Hyperkeratosis in nude mice, associated with a coryneform bacterium, was first reported in 1990 as a severe disease resulting in nearly 100% mortality in suckling and transient disease in weanling mice. The disease is said to have been described as early as 1976 at Charles River Laboratories. In 1998, the causative agent was identified via 16S rRNA sequencing as *Corynebacterium bovis* - an aerobic, Gram positive, pleomorphic rod.

Within the MSKCC vivaria, *C. bovis* has been an endemic problem with severe outbreaks of disease occurring in the fall of 2005 and the spring of 2006. The methods of *C. bovis* introduction into the facility remain elusive. There are conflicting reports regarding the possibility that immunocompetent mice are carriers of the bacterium. Additional sources of the agent may include immunodeficient mice, which are not tested for *C. bovis*, and tumor and cell lines that are not screened appropriately. There are also anecdotal reports that humans can be carriers of *C. bovis* in their nasopharynx.

Once established within a facility, eradication has thus far only been successful with depopulation and restricted room access. *C. bovis* is highly resistant to dry environments where it has been reported to survive more than 30 days. The bacterium has been shown to persist on infected mice for at least 33 days following the onset of infection and clinically affected animals have been shown to remain infected after disease resolution. Transmission can occur by direct contact of infected mice and by various fomites, including contaminated gloves, gowns, and instruments.

Both immunocompetent and immunodeficient mice and rats have been reported to be capable of infection, but it is the clinical manifestation in nude mice that accounts for the term “Scaly Skin Disease.” Seven to 10 days post-exposure, athymic nude mice develop yellow-white flakes adherent to their skin that begin on their dorsum and spreads along their back and flanks. Nude mice can also exhibit weight loss, dehydration, and generalized weakness. Untreated, clinical disease is
When the Staff is Away the Mice Still Play!

A Vacation Reminder

Summer is here and the time is right... for vacation! This means that at some point during the coming months you or your colleagues may be away from your laboratories.

PLEASE remember that your animals in the vivarium need to be observed at least weekly and often on a more frequent basis depending on their research use. This is imperative especially if you manage a breeding colony as overcrowded conditions can develop quickly.

Please make contingency plans to ensure your animals are being monitored during your absence.

If you find you need help, RARC’s Veterinary Services section may be able to assist.

Contact Veterinary Services to discuss your needs at RARC_VS@med.cornell.edu or 212-746-1079.

RARC’s Veterinary Services section, in conjunction with Husbandry and Operations, maintains a stock of various medicated diets. Many of these are specially compounded and manufactured to RARC’s standards. To produce these diets, specific pharmaceutical agents are added to a grain based or purified diet, and are then pelleted. The medications are added at specific concentrations to ensure accurate dosing. Before distribution, medicated diets are gamma irradiated to prevent introduction of unwanted infectious agents which may have contaminated diet components. Because medicated diets contain prescription medication, these diets are available only after consultation with Veterinary Services staff. To ensure medicated diets are not mixed with one another or standard diets, food coloring is added so that each diet is a distinct color. If you have ever wondered about the rainbow of colored diets, the following is a list of diets that you might encounter:

Red diet contains AMOXICILLIN & VITAMIN E. This diet is frequently used to treat mice with ulcerative dermatitis, and other forms of skin disease.

Green AMOXICILLIN diet is used for the treatment of Corynebacterium bovis infections, but is also used to treat other infections caused by bacteria sensitive to this agent.

Purple diet contains Sulfadiazine antibiotic. Trimethoprim and sulfamethoxazole are used to prevent and treat Pneumocystis murina pneumonia in immunocompromised mice. This diet has other uses, including treatment of susceptible skin infections.

Dark Blue diet contains the anthelminthic IVERMECTIN. Ivermectin feed is used to control and eradicate internal and external parasites.

Yellowish DOXYCYCLINE diet (below left) is similar in appearance to non-medicated rodent feed (below right). Doxycycline, although also to treat bacterial infections, is most commonly used to modulate gene expression in conditionally mutant mice.

