

Laboratory Animal Allergy

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Abstract: Ranging from mild respiratory allergy to anaphylaxis, laboratory animal allergy (LAA) can adversely affect an individual's health and career. LAA can be prevented through a hierarchy of controls. However, workers remain at risk as many, if not most, workplaces have not fully adopted needed prevention practices. To address this risk, organizations should use a multidisciplinary leadership team. Along with participation on the leadership team, occupational medicine physicians should oversee a medical surveillance program that identifies workers with LAA including incident cases, as well as workers with LAA who are symptomatic in the workplace. One indication that medical surveillance may be effective in identifying incident cases is that it is detecting prevalent cases, usually in the range of 10%–20% or higher. Programs with lower detection rates of prevalent cases should adjust their approach to medical surveillance. The results of medical surveillance, including the incidence and prevalence of LAA, should be shared within the organization and used to guide the use of controls. Periodic self-audits are recommended to better protect workers by identifying and addressing opportunities for program improvement.

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Allergy to animals is common with 10%–20% of individuals being allergic to dogs and cats.¹ Animal allergies are also a significant concern in the workplace where a variety of animals are utilized in research studies. In the research setting, scientists, veterinarians, technicians, and others who work with animals or in animal facilities are at risk of developing LAA that can affect their health and career.^{2–4} It is estimated that between 11% and 44% of lab animal workers will develop LAA.⁴ LAA can manifest as rhinoconjunctivitis, sinusitis, asthma, dermal allergy, or anaphylaxis. Workers are also at risk of developing allergies to more than one species,^{5,6} which can further limit their career.

LAA has been recognized as a hazard since at least the 1970s.^{7–10} In 1998, the National Institute for Occupational Safety and Health issued a hazard alert warning about the need to protect laboratory animal workers from asthma.¹¹ There is extensive literature addressing approaches to prevention of LAA;^{2–5,12–19} however, it remains a significant workplace challenge.^{17,18,20,21} National surveys suggest that while some organizations may have excellent prevention programs, many, if not most, can improve their programs to better protect workers.^{17,18,21}

This guidance statement addresses the causes of allergy, approaches to exposure control, occupational medicine programs for animal research related to allergy including medical surveillance, and a programmatic approach to worker protection through prevention.

THE ALLERGENS

Allergic reactions from animal allergens occur when an allergen binds to and crosslinks IgE molecules already bound to mast cells. This leads to degranulation and release of mediators. While new animal allergens continue to be identified, the most common IgE molecules that cause LAA have been well described. Most of these allergens are members of the lipocalin family, including the major rat (Rat n 1) and mouse (Mus m 1) allergens.^{4,6,22,23} These molecules have a common tertiary structure with substantial sequence homology.^{6,22} Along with the rat and mouse allergens, other lipocalin allergens include guinea pig (Cav p 1, Cav p 2, Cav p 3, Cav p 6), hamster (Mes a 1, Phod s 1), rabbit (Ory c 1, Ory c 2,

Ory c 4), dog (Can f 1, Can f 2, Can f 4, Can f 6), and cat (Fel d 4, Fel d 7).²² However, animal allergens also come from other protein families, including the primary cat allergen, Fel d 1 (secretoglobulin)²⁴ and a major dog allergen Can f 5 (kallikrein).²⁵ Other allergens come from the albumin family including Fel d 2 (cat) and Can F 3 (dog).^{22,26} Because many allergens come from a small number of protein families and have similar sequences, there can be cross reactivity of specific IgE molecules within and across species, which may increase the risk of developing additional allergies after a first allergy develops.^{5,6,22,26} These allergens can be found in saliva, dander, hair, and urine, as well as places where animals have been, or allergens have migrated.

ALLERGENS IN THE WORKPLACE

Laboratory animal husbandry staff, veterinarians, researchers, technicians, and others who work with laboratory animals or in animal facilities are routinely exposed to a wide range of sensitizing protein allergens, particulates, and endotoxins from animals, their bedding and waste. Since these can be present in the air and on laboratory surfaces, workers can be exposed via inhalation, ingestion, contact, and occasionally via percutaneous exposures. Additional sources of allergenic exposures can include research materials used with the animals, their food, and even contaminated personal protective equipment (PPE). Moving animals outside the animal facility to conduct research in other laboratories creates additional risk of exposure both during transportation and when performing research. Other sources of exposure include animal area exhaust ventilation, which may expose people in the workplace and in nearby locations if ventilation is exhausted improperly. Allergens can be transported to nonanimal worksites and into homes on the clothing or hair of animal workers, especially when PPE is not correctly worn or removed at the worksite. All of these exposure mechanisms can create allergic sensitization or produce symptoms.

Mice and rats are the most commonly used research animals and by far the most common sources of sensitization and allergic reactions.³ Other small rodents (such as hamsters and guinea pigs) and lagomorphs (such as rabbits), which are frequently used in lab research, are also highly allergenic. Cats, dogs, and primates can also produce allergic sensitization, although their lower frequency of use

in research is reflected in smaller numbers of reported occupational allergy diagnoses. Any animal can cause allergic reactions in susceptible individuals.

