Acknowledgments

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References

1. **Gordon, J. W.** 2002. Barrier facilities for transgenic rodents in academic centers—a two-edged sword. Comp. Med. **52:**397-402.
2. **Jacoby, R. O. and J. R. Lindsey.** 1997. Health care for research animals is essential and affordable. FASEB J. **11:**609-614.
3. **Jacoby, R. O. and J. R. Lindsey.** 1998. Risks of infection among laboratory rats and mice at major biomedical research institutions. ILAR J. **39:**266-271.
4. **Hailey, J. R., J. K. Haseman, J. R. Bucher, A. E. Radovsky, D. E. Malarkey, R. T. Miller, A. Nyska, and R. R. Maronpot.** 1998. Impact of *Helicobacter hepaticus* infection in B6C3F1 mice from twelve national toxicology program two-year carcinogenesis studies. Toxicol. Pathol. **26:**602-611.
5. **Fox, J. G., X. Li, L. Yan, R. J. Cahill, R. Hurley, R. Lewis, and J. C. Murphy.** 1996. Chronic proliferative hepatitis in A/JCr mice associated with persistent *Helicobacter hepaticus* infection: a model of helicobacter-induced carcinogenesis. Infect. Immun. **64:**1548-1558.
6. **Diwan, B. A., J. M. Ward, D. Ramljak, and L. M. Anderson.** 1997. Promotion by *Helicobacter hepaticus*-induced hepatitis of hepatic tumors initiated by N-nitrosodimethylamine in male A/JCr mice. Toxicol. Pathol. **25:**597-605.
7. **Franklin, C. L., P. L. Gorelick, L. K. Riley, F. E. Dewhirst, R. S. Livingston, J. M. Ward, C. S. Beckwith, and J. G. Fox. 2001.** *Helicobacter typhlonius* sp. nov., a novel murine urease-negative *Helicobacter* species. J. Clin. Microbiol. **39:**3920-3926.
8. **Shomer, N. H., C. A. Dangler, M. D. Schrenzel, M. T. Whary, S. Xu, Y. Feng, B. J. Paster, F. E. Dewhirst, and J. G. Fox.** 2001. Cholangiohepatitis and inflammatory bowel disease induced by a novel urease-negative *Helicobacter* species in A/J and Tac:ICR:Has*cid*fRF mice. Exp. Biol. Med. (Maywood) **226:**420-428.
9. **Barthold, S. W.** 2002. "Muromics": genomics from the perspective of the laboratory mouse. Comp. Med. **52:**206-223.
10. **Baker, D. G.** 1998. Natural pathogens of laboratory mice, rats, and rabbits and their effects on research. Clin. Microbiol. Rev. **11**231-266.
11. **Hamm, T. E. Jr. (ed.).** 1986. Complications of viral and mycoplasmal infections in rodents to toxicology research and testing. Hemisphere Press Publishing Corp., Washington, D.C.
12. **Ward, J. M.** 2002. Comment on the muromics "garden path." Comp. Med. **52:**302.

Author's Response

I am grateful to Dr. Shoeb and Dr. Davis for the effort they made to provide a response to my article. Exchanges such as these can only improve animal management. I do not feel compelled to argue the question of how to define "clean" animals. Clearly, every barrier needs to develop such a definition before proceeding to develop maintenance protocols. Of course, the "cleaner" the animal is required to be, the more difficult it becomes to maintain that state of cleanliness.

The comment that too little is known about the impact of infectious agents on animal experiments to expect papers to have been withdrawn because of problems with animal pathogens is interesting, and I entirely agree that we need to know more about the physiological manifestations of infection with common rodent pathogens. However, if we balance the absence of negative information on the affect of pathogens against the documented finding of transgene phenotypes that do not appear when animals are clean, I believe the most rational approach is to produce transgenic animals and evaluate these animals under conventional conditions, where transgene phenotypes are less likely to be missed. It is important to recall in this regard the several examples I cited of trangene-related phenotypes that do not appear in an artificially clean setting. This strategy not only takes potentially undisciplined personnel out of the barrier, it also facilitates barrier maintenance by eliminating complex equipment and elaborate experimental manipulations from the facility. Lines of animals can always be rederived to whatever level of cleanliness is required for specific experiments after the production and initial evaluation period. In addition, while it is true that the absence of evidence is not the evidence of absence, we should not simply assume that barrier housing is superior because it avoids imagined rather than documented problems.

I also agree, of course, that barrier housing should be justified. If the decision to perform experiments within a barrier is made judiciously, barrier use can be more efficient, more cost-effective, and more adaptable to progress in both the scientific and technological arenas.

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