you regularly have any of the following symptoms? ___ Yes ___ No Please indicate if the symptom is present and the year of onset. Also check in what location or time "period" the symptom(s) is/are present.

Symptom	Yes/No Present	Year of Onset	Symptoms Are Present At Work	At Home	On Vacation	No Difference
Cough	___	___	___	___	___	___
Sputum Production	___	___	___	___	___	___
Shortness of Breath	___	___	___	___	___	___
Wheezing	___	___	___	___	___	___
Chest Tightness	___	___	___	___	___	___
Asthma	___	___	___	___	___	___
Nose Congestion	___	___	___	___	___	___
Runny Nose	___	___	___	___	___	___
Sneezing	___	___	___	___	___	___
Itchy Eyes	___	___	___	___	___	___
Sinus Problems	___	___	___	___	___	___
Hay Fever	___	___	___	___	___	___
Frequent Colds	___	___	___	___	___	___
Hives	___	___	___	___	___	___
Skin Rash	___	___	___	___	___	___
Swelling of Eyes or Lips	___	___	___	___	___	___
Eczema	___	___	___	___	___	___
Difficulty in Swallowing	___	___	___	___	___	___

Were you ever told by a doctor that you had allergies? ___ Yes ___ No

Have you ever been skin tested for allergies? ___ Yes ___ No If yes, what substances were you found to be allergic to or sensitized to?

___ Ragweed ___ Grass ___ Trees ___ Mold
___ Dust ___ Cat ___ Dog ___ Mice
___ Other _____

Have you ever received allergy (desensitization/immunotherapy) shots? ___ Yes ___ No

Has a doctor ever said you have asthma? ___ Yes ___ No
If yes, when did your asthma start? _____ (year)
Are you currently taking medication (either over the counter or by prescription) to control your asthma? ___ Yes ___ No

Has a doctor ever told you that you have a medical condition caused by your working conditions? ___ Yes ___ No

Do any of your blood relatives (grandparents, parents, brothers/sisters) have allergies or asthma? ___ Yes ___ No

Are you under a doctors care for any other illnesses? ___ Yes ___ No
If yes, please list illnesses: _____
_____

Do you take blood pressure medication(s)? ___ Yes ___ No

Do you regularly use "over the counter" (nonprescription) nose drops or nose sprays (e.g., Afrin, Neosynephrine)? ___ Yes ___ No

Do you smoke cigarettes? ___ Yes ___ No If yes, how many cigarettes per day?_____
How many years?_____
If not presently smoking, did you ever smoke? ___ Yes ___ No
If yes, when did you stop smoking cigarettes? _____ (year)
How many years did you smoke? _____ years

Comments _____
_____
_____

Reviewed By:_____ Date:_____

[a]From Bush RK, Wood RA, Eggleston PA. 1998. Laboratory animal allergy. J Allergy Clin Immunol 102:99-112.

allergens, such as mouse urinary protein, which may be more sensitive.

Clinical immunological assessment of workers suspected for LAA should include in vivo or in vitro tests as they are available. The skin prick test is the most commonly used in vivo test to assess IgE-mediated sensitivity responses to laboratory animal allergens (Bernstein 1993; Bernstein et al. 1996; Grammar and Patterson 1993). Concentration of the material used in the test usually ranges between 0.1 and 10 mg/mL of the protein (Grammar and Patterson 1993). The test consists of placing a drop of the extract prepared from the animal allergen source on the skin, pricking the skin with a needle, and observing the response after approximately 10 to 15 min (Bush 1999). If the individual is sensitized to the specific allergen, the allergen extracts with IgE molecules on the surface of the mast cells in the patient's skin, which leads to the release of histamine and the production of a wheal and flare response at the site. This response is confirmed by the use of both a positive (histamine) and a negative (saline) control skin test. The presence of a positive response to the allergen and histamine with a negative response to saline indicates that the individual is allergic to the specific allergen tested.

Rarely, an intradermal skin test may be used if an exposed worker is suspected of having LAA and has a negative skin prick (Bush 1999). In such cases, a small amount (0.03 mL) of the laboratory animal allergenic extract is given by intradermal injection along with appropriate control solutions. Results are interpreted as described for the skin prick test. Intradermal skin testing carries a risk for anaphylaxis, albeit small, and therefore should be performed only by physicians who have training and experience with the technique.