LABORATORY ANIMAL ALLERGY PATHOPHYSIOLOGY

Clinical allergy is preceded by sensitization, the development of IgE against animal allergens. However, not everyone who is sensitized will develop clinical symptoms. Allergy to laboratory animals has been recognized as an occupational illness for decades and includes primarily the first of the four standard allergic responses: type I IgE-mediated hypersensitivity. IgE-mediated syndromes include rhinoconjunctivitis, sinusitis, asthma, dermal, and anaphylactic reactions. Other types of allergic reactions are less common: type II IgG or IgM-mediated cytotoxic hypersensitivity, such as transfusion reactions or autoimmune hemolytic anemia; type III immune complex-mediated hypersensitivity such as serum sickness, Arthus reactions; and type IV cell-mediated hypersensitivity reaction, such as contact dermatitis.

Immediate (type I) hypersensitivity reactions begin when a susceptible individual is exposed to the animal allergen protein, usually by inhalation, although mucous membrane and dermal exposures can also trigger sensitization. Whatever the route of exposure, allergens are then taken into antigen-presenting cells, such as alveolar macrophages and dendritic cells. Antigen presenting cells process the proteins into smaller peptide fragments and display them on their outer membranes in combination with major histocompatibility proteins. Upon encountering these antigen presenting cells, naive T-helper cells with compatible surface protein complexes are activated to mature and replicate. When re-exposed to the inciting antigen, the activated T-cell release cytokines and induce specific IgE production by B cells. IgE then binds to mast cells and basophils, stimulating them to release histamines and a range of other preformed inflammatory biochemicals, which can produce immediate symptoms, varying with the site of inflammation. The cytokines also attract eosinophils to the affected tissues, facilitating subsequent release of inflammatory compounds with ongoing symptoms.

Working with animals may also expose workers to endotoxins, which are inflammatory lipopolysaccharide complexes found in the outer cell walls of gram-negative bacterial species. These bacteria and the endotoxins they produce are common in areas that house animals, and environmental endotoxin exposure can induce mucous membrane irritation, dyspnea, cough, and wheezing, all of which may overlap IgE-mediated allergic symptoms.²⁷ Although the pathophysiology differs, with endotoxin-induced inflammation arising from

a cascade of cytokines and neutrophil recruitment without IgE dependence, the clinical manifestations may be indistinguishable from allergy or may coexist and worsen illness. The need for exposure controls and medical surveillance are identical for endotoxins and allergens.

CLINICAL MANIFESTATIONS

Rhinoconjunctivitis, the most common allergic syndrome among laboratory animal workers, presents with coryza, sneezing, tearing, mucosal itching, and eye redness, occurring alone or in combination. Asthma, manifested by dyspnea, wheezing, coughing and/or chest discomfort, may occur de novo or—more often—following rhinoconjunctivitis symptoms. Sinusitis usually presents with a frontal headache or pressure and symptoms may be delayed. Dermal allergy can include a pruritic maculopapular rash or urticaria alone, or in combination with mucosal or respiratory symptoms. All may present acutely or subacutely with a broad range of severity and always with the risk of progression.

Anaphylaxis after lab animal exposure may occur with or without prior symptoms, may follow a first animal bite or contaminated percutaneous injury, or may occur without warning after prior uneventful exposures including bites.^{28,29} This life-threatening condition can be mistaken for anxiety or a panic attack by the individual experiencing symptoms as well as less experienced clinicians. Presentations can be catastrophic or progressive with a range of syndromes and symptoms. Angioedema can present with skin or mucosal swelling that can cause upper airway obstruction if the tongue, larynx, or trachea are severely affected. Lower airway swelling and obstruction can present with wheezing or severe dyspnea. Gastrointestinal involvement may present with cramping, diarrhea, nausea, and/or vomiting. Dropping blood pressure may present with light-headedness or syncope. Anaphylaxis may be treated initially on the scene with injected or auto-injected epinephrine or nasal epinephrine, but in some cases, the therapeutic effect may wane within minutes. Guidelines published in 2023 from the Allergy Immunology Joint Task Force state that calling emergency services after use of an epinephrine auto injectors “may not be required if the patient experiences prompt, complete, and durable response to treatment and has access to additional epinephrine auto injectors. Situations that would warrant EMS activation include severe anaphylaxis, symptoms that do not resolve promptly, completely or nearly completely, or symptoms that return or worsen.”^{30,31}

Presenting symptoms of LAA may overlap with seasonal or other environmental allergies. Determining the etiology of symptoms may also be complicated by co-existing sensitization and exposure to pets or farm animals at home.

For these reasons, primary care providers, urgent care providers, and emergency department clinicians may fail to recognize workplace causality and miss opportunities to prevent further exposure and worsening pathology. An occupational history is an essential component of the assessment of patients evaluated for allergic symptoms.

DIAGNOSIS

Respiratory LAA usually presents as rhinoconjunctivitis. Diagnosis of LAA relies on a history of symptoms developing in conjunction with workplace exposure. The timing of the onset of symptoms can be variable and sometimes delayed but often occurs shortly after or within 30 minutes of exposure. Workers may report nasal congestion, runny nose, sneezing, itching, or red and itchy watery eyes.⁴ The differential diagnosis of allergic rhinitis includes nonallergic, infectious, and medication-induced rhinitis.³² Symptoms due to LAA need to be distinguished from symptoms caused by seasonal allergy, allergy to other allergens in the workplace, or reactions to other workplace environmental exposures, including endotoxins.³³ LAA may also coexist with other conditions causing similar symptoms.

