Origins of the M.I.C.E. SYSTEM

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Ten years ago, I was sitting in a luxurious conference room at the prestigious NCRR-National Center for Research Resources department of NIH-National Institute of Health. As a participant in a study called "Enhancing the Design of Animal Research Facilities" and since published (Ventilation Design Handbook on Animal Research Facilities. Volumes I and II, 800 pages, NIH, 1998 by Farhad Memarzadeh, P.E.), I was proud to find myself among the best in laboratory animal science veterinarians, animal facility directors, scientists, architects, and engineers. I was very excited about this NIH study because it might be a prelude to improving quality of data and quality of life in and out of cages.

As a veterinary scientist and director of animal facilities, I was invited by my post-doctoral mentor, Dr. Harry Rozmiarek who is an author of the *Guide* revised in 1965 under the title *Guide for the Care and Use of Laboratory Animals*, NRC. My qualifications to participate at this NIH study came from two funded grants on upgrading animal care and improving animal resources. My first award was a NSF-National Science Foundation grant titled: Upgrade of Animal Facility to a Barrier Facility and my second award was a NIH grant titled: Upgrading Conventional Animal Housing Facility. Both grants addressed engineering controls of airborne contaminants to preventing cross-contamination and lab animal allergies (LAA) as well as ways of expanding animal population in limited space.

Conclusions of the NIH study revealed a great deal of facts. First, animal airborne contaminants such as odors, biohazards, and heat loads are the limiting factor to housing and expanding a rodent population. Second, our tools against airborne contaminants consists of caging system; personnel protective equipment (PPE) and standard operating procedures (SOP); and HVAC (heating, ventilation, air conditioning) control to diluting, filtering and pressurizing air. Third, except for wire-bottom and open shoebox cages, all types of 'petri-dish' and sealed caging with filter-top whether static or individually ventilated are independent from the HVAC-controlled room conditions. In fact, we build animal facilities with HVAC system that provides high air dilution factor in the range of 15 to 20 ACH (air changes per hour) of (high efficiency particulate air) HEPA-filtered air at cost averaging 40% worth of the total construction or renovation budget. Occupants of filter-top cages, either static or individually ventilated (IVC) caging, do not benefit from that costly air dilution factor. On the contrary, the NIH study suggests that when increasing air dilution factor from 10 to 15 ACH, the extra pressure surrounding static cages prevent them to leak out odors, contaminants, and heat loads. It has been found that an increase in room ventilation rates would decrease airborne contaminants in the occupied zone (animal room) but increase ammonia concentration in static cages. In fact, rack variations are 3 ^{0}F, 10% Relative Humidity (RH), 2,256 ppm of CO_2, 4.8 ppm of NH_3-ammonia, and 50% ACH. With IVC cages, the cool air necessary to dilute odors and heat loads from animal, human, and blowers affect the temperature at which the forced-air is delivered to the cages. Top- or bracket-mounted blowers are the worst with their air intakes in the vicinity of ceiling air supplies. Accordingly, temperature, RH, CO_2, NH_3, and ACH vary from cages to cages and across racks depending of cages location on a rack and in a room. The benefit of higher air dilution ventilation and better air filtration are strictly for us in the animal room. Higher room ventilation rates dilute odors, contaminants, and heat loads in the animal room instead of in the cages. Since we do not feel cold temperature or smell mice in a room, we assume that they are fine. We make the mistake of thinking of our own comfort first, then those of animals that we care for.

From a mouse point of view, many stressful contaminants exist in the static cages. There are accumulations of heat, moisture, and waste gases in stall air over time. Besides providing poor air quality and environmental conditions, it creates variations at each cage changes to confounding experimental data with varying and uncontrolled levels of ammonia and other waste gases. Also, static cages are changed once to twice-a-week with aggressive behavioral consequences such as marking, barbering, and fighting among cagemates. In the IVC cages, there is incomplete air exchange with high turnover of dry air letting the cage occupants in a stressful and cold environment with air drafts, turbulences and dead-air spaces. For instance, when observing smoke distribution patterns in an IVC cage set at 60 ACH, smoke sinks in the bottom of the cage and takes up to 20 minutes before being diluted by HEPA forced-air. This would correspond to 3 ACH whereas odors, contaminants, and heat loads accumulate over time. To a lesser degree than static cages, IVC provides poor air quality and environmental conditions. It also creates variations at each cage changes to confounding experimental data with varying and uncontrolled levels of ammonia and other waste gases. IVC cages are changed every 10 to 15 days with similar aggressive behavioral consequences.

From a researcher point of view, those stressful contaminants are variables in experiments as well as potential risk of cross-contamination. Also, researchers have documented decreased growth rates, low body fat, loss of established pregnancies, and decreased fertility which can be associated with stressful contaminants and/or dehydration created by the caging system.

Six years ago, I found a solution to 1) room odors, contaminants, and heat loads; 2) cage contaminants and poor air quality and environmental conditions; 3) experimental variables; and 4) animal's needs. I invented the M.I.C.E. system- Mi(a)croenvironmental comfort, Isolation, Containment, and Enrichment. It consists of a closed-system caging on exhaust ventilated rack that eliminates animal-contaminants at the source, i.e. the cage. I use direct exhaust ventilation of closed-system cages to eliminate (and not dilute or reduce) contaminants that include room odors, contaminants, allergens, and heat loads; cage accumulation of contaminants, heat, moisture, and waste gases loads; and experimental variables. Also, the M.I.C.E. cage provides a low-stress environment to meeting species-specific needs. Moreover, it meets the convenience needs of their caretakers and users.

We followed a challenging and demanding course of actions. First, we created a barrier-cage that prevents in-and-out air leakage under active exhaust ventilation. Second, we optimized natural airflow by convection that is fail-safe, reliable, and controllable. Third, we provided vent air filter units that optimize airflow, are washable / autoclavable, and protect the animals, their users, and the environment. Fourth, we developed active exhaust ventilation that provides an adequate, efficient, one-pass/total-volume, and breeze-like airflow. Lastly, we designed integrated environmental enrichment structures that fulfill species-specific needs and minimize stress of confinement and variables. The resulting design is quite different from any cage in use then or now. It follows the animals, their users, and the research/testing needs throughout. The M.I.C.E. caging system improves quality of data and quality of life in and out of cages; prevents cross-contamination and LAA; and provides ways of expanding population in limited space.