In vitro tests can also detect IgE antibodies to laboratory animal allergens. The radioallergosorbent test (RAST[1]) requires binding of the specific laboratory animal allergen material to a solid phase, which is then incubated with the subject's serum and a radiolabeled anti-IgE antibody to human IgE. The amount of radioactivity bound to the solid phase material is directly proportional to the amount of the serum-specific IgE antibodies. The RAST test has largely been supplanted by enzyme-linked immunosorbent assays because of the risk of radiation exposure. In this assay (Grammar and Patterson 1993), the allergenic material is bound to plastic wells, is then incubated with patient's serum, and anti-IgE human IgE antibodies are conjugated to alkaline phosphatase. The colorometric change is measured by spectrophotometry. The optical density is proportional to the amount of specific IgE in the patient's serum.

In general, skin tests are more sensitive than in vitro assays. The introduction of the CAP-RAST (Pharmacia, Piscataway, New Jersey) and similar assays has increased the sensitivity of the in vitro assays. False-positive reactions from in vitro assays can occur in the presence of high serum total IgE levels due to nonspecific binding, and false negatives can occur as a result of binding of a specific isotypic antibody other than IgE (Grammar and Patterson 1993). Proper standardization of both in vitro and in vivo skin tests requires the use of well-established positive and negative controls. In the case of the in vitro assay, positive and negative control sera are used (Sarlo et al. 1990). For the skin test, the histamine control is the positive and a saline diluent serves as the negative control.

Assessment of Lung Function

For individuals who have lower respiratory-related complaints of cough, wheezing, and shortness of breath related to their laboratory animal exposure, lung function measurements should be performed (Figure 1) to determine whether laboratory animal allergen-induced asthma exists. Pulmonary function testing may also be useful in detecting subclinical asthma in workers with only upper airway rhinitis symptoms (sneezing, nasal congestion, "runny nose"). Ideally, lung function measurements should be monitored in the workplace if laboratory animal allergen-induced asthma is suspected (Malo and Chan-Yeung 1993). However, these measurements can create logistical problems and are usually not suitable for routine use. Frequently, the personnel and equipment to perform proper pulmonary function testing are not readily available.

Spirometry is the gold standard for assessing lung function and should include the measurement of forced expiratory volume in 1 sec (FEV_1)[1], forced vital capacity, and maximum midexpiratory flow rate (FEF_{25-75})[1]. Assessment of lung function before and after an employee's work shift has been used to correlate asthma symptoms with the workplace, but such correlation may lack sensitivity. Multiple assessments of the PEFR during a workday are more likely to capture enough data to diagnose or exclude asthma related to work exposure (Malo and Chan-Yeung 1993). Changes in a worker's lung function over the course of a workshift have been shown to be directly proportional to the level of exposure to laboratory animal allergens or to the sensitizing agent (Enarson and Chan-Yeung 1985).

Serial measurements of PEFRs, when properly performed, have been shown to correlate moderately well with the results of provocation challenges (Cote et al. 1990; Perrin et al. 1990). However, limitations of the peak expiratory measurement include patient noncompliance and the potential for falsification of measurements (Cartier 1984; Malo and Chan-Yeung 1993). These problems can be decreased by using computerized peak flow meters or spirometers that record the exact measurement and time of the reading.

Occasionally, another test known as nonspecific bronchial hyperresponsiveness may be performed. Although this test is not diagnostic because it may occur in other conditions (e.g., allergic rhinitis), it may be useful for confirming the absence of asthma (Bernstein 1993; Bernstein et al. 1996; Malo and Chan-Yeung 1993). Testing is conducted with methacholine or histamine. Individuals inhale the agent and perform pulmonary functions before and after the challenge. Gradually increased doses are used until the individual's pulmonary functions decrease by 20%. The threshold levels

that induce this decrease in lung function have been established. A positive methacholine test is not diagnostic of asthma; however, individuals who have specific IgE antibodies to laboratory animal allergens and a positive methacholine challenge test are more likely to exhibit a positive bronchoprovocation challenge with a laboratory animal allergen. A negative test for nonspecific bronchial hyperreactivity is more useful in excluding the current diagnosis of asthma in a symptomatic exposed worker (Bernstein 1993; Bernstein et al. 1996; Malo and Chan-Yeung 1993).