Occupational asthma associated with laboratory animals can have a similar time to onset following exposure and appears similar to other forms of asthma. Spirometry and other pulmonary tests may not be necessary to make a diagnosis of asthma when the history and physical exam are straightforward but are often helpful to confirm the diagnosis.

Anaphylaxis associated with laboratory animal exposure is clinically the same as anaphylaxis from any other cause.²⁹ Anaphylaxis is most often associated with animal bites but can occur with airborne exposure.^{28,34,35}

Skin reactions include hives or maculopapular rashes. These usually occur at the site of contact with animal urine, dander, animal bodies or tails, or as the result of scratches.³

A diagnosis of LAA may be based on history and clinical findings alone. Laboratory testing for IgE or skin prick testing can be helpful to support a diagnosis of LAA (IgE measurement has largely replaced radioallergosorbent testing). If tests are ordered, it is important to understand which antigens are being tested for as some tests assess specific proteins while others test “epithelium” or “urine.” However, a positive test is not necessary for diagnosis. A negative antigen test does not exclude the diagnosis in the presence of a clear history and exam findings. Negative results in the setting of true allergy may occur because the symptoms are due to an antigen that was not tested for, including novel allergens.

EXPOSURE RISK BY JOB AND TASK

Identifying the activities and job roles in a research facility with the highest exposure

levels can help to prioritize risk mitigation efforts. Activities resulting in the greatest exposure to rat and mouse allergens have been identified through aeroallergen monitoring, and include emptying, changing, and washing used cages, as well as animal husbandry activities such as handling and feeding. These activities occur in various locations throughout a research facility including housing areas, laboratories, cage wash areas, and procedural areas. Surgery, sacrifice, and handling dead animals or tissue also result in allergen exposure but usually at a much lower level.³⁶⁻³⁹ Workers may also experience higher levels of exposure if they are working with mostly male rodents due to the higher urinary allergen concentration excreted by male versus female animals.³⁹

Based on typical job tasks, animal care and cage wash technicians have the most exposure, followed by veterinarians and veterinary techs, while research personnel sustain less exposure. However, exposure can vary significantly between workers performing the same roles.^{36,37} Even when no high-risk activities are underway, allergen levels in the laboratory may remain higher than in adjacent corridors and offices, putting workers entering the laboratory or animal housing space at risk.³⁶

EXPOSURE AND HEALTH EFFECTS

Occupational exposure to laboratory animal allergens, particularly mouse or rat urinary aeroallergens, is clearly associated with allergic sensitization (elevated IgE against animal allergens with or without clinical symptoms) and clinical allergy.⁴⁰⁻⁴³ Sensitization, usually measured through skin prick testing, has been consistently found to be associated with increasing levels of exposure, as well as current and cumulative exposure.^{40,43,44}

While individual and occupational risk factors have been identified, the nature of sensitization and allergic response is such that LAA can occur at extremely low exposure levels, such that no “safe” exposure level can be determined. Measuring mouse or rat urinary aeroallergens can be useful to identify higher and lower-risk work areas and assess the effectiveness of mitigation activities. While some facilities aim for aeroallergen levels below 2.5 or 5.0 ng/m³,^{45,46} levels should generally be reduced to as low as reasonably achievable. Even with improvements in hazard control that lead to a reduction in the incidence of LAA, sensitization rates may not be significantly reduced,⁴⁴ and the prevalence of LAA among animal workers with the lowest exposure levels may still exceed 10%.⁴⁵

Incidence rates of LAA are highest in younger workers and new employees within the first 3–4 years of rodent work, those with atopy, and workers without previous rodent

exposure or sensitization.^{40-42,47-49} The exposure-response curve may be steeper for workers with less than 4 years of experience working with rodents, and individuals with atopy are at higher risk of sensitization and LAA at every exposure level.^{40,42,48} However, workers can develop LAA at any point in their career.

Workers with LAA are at risk of developing allergy to additional species, even at a level of exposure that prevents development of a first allergy.⁵ In a longitudinal study, 25% of workers developed a second allergy within 2 years after the initial diagnosis and 50% had at least one additional allergy at 10 years.⁵

The risk of LAA correlates with the duration, frequency, and intensity of acute and cumulative exposure.^{41,49,50} Since male animals produce more allergens than females, sensitization and symptomatic allergy are associated with exposure to male rodents.⁴⁹

Some early cross-sectional studies suggested that sensitization and LAA are associated with consistent moderate-intensity exposures rather than infrequent high-intensity exposures.^{51,52} This alleged “beekeeper effect” was hypothesized to be attributable to protective levels of IgG4 stimulated by intermittent high-intensity exposures. However, further longitudinal analysis has confirmed that high levels of IgG4 precede sensitization. Neither high exposure levels nor high IgG4 protects workers against sensitization or symptoms.⁵³

The factors that trigger an immune response rather than tolerance to animal allergens are complex and incompletely understood. Further study is needed to determine the impact of exposure variability and exposure holidays. Nevertheless, the evidence is clear that animal workers exposed at any level to animal allergens are at risk of sensitization and LAA.

