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Control of biohazards associated with use of Experimental animals

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Introduction

Laboratory animal facility workers are continuously exposed to biological hazards. The laboratory animals can act as transmission source of infections to workers (i.e. zoonosis) or source of biological materials inducing allergies often referred as Laboratory Animal Allergens (LAA). Understanding the mechanism of development of allergies and critical control points helped in formulating control strategies a lot. Recent advancement in technology greatly helps in controlling these biohazards and ensure safety of laboratory workers. Zoonoses are uncommon in laboratories practicing good hygiene measures.

Laboratory Animal Allergies

These are common health problems associated with biomedical research and their prevalence can go up to 56% in animal exposed workers. However, usually the prevalence ranges between 20% - 30%. Symptoms can vary from slight rashes to severe anaphylactic shock or chronic illness like asthma. LAA are costly to both the employer and employees and controlling the risks associated is desirable from both moral and economic point of view. LAA can be related with any animal species but most commonly associated with mice and rats. The allergens are present in feces, urine, skin, hair or any other material from the animals. Urinary proteins are the most important rat and mice associated allergens.

These allergens lead to production of specific IgE antibodies in body of exposed persons when activates a cascade of events on binding with allergens leading to production of allergy signs. Majority of studies indicated that workers having allergies against other substances are three to five folds more prone to develop LAA and within a short duration of time. A number of occupational risk factors (including high risk tasks like cleaning of cages) have been identified. Aeroallergens are most commonly associated with LAA and therefore, most of control studies focus primarily on their control. Allergen control strategies generally focus on measures to control total exposure of workers to

allergens by a combination of engineering, procedural and personal control measures. There are no reports regarding the cost-effectiveness of allergen control programs.

Engineering controls

Minimizing the influence of human factors is the prime objective of engineering controls. Design of animal facilities should incorporate engineering controls to the extent possible. The need for significant capital investment and the constraints imposed by existing animal facilities are the most likely limitations experienced. One of the problems associated with evaluation of engineering controls is the relatively little evidence about a specific building system (ventilation or architect design) may contribute in reduction of total exposure to allergens actually help prevent allergies.

Table 1. Likelihood of Exposure in the absence of specific Control Measures

Exposure	Task
Low	Postmortem and surgery
	Slide preparation
	Laboratory work (low number of animals)
	Automated cage cleaning
Medium	Cleaning
	Indirect contact in animal room
	Feeding
	Taking specimens
High	Injections
	Handling animals
	Changing and cleaning cages
	Changing filters
	Washing cages

Table 2. Preventing Allergies in Animal handlers

Animal Handlers Should:
Perform animal manipulations within ventilated hoods or safety cabinets when possible
Avoid wearing street clothes while working with animals
Leave work clothes at the workplace to avoid potential exposure problems for family members
Keep cages and animal areas clean
Reduce skin contact with animal products, such as dander, serum, and urine, by using gloves, lab coats, and approved particulate respirators with face shields
Employers of Animal Handlers Should:
Modify ventilation and filtration systems:
Increase the ventilation rate and humidity in the animal-housing areas.
Ventilate animal-housing and -handling areas separately from the rest of the facility.
Direct air flow away from workers and toward the backs of the animal cages.
Install ventilated animal cage racks or filter-top animal cages.
Decrease animal density (number of animals per cubic meter of room volume).
Keep cages and animal areas clean.
Use absorbent pads for bedding. If these are not available, use corncob bedding instead of sawdust bedding.
Use an animal species or sex that is known to be less allergenic than others.
Provide protective equipment for animal handlers: gloves, lab coats, and approved particulate respirators with face shields.
Provide training to educate workers about animal allergies and steps for risk reduction.
Provide health monitoring and appropriate counseling and medical follow-up for workers who have become sensitized or have developed allergy symptoms.

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Principal Elements of an Occupational Health and Safety Program[c]

Administrative procedures
Facility design and operations
Exposure/control methods
Education and training
Occupational health services

Principal elements of an occupational health and safety program[c]

Equipment performance testing
Information management networks
Emergency procedures
Program evaluation and audit

Separation

Separation of the potential population at risk from the hazard should be the prime consideration concerning the spread of allergen within the facility. Clear segregation of work involving contact with animals either directly or indirectly from other tasks within the facility can be of considerable help. Boundaries can be established and only the trained non-atopic persons are assigned the animal related tasks and rest workers should remain at distance. Two corridor system will facilitate the separation, whenever possible, with one corridor for clean and the other one for dirty activities. High risk areas include cage waste handling site, laundry and at exhaust points from ventilation systems.

General ventilation

Ventilation of the animal house controlling the relative humidity and temperature of the microenvironment contribute in general control of allergens. The principal control method is task specific local exhaust ventilation as it is of low cost, more effective and is easier to implement. Air-change frequency may help in reducing the allergen levels in the facility but it is not a consistent finding. One- way airflow system with perforated sliding screens works perfectly leaving minimum level of allergens in the facility.