It is rarely necessary to perform bronchoprovocation challenges with a laboratory animal allergen. However, a positive test is the gold standard for confirming a diagnosis of occupational asthma due to laboratory animal exposure when the diagnosis is in doubt. In such a test, the individual is tested for lung function (usually spirometry or peak flow rate) before and after inhaling a control saline solution. The individual then inhales gradually increased doses of the allergen, and lung function is measured at 10- to 15-min intervals after each dose. A positive test is determined by a decrease in lung function ($\geq$20% decrease in FEV_1 or $\geq$25% decrease in PEFR). The individual's lung function may be monitored for up to 12 hr after the challenge to detect a late-phase response. These tests should be administered only in specially equipped centers and when supervised by experienced physicians (Malo and Chan-Yeung 1993).

Bronchoprovocation testing is time consuming and expensive to perform. If performed properly, it can be done with minimal risk. Several patterns of response have been noted, including isolated early asthmatic response characterized by the rapid onset of asthma symptoms and decrease in lung function after exposure to the allergen. This response is usually associated with LAA due to IgE-mediated sensitivity (Bernstein 1996). The diagnostic utility of an isolated early response is limited because sensitized individuals without asthma can have a positive challenge. Very rarely, a late asthmatic response can occur as an isolated event 4 to 12 hr after exposure, but this response is not usually characteristic of LAA. It is more likely to occur with exposure to chemical agents (e.g., isocyanates) in the work environment (Bernstein 1996). Finally, individuals may exhibit a dual response characterized by both the immediate and late-phase response. This response has been observed to occur with multiple types of occupational asthma including LAA.

Clinical Assessment of the Laboratory Animal Allergic Individual

One approach for the clinical assessment of LAA causing asthma is summarized in Figure 1 (Bernstein and Bernstein 2000). This approach may be used with workers who have work-related symptoms and are currently exposed to the suspected agents at work. The first step is to carefully administer a questionnaire or otherwise obtain a thorough medical history. As discussed above, a questionnaire can help capture and determine the appropriate clinical and exposure information. Upper airway symptoms, such as runny nose, nasal congestion, and/or itchy eyes, suggest that the individual is most likely allergic to laboratory animal allergens. Individuals with symptoms that begin immediately after starting work or within a few hours are also likely to be sensitized (Bernstein 1993).

If the patient has symptoms of dyspnea, chest tightness, cough, and wheezing, a test for nonspecific bronchial hyperresponsiveness with methacholine or histamine should be performed at work or within 2 hr after the workshift ends, provided the baseline lung functions are normal (Bernstein and Bernstein 2000). A negative methacholine challenge test excludes asthma, and no further evaluation is necessary. A positive test is consistent with asthma but is by itself nondiagnostic. In such a case, assessment of lung functions performed at and away from the workplace is essential for a diagnosis of laboratory animal allergen-induced asthma. If possible, supervised measurements of lung function (FEV_1) should be made at the actual worksite before and during workshifts for at least 1 wk of work exposure. These measurements are called a "workplace challenge." Improvement in symptoms and lung function after removal from the workplace with subsequent deterioration after returning to work supports the diagnosis of occupational asthma (Bernstein 1993).

If it is not possible to perform the workplace challenge, peak expiratory monitoring should be conducted over 2 to 3 wk (Bernstein and Bernstein 2000). The worker should measure and record peak expiratory flow measurements every 3 hr while awake or at least four times a day as a minimum (Bernstein 1993). Work exposure symptoms and use of any medications should be recorded. A variability of 20% in PEFR at work compared with the normal variability at home is consistent with occupationally induced asthma. A consistent pattern of declining PEFR at work with improvement when away from the exposure confirms the diagnosis. However, PEFR measurements should be interpreted with caution because there is the potential for falsification of readings by workers seeking compensation.