EXPOSURE CONTROL

Exposure control is the key to LAA prevention and control of symptoms. Implementing a structured hierarchy of controls is essential for reducing allergen exposure. This approach involves a combination of elimination, engineering controls, administrative controls, and PPE, including respiratory protective equipment (RPE), tailored to the specific laboratory setting (Table 1). Organizations should regularly review and update control measures based on new research, technological advancements, feedback from personnel, and program audit findings. While this guidance is focused on LAA, additional controls may be needed to address other chemical, physical, biological, and radiation hazards that may be present in the workplace.

The most effective control measure for prevention of LAA is elimination and involves

removing all sources of animal allergens. This includes employing alternative research methods that do not involve the use of animals, such as *in vitro* studies or computer modeling.⁵⁴

Engineering Controls

Engineering controls are used to remove allergens from the environment and a worker's breathing zone. These include containment devices, biological safety cabinets (BSCs), ventilation systems, and facility design.³⁹ Heating ventilation and cooling (HVAC) systems aid in reducing airborne allergens. General ventilation dilutes contaminants in the overall room environment. Effective ventilation controls temperature, humidity, and airflow to ensure both animal and worker well-being. The facility design and physical layout of the laboratory should minimize cross-contamination. This can be achieved by separating animal holding areas from other work areas and using barriers or enclosures to contain allergens. Specialized facility design can include airlocks and negative pressure rooms to prevent allergen spread. Enhanced containment systems can be used for specific areas where high allergen generating activities take place.

Local exhaust ventilation can remove allergens from a worker's breathing zone at the point of generation. Laminar flow benches, automated cage emptying/cleaning systems, and centralized vacuum cleaners are effective in reducing exposure, as are individually ventilated cages (IVCs) under negative pressure.^{38,39,55,56} However, if IVCs are under positive pressure (IVC+) for the animals' protection, workers can sustain increased exposure to allergens, especially if the IVCs are not well-sealed or if they are intermittently opened outside a BSC.^{38,57} Opening IVCs maintained under negative pressure can also result in exposure. While class I BSCs reduce exposure somewhat, class II BSCs with 70% air recirculation can eliminate detectable animal allergens as measured by personal air sampling of workers.⁵⁵ When working with unsealed IVC+ cages, static housing systems, or cage clean-out performed in a class I BSC, respirators can reduce exposure.

Administrative Controls

Administrative controls include approaches to work procedures that reduce the duration, frequency, and intensity of exposure. These can be divided between policies that affect all workers and specific work practices that affect workers performing specific tasks. Examples of broadly applicable policies include restricting animal use to dedicated animal facilities when feasible, restricting access to areas where animals are housed, or research is conducted, and maintaining separate lockers for street clothes. Standard operating procedures (SOPs) for facilities and tasks related to

TABLE 1. Approach to Prevention of Laboratory Animal Allergy

Elimination

- Computer models simulations
- In vitro: Culture cell lines, tissue culture, microbiological systems, stem cells, DNA chips, microfluidics (including organ-on-a-chip), plant-tissue based materials
- In silico: Computer analysis models, epidemiological surveys

Environmental controls

- Building design and/or directional airflow to separate animals and animal work from “clean” areas
- Negative pressure environments
- Increased air exchange
- Local exhaust ventilation
- Ventilated equipment (including individually ventilated cages)
- Biological safety cabinets
- Filter-topped cages
- Downdraft and backdraft tables
- HEPA filter vacuums
- Cage changing stations
- Robotic cage cleaning and waste handling equipment
- Bedding that reduces exposure

Administrative controls

- Minimize animal use to extent feasible
- Limit animal density
- Training and education of workers
- Restricted access to vivarium and animal rooms
- Limit animal use to the animal facility (when not possible, limit animal transport to “dirty” corridors and minimize exposure during transport)
- Restrict contaminated PPE to animal facility
- Locker facilities that separate “clean” and “dirty” clothing and PPE
- Shower facilities

Work practice controls

- Work process design to reduce animal handling and exposure
- Wet prep or HEPA vacuum shavers for shaving
- Room cleaning procedures that minimize exposure, including wet mopping for room cleaning (and avoiding dry sweeping)
- Hand washing
- Dedicated clothing
- Showering out of facility

Personal protective equipment (PPE)

- Respirators - N95, N99, half-face, full-face, powered air purifying respirators (PAPRs)
- Gloves
- Shoe covers
- Hair covers
- Eye and face protection
- Protective clothing
 - Protective sleeves
 - Lab coats
 - Gowns
 - Protective suits

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animal care and research should be developed. Standardizing practices across the organization can help ensure uniformity in safety measures and promote a culture of health and safety. Regular training programs should educate Principal Investigators and staff about the risks associated with animal allergens, including the risk of developing allergies to additional species for those with LAA. Training should encourage proactive reporting of symptoms or hazards to address issues before they escalate.⁵⁸ This training can be combined with biological safety training and should be updated regularly to reflect new findings and best practices.

