



March 2008
Volume 1, Issue 2

WEILL CORNELL MEDICAL COLLEGE EDITION

RARC NEWS

Research Animal Resource Center

Special Interest
Articles:

Biosecurity-
Emerging
Murine
Pathologies

A message from the Director

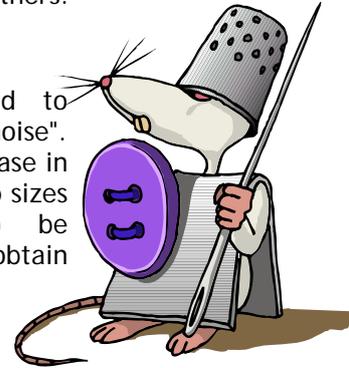
With spring approaching many begin to think about warmer weather and spending time out of doors. At RARC, we are investing time and effort improving and enhancing the resources we provide in support of animal care and use. We will be updating and enhancing our web site. It will be more user-friendly and provide additional resources. For example, you will be able to access various training

resources, schedule training classes, and view health information on your rodent colony. In coming months, we will also roll out a new web-based colony health certification system. This system will allow you to instantaneously generate health reports for your colony and electronically distribute them to colleagues to whom you would like to export animals. We appreciate your feedback on planned enhancements and suggestions for others.

Emerging Diseases Series

Beginning with the item below, a series of articles focusing on emerging infectious agents found in research rodent colonies will be presented in **RARC NEWS**. Some agents such as mouse norovirus (MNV) or *Helicobacter spp.* are found ubiquitously in many US animal facilities including ours. Others, such as fur mites or mouse parvovirus have caused outbreaks at WCMC in the past. Yet others, such as *Corynebacterium bovis*, that cause corynebacterium-associated hyperkeratitis aka "scaly skin disease" (Look left for upcoming seminars on this topic!) affect only a subset of animals, mainly nude mice. Most of these agents have a direct or indirect impact on research conducted in animals. Not every study is affected to the same degree, but infectious agents may alter the physiology of the affected

animal and add to background "noise". Due to this increase in variability, group sizes may need to be increased to obtain statistical significance.



Each article will be dedicated to one disease, discussing the etiologic agent, mode of transmission, and the clinical signs they may cause. It will also address the potential impact on research providing references where available and elaborate on the measures RARC is/has been taking in response to each agent. Comments and suggestions from the investigative staff are appreciated.

SPECIAL TOPIC SEMINAR:

Hyperkeratotic Dermatitis "Scaly Skin Disease"

This seminar is presented on
two occasions:

Tuesday, March 25th
2:00 - 3:00 PM
&

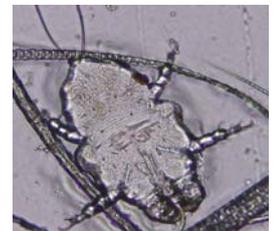
Wednesday, April 2nd
11:00 - 12:00 PM

Zuckerman Research Center
Room Z-911

Fur Mites

Fur mites are the most common ectoparasites of laboratory rodents. Mice are generally infested with *Myocoptes musculus* and *Myobia muscili*, frequently in combination. Other mites found on laboratory mice include *Radfordia affinis* and *Ornithonyssus bacoti*. Fur mites complete their entire life cycle on their host. Unlike other mites, fur mites do not burrow into the skin, rather their first (in *Myobia*) or their third and fourth (in *Myocoptes*) pair of legs (mites have a total of 8 legs) are specifically adapted to securely clasp the host's hair shafts. They do not feed on blood, but rather on skin excretions and exfoliated dead skin. Mouse fur mites may infest rats but not other animals or humans.

MYOCOPTES

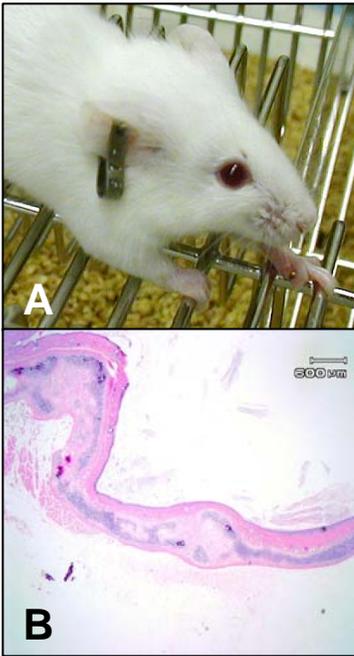


MYOBIA

Fur mites are transmitted through direct contact between animals and less efficiently via fomites (mites are only able to survive off of the host for a few days). After mating, the adult female attaches her eggs permanently to the hair shafts of the host. After 5-8 days egg hatches and a mite larvae emerges. As they grow they shed their exoskeleton several times and transform into nymphs. Larvae and nymphs

Cont. on pg. 3

Pertinent Pathology ~ To Tag or Not To Tag?



