

Tradeline Publications: Trends Driving Animal Facility Design

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One of the obvious trends in new animal facilities is the increasing emphasis on mice, especially the transgenic variety. It's not unusual to find vivariums where the mouse population accounts for two-thirds or more of the total animal holding space, according to Stan Dannemiller, DVM, director of the biological resources unit of the Cleveland Clinic's Lerner Research Institute (LRI), which recently brought a new 100,000-sf animal facility online.

But mice haven't always been such a strong presence in the animal environment.

"Back in 1965, people would have laughed to hear that a facility like ours had over 10,000 cages of mice and only 30 or 40 dogs," he remarks. "Looking at the mix 30 years later, back in the mid-1990s, we had approximately equivalent amounts of square footage for dogs, rats, mice, and agricultural species."

By 2006, however, the species census had changed considerably. Over the past 10 years, Dannemiller has seen the real estate occupied by mouse housing in his facility more than double, rising from 31 percent to 65 percent of the total. Meanwhile, the square footage allotted to rats declined from 22 percent to five percent, and the space for large animals, including dogs, has dropped as well (although not as dramatically).

He attributes this metamorphosis to the progress of medical research, which the large, tertiary-care human hospital has experienced first-hand. Historically, the clinic's animal population had been comprised primarily of dogs, pigs, and ruminants (sheep, goats, and cows) which were used in pioneering advances like heart valves, artificial organs, orthopedic devices, and minimally invasive surgery. These large animals would be transported to the operating room and then go back to a holding room after surgery.

With the inauguration of the LRI in the early 1990s, investigations took a different turn, targeting the mechanisms of disease and pathology. The subsequent focus on the cellular and subcellular levels prompted a species shift to transgenic mice, and the operating room gave way to the laboratory full of sophisticated equipment.

Now, stem cell and genetic research hold the promise of individualized medicine, in which a patient's genetics will determine the kinds of drugs or treatment that will be most effective. Researchers have much to learn about how to tap this potential, and Dannemiller predicts a new reliance on mice as the model for such studies. Looking ahead, advances like automated gene chips and nanoscale

science will only intensify the growth in mice numbers.

"Suddenly, the mouse is becoming a large animal. If you only need five microliters of blood to run 50 different tests, dogs may not be necessary," he says.

Flexibility Defined

It's not just the predominance of the mouse that has occasioned changes in vivarium design. The development of new technologies, along with the push to prolong building life—expectations of 25 to 40 years are now the norm—also exert a strong influence over planning efforts, making flexibility a critical attribute that must be incorporated from day one.

The unanticipated need to accommodate different species often crops up. For example, during the original design of the Cleveland Clinic's new animal facility, intentions were to fill the facility with mice. But then it was decided to make space for dogs, pigs, and ruminants while the old facility was being renovated. In addition, recruiting a new principal investigator introduced the need to house primates in the new building.

The Clinic was able to do all this thanks to the flexibility features incorporated in the new facility design.

"Flexibility is all about planning for the future, because we know that change is inevitable," comments Yun Lee, senior lab planner in the Atlanta office of CUH2A, which has designed many recent vivariums, including the one at the Cleveland Clinic.

"Merriam Webster's dictionary defines flexibility as 'a ready capability to adapt to new, different, or changing requirements,'" Lee explains, noting its four primary characteristics: versatility, adaptability, interchangeability, and expansibility.

Versatility is defined as the ability to have many uses or applications, she points out. In the vivarium, this means thinking about optimal room sizing to accommodate different cages for different species. While the actual dimensions of the rooms will vary with each project, the need for different temperature and humidity ranges must be considered. Another "must" is having adequate mechanical, electrical, and plumbing infrastructure to support the gamut of housing options, from racks, pens, and mobile cage change equipment to flexible isolators for containment, she says.

Adaptability is making adjustments to suit new condi-

tions, often via modification. As an example, Lee cites adding or removing partitions—not only to make rooms bigger or smaller, but also to group rooms together. These kinds of changes typically entail modifying airflows to alter pressure relationships with adjacent areas. Once again, having the infrastructure already in place will make the adaptation easier and more cost effective to implement.

