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The purpose of this BRL Bulletin is to review the definition of ecological status, describe the current status of rodents at UIC, and explain our future goals as it relates to UIC rodents. Ecology is defined as the branch of biology that deals with the relationship between living organisms and their environment. For this discussion, ecological status is the association between the rodent and its microbial environment. Terms such as specific pathogen free (SPF) and viral antibody free (VAF) can be used to define the ecological status, but at best, they are loose definitions which may be variably defined by institutions and vendors. SPF and VAF help conceptually define situations in which agents are excluded from rodent facilities. Excluded agents are microorganisms that may be pathogens under certain situations or may influence experimental results. Excluded agents come from every microbial class including viruses, bacteria, parasites, and fungi. Almost all research institutions and commercial suppliers have a list of microbial agents that are excluded from their facilities. The list of excluded agents often differs between facilities, but there are some agents that are universally excluded. Please note that the hundreds of commensal bacterial species, so called normal flora, that have not been linked to pathogenic effects are of no concern and will not be included in this discussion.

Almost all rodent research colonies exclude horizontally transmitted viruses. The UIC veterinary staff tests for twenty-two mouse and rat viruses using serologic assays. One example, mouse norovirus, is a recently described virus that is enzootic in approximately 85% of academic rodent research facilities. However, UIC is mostly free of mouse norovirus, so rodents received from many other academic institutions must be rederived upon arrival. It is likely that most academic institutions will eliminate this agent with time. Although most institutions are free of horizontally transmitted rodent viruses, be aware that vertically transmitted viruses such as retroviruses cannot be eliminated. Therefore, there is no such thing as a truly viral-free rodent. In fact, it is estimated that over 37% of the mouse genome is made up of retroviral

elements.

Bacterial agents are more difficult to exclude, but *Mycoplasma pulmonis*, *Clostridium piliforme*, *Salmonella* spp., CAR-bacillus, and *Corynebacterium kutscheri* are examples of rodent pathogens that are particularly pathogenic and are excluded from virtually all facilities. One problem with testing for this group of agents is that serologic assays are less reliable since surface antigens of pathogenic species can cross react with other less pathogenic bacterial species. PCR testing is proving to be more reliable than serologic testing for many bacterial agents. However, one of the major bacterial pathogens in rats, *Mycoplasma pulmonis*, may be reliably detected using serologic methods due to the simple surface antigens of this agent.

More ubiquitous bacterial agents such as *Staphylococcus* spp. and *Pseudomonas aeruginosa* are difficult to eliminate from rodent colonies since humans and the environment are sources of these agents. *Pseudomonas*, in particular, is often cultured from water that has come into contact with animals. This organism can grow in water contaminated with food from the mouths of rodents who drink the water. As a precaution, some rodents may be provided acidified water to decrease *Pseudomonas* levels. Water is acidified with hydrochloric acid to a pH of 2.5. This husbandry practice is common for rodents used in irradiation projects. Rodents find this water palatable, but there are reports of heavy metal leaching from water bottle components and potential effects on immune function, weight gain, water consumption, and tooth enamel.

Not many fungal agents are reported as pathogens, but *Pneumocystis* sp. is one that can cause disease. Much like human patients with immunodeficiency disorders, immunodeficient rodents, whether genetically or experimentally induced, are susceptible to disease caused by this agent. Recently, this agent has been shown to be the causative agent of rat respiratory disease in immunocompetent rats. Rat respiratory disease is characterized as an interstitial pneumonia that is histologically identified in immunocompetent

rats six weeks after naive rats enter a contaminated facility. The UIC Animal Care Program is taking initial steps to determine the procedures required to eliminate this agent. Each species of rodent has its own species of *Pneumocystis*. Rats, for example, are most often infected by *P. carinii* whereas mice are typically infected with *P. murina*. Protozoan parasites such as *Entamoeba muris*, *Giardia muris*, and *Spironucleus muris* are common pathogens in institutional and vendor colonies. Testing and culturing modalities for these agents are not well established, and for this reason, very little is known about the pathogenicity and experimental influences on rodents. These agents may take on more importance as more is discovered about the biological effects of these agents.

Helminth parasites are excluded from most academic and commercial animal facilities. The only parasite still commonly seen in academic rodent facilities are pinworms. These parasites reproduce rapidly, spread via aerosol, and the eggs are resistant to environmental decontamination. Historically, testing methods include the perianal tape test, fecal flotation, and direct observation of intestinal contents at necropsy. These tests are not very sensitive, which is yet another reason these organisms are still common in rodent research facilities. A PCR test for pinworms has recently been developed that is much more sensitive, and may help achieve elimination of these parasites from rodent colonies. At UIC, rats and mice from unapproved vendors are routinely fed a diet containing the anthelmintic fenbendazole for six weeks upon arrival. Investigators pay for the cost of this diet.

External parasites such as ticks, fleas, and mites are excluded from most academic and commercial animal facilities. However, fur mites are still common in many academic rodent colonies. Historical testing methods include microscopic evaluation of skin scraping and fur samples and direct observation of the pelt at necropsy. These tests are not sensitive and limit the ability to diagnose an infestation. A PCR assay has recently been developed that is much more sensitive than historical tests. Rats and mice from unapproved vendors are routinely treated with a topical anti-parasitic medication (moxidectin) when they arrive on campus. Investigators pay for this treatment through the per diem charged during the quarantine period.