As noted above, the ultimate diagnostic test for laboratory animal allergen-induced occupational asthma is the bronchoprovocation test (Bernstein 1993; Bernstein et al. 1996; Malo and Chan-Yeung 1993). This test may be necessary to document causation of laboratory animal allergens by new exposures in index cases and, rarely, for medical-legal proof or disproof of a worker's eligibility for workers compensation. It is important to perform the bronchoprovocation test either before or shortly after removing the worker from exposure of the workplace because if the worker is removed from exposure, the response may wane over time. Another potential problem is the lack of standardized material available for such inhalation challenges. It may be impossible to reproduce work exposure conditions in the laboratory because other technical factors (e.g., temperature, atmosphere, and pressure) cannot be controlled.

In addition to assessing lung function, it is important to identify whether the individual is allergic to common

aeroallergens outside the work environment. In vitro assays to measure specific IgE to various allergens can be performed but are less sensitive than skin testing. It is important to note that the presence of a positive skin prick test or specific IgE antibodies by in vitro testing indicates only that sensitization has occurred and does not prove a clinical diagnosis of LAA or occupational asthma (Bernstein 1993).

Treatment

As soon as a diagnosis of LAA or asthma has been confirmed, treatment should be directed toward removing the worker from continued exposure. Studies evaluating the clinical course of workers with occupational asthma after removal from exposure have shown that persistence of the symptoms frequently depends on the duration of symptoms before diagnosis (Bernstein et al. 1996). The longer patients have symptoms, the less likely they are to recover completely. With early diagnosis, prognosis is much better, lung function is preserved, and the degree of nonspecific bronchial hyperresponsiveness is reduced. In contrast, individuals who remain in the workplace for longer periods of time and experience deterioration of lung function develop chronic persistent asthma, which often requires continued medication use.

Exposure Reduction and Avoidance

Reducing exposure to animal allergens in the workplace is particularly important in preventing the development of sensitization and symptomatic disease (Bush et al. 1998). Elsewhere in this volume, Seward (2001) discusses several of these methods, and Harrison (2001) describes specific engineering controls.

Personal protective equipment (PPE[1]) can reduce an individual's exposure to laboratory animal allergens. PPE includes respirators, eye protection, and protective clothing. Although these pieces of equipment may reduce exposure, their effectiveness is dependent on the users' willingness to wear them.

Respirators such as airstream helmets may provide some degree of protection but are expensive. Because the particles containing animal allergens are small and easily respirable, more than a dust mist type of mask may be necessary to prevent exposure (Bush et al. 1998). Such respirators require a respiratory protection program, which should include medical approval for use and test fitting (Bush et al. 1998; Seward 1999).

Experimentally, it has been shown that dust mist masks that have been approved by the National Institute of Occupational Safety and Health can remove up to 98% of rodent urinary allergens from the air (Sakaguchi et al. 1990). However, in individuals who have symptomatic disease, a more efficient respirator or air filtering hood affords better protection than a dust mask (Seward 1999). Nevertheless, use of such respirators has not been shown to prevent the progression of disease and is not a substitution for removal of the symptomatic individual from exposure.

Comprehensive programs that include education and training of workers, modification of work practices, engineering controls (Reeb-Whitaker et al. 1999), and use of PPE (including the mandatory use of respiratory protection in the form of dust mist respirators) have been shown to prevent laboratory animal allergen sensitization (Fisher et al. 1998). Unfortunately, prospective studies of such practices have not been performed.

Pharmacological Management

Pharmacological treatment of acute or chronic symptoms due to LAA is similar to treatment of those individuals who have nonoccupational allergic diseases. Antihistamine medications may be useful in controlling symptoms. A worker's premedication with antihistamine before entry into the environment may be particularly useful in minimizing nasal and ocular symptoms of sneezing and itching as well as reducing skin rashes. Traditional antihistamines used in the treatment of allergic diseases block the effect of histamine on the H1 histamine receptor in tissues (Bush and Georgitis 1997). Antihistamines mainly treat symptoms of pruritus and sneezing and have little effect on nasal congestion. Similarly, they have minimal effects in the treatment of asthma. These medications are most effective when taken before exposure because they are competitive antagonists for histamine on the H1 receptor. Many so-called "second generation" antihistamines have been developed (Slater et al. 1999) and have the advantage of lessening the sedative effects of antihistamines compared with products developed earlier. They produce less drowsiness and sedation, which may be particularly important in preventing work-related accidents that the worker must be fully functional to avoid.

In addition to oral forms of antihistamines, ocular antihistaminic drops are also available (Gern and Busse 1998). Use of these ocular antihistamine preparations before exposure may also reduce symptoms of ocular itching.