Interchangeability permits the mutual substitution of components, on many levels and scales. For instance, holding rooms and procedure rooms are often interchangeable, as are ABSL-3 suites, quarantine suites, and specific pathogen-free suites. This attribute can extend all the way from casework components to filters for animal dander to insect screens.

Expansibility is the ability to enlarge, either horizontally or vertically. Provisions for growing room should be kept in mind in the earliest planning stages, starting with site selection. Adequate engineering systems—structural, mechanical, electrical, and plumbing—are also critical for future expansion. A building that is organized in modules with identifiable rhythm and logical progression is very helpful when it's time to connect new systems into existing ones, she advises.

Room Blends and Neighborhoods

When it comes to animal housing rooms, a one-size-fits-all approach is unlikely to be very effective, not just because of species differences but because of the disparity in individual animal populations maintained by various building occupants, according to Mike Mottet, director of lab planning for CUH2A's Atlanta office. As an example, he cites a two-level, 100,000-nsf vivarium now under construction in which researchers will have as few as 25 or as many as 1,000 mice.

"We did not want to give up a large room to the researcher who had perhaps 50 mice," he says. "Also, cubicle rooms are not the most efficient way to design a facility because they are very expensive and less flexible."

The answer is a blend of room sizes—small, medium, and large—affording the flexibility to accommodate investigators who have different numbers of animals yet similar protocols and research. For instance, a set of half a dozen rooms can be ganged into what Mottet calls a "six pack," with an anteroom in the center that can be used as a common procedure space. The scheme is flexible enough to fit a rack of primates in the small housing rooms, which can also be set up as procedure space, or even designated for storage. A similar organization can be applied to the larger room clusters, making, for example, a "four pack" that combines both large and small rooms.

Superimposed on the room blends is the concept of neighborhoods, which provide for separation of species for both security and environmental purposes. A neighborhood can be designed to segregate animals vertically, by stacking (the two-level vivarium project Mottet mentions has large animals on the lower floor and small

animals above), and/or horizontally, with doors, sound attenuation, and structural features, such as placing core facilities in the middle to create a dividing line between different zones.

Because HVAC systems consume so much of the project budget, Mottet recommends incorporating as much flexibility and adaptability as possible right from the start. Rooms initially intended for larger animals, with a standard of 15 air changes per hour, can easily be converted to ventilated racks with 10 air changes per hour if rack exhaust ports with appropriate engineering systems are designed, budgeted, and installed.

Finances permitting, each room should also have individual temperature and humidity control. While a zone arrangement is less expensive, being able to maintain temperature and humidity control at the room level makes a significant contribution to flexibility.

"It allows you to house rabbits at, say, 65 degrees, and then raise the temperature up to the mid-70s if you have rodents instead," Mottet emphasizes.

Plumbing should also be provided, "even if you don't have a need for it on day one," he adds. Rooms already equipped with trench drains and hot and cold water mixing stations facilitate the shift from rodents to larger animals and non-human primates.

"Even if it is just a hose bib, it is ideal to put a water source close to the room. It might be used infrequently with the smaller animals, but it is essential for the day-to-day wash down of large animals," he points out.

Some provision should also be made for an automatic watering system, which again might not be necessary upon occupancy but may be desired in the future. Setting aside a room for the system's filtration devices and storage tanks initially means not having to give up equipment and vivarium storage space later. Sometimes, that equipment can be located in an interstitial or mechanical floor, but there is a limit on how far the water can travel or be pumped. Mottet suggests piping the main distribution runs in the corridors, leaving room penetrations for future system installations.

Open Issues

Dannemiller points out that innovation in animal caging have made room blends much more feasible.

"On the large animal species, we have been able to become much more modular, so we have one cage that can house a pig, a dog, a sheep, a goat, or a cow, instead of having to have a different room for the different species," he observes.

