# ❖BRL BULLETIN❖

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*T*his issue of the BRL Bulletin will discuss allergies due to exposure to laboratory animals. Laboratory animal allergy (LAA) is the most common medical condition that affects individuals who work with animals in the research environment. It has been estimated that 11 to 44% of individuals who work with laboratory animals will develop an allergic condition to these animals. Of those who develop allergies, four to 22% will eventually develop occupation-related asthma, a serious, life-long respiratory disease. In other words, more than one out of ten people who work with laboratory animals will develop allergic symptoms and of these individuals, at least one out of twenty will develop asthma. It has been reported that the prevalence of asthma subsequent to LAA might be decreasing because of reduced allergen exposure. However, due to the high prevalence of LAA in the laboratory environment, this *Bulletin* will discuss various aspects of this condition, including how allergies develop, symptoms, associated risk factors, animals involved, and methods to minimize exposure.

**How Do Allergies Develop?**

There are two steps involved in the development of allergies. First, the person must become sensitized to the substance that causes the allergy (allergen). With animals, these substances are often found in the dander, hair, urine, saliva, or blood. During the sensitization process, the allergen is inhaled into the lungs where it is presented to T-cells. These activated T-cells stimulate B-cells to produce specific IgE antibodies against the allergen. The IgE antibodies bind to mast cells and basophils, which are found in high concentrations in certain areas of the body. Once the IgE antibodies bind to these cells, the person is sensitized to the allergen. During the second step, the sensitized individual is exposed to the allergen again. The allergen binds to the IgE antibodies which causes the release of histamine and other inflammatory mediators from the mast cells and basophils. Since mast cells and basophils are abundant in the skin, conjunctiva, respiratory tract, and gastrointestinal tract, these areas are the sites for allergic reactions. In these areas, it is the histamine released by the mast cells and basophils that causes the symptoms commonly seen in allergic individuals, including constriction of airways, tissue edema, increased mucus secretion, itching, and sneezing. Once a person is sensitized to an allergen, he/she will develop allergic symptoms within 10-15 minutes of subsequent exposure to that allergen. In addition to this early phase reaction, approximately half of allergic individuals will also develop a late phase reaction three to four hours following exposure to the allergen. This reaction typically reaches its maximum intensity four to eight hours following exposure, and resolves after 12 to 14 hours. Symptoms experienced during the early and late reactions are similar; however, an individual may not realize that the allergic symptoms he/she has outside the work environment are directly related to exposure to allergens at work. Although the symptoms are similar, the late reaction can lead to more severe problems due to the entry of inflammatory cells into the tissues. Over time and continued exposure to the allergen, a chronic inflammatory condition such as asthma may develop.

**Symptoms of LAA**

As discussed above, histamine and the production of an inflammatory response cause allergic symptoms in the target areas of the body. The majority of individuals who become sensitized develop symptoms of LAA within three years of initial exposure to laboratory animals, of which one-third develop allergies within the first year. Although most sensitized individuals develop symptoms of LAA within three years, certain individuals may develop allergies several years after initial exposure. The most common sites for an allergic response are the nasal passages and the eyes. Common nasal symptoms are congestion, sneezing, nasal

drainage, and itching, which collectively are termed allergic rhinitis. The common ocular symptom is watery, itchy, red eyes, which is called allergic conjunctivitis. In individuals who have allergic reactions in the skin, common symptoms are redness, itching, rashes, welts, and hives. This combination of symptoms is collectively termed contact urticaria. Skin allergies usually appear after the allergen has come into contact with the exposed skin of the allergic person. Some allergic individuals may develop a more serious manifestation of allergies known as asthma. Symptoms of asthma include coughing, wheezing, tightness in the chest, and shortness of breath. Due to the chronic changes to the lungs that take place in asthmatic individuals, the symptoms often persist for several hours after exposure to the allergen. Sometimes, a severe generalized allergic reaction known as anaphylaxis may occur. Although extremely rare, an anaphylactic reaction can occur following a bite or puncture wound with a needle or other sharp object contaminated with allergens. The symptoms can range from generalized itching and hives to life threatening swelling of the larynx and airways and shock. Other symptoms of an anaphylactic reaction include flushing of the skin, swelling of the lips and eyes, difficulty swallowing, dizziness, fainting, nausea, and diarrhea. Rhinoconjunctivitis is the most common expression of LAA (53-100% of people with LAA symptoms) with contact urticaria and asthma second (13-70% and 13-71%, respectively). More than 60% of persons with LAA (and almost all asthma cases) have specific IgE antibodies to animal allergens. Not all people with LAA symptoms have specific IgE antibodies to animal allergens, which suggests that LAA-type symptoms might also result from reactions to other environmental agents such as dust, disinfectants, formaldehyde, or ammonia.

