# Recent Developments in Laboratory Mouse Welfare

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## Introduction

The use of mice in laboratory experiments is a common practice in myriad research disciplines. It is therefore important that optimal welfare of these animals is maintained such that alterations in physiology and behaviour, as a result of poor welfare conditions, do not skew experimental results. Many different inbred and outbred strains are utilised in research, and it is known that mice of differing strains have different physiology and behaviour (Wilson & Mogil, 2001). As it is difficult to formulate generalised guidelines applicable to all laboratory mice, it is generally left to the discretion of researchers to assess the welfare of their charges and make changes accordingly (Brown & Murray, 2006). Recent developments in laboratory mouse welfare have focused on living space, ambient temperature and environmental enrichment.

## Discussion

The effect of housing density on corticosterone concentrations differs for inbred and outbred mice. Increased housing density when comparing 2, 5 and 10 mice per cage resulted in significantly increased plasma corticosterone concentrations for inbred mice of C57BL/6 and BALB/c strains (Laber *et al*., 2008*)*. In comparison, high housing density due to large litter size did not significantly affect faecal corticosterone concentrations in outbred mice (O'Malley *et al*., 2008). Corticosterone influences aspects of physiology and behaviour, such as immune system function, reproduction and exploratory behaviour. Consequently, housing density affected corticosterone concentrations, which, in turn, affected certain aspects of the animals' physiology. Corticosterone has the ability to suppress immune function by suppressing cytokine secretion by immune cells. It also causes sequestration of lymphocytes within lymphoid tissue and lymphocytolysis at high concentrations. Thus, inbred mice housed in conditions of increased housing density had a decreased number of CD4+ T helper cells (lymphocytes) within their bloodstream, as a result of elevations in corticosterone concentrations (Elenkov, 2004).

Corticosterone is also one of the factors that suppresses reproductive performance, specifically fertility rates (Politch & Herrenkohl, 1984). Therefore, as outbred mice did not have significantly increased faecal corticosterone, their reproductive performances were not affected. Finally, elevated plasma corticosterone concentrations are known to enhance exploratory behaviour (Skorzewska *et al*., 2006), which is converse to the findings of Laber *et al*. (2008), who concluded that increased housing density significantly decreases exploratory behaviour. This indicates that plasma corticosterone was not likely to be the major factor in causing the change in exploratory behaviour in this experiment. These two studies support the notion that mouse strain has a significant effect on stress responses, which, in turn, can alter physiology, emphasising the need to tailor habitat to suit the physiological needs of each strain.

Mice are often housed at temperatures between 20°C and 26°C (National Research Council, 1996). However, the mouse's thermoneutral zone is between 26°C and 34°C (Gordon, 1993). Gaskill *et al*. *(*2009) studied 48 C57BL/6 mice initially placed in cages with ambient temperatures of 20°C, 25°C and 30°C for one day at a time in random order. The mice were then allowed to move freely between cages of different ambient temperatures. They spent significantly more time in the 30°C cage, and preferred to conduct inactive activities, such as sleeping, and maintenance activities, such as grooming and nest building, in an ambient temperature of 30°C. Sex and time of day were also major determinants of thermal preference. Conclusions drawn from this study highlight the need to increase the housing ambient temperature range to 25°C-30°C. However, further research must be conducted to quantitatively assess the effect of prolonged exposure to low ambient temperatures on physiology. In low ambient temperatures, mice attempt to maintain core body temperature by shivering, vasoconstriction of peripheral vessels, activation of brown adipose tissue, and increased secretion of thyroid hormone (Sjaastad *et al*., 2003). These responses have significant effects on the way energy is utilised. The thermal stress may increase the disparity between *in vitro* and *in vivo* situations, therefore potentially compromising the credibility of research based upon laboratory mice. Investigation into the thermal preferences of other strains of mice should also be conducted, as genetic aberrations may be expressed as alterations of the thermoneutral zone, thus affecting the ambient temperature required for other strains of mice.

For environmental enrichment to be successful and improve animal welfare, it must first enhance the range of normal behaviour of an animal, and second, not be habituated to by the animals (Nicol *et al*., 2008). Upon investigation of 128 inbred and outbred female mice, Nicol *et al*. (2008) determined that the "hammock" was the most favoured form of enrichment for these animals. This enrichment was characterised as soft, replaceable and chewable. The preference for this enrichment was indicated by two behaviours known to be exploratory to novel stimuli, rearing on the enrichment and resting on the enrichment (Crusio, 2001). These behaviours were most frequent for this enrichment in comparison to 24 other enrichments presented to the mice.

However, the presence of enrichment had no beneficial effect on the amount of stereotypic activities or the level of aggression observed. Howerton *et al*. (2008) found that aggression was increased and social structure disturbed when enrichment was introduced into cages housing male CD-1 mice. The difference in findings can be attributed to the investigation of different sexes in each study, and highlights the need to assess the appropriateness of a given enrichment to each different social situation and for different strains of mice. Additionally, further study must be conducted to determine the specific characteristics that render a particular enrichment successful. It has been established that the presence of enrichment does not augment basic maintenance behaviours, such as feeding, drinking, self-grooming, social behaviour, resting in the cage and locomotion. Consequently, for experiments where data collection examines these behaviours, the presence of environmental enrichment does not alter experimental results (Nicol *et al*., 2008).

## Conclusion

The above studies highlight the difficulties in formulating universal husbandry guidelines for laboratory mice due to the number of strains available and the varying housing units in which mice are placed. In order to optimise welfare, the physiology and social behaviour of each strain must be investigated, in order to form the basis for formulating strain-specific guidelines for laboratory mouse welfare.

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