One of the more common methods for individually identifying research rodents is ear tagging (Figure A). Tags with stamped or laser etched numbering and lettering (available through National Band & Tag Company or Kent Scientific Corporation) are typically composed of monel, a nickel-copper alloy with excellent corrosion resistance, strength and ductility. Although ear tags can sometimes fall or tear out, they are inexpensive as well as quick and easy to apply. Nonetheless, investigative staff should be aware of potential inflammatory and neoplastic conditions which can develop at or near ear tag sites in mice and rats. Auricular chondritis, also known as auricular chondropathy, has been reported as a spontaneous condition associated with ear tags in various strains and ages of rats and mice. It is characterized grossly

by nodular to diffuse thickening of the pinnae as early as 3-5 weeks post-tagging. Histologically, lesions consist of granulomatous inflammation, chondrolysis, formation of new cartilaginous nodules composed of hyaline versus normal elastic cartilage, and osseous metaplasia (Figure B). Interestingly, although animals are tagged unilaterally, lesions can occur bilaterally with variable incidences. Auricular chondritis in rodents shares some clinical and pathologic similarities with relapsing polychondritis in humans. Affected humans develop episodic inflammation of cartilaginous structures throughout the body, typically due to the formation of autoantibodies against collagens type II, IX or X. Rats inoculated with incomplete Freund's adjuvant and collagen type II, as well as various

Cont. on pg. 4

Diamonds in the rough- the GEM database!

We have established a web-accessible database for all Genetically Engineered Mice, maintained at WCMC, MSKCC, and RU to 1) Assist investigators in identifying sources of genetically engineered mouse lines of interest within the local research communities thus helping to avoid on-site production and/or importation from outside institutions, and 2) Document phenotypic abnormalities, which will aid the husbandry and clinical vet staff in monitoring the overall health and well being of the animals.

We hope this will be a resource to investigators searching for mouse models exhibiting a specific phenotype. Please use the link on our website to access the online form for providing information for each genetically engineered mouse line already characterized and used in your laboratory. Contact RARC at 646-888-2400 if you identify a line in the database in which you have interest.

Education & Quality Assurance

The Education & Quality Assurance (EQA) Specialist is the "go to" member of the EQA team for all of your training needs. The EQAS is the first person you will meet at RARC's New Investigator Orientation session and then on numerous and varied other occasions throughout your work experience with animals at this institution.

If you find that you are having difficulty mastering a specific technique or just need some practice animals to hone your skills contact your EQAS. RARC maintains a protocol to allow for such occasions and we can usually meet your needs within 24- 48 hours.

For more information on this program or to schedule a special session please call 212-746-1369, or contact us at rarc_ega@mskcc.org

TRAINING SESSIONS: MARCH - APRIL 2008

RARC Orientation

Tuesday, 3/4/08, 2:00-4:00

Thursday, 3/13/08, 10:00-12:00

Tuesday, 4/2/08, 2:00-4:00

Thursday, 4/17/08, 10:00-12:00

Xenograft Training

Monday, 3/10/08, 2:30-3:30

Monday, 4/21/08, 2:30-3:30

Hazardous Materials Training

Wednesday, 3/26/08, 2:45-3:45

Wednesday, 4/23/08, 2:45-3:45

Rodent Surgery

Friday, 3/7/08, 10:30-12:00, wet lab

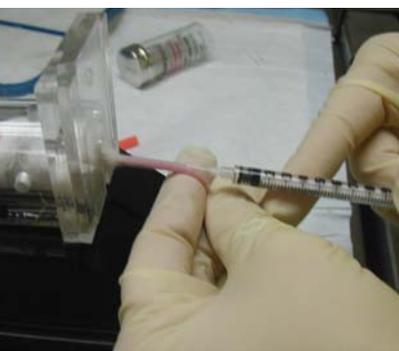
Monday, 3/17/08, 10:30-11:30

Friday, 4/4/08, 10:30-12:00, wet lab

Monday, 4/21/08, 10:30-11:30

Rodent Breeding

Wednesday, 4/23/08, 10:00-11:30



EQA Specialists provide numerous "Special Technique" sessions such as rodent gavage, blood collection techniques and mouse IV tail vein injection, shown above, to name just a few.