**Risk Factors**

The most important risk factor for the development of LAA is the level of exposure to animal allergens. Certain tasks such as changing cages and handling animals cause the individual to be exposed to high levels of allergens, which may hasten the onset of allergic symptoms. Although some controversy exists, most studies indicate that individuals with allergies to substances outside the workplace (i.e. pollen, ragweed, and pets) have an increased risk for the development of LAA. Some people also have atopy, which is a genetic predisposition to develop IgE antibodies. Individuals who have a family history of allergies are likely to have atopy, which is another risk factor. Finally, some suggest that smoking is a risk factor, as the development of allergies and asthma is potentially more likely to occur in a respiratory system damaged through the effects of smoking.

**Animals and their Allergens**

It is important to remember that any animal can potentially cause an allergic reaction. Most people associate LAA with certain animals such as mice and rats. Since mice and rats are the most commonly used animals in biomedical research, they are implicated in most cases of LAA. However, mice and rats are no more allergenic than any other animal in the laboratory environment. In fact, multiple allergens produced in multiple tissues have been identified from most of the commonly used animals. Most of the allergens produced by animals are very small, so they remain suspended in the air for long periods of time and can penetrate deep into the airways. For this reason, they are easily inhaled into the respiratory system when a person enters a room housing animals. In mice, there are three allergens that have been identified. The major allergen is a protein found in the urine as well as in the hair follicles and dander called Mus m 1 or mouse urinary protein (MUP), which exists in multiple isoforms. Male mice produce up to four times more of this allergen because its expression is dependent on testosterone. The other two mouse allergens are found in hair and dander (Mus m 2), and albumin, which is a protein found in the blood. The three main rat allergens are found in the urine (Rat n 1.01 and Rat n 1.02, also found in exocrine glands) and serum (rat albumin), with other allergens occurring in the saliva and fur. Like mice, male rats produce greater amounts of allergens than females and rat albumin has the ability to cause an allergic reaction in some individuals. Three allergens have been identified from the urine, hair, saliva and dander of guinea pigs (Cav p 1, Cav p 2, and Cav p 3). Rabbits have two main allergens found in their saliva and fur (Ory c 1) and saliva, fur and urine (Ory c 2), along with

others that have not been fully characterized. One of these allergens is found in the saliva, hair, and dander, and the other is found in the hair, dander, and urine. There are 10 cat allergens that have been identified, although only one allergen (Fel d 1) has been implicated in most allergic reactions. This protein is produced in the sebaceous glands of the skin and is secreted onto the skin and hair. It is also produced in the salivary glands and is secreted into the saliva. Like male mice and rats, male cats produce greater quantities of this allergen than female cats. Cat albumin can also elicit an allergic response in some individuals. There are six dog allergens (Can f 1 through Can f 6) found in the hair, dander, saliva, and urine. In addition, dog albumin can cause an allergic reaction in some people. Other animals in the laboratory environment can cause allergies, but their allergens have not yet been identified. It is prudent to be aware that any animal can cause allergies in sensitized individuals; no animal is any less or any more allergenic than any other animal.

