Laboratory animal: an integral but probable hazardous component of biomedical research

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Animals are not only an integral part of the ecosystem, but are also of tremendous use to humans in many ways. Besides conventional uses, they also play pivotal roles in numerous medical and biological researches as animal models. An animal model can be defined as a living organism that is closely related phylogenetically to humans, and that can be used to study shared biological systems in relation to health and disease. The ultimate goal of all biological research is promotion or welfare of mankind. All outcomes of research, like drug discovery, prosthetic implants, evaluation of cosmetic agents, etc. cannot be directly used on human, though researchers prove their efficacy in vitro; as this may have harmful or negative effects. Again, legal and ethical hurdles as well as social complications restrict their evaluation directly on humans. One has to pay attention while working with human volunteers, as some poor people may become victims of such experiments due to their economic predicaments. In this context, the drug experimentations on the poor Jews by the Nazi doctors can be remembered. To deal with such situations and to have a preliminary in vivo data, researchers use laboratory (lab) animals. At present lab animals are one of the integral components of biomedical research, especially translation research. Different types of animals like mice, rats, rabbits, etc. are used as experimental lab animals. Veterinary science and other branches of life sciences are also using lab animals for drug testing, disease model studies, surgical investigations, etc. Nowadays, nearly all life sciences institutions have developed small or large, organized or non-organized animal houses. Probably due to improper communication between veterinarian/lab animal experts and research workers, or lack of awareness, many a times it is seen that there is inappropriate handling, and animal handlers or research workers unknowingly become vulnerable to some of the hazardous allergens or zoonotic diseases. Therefore, proper handling of lab animals and following proper guidelines are vital criteria for public health

importance and accuracy of research findings.

Hazards of lab animals and safety measures to be taken

Those who deal with lab animals must be aware of various types of hazards, as it may cause serious health issues. Research workers should have a sound knowledge on precautionary measures so that they can keep themselves as well as their co-workers or assistants safe. The hazards that may arise from handling lab animals may be divided into three categories: (i) Physical and protocol-related hazards; (ii) Laboratory animal allergy (LAA); (iii) Zoonotic diseases.

Physical and protocol-related hazards

Individuals involved in animal handling may get scratches or wound from physical items like sharp edges, knives and surgical instruments if they are not careful. This may cause iatrogenic infections/ systemic allergic reactions referred to as anaphylaxis. Carelessness may also lead to bites and scratches from animals, leading to rat bite fever (generally due to *Spirillum minor* and *Streptobaccilus moniliformis*).

Laboratory animal allergy

Inappropriate immune response to otherwise harmless protein (allergen) present in the urine (urinary protein – lipocalins), fur, saliva, etc. of lab animals, particularly of rodents, is referred to as laboratory animal allergy¹. Different types of agents that may lead to LAA are fur, urine, saliva, serum proteins, tissues (necropsy) and dander.

Individuals may encounter these in day-to-day work like animal handling, changing bedding material, cage cleaning/dumping, etc^2 . Improper handling may even cause serious health problems or ailments (Table 1).

Zoonotic diseases

Zoonotic transmissions to individuals in contact with lab animals are infrequent and sporadic. However, many zoonotic disease episodes have likely remained unreported and those reported showed serious disease and even fatalities. Thus, individuals in contact with lab animal should be aware of these diseases (Table 2) and take appropriate precautionary measures^{2–5}. Animal handlers or researchers may be infected by the following means^{3,4}.

- Injection (contaminated sharps).
- Inhalation (airborne contaminants).
- Ingestion (eating lunch with dirty hands).
- Skin contact (directly while handling animals or contact from bedding materials).
- Mucous membranes (rubbing eyes with dirty fingers).

Safety measures to be taken

The only way to deal with these hazards is to take precautionary/safety measures which include Administrative control, engineering control, proper hygiene and personal protective equipment (PPE)^{6,7}.

Administrative controls

It is the responsibility of the administration to provide regular and proper training to those involved, which will increase their awareness, make them responsible and keep them alert. At the same time, all animals must be procured from reliable source which will reduce their chances of carrying infections.

Engineering controls

This includes proper ventilation, adequate space management according to the available guidelines, provision for quarantine and isolation, etc. The animal house should be constructed in such a way that wild rodents or any other

Disorders	Symptoms	Signs			
Contact urticaria	Redness, itchiness of skin, welts, hives	Raised, circumscribed erythematus lesions			
Allergic conjunctivitis	Sneezing, itchiness of skin, welts, hives	Conjunctival vascular engorgement, cheminosis, bilateral ocular discharge			
Allergic rhinitis	Sneezing, itchiness, clear nasal drainage, nasal congestion	Pale or oedematus mucosa, clear rhinorrhoea			
Asthma	Cough, wheezing, chest tightness, shortness of breath	Decreased breath sound, prolonged expiratory phase or wheezing, reversible airflow obstruction, airway hyperresponsiveness			
Anaphylaxis	Generalized itching, hives, throat tightness, eye or lip swelling, hoarsness, shortness of breath, dizziness, fainting, nausea, vomiting, abdominal cramps, diarrhoea	Flushing, urticaria, angioedema, stridor, wheezing hypotension			