To reduce allergen accumulation, regular cleaning protocols should be established,

using approaches like wet mopping instead of dry sweeping, and using HEPA-filtered vacuums. Equipment should be routinely inspected and maintained to ensure it is functioning correctly.

Additionally, conducting regular audits and inspections helps ensure compliance with health and safety protocols. Any non-compliance issues should be addressed promptly, and corrective actions should be documented.

Personal Protective Equipment

To avoid contaminating street clothing, laboratory personnel should wear protective

clothing, such as gowns, gloves, protective sleeves, and shoe covers. Changing from street clothes to clothing only worn for animal work can further reduce the risk of contamination. Eye and face protection may be needed, depending on the tasks or types of animals (eg, work with nonhuman primates requires eye and face protection because of the risk of herpes B virus transmission). Hair coverings prevent allergens from attaching to hair and also reduce allergen transfer from the workplace to homes.^{59,60} Respiratory protective equipment (RPE) should be used in environments where allergen exposure remains a concern after implementing other controls. While the goal should be to create an environment that does not require RPE, the only published programs that have demonstrated a reduction in LAA mandated the use of respirators in addition to other controls.^{5,12,16} Appropriate RPE includes the use of National Institute for Occupational Safety and Health-certified respirators, such as N95 or N99 masks, or powered air-purifying respirators (PAPRs).¹⁷ Training on the correct use, storage, and maintenance of PPE is crucial to ensure its effectiveness. Workers should understand how to properly don, doff, and dispose of PPE to minimize contamination.

A written respiratory protection program should be in place, including Occupational Safety and Health Administration (OSHA) required medical clearance, annual fit testing, regular training, and proper maintenance of equipment. Organizations may find it convenient to conduct respirator clearance in conjunction with medical surveillance.

MEDICAL SURVEILLANCE

A medical surveillance program is an essential component of occupational health programs serving animal workers.^{19,21,61,62} Medical surveillance is the primary mechanism to identify individuals with signs or symptoms of LAA who need further medical evaluation. Aggregate, deidentified surveillance data can identify work areas or jobs needing further mitigation efforts. Tracking data trends, including incidence and prevalence, support the evaluation of targeted interventions and the overall animal allergy prevention program.^{17,18,21,58}

Medical surveillance should begin with a preplacement assessment before animal work begins and continue throughout the individual’s career working with animals. Exit evaluations are recommended at termination of employment or discontinuation of animal work to detect previously unreported LAA.¹⁹ This requires a notification system so that surveillance can be conducted while the worker is still employed.

The baseline assessment can be incorporated into the preplacement evaluation for infectious diseases and other work requirements.

A mechanism to conduct baseline evaluations should also be in place for existing personnel anticipating new animal exposure, such as job transfers or additions to research protocols. Surveillance is typically conducted annually, although the frequency can be adjusted based upon a risk assessment.⁶²

Institutions vary widely in the implementation of medical surveillance.^{17,18} Mandatory participation policies have increased over the past decade to over 70%, with larger organizations being more likely to conduct medical surveillance and require participation.¹⁷ However, the ability of institutions to analyze and interpret meaningful population-level data is limited and has stalled; only 25% of institutions responding to a 2022 US national survey were aware of their LAA incidence and prevalence rates.^{17,21} Among those reporting the prevalence rate, many indicated it was 0%, which is substantially below the expected prevalence rate of 10%–20% or higher,^{4,44,63,64} raising the concern that some surveillance programs may not be detecting incident and prevalent cases.^{17,21} If an organization relies on questionnaires as a screening tool to identify workers with LAA symptoms, assessing whether the prevalence rate is within the expected range can be an indicator of whether surveillance is likely to be identifying incident cases. If questionnaires do not appear to identify incident and prevalent cases, interviews with workers may yield better results.^{63,65}

Institutions enrolling workers in medical surveillance need to develop a process for the systematic and comprehensive identification of all exposed workers and define the minimum exposure threshold for enrollment. While many exposed workers can be identified by their inclusion in a research protocol or by their job title or department, some workers such as facilities or housekeeping staff, are not as easily identified. Since access to laboratory animal housing facilities is restricted, the facility access list is one way to identify potentially exposed workers.

Workers who are not employees, including contractors and students with animal exposure present an additional challenge, in that they may not be tracked in the human resources or occupational health systems and may not be eligible for medical surveillance services provided to employees through the occupational health service. Organizations should implement methods to identify and train these individuals regarding animal allergy risks and symptoms and direct them to appropriate medical care for symptoms or routine surveillance.

While symptoms can occur at any frequency of exposure, for practical reasons institutions need to identify a minimum exposure threshold for enrollment in medical surveillance. This threshold need not be defined through measurement of animal aeroallergens

in the work area or through personnel monitoring but can be designated as some minimum time or frequency working with animals or in areas at risk of exposure, including but not limited to, animal housing areas, laboratories, procedural, or cage wash areas. A minimum exposure frequency to warrant medical surveillance is not defined in regulatory or accreditation guidance and requires a facility-specific risk assessment. Thresholds commonly range from exposure once per quarter to 2 hours per week⁶² and depend upon the effectiveness of hazard controls in place and trends in LAA incidence rates.