And thanks to collaboration with caging vendor Lab Products, the clinic now has the ability to fit larger numbers of mice into a given footprint than it did in the past. Dannemiller also notes that while micro-isolators might be necessary to protect immuno-suppressed or other high-investment animals, some facilities do not need to operate on a cage-level barrier, an indication that the conven-

tional cage still has a role to play in the contemporary animal environment.

A lingering uncertainty is the prospect of rats and mice being brought into the USDA's regulatory fold, creating the need to comply with protocols imposed by an external authority. Of all the potential agency changes, this is the one that most concerns him, Dannemiller admits.

"I think is going to have a huge impact on us potentially," he says, "and in my mind the issue is not 'will this happen?' but 'when will it happen?' I do not know how far down the road it is."

A further challenge to be faced is the push to produce "green" buildings. The vivarium is typically a large consumer of energy and water, and the drive to reduce the environmental impact through architects and engineers who are LEED certified is mounting.

A final factor to affect species selection and their housing is public perception. Animals like dogs, cats, and monkeys rank high on the "cute" scale, making them less desirable as research subjects, Dannemiller explains. Rodents, on the other hand, don't incur the same objections, at least not yet—another reason for the growing popularity of mice.

Biographies

Dr. Stan Dannemiller is the director of the Biological Resources Unit at Cleveland Clinic in Cleveland, Ohio. He has a broad variety of experience in laboratory animal science having worked in contract research, industrial, and agricultural chemical industry, medical devices, pharmaceutical, and consumer products companies. Dannemiller received his Master's in zoology/comparative physiology, Doctorate in veterinary medicine from The Ohio State University, and completed a residency program in laboratory animal medicine and a Master's in comparative medicine/toxicology from the University of Pennsylvania.

As a senior laboratory planner with CUH2A, Yun Lee has extensive experience in the programming, planning, and designing of research facilities. As a vivarium planner she works closely with both scientific users and facility managers to develop needs assessment reports and

program documentation. Lee received a Bachelor of Arts degree in architectural studies, art and art history from Rice University, and a Master's degree in architecture from the Georgia Institute of Technology. She has worked on projects for the Centers for Disease Control and Prevention, the United States Army Medical Research Institute for Infectious Diseases, Emory University, and the University of Georgia.

Mike Mottet is director of laboratory planning with CUH2A in Atlanta. He has more than 10 years of experience in the science and technology marketplace with a strong background in the planning and design of lab animal environments. He is particularly knowledgeable in the areas of vivarium design, equipment design and installation, and engineering coordination. Mottet received a Bachelor of Science in architecture from Iowa State University, and has worked in the pharmaceutical, academic, and government arenas. Clients include the Cleveland Clinic Foundation, Emory University, the Georgia Institute of Technology, the University of Georgia, and the University of South Carolina.

This article is based on a presentation given by Dannemiller, Lee, and Mottet at the *Tradeline Animal Research Facilities* conference in November 2006.

For more information, please contact Stan Dannemiller, DVM, MS, DACLAM, Director, Cleveland Clinic, Biological Resources Unit, Lerner Research Institute, 9500 Euclid Avenue, MS NC50, Cleveland, Ohio 44195, 216-444-2055, dannems@ccf.org, or Yun Lee, Senior Laboratory Planner, CUH2A Inc., 1201 Peachtree Street, NE, 400 Colony Square, Suite 600, Atlanta, Georgia 30361-3500, 404-815-1212, ylee@cuh2a.com, or Michael P. Mottet, Director of Laboratory Planning, CUH2A Inc., 1201 Peachtree Street, NE, 400 Colony Square, Suite 600, Atlanta, Georgia 30361-3500, 404-815-1212, mmottet@cuh2a.com.

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Figure 1

Animal facilities have to be flexible to accommodate not just the upsurge in mice populations but also the increasingly broad array of species, from ticks to ruminants, with their intrinsic extremes in scale. (Image courtesy of CUH2A and Cleveland Clinic.)