Microbial agents that are excluded from rodent colonies vary over time. Pathogenic agents are discovered when

new diagnostic techniques are developed. Certain parvoviruses were identified when a new PCR test was developed and other new pathogens will likely be discovered in the future. For example, mouse norovirus was identified as a pathogen about a decade ago. Since that time, reputable vendors such as Harlan, Charles River, Taconic, and Jackson have tested their colonies and determined that many of their colonies are free of this agent. These vendors have regular programs to rederive their colonies and have eliminated this agent during these procedures. Typically, academic institutions accept the microbial status of reputable vendors because they regularly receive rodents from these sources, which influences the agents excluded from their rodent facilities.

Currently, UIC has 11 rodent facilities that are approved for housing animals. The Biologic Resources Laboratory (BRL) and the Brain Body Center (BBC) on the west side of campus and the Behavioral Sciences Building (BSB) and Science and Engineering South (SES) on the east side of campus are multi-room animal facilities with self-contained cage wash support. In addition to these facilities, the Molecular Biology Research Building (MBRB) and College of Dentistry are multiple room facilities supported by BRL staff and cage washing operations. Finally, there are single-room rodent facilities that support the research requirements of specific investigators.

The Jesse Brown Veterans Administration (JBVA) animal facility is not a UIC facility, but is important strategically for several reasons. First, a number of UIC faculty have dual appointments at UIC and JBVA. Second, collaborative opportunities often arise for faculty as the institutions are in close proximity. Third, UIC staff provide veterinary support to the JBVA. As a result, we are integrally involved with the management of this facility and can readily determine the risks involved with movement of equipment, staff, and animals.

From a management perspective, facilities on campus have similar management practices and use similar equipment. Every facility houses laboratory rodents such as rats and mice, but only two facilities on campus have USDA-covered species (BRL and SES). Each facility is evaluated on its own merit in terms of the risks involved with maintaining a certain microbial status.

UIC began rederiving campus rodent colonies in 2003 when the College of Medicine Research Building (COMRB) opened. Mice were rederived to eliminate mouse hepatitis virus, mouse norovirus, *Helicobacter* spp., pinworms, and fur mites enzootic in the BRL rodent colony and were transferred to this facility. The institution was on the leading edge of eliminating microbial agents such as *Helicobacter* and mouse norovirus. As a result, we are the only academic institution in the Chicago area that is free of these agents.

By 2006, the BRL rodent colony had excluded mouse hepatitis virus, mouse norovirus, pinworms, fur mites, and *Helicobacter* so its microbial status matched that of COMRB. The animal facilities at SES, BSB, and Pharmacology followed suit shortly thereafter. We have almost completed the rederivation of MBRB and College of Dentistry animal facilities. Animals currently housed in MBRB are the same microbial status as the animals in COMRB, BRL, SES, BSB, and Pharmacology. This allows investigators to take advantage of the new magnetic resonance, echocardiogram, and bioluminescence imaging modalities in the BRL without undergoing a costly rederivation procedure. The institution can offer these shared equipment resources to a wide range of investigators by maintaining rodents at the same ecological status at all animal facilities.

Our future plans include renovating the College of Dentistry animal facility and rederiving all the BBC and JBVA mice. There are currently no animals in the College of Dentistry animal facility because of the ongoing renovation project. This facility will be expanded by three animal housing rooms and several procedural areas to supplement the existing two animal housing rooms and one procedure room. The rodents housed in this facility will have a similar microbial status to other rodent colonies on campus.

At BBC, the vole colony will be closed this summer due to the investigator leaving UIC. However, as one door closes another opens, and an opportunity presents itself. The voles were the reason we tolerated *Helicobacter* in this facility as there are no proven methods of rederiving voles. We plan to rederive the breeding mice and rats to make this facility the same ecological status as other facilities on campus.

Finally, the JBVA has plans to rederive their rodent stocks and strains. Currently we are working out contractual issues, but our hope is to complete rederivation by this time next year. Once this facility is rederived there will be less risk for pathogen contamination and greater opportunity for investigators to collaborate.

When all campus facilities attain the same microbial status, the quarantine room at the BRL will be the only location that houses contaminated mice. The BRL staff has worked diligently to rederive newly acquired contaminated rodent strains. When University departments recruit new faculty who transfer large numbers of contaminated rodents, the quarantine space will be expanded to accommodate these additional animals. We will always have at least one quarantine room, but additional rooms will be recruited based on faculty needs.

In summary, UIC has a high quality animal care program that excludes agents not excluded from other academic institutions in the country. Because of the consistency of care and microbial standards, animals can move throughout the campus more freely, and collaborative opportunities are possible between investigators from different departments on campus.

ANNOUNCEMENTS

Happy Retirement - On June 30th the BRL will lose approximately 105 years of animal care experience as Larry Rias (34 years), Volta Perkins (29 years), Lee Bailey (22 years) and Larry Reed (20 years) retire from UIC. The staff of the BRL would like to thank them for their dedicated service to the animal care program and the research community. Enjoy your retirement — you deserve it!!!