A well-constructed and optimally managed survey questionnaire can provide a useful screening tool to identify individuals needing further evaluation while collecting population-level data. Surveys are the primary tool for medical surveillance in over 96% of surveyed facilities.¹⁷ Surveys are noninvasive, inexpensive, and convenient. Electronic surveys have additional advantages: they can be accessed at any work location or shift; they can utilize branching logic to cascade follow-up questions based upon initial responses; they can import results directly into an occupational system to track completion and analyze aggregate data; and an algorithm can flag individual responses to prioritize for follow-up by occupational health staff. Free options are available to develop and administer electronic surveys (eg, REDCap⁶⁶).

Organizations using an electronic questionnaire for medical surveillance have the option of selecting a simpler screening approach with a small number of questions to identify workers who need further evaluation (see Supplemental Digital Content 1, <http://links.lww.com/JOM/B869>) or more detailed questionnaires that are intended to capture more extensive data. In either case, workers with LAA require follow-up including a more detailed history of tasks, exposure, and symptoms. More extensive surveillance questionnaires have been published that can also be adapted (questions covering family history would need to be removed).^{3,4}

Organizations should determine which approach, or a variation of these approaches, is most effective in identifying incident and prevalent cases, including cases of allergy to additional animal species. Medical surveillance should be detecting prevalent cases in the range of 10%–20% or higher. Since many organizations may not be fully detecting incident and prevalent cases through their current surveillance practices,^{17,21} organizations should evaluate their approach and pursue a continuous improvement process so that their medical surveillance program achieves the goals of case identification and the reduction or elimination of incident cases. Medical surveillance should also ensure that workers with existing LAA are not experiencing symptoms.

The occupational health service is responsible for medical surveillance survey interpretation. Workers reporting symptoms that have not been previously evaluated require further medical evaluation, as do all workers experiencing symptoms in the workplace. If using an electronic survey, the system can be programmed to flag individuals needing timely attention. The occupational health service should provide or facilitate medical evaluation for individuals with symptoms consistent with LAA, and for referral to an allergist if warranted.

When selecting or designing an electronic survey, it is important to ensure information privacy and security, collection of an electronic signature, long-term data storage, and, if possible, interoperability with the occupational health system. Instructions for contacting an occupational health nurse or clinician during business hours, or accessing emergency services after hours, should be provided. Ideal features include electronic notification of survey availability and completion, compatibility with common mobile devices, and an option to view the survey in another language, as pertinent to the workforce demographics. An alternative to the electronic survey should be readily available for individuals with low literacy or lack of access to technology.

Participation in medical surveillance should be defined as mandatory or voluntary by institutional policy. Mandatory participation ensures broader awareness of LAA risk by employees, a greater likelihood of identification of individuals with LAA, and more robust surveillance data. Mandatory medical surveillance policies can be implemented at the institutional level by Human Resources in collaboration with occupational health or could be an Institutional Animal Care and Use Committee or departmental policy. The policy should ensure the privacy of individual health information, define criteria for enrollment, designate responsibility for enrollment and for monitoring and enforcing individual compliance, state whether individuals can decline participation, and identify the consequences of nonparticipation.

RECOMMENDATIONS FOR WORKERS WITH LAA

The goal in all workplaces should be preventing workers from developing LAA by eliminating exposure to allergens. However, as many, if not most, workplaces do not appear to be meeting this standard,¹⁷ workers continue to develop LAA. In addition, workers may come to a new job with previously acquired LAA. It should be possible for most workers with nonasthma respiratory LAA or dermal LAA to continue to work with animals if existing workplace controls are sufficient or modifications can be made so that workers are symptom-free.^{16,65}

For workers with dermal LAA, the recommendation to keep skin covered may be sufficient. For those with non-asthma respiratory LAA, generic recommendations, such as requiring the use of a respirator and certain engineering/work practice controls, may be helpful, but a preferred approach is to individualize recommendations based on the specific workplace conditions, tasks, and work practices.

Informed decisions can be made by involving the worker in collaboration with the occupational health department, environmental health and safety, facilities and engineering, and their supervisor who possesses knowledge of the work and worksite. A worksite visit is especially helpful to thoroughly understand how work is being conducted and what controls can be implemented to reduce exposure. While the focus is on protecting an individual worker, this is also an opportunity to identify modifications to controls and tasks that can protect all workers.

Workers who develop asthma associated with animal allergens face a greater challenge. Asthma can worsen with continuing exposure and can sometimes progress after exposure ceases.⁴ The best outcomes after a diagnosis of asthma occur with no further exposure to the allergens.^{67,68} If workers with asthma associated with animal allergens wish to continue to work with animals, and this is supported by the organization, work should be limited to only essential tasks. Stringent work modifications may be required, such as work only within engineering devices that provide directional airflow and filtration, wearing of PPE and RPE designed to protect respiratory and mucous membranes, having a rescue inhaler immediately available at all times when working with the implicated species, and adding focused physical exams to confirm effectiveness of these and other control measures.⁶⁵ Continuing work under these circumstances requires that the worker becomes and remains free of any LAA symptoms.

Recommendations for workers with LAA may include restrictions, exclusions, or modifications to conducting work with specific species, and/or activities (eg, no entering animal facility, avoid specific species, no animals in work area, no animal handling, or must wear specified PPE or use RPE). Restrictions may be permanent or may be temporary while undergoing medical evaluation and/or implementing controls.