 Table 1.
 Different ailments due to laboratory animal exposure and signs as well as symptoms

Table 2. Common laboratory animal species and diseases

Species	Diseases								
Mice and rats	Dermatophytosis, ectoparasitism, hantaviral diseases, leptospirosis, lymphocytic choriomeningitis, rat bite fever, salmonellosis, rodentolepsis								
Rabbits	Dermatophytosis, ectoparasitism, pasteurellosis, salmonellosis								
Hamsters	Campylobacteriosis, ectoparasitism, lymphocytic choriomeningitis, leptospirosis								
Guinea pigs	Balantidiasis, chlamydiosis, dermatophytosis, ectoparasitism, lymphocytic choriomeningitis, salmonellosis								

animals do not get the chance of entry to it. The size of the animal house must be according to the guidelines of the Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA).

Hygiene

Animal handlers must clean their hands with antiseptic soap or solution before and after handling animals, to reduce the chances of infection. All animal cages, floor of animal houses as well as drainage system must be regularly cleaned and should be disinfected once in a month. Research workers should also maintain the protocol of animal handling strictly and maintain good records.

Personal protective equipment

These include nitrile gloves, lab coat, N95 dust and mist respirator, hair cover and goggles. Items used in the animal house should not be used in other laboratories. All PPE should be removed and kept inside the animal house only. There should be individual PPE for each worker/handler. These items must be cleaned or disinfected once every fortnight.

Individuals involved in animal handling should immunize themselves at least against the two deadly diseases, i.e. tetanus and rabies. (Recommendation according to the World Health Organization, Department of Communicable Diseases Surveillance and Response, November 2002.)

Tetanus vaccination consists of a primary course of three injections usually received during childhood and followed by booster doses every 10 years. If an individual is not sure of having received tetanus vaccination in the past 10 years, she/he must get vaccinated.

In case of rabies, three injections on day 0, day 7 and day 28 must be given as pre-exposure dose and booster injection one year later and continue booster annually. The injection scheduled on day 28 may also be administered on day 21.

Ethical issues and CPCSEA guidelines for lab animals

Nowadays, nearly all biological institutes use experimental lab animals for a variety of *in vivo* experiments. Due to lack of awareness, these animals are not handled following the prescribed guidelines. This unknowingly exposes researchers to various types of hazards related to lab animals. Therefore, it is important to follow the prescribed guidelines of CPCSEA under the Animal Welfare Board of India. CPCSEA guidelines were prepared considering all issues of animal and human health, including ethical aspects (https://www.aaalac.org/resources/SOP_CPCSEA.pdf). Researchers must use it as baseline information to conduct their experiments involving various lab animals.

The main goal of the CPCSEA guidelines is endorsement of humane care of animals used in biomedical and behavioural research. It is aimed to provide specifications that will enhance animal well-being.

The guidelines provide information regarding construction of animal houses, animal transportation, floor space requirement, anaesthetic managements, including euthanasia as well as constitution of the Institutional Biosafety Committee (IBSC).

All institutions, involved in *in vivo* research activities must have Institutional Animal Ethics Committee (IAEC) for regular monitoring of all experimental procedures, including ethical issues. IAEC is recognized and registered by the CPCSEA and consists of a group of persons, including a biological scientist, two scientists from different biological disciplines, a veterinarian involved in the care of animal, scientist in charge of the animal facility of the establishment concerned, a scientist from outside the institution, a non-scientific, socially aware member, and a nominee of CPCSEA.

All types of research proposals involving *in vivo* experimentation are to be reviewed before and throughout the experiment (details about IAEC for India are available at <u>http://cpcsea.nic.in/</u><u>Content/55_1_GUIDELINES.aspx</u>). It is mandatory to constitute an IAEC in all institutions where animal experimentation is being done.

Conclusion

It is our prime responsibility to follow the ethical rules and regulations of handling lab animals. At the same time IAEC should monitor research activities involving lab animals at regular intervals. Improper handling or managing lab animals may lead to serious public health concerns. Therefore, those engaged in *in vivo* research must strictly follow the procedures and rules of animal experimentation.

- Bush, R. K. and Stave, G. M., *ILAR J.*, 2003, 44(1), 28–51.
- Hime, J. M. and O'Donoghue, P. N., Handbook of Diseases of Laboratory Animals, Diagnosis and Treatments, William Heinemann Medical Books Ltd, London, 1979, 1st edn.
- Hankenson, F. C., Johnston, N. A., Weigler, B. J. and Di Giacomo, R. F., *Comp. Med.*, 2003, 53(6), 579–601.
- Weigler, B. J., Di Giacomo, R. F. and Alexande, S., Comp. Med., 2005, 55(2), 183–191.

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 gen and Zoonosis Online Training 2012 SCC.pdf (accessed on 16 May 2016).
 7. Laboratory Animal Allergy Prevention Guidelines, University of Otago, 2012; http://www.otago.ac.nz/administration/policies/otago036441.html (accessed on 16 May 2016).

management/ehso/media/Lab Animal Aller-

5. Poole, T., The IFAW Handbook on the

Care and Management of Laboratory Animals, Lingman Scientific & Technical,

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