Positive pressure ventilation systems are common findings in various laboratories and effectively control allergens. Negative pressure sinks can also be used. Ensure the capacity of supply and exhaust systems should be equal to maintain the indoor pressure balance. Exhaust air should always be filtered before recirculation.

Task ventilation

In the task ventilation/ local exhaust ventilation, allergens are removed at their source and these systems can be designed of lower cost. It includes ventilated workstations (using downdraft or backdraft systems), biosafety cabinets and fume cupboards. Usually these systems are mobile and can be easily installed in the already established facilities. However, it may be difficult to demonstrate the effectiveness of these systems, especially novel designs such as downdraft benches, which rely on undisturbed laminar flow.

Automation

Tasks which are labor intensive and pose significant health risk will benefit much more on automation. Many laboratories have now automated various high-risk tasks like cage cleaning and waste removal systems and have shown significant reduction in ambient allergen levels and personal exposure to operators.

Cage systems

Studies have shown that greater than 75% reduction in allergen level is noticed when the filters are installed with open-top cages. Individually ventilated cages are now being widely used in many studies and shown significant reduction in background aeroallergen levels in a number of studies. Almost 100% reduction is noticed in undisturbed animal rooms with cages operated under negative pressure system. Installation of filtered exhaust ports further enhances the effectiveness of system. Transmission of infectious diseases can be reduced by using these cages operated under negative pressure system.

Procedural controls

As the risk of LAA cannot be completely eliminated by removing the allergen source; therefore, there is requirement of some additional controls. Managing the work choices so as to ensure the performance of essential job duties in a way that minimize the level and spread of environmental allergens.

Reduction of number of exposed persons

It is the first strategy of prevention and can be accomplished by reduction in number of animals used, using alternative methods like cell lines or by using tests not involving use of animals. Atomization of facility at the high-risk points and labor-saving devices also helps to reduce persons required. Workers with expertise in animal handling causes minimum discomfort to animals and thereby, help in controlling the allergen levels.

Bedding, Animals and Stock density

Studies have reported that mature male animals tend to produce higher levels of allergens in their urine and therefore, there is higher risk of contacting LAA while working with male animals. Preferably, male animals are substituted with females or the younger animals if the study permits.

Several studies have shown an association between allergen levels and the tock density. Maintaining control of ambient level of aeroallergens even with increased stock density is made feasible with the advent of individually ventilated cage systems.

Bedding is an important variable in controlling LAA and studies have shown that the absorbent pads results in significant reduction in aeroallergen levels than the sawdust or wooden chips.

Housekeeping

Design of animal facility should be the one that can be cleaned effectively and safely. Avoid the dry cleaning of facility as it results in generation of high concentration of allergen laden dust

particles. Power washing systems generate high amount of aerosol; therefore, it is necessary to wear personal protective equipment's near the power washing systems. Another important potential source of allergens are contaminated records and archives.

Low level of allergens during floor cleaning can be ensured by using vacuum cleaning systems not generating local contaminated exhaust.

Movement within the facility

Procedural design should ensure the prevention of spread of allergens in the environment and to adjacent areas such as rest areas, corridors and office rooms. Dirty corridors should be designated for transport of soiled cages to washing area. Transportation of animals through corridors should be done using cabinets/ cages equipped with filters to prevent allergen spread.

Work permits and Visitors

Unnecessary visits to the animal room should be avoided and only the required designated workers should enter the animal holding rooms. Irregular tasks like ventilation maintenance should be assessed individually.

Environmental monitoring

Regular monitoring of allergen levels in the facility should be done to access the efficacy of control mechanisms. Unfortunately, the assessment of allergen samples is time consuming and expensive. Rather, the measurement of particle concentration is relatively easy, can be done in real time and gives the clear indication of personal exposure to particles on the working day. It is important to consider the extent to which particles may be contaminated with allergens for risk assessment based on particle concentration. At present, there are no internationally accepted standards for analytical methods or acceptable exposure levels of aeroallergens. Because of the involvement of many other factors like genetic predisposition and environmental influences, a single threshold level will not be able to protect every worker for allergies.

Personal controls

Personal hygiene

Activities like smoking, drinking, eating and application of cosmetics should not be permitted within the animal facilities. Separate dress should be there for working in the animal facility to prevent the spread of allergens in the surrounding areas and the entry of external pathogens in the facility. Shower should be mandatory for at least the heavily exposed workers before leaving the facility and handwash should be must for all. Take care to prevent the development of small skin fissures from frequent hand-washing as they will increase the exposure levels. So, it is advised to use moisturizer creams after handwashing which are free from harmful chemicals.