Workers who develop anaphylaxis from animal exposure, which most often occurs following animal bites, should be assigned to jobs that do not involve a risk of bites.^{29,69} All potential alternative work arrangements should be explored and discussed with the worker and their supervisor in order to ensure no further exposure risk. In the uncommon situation that elimination of bite risk is not feasible, the risk should be minimized. A review of work practices, administrative controls,

engineering controls, and PPE should be performed, preferably including a worksite visit. All needed modifications should be made. As part of the occupational history, workers should be asked about prior respiratory symptoms (allergy or asthma) or dermal allergy associated with animal work and, if present, these should be addressed. Workers who return to work with animals implicated in causing anaphylaxis should be required to keep injectable or epinephrine with them. A recently approved epinephrine nasal spray may be an alternative option. At-risk workers should not work alone in settings where bites or sharps exposures may occur. Puncture resistant gloves may be helpful if they do not excessively limit dexterity. Co-workers and first responders should be trained in how to recognize and address possible cases of anaphylaxis, including the administration of injectable or nasal epinephrine.⁶⁹

Some workers may ask about the role of immunotherapy for LAA. In general, for many patients, immunotherapy is effective in reducing “asthma symptoms, asthma medication usage, rhinitis/rhinoconjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhinoconjunctivitis disease-specific quality of life in comparison to placebo or usual care.”⁷⁰ For those who have improvement in symptoms with immunotherapy, benefits may wane over time.⁷¹ There is limited published data on immunotherapy for rodent allergy. A small cases series of immunotherapy for mouse allergy demonstrated improvements in rhinitis and asthma symptoms with some patients reporting resolution of symptoms.⁷² A case report indicated that immunotherapy was successful in resolving allergy and asthma symptoms for a scientist working with laboratory rats.⁷³ Immunotherapy should be continued for at least 3 years.⁷⁴ Workers interested in immunotherapy can be referred to an allergist for consultation.

PROGRAM SELF-AUDITS

Self-audits are a means to assess and measure one’s LAA program against regulatory requirements and recommended best practices, as well as internal goals and policies. A self-audit is a planned, documented, and objective review of workplace health and safety hazards by competent individuals. The aim of self-audits is to prevent, identify, and correct exposure to hazards by uncovering gaps for corrective action. Program evaluation through self-audits should occur on a routine basis to ensure both compliance and successful outcomes.^{11,75} They can also help organizations prepare for internal and external audits.^{61,76,77} The Occupational Safety and Health Administration (OSHA) and related state plans include provisions to treat voluntary self-audits as evidence of good faith and will refrain from issuing citations when a

hazardous condition is identified, and corrective action has been implemented, prior to an inspection.⁷⁸ Organizations should seek legal counsel to fully understand how this policy applies to their program.

External audits may be conducted by a number of organizations including AAALAC International.⁷⁹ Many research organizations seek voluntary accreditation by AAALAC International, which requires semi-annual program audits that include review of the occupational health and safety program. It also provides an ongoing mechanism to ensure compliance with applicable animal care and use policies, guidelines and laws.⁷⁹ The United States Public Health Service Policy and Animal Welfare Regulations stipulate that the Institutional Animal Care and Use Committee must review the program for humane care and use of animals at least once every 6 months, using the National Research Council’s *Guide for the Care and Use of Laboratory Animals* as the basis for evaluation.^{61,76,77}

The hazard evaluation and risk assessment process guide the LAA program content and scope to manage the risks of LAA. This also directs the audit content, variables to measure, and frequency. The findings of the self-audit will help determine if controls have made an impact or decreased the risk of exposure and identify areas that need improvements and/or application of further controls. A self-audit process should be part of continuous process improvement. Self-audits should cover all aspects of the LAA prevention program including training and education of workers, implementation of controls, maintenance and certification of engineering controls, the medical surveillance program, and overall program effectiveness based on the incidence of LAA.^{4,14,17–19} Self-audits should address the LAA prevention program for the vivarium and all study areas outside the vivarium where work with laboratory animals is conducted.

The self-audit should include effective and timely communication with stakeholders, defining their respective roles and responsibilities, ensuring agreement with and communication regarding the requirements for the LAA program, goals to measure, and criteria to audit.^{4,14,75} Steps for conducting a self-audit should capture both visual inspection of the workplace and discussions with workers, review of written documentation and policies, examination of incidence and prevalence data from medical surveillance, as well as workers’ compensation and OSHA recordability records, evidence of participation in the LAA program (enrolled in surveillance, participation in periodic surveillance, assignment to respirator clearance), evidence of leadership support, and documentation of findings.^{18,76,77,79,80}

The post self-audit process should include reviewing the findings and sharing

them with stakeholders, identifying deficiencies based on the audit elements or goals, setting priorities and a timeline to address deficiencies, securing resources for improvements, a postimplementation assessment, and ensuring leadership oversight and commitment.^{14,79} The self-audit should answer the question of whether the LAA program is meeting its goal of preventing exposure to allergens and reducing the incidence of LAA. Audits should also assess whether the needed corrective measures identified by the prior audit were completed.