Fur Mites, Cont. from pg. 1

have only three pairs of legs and are not sexually mature. Second stage nymphs finally molt to become sexually mature adults with 4 pairs of legs. The entire life cycle lasts 8 days for *Myocoptes* and 23 days for *Myobia*.

In many cases affected animals do not show clinical signs. Clinical disease may occur in select strains of mice or if the parasite burden is very large. Some mouse strains may also have an allergic reaction. Mice develop pruritus and secondary to scratching, hair loss and ulcerative dermatitis. The latter may become severe enough to require euthanasia. Like with other infectious agents, clinically normal mite-infested animals may have an altered physiologic state that potentially could interfere with the research in which they are used. Adverse effects of fur mites have not been extensively studied; however, it is well documented that affected mice exhibit elevated IgE levels and some immunological responses are altered.

As most of you know, we experienced an outbreak of both *Myocoptes musculus* and *Myobia musculi* in a limited number of

rooms at WCMC in late 2006. Many other facilities in the country were affected at around the same time and we now believe that the parasites came in through an importation from an atypical source. In retrospect, we have found that our diagnostic and quarantine procedures, at the time were considered appropriate according to industry standards, were inadequate. We have modified our procedures accordingly. We believe these improvements are effective as we have identified two groups of infested animals where the sending institution had reported the colony to be mite-free. In both instances, the sending institution was able to confirm the finding after they were informed. In addition, we have been reluctant in the past to treat mice in quarantine as the efficacy of the drugs employed yielded inconsistent results. However, as the prevalence of mite infestations have grown worldwide and recent studies, including our own, have demonstrated the effectiveness of newer anthelmintics, we now routinely treat all incoming animals prophylactically.

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Technique Update**Submandibular Venipuncture**

Why should your lab consider submandibular venipuncture as an alternative to retro-orbital bleeding? This procedure is safe and there are far fewer potential complications. Mice that were sacrificed one week following submandibular bleeding had no gross evidence of the procedure having been performed. The procedure is easy to learn and works consistently. And, unlike retro-orbital bleeding, mice do not have to be anesthetized for blood collection. The recovery is quick, and the same animal can be bled multiple times. As a result, learning and perfecting this technique can significantly increase your lab's bleeding efficiency.

How is submandibular venipuncture performed? The correct location for the puncture is slightly behind the end point of the jaw bone. Once located, the lancet is used and the blood sample collected. Light pressure is applied following the procedure to ensure hemostasis. More than one sample can safely be collected on the same mouse by alternating sides.

However, please keep in mind that the amount of blood collected over a two week period should still not exceed 1% of the total body weight of the mouse (10mls/Kg). So, if you have a 20 gram mouse, the amount of blood that you are sampling should not exceed 0.2 mls.

If your lab is interested in being trained on the technique, please contact Rochelle Torrence at rot2003@med.cornell.edu or (646) 888-2418.

NEW A better way to draw blood from small animals

Goldenrod™
ANIMAL LANCET®

For taking
Submandibular Blood Samples

Submandibular
There is a vascular bundle located at the rear of the Jaw Bone providing a convenient and consistent source of blood

Ear Tags, cont. from pg. 2

genetically engineered mice, more closely resemble the condition in humans due to the concurrent development of polyarthritis and auricular chondritis.

Ear tags, similar to other metal surgical implants, have been associated with the development of neoplasms in rodents. Two distinct groups of Wistar rats developed tumors at ear tag sites with incidences up to 8.3%. The spectrum of neoplasms reported included various osteosarcomas as well as a histocytic sarcoma and a cutaneous papilloma. Metastasis to regional lymph nodes was noted with 5/14 tumors. Squamous cells carcinomas at ear tag sites have also been reported in 9% of aged FVB/N mice with metastasis to a kidney noted with 1/14 tumors.

The exact pathogenesis of the inflammation and neoplasia at ear tag sites is unknown; however, it likely

involves release of metal ions from the tags. Although monel is reported to be a nickel-copper alloy, tags have been shown to also include iron, manganese +/- chromium when metal content was actually analyzed. Iron and copper are known suppliers of reactive oxygen species which can induce inflammation and fibrosis. Subsequent oxidation of collagen results in brittle fibrils prone to mechanical failure. Degeneration of collagen proteins can serve as a nidus for the formation of autoantibodies and subsequent involvement of untagged ears. The development of neoplasms seems to be related directly to the presence of ear tags since they only occurred in tagged ears. However, persistent inflammation and fibrosis could also be synergistic. References are available upon request to lcp@mskcc.org or (646) 888-2422.

Fur Mites, cont. from pg. 3

We have treated mice in the affected WCMC rooms with a treatment regime that was published recently and which we modified to reduce side effects. The treatment regime used three drugs