Protective clothing

Wearing of protective clothing is the requirement in most modern laboratory animal facilities to prevent the microbial contamination of animals residing in the facility. Failure to do so can lead to

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distant spread of LAA. The type of clothing varies as per the degree of protection required and may range from simple changing of conventional laboratory coat to full-proof clothing including face mask, head cap, gown and shoe cover. The protective clothing should be designed such as not to allow the trapping of allergens inside the arm surface. So, it is required that the sleeves should be having elastic hem or other suitable mechanism. Non-latex gloves should be preferred over the latex ones to prevent the development of latex allergy.

Training and education

Any risk control program will succeed only with the collaboration of the staff and effective training and education will greatly help in this regard. Workers must understand the nature of risk associated with their job and should report promptly if any symptom of allergy is noticed. It is seen that workers are more willing to adopt the control mechanisms if they get proper education about the nature of risk involved.

Preplacement risk assessment

The prevention of allergy should begin before the actual exposure to an allergen. It is considered a good practice as well as legal duty (in some jurisdictions) to assess the potential animal workers before the commencement of working with animals. The purpose of this assessment is to find the atopic persons to prevent the onset of allergic symptoms which can be lethal to some individuals in some cases.

Atopy is the genetic predisposition of an individual to develop specific IgE and allergic signs (like skin rashes, rhino conjunctivitis, asthma, etc.). Many studies reveal that the persons having history of atopy are more likely to develop LAA. Some investigators have identified a relation between the family history of atopy and the development of LAA but it is likely to be weak. Studies have shown that a combination of positive RAST (radio-allergo-sorbent test) and positive skin test is 897.4% predictive of the development of LAA.

Health surveillance

It is worthwhile conduct regular health surveillance of exposed workers. It provides an opportunity to raise awareness among workers. Annual surveillance of exposed workers is advised. More frequent surveillances are required in the first two years as most of predisposed individuals will develop symptoms within this period. A predesigned questionnaire will be of great help in the times of surveillance and can help in identification of workers at high risk.

Zoonoses

Diseases which can transmit from animals to man and from man to animals. While most of the organisms harbored by laboratory animals are harmless to both the animal and the handler but some have the ability to result in infection and are usually species specific. Zoonoses in laboratory animal facilities are rare because of good hygiene standards being practiced in most of the facilities but vigilance is important.

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These diseases can be directly transmitted by direct contact with the animal, contaminated surroundings or by ingestion or indirectly by the vectors such as flies, ticks, etc.

It is seen that of all the diseases known to infect humans, zoonotic diseases comprise almost 61% of total and nearly 75% of newly emerging diseases. The likelihood of transmission of animal disease to human is directly proportional to the phylogenetic relationship between that species of animal and human (i.e. highest from the primates). This likelihood is inversely proportional to the immune status of the individual.

Table 3. Some important Zoonotic infections

Viruses	Bacteria	Protozoa	Fungi
Herpes B	Tuberculosis	Amebiasis	*Trichophyton*
Rabies	*Streptobacillus* (rat bite fever)	Toxoplasmosis	
Hantavirus	Brucellosis		
Lymphocytic choriomeningitis	Leptospirosisosis		
Hepatitis	Campylobacteri		
Simian immunodeficiency	Salmonellosis		
	Shigellosis		

Prevention

Zoonoses can be identified managed by the close collaboration of veterinarians, physicians and animal workers. Standard biosafety practices reduce the chances of development of infections in animal facilities and these should include: -

- Establishment of biosafety level
- Use of aseptic techniques and procedures
- Good personal hygiene and use of personal protective equipments
- Use of biosafety cabinets
- Decontamination
- Appropriate management of waste
- Learning from previous incidents
- Immunization of workers with existing vaccines
- Post-exposure treatment

Disease-free animals

Preference should be given to selection of animals at lower risk of disease whenever possible and special precautions are needed when animal-human diseases are being studied i.e. animals are known to be infected. Use of live vaccines is not preferred to protect animal health as they can pose risk of development of infection in the handlers. Regular screening of animals and handlers is must.

Awareness

Education and awareness of workers is must to prevent them from zoonotic infections and should know that a good-looking animal can be in a carrier state and can transmit the infection;

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therefore, care should be taken while handling each and every animal and the contaminated materials like cages.

Personal protective equipment's

The main purpose of PPE is to prevent the individual from pathogen and allergen exposure.

Health care of workers

Assessment of vulnerability of workers should be done at the start of employment and monitoring should be done at regular intervals. Regular immunization of workers with existing vaccines should be practiced.

Protecting animals from human diseases

It is essential to consider that some laboratory animals are also susceptible to human diseases. Close phylogenetic relationship of primates to human proves the high vulnerability of primates to human diseases. Standard biosafety measures also prevent the animals from human diseases. This sensitivity of some species to human diseases gives an opportunity to study pathogenesis and treatment of diseases in animal models.

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