Routine, periodic program self-audits should be designed to observe trends (individual workers and groups) and with ongoing review of goals and outcomes. The frequency of self-audits should be set to ensure thorough evaluations of the program and facilities, enabling corrective measures to be taken in a timely manner to achieve compliance and gain successful outcomes.^{75,79}

A sample set of self-audit checklist topics is provided that can be adopted or modified by organizations. (Supplemental Digital Content 2, <http://links.lww.com/JOM/B870>)

LEADERSHIP: A MULTIDISCIPLINARY APPROACH

Effective leadership is crucial in managing and controlling hazards in laboratory environments. A broad, multidisciplinary team approach ensures that all aspects of health and safety are addressed, leveraging the expertise and perspectives of various stakeholders within the organization. This comprehensive approach ensures the health and safety of all workers, ultimately enhancing the overall effectiveness and sustainability of the organization's health and safety programs.

A robust LAA leadership team should include representatives from the following key areas:

- *Occupational Health*: Provides medical assessments and services, including vaccines, medical clearance, medical surveillance, injury and illness trends tracking and feedback, and management of work-related health issues.^{75,81}
- *Environmental Health and Safety*: Provides hazard assessment, hazard control recommendations, PPE management, and environmental monitoring for biological, chemical, physical and radiological hazards.
- *Institutional Animal Care and Use Committee*: Provides research protocol oversight and ensures compliance with animal welfare regulations.⁶¹
- *Animal Care and Veterinary Medicine/Comparative Medicine*: Responsible for the health and welfare of laboratory animals.
- *Facilities/Engineering*: Responsible for the physical environment and infrastructure.

- *Senior Laboratory Leadership*: Oversees laboratory operations and compliance with safety protocols.
- *Regulatory Staff/Risk Management/Compliance Officer*: Ensures adherence to local, state, and federal regulations.
- *Biosafety Officer*: Supports institutions in managing biosafety programs.⁸²

The leadership team can align goals across departments to foster a unified approach to worker protection, monitor findings from audits and medical surveillance, and track continuous improvement efforts. These should include the adoption of best practices for engineering controls, facilities improvements (including conducting all work in a centralized facility), administrative controls, and use of PPE. This multidisciplinary group can identify barriers that may require an institutional investment and assemble the data necessary to justify capital budget requests. The team should meet regularly and maintain minutes documenting institutional efforts to continually improve the health and safety of animal workers. A standing agenda allows the team to monitor continuous improvement on long-term issues.

Institutions receiving research funding from the National Institutes of Health must meet the requirements of the Office of Laboratory Animal Welfare.⁸³ To meet these requirements, many organizations choose to pursue voluntary accreditation by AAALAC International. AAALAC International expects institutions to have a robust health and safety program including comprehensive animal allergy risk mitigation and medical surveillance.⁸⁴ It is important to maintain ongoing communication between the leadership team and the designated Institutional Official for the animal research program and keep the Institutional Official informed about risks, mitigation efforts, and institutional investment needs beyond and between regular inspections and accreditation visits.

This approach promotes a safety culture that permeates all levels of personnel and supports the implementation of comprehensive safety practices. The leadership team should follow best practices to facilitate a culture of safety by:

- Engaging front-line workers for feedback on administrative controls and effectiveness.
- Promoting a culturally sensitive and inclusive approach to safety and training.
- Accommodating the needs of diverse populations, including non-English speakers, different age groups, and workers with disabilities.
- Including all Principal Investigators and workers, including volunteers, students, maintenance, and housekeeping/environmental services staff.

The commitment to health and safety must be reflected in every aspect of the organization, from the allocation of budgets to the involvement of all personnel, including those in traditionally overlooked roles. This comprehensive approach ensures the health and safety of all workers, ultimately enhancing the overall effectiveness and sustainability of the organization's health and safety programs.

CONCLUSION

Laboratory animals produce protein allergens that are a significant occupational hazard. Exposure can lead to allergies that affect health and career. Laboratory animal allergy can manifest as rhinoconjunctivitis, sinusitis, asthma, dermal allergy, or anaphylaxis. Although approaches to prevention of LAA through a hierarchy of controls have been well documented, and some organizations have demonstrated the success of this approach, workers remain at risk as many workplaces have not fully adopted these prevention practices.

The goal of an LAA prevention program is preventing new cases of allergy. A multidisciplinary leadership team should oversee the program to ensure that there is a full understanding of the problem and institutional commitment to addressing LAA. Occupational medicine physicians can play a valuable role on the leadership team and through oversight of medical surveillance. Medical surveillance should identify workers with existing allergy, new cases of LAA, and workers with symptoms despite controls. Effective medical surveillance should identify an LAA prevalence of 10%–20% or higher. The approach to surveillance should be modified as needed to ensure it is identifying all cases. This may require supplementing the use of questionnaires with interviews of workers. The findings of the surveillance program, including the incidence and prevalence of LAA, should be shared across the organization and can be used to inform the overall prevention efforts by assessing the effectiveness of controls and identifying areas for improvement. Additional opportunities for continuous improvement should be identified through periodic self-audits of all elements of the prevention program followed by a process that ensures timely implementation of needed improvements.

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