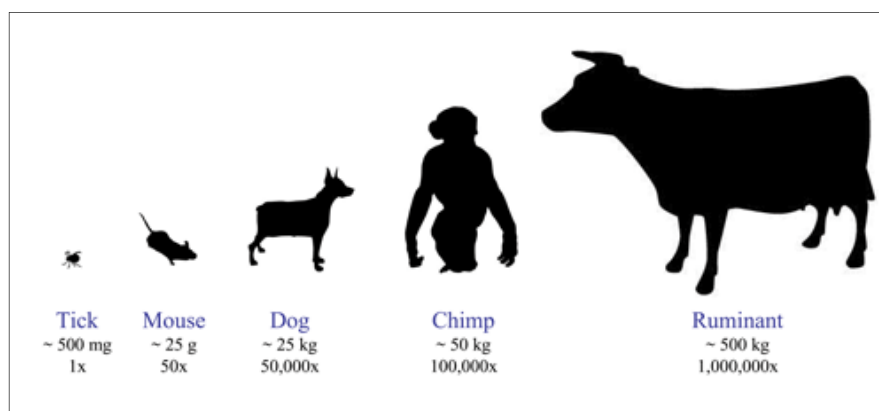


Figure 2

A mix of small, medium, and large animal housing rooms with common procedure space is one way to co-locate investigators with similar protocols and research. Ganged together, the room blends create larger neighborhoods that separate species for both security and environmental purposes. (Image courtesy of CUH2A and Cleveland Clinic.)

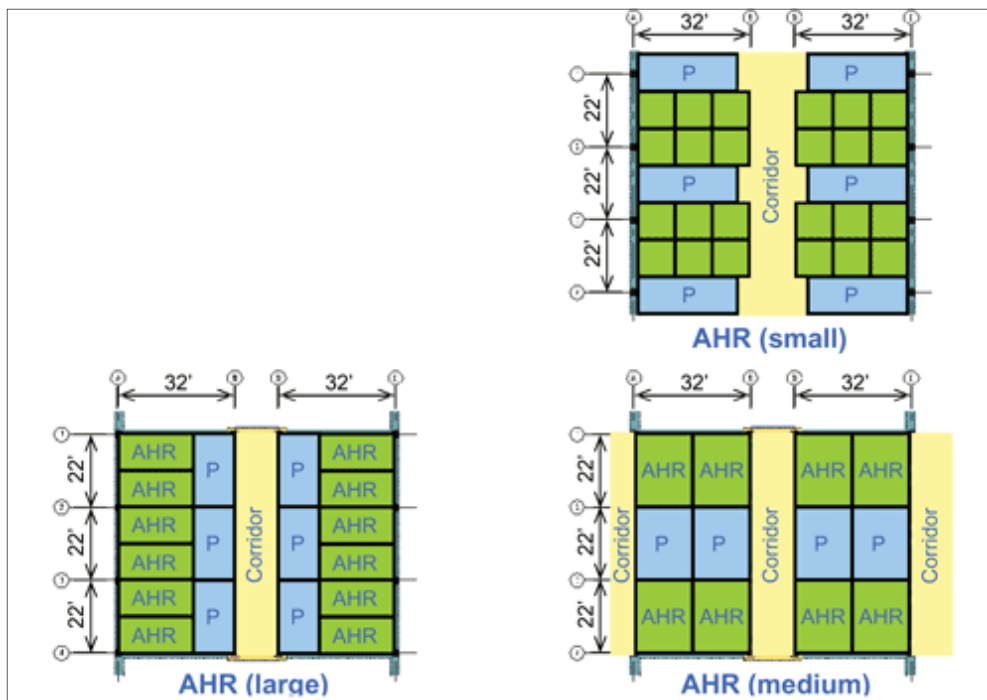


Figure 3

The development of new technologies, along with the push to prolong building life up to 40 years, are major drivers of vivarium planning, making flexibility a critical attribute that must be incorporated from day one. (Photo courtesy of CUH2A and Cleveland Clinic.)