**Minimizing Exposure to Allergens**

The key to controlling LAA in the workplace is to minimize exposure to allergens. The most successful strategy is to remove the employee from areas where he/she is exposed to allergens. If task reassignment is not possible, there are methods to minimize exposure to employees. Selection of animals, animal density, type of bedding, type of caging, ventilated hoods, method of cleaning, control of animal movement, and personal hygiene all play important roles in minimizing employee exposure to allergens. For example, male mice, rats, and cats produce greater amounts of allergen than their female counterparts. If possible, studies should use young female animals of these species. Decreasing the density of animals will also decrease the level of allergens in the animal room. If space is available, it is better to spread the animals among several rooms or cubicles rather than pack them all together in a single room or cubicle. The choice of bedding can greatly impact the level of allergen in the animal room. Reduction in allergen levels has been demonstrated with the use of absorbent, noncontact pads and corncob bedding. The type of caging used can also help prevent the escape of allergens into the environment. Two choices are the filter top microisolator cage and the individually ventilated cage. Ventilated hoods, the laminar air flow cabin in particular, also greatly reduce the amount of rodent allergens in the breathing zone by at least 90-95%. The method used to clean in the animal facility can either increase or decrease the amount of allergen suspended in the air. Dry sweeping and vacuuming both re-suspend allergens that have settled on surfaces. If a vacuum is used, it should have a HEPA filter that will trap allergens and prevent their escape with the exhaust. Wet mopping is a better method of cleaning because it reduces the level of allergens by trapping allergens in water molecules. The movement of animals and their allergens around the facility should be minimized. The frequent movement of animals may contaminate corridors with allergens, which can lead to their spread to non-animal areas of the facility. In such a manner, employees who have no exposure to animals may develop symptoms consistent with LAA. Finally, personal hygiene is an important method to reduce exposure to allergens. All personnel should wear appropriate protective equipment over their uniform or street clothes while working with animals. This equipment includes a long-sleeved lab coat or gown, hair covering, shoe covers, and gloves. These items should be discarded and hands washed before leaving the animal room. In addition, it is recommended that individuals wear eye and respiratory protection to avoid allergen exposure to the eyes and lungs. It is important to stress that not all masks are created equal in terms of protecting the wearer from allergens. Surgical masks and cone-style dust masks do not provide effective respiratory protection. These masks do not seal around the face, so the wearer easily breathes in allergens around the edges of the mask. Rather, a respirator mask must be worn to protect the wearer from inhaling allergens. The National Institute for Occupational Safety and Health (NIOSH) certifies air-purifying respirator masks to demonstrate a minimum filter efficiency of 95% for particles 0.3 m in size, which will filter out most allergens. If worn properly and at all times when exposure to allergens is expected, respirator masks can help control allergic reactions in sensitized people. In order to wear NIOSH-approved respirator masks, the wearer must be fitted, trained, and receive medical clearance to wear the respirator. With appropriate

respiratory protection, allergic individuals may be able to continue working with laboratory animals without further endangering the health of their lungs. Lastly, it is important to minimize contamination of the home environment with laboratory animal allergens brought home from the workplace. Wearing appropriate protective clothing while working with animals and showering at the end of the workday or immediately upon arriving home will reduce allergen contamination of the home environment. If an individual brings home allergens on his/her skin, hair, or clothing, LAA may develop in persons living in the same home who have no exposure to laboratory animals.

If you feel you may be developing allergies to laboratory animals, it is important to be evaluated by your physician and University Health Services. Given that LAA is an important cause of lost time from work, it is vital that the allergies are diagnosed and treated by a specialist. If you already have been diagnosed with allergies, you may wish to wear an air-purifying respirator (NIOSH 95 respirator mask). Please contact Employee Health Services (6-7420) to receive medical clearance and the Environmental Health and Safety Office (6-7411) for respirator fit testing. Remember that allergies may seem to be nothing more than an annoying nuisance, but they can progress to serious, chronic lung disease. It is important that you intervene early to avoid more serious problems down the road.

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**ANNOUNCEMENTS**

**Happy Retirement:**

After 24 years of dedicated service, Ms. Maria Lang (supervisor of the BRL Veterinary Technical Service) has decided to hang up her lab coat and enter the world of retirement. Enjoy your retirement, you deserve it!!! You will be missed by all.