If you would like to request one of these diets please fill out a Special Husbandry Form which can be found on RARC’s intranet site; go to Husbandry & Operations and click on special water and diets. If you would like more information about our special diets and or medicated water please contact veterinary services at RARC_VS@med.cornell.edu.
reported to resolve 7 to 10 days later, but our experience is that mice may suffer a more severe illness, potentially leading to death, due to stress from experimental manipulation.

Haired immunodeficient mice (e.g., SCID) can develop a less severe form of the disease, exhibiting alopecia and scaling dermatitis on the back, flank, neck, and face.

There are implications for research when animals are infected with Corynebacterium-associated-hyperkeratosis. Mice can exhibit significant weight loss or a depressed rate of growth. Pertinent to cancer research, tumor growth rate may be depressed and the toxicity or efficacy of chemotherapeutics may be affected sometimes with an associated increase in mortality. Natural killer cell activity may also be affected.

RARC is currently conducting studies to better understand the epidemiology of C. bovis infection to improve rodent health and minimize research complications. Nude sentinels have been placed in various mouse holding rooms to examine the possibility that immunocompetent mice may serve as carriers. The efficacy of our cage change SOP for preventing cross-contamination is being evaluated. We are also currently evaluating the efficacy of the two week amoxicillin diet prophylaxis for all incoming nude mice. In the near future, we will determine if antibiotic treatment effectively clears C. bovis from infected animals, or if only clinical signs resolve. With new information, we hope to more effectively manage this disease.

### Why it is important to adhere to WCMC’s Policy for Maintaining Mouse Cage Populations.

1. Density standards provided in the Guide for the Care and Use of Laboratory Animals (Guide) are designed to ensure that animals are housed in a manner that promotes their health and well being. WCMC is required to adhere to these standards.

2. NIH’s Office for Laboratory Animal Welfare (OLAW), specifically states that chronic failure to provide space for animals in accordance with the Guide’s recommendations, unless approved by the IACUC and based on written scientific justification, is a reportable offense and may place institutional funding at risk.

3. Pups born into a cage containing an older litter may not be able to compete for the dam’s milk. This may be particularly problematic for delicate transgenic lines.

4. There is a higher incidence of morbidity and mortality in young litters stepped on by older animals.

5. The added workload on RARC’s Husbandry & Operations and Veterinary Services staff addressing overcrowded cages results in higher per diem costs for investigators and takes precious time away from other duties. This results in inequity for those laboratories properly managing their breeding protocols.

6. Excessive food and water consumption may lead to animals going without food and/or water.

7. The excessive heat generated by large numbers of mice and noxious build up of ammonia and carbon dioxide in these cages can significantly impact the health and welfare of both young and old animals and could potentially interfere with research results.

8. The best way to ensure a healthy, uncompromised animal model suited for generating quality experimental data is to provide a clean, healthy environment.
**UPCOMING SEMINARS**

**HANDLING AND EXPERIMENTAL TECHNIQUES IN RODENTS**

Speaker: Caroline Murray, BS, RLATG, CMAR, Education & Quality Assurance Specialist  
Date: Wednesday, July 16  
Time: 2:00 - 3:30 PM  
Place: MSKCC campus, RRL, Room 101

**GENETICALLY ENGINEERED MOUSE MODELS: ADVANCING AND UNDERSTANDING OF HUMAN DISEASE**

Speaker: Ravi Tolwani, DVM, PhD, Diplomate ACLAM. Research Associate Professor, Associate Vice President and Senior Director of CBC, The Rockefeller University  
Date: Wednesday, August 20  
Time: 2:00 - 3:30 PM  
Place: Rockefeller campus, Weiss 302

**STRATEGIES FOR BEHAVIORAL PHENOTYPING OF TRANSGENIC AND KNOCKOUT MICE**

Speaker: Jacqueline N. Crawley, Ph.D., Chief, Laboratory of Behavioral Neuroscience, National Institute of Mental Health  
Place: ZUCKERMAN RESEARCH CENTER (ZRC), RM. 105  
Date: Wednesday, September 17  
Time: 2:00 - 4:30 PM

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