

Limits of animal models

(Influence of non experimental factors on the quality of the animal Model)

When conducting research, investigators want experimental and control groups to be exactly the same, except for the variable they are interested in. However, laboratory animals are influenced by many non-experimental factors that might potentially affect the outcome of the study. Those factors should be identified and accounted for at all stages to ensure they do not increase the variability or adversely affect the outcome of the experiment.

The many non-experimental factors that can influence the response of the animal model in an experiment can be grouped as:

- Animal related factors

- Physical / environmental factors

- Experimental handling factors

Animal related factor

-Genetic constitution: It is preferable to use inbred strains (successive breeding of related animals) than outbred strains since this reduced genetic diversity leading to reduced inter individual variability, means that smaller numbers of animals can be used to obtain statistically significant results.

-Age, sex, reproductive status: the response of animals could be affected by these factors so it is important to homogenize these factors between animals of the study.

-Circadian rhythm: the animal's metabolism varies with the time of day, according to a circadian rhythm that is entrained by the light cycle. This means that drugs, such as anesthetics for example, can have a variable effect depending on the time of day they are administered. Thus it is very important to perform research manipulations at the same time of day for all animals.

Microbial Flora: Most research animals carry a mixed microbial population that depends in part on housing conditions, diet, exposure to microbes, and other factors. These microbes may be a source of variability between animals housed in different facilities, and can influence parameters such as nutritional requirements and drug metabolism. Thus it is important to use animals that come from the same source and kept in the same conditions

Diseases (subclinical or silent): is one of the most important variables that interfere with research. Disease in research animals can be clinical, meaning that it is readily apparent, and the animals actually look sick or silent. Sick animals must be excluded of the experiment since their responses will be influenced by the presence of the disease.

For example fur mites (*Myocoptes musculinus*, *Myobia musculi*, *Radfordia affinis*) infestation in mice is an infectious disease of the skin which causes alopecia, pruritus and ulcerative dermatitis. Interference with research: Animals with mites and severe clinical signs such as ulcerative dermatitis are not suitable for use in research. For example, mice may have an increased IgE response, an increase in the formation of secondary amyloid, hypoalbuminemia, and a decreased mean hemoglobin concentration.

Physical and environmental factors (housing conditions)

To reduce animal stress and risk of diseases and infection environmental factors have to be controlled. Inappropriate housing conditions could increase interindividual variability and interfere with the experimental results. Housing conditions should be as:

Ambient temperature (25 C)

Relative humidity (Standards $55 \pm 15\%$)

Ventilation

Proper Lighting (intensity, wavelength, photoperiod) and minimum of Noise

Free access to Food and Water (unless otherwise indicated in the experimental protocol)+

Nutritional quality of food and clean water

Quality of recipients of food and water (Ex risk of contamination by bisphenol A)

Dry and clean cage litter

Proper size of cages and proper density of animal per cage

Experimental handling

-Ovoid the stress of animals during experimental procedures (pain and noise) and minimize the stress of transport by allowing and adaptation period as it could affect results.

-Good practice of experimental techniques such as routes of administration of substances and blood collection to avoid animal pain and stress, animal injury and related infections and inflammation ; to avoid variability in results ..

-Duration of manipulation must be minimized and consistent between animals. For example studies have shown that some hematological changes start happening when an animal is taken from its cage and these changes for minutes to hours and will be reflected in the results obtained.

References

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