Mast cell stabilizers, such as cromolyn and nedrocrimil, are pharmacological agents that prevent degranulation of mast cells in response to allergen exposure. Cromolyn is available as an ocular preparation, a nasal spray, and an oral inhaler. Nedrocrimil is available as an ocular preparation and an oral inhaler. Use before exposure to laboratory animal allergens may prevent or reduce symptoms. These compounds, however, cannot be used to treat acute symptoms. To be effective, they must be used as premedication before the allergen exposure (Bush and Georgitis 1997).

Gross (1980) has performed a double blind, controlled trial of cromolyn in the prevention of asthma symptoms in laboratory animal workers with animal sensitivity. In this controlled trial of 10 subjects with laboratory animal-induced asthma, the prior use of inhaled cromolyn afforded considerable or complete protection against both immediate and

late-phase bronchial responses in nine subjects. Therefore, the use of cromolyn or nedrocrimil to prevent asthma symptoms may be appropriate in some circumstances, such as when reduction of exposure has not proved beneficial. However, as previously mentioned, complete avoidance is the treatment of choice, and the use of symptomatic medication should not be considered a substitute.

Occasionally, individuals with occupational asthma will experience acute symptoms, in which case a short acting beta-receptor agonist bronchodilator may be useful to control symptoms (Bush and Georgitis 1997). Such medications provide only temporary relief of symptoms and are not appropriate for long-term treatment of the symptomatic individual. Although these medications have shown some benefit in preventing or reducing the severity of an immediate bronchospastic response, they do not affect the late-phase response to allergen exposure.

For individuals who have more chronic disease (i.e., daily symptoms while at work), inhaled corticosteroids along with a long-acting beta-receptor agonist bronchodilator may be used. The nature and severity of the worker's symptoms will dictate the need for these medications (Tavakkoli and Rees 1999). Inhaled corticosteroids reduce the inflammatory changes in the airway in individuals with asthma (Bush and Georgitis 1997). Inhaled corticosteroids reduce the late-phase response to allergen challenge. With long-term use, they may also reduce some of the immediate response (Bush and Georgitis 1997). However, none of the medications act as substitutes for the long-term solution to the problem because deterioration of lung function and symptoms can increase with prolonged exposure.

In some individuals, immunotherapy to cats and dogs has been undertaken with some degree of success (Bush et al. 1998). Immunotherapy consists of administration of allergenic extracts to sensitive individuals to reduce their sensitivity. The results of immunotherapy for animal danders are most applicable to individuals with intermittent exposure and have not been applied to chronically exposed laboratory workers. Uncontrolled studies of immunotherapy to laboratory animals such as mice, rats, and rabbits have demonstrated some improvement (Wahn and Siriganian 1980). The use of immunotherapy to protect laboratory workers from progression of symptoms and deterioration of lung function, however, has not been established.

Emergency Procedures

On rare occasions, an individual may experience an anaphylactic reaction from an animal bite (Teasdale et al. 1993) or from needle punctures contaminated with laboratory animal allergens (Watt and McSharry 1996). Because these reactions can progress rapidly and become fatal, physicians may recommend that the worker carry a self-administered form of epinephrine such as Epi-Pen (Dey, Napa, California) or Ana-Kit (Bayer Corp., West Haven, Connecticut) (NRC 1997). In appropriate circumstances, it may be useful to instruct coworkers in emergency procedures such as cardiopulmonary resuscitation.

Prevention

As noted in *Occupational Health and Safety in the Care and Use of Laboratory Animals* (NRC 1997), prevention of the development of LAA should be the aim of all facilities engaged in the use of laboratory animals. Cooperation between facility management and workers and the implementation of good industrial hygiene measures aimed at preventing exposure to inhalant material have the potential for reducing LAA. Workers should be continually educated about the importance of adhering to appropriate procedures that reduce exposure. Preplacement screening of hired workers for allergy to other antigens such as pollens, molds, and animal danders may be considered before assigning employees to specific jobs in an effort to reduce risks for development of laboratory animal sensitivity. Comprehensive surveillance programs for detecting and monitoring workers at increased risk for sensitization may reduce the frequency of laboratory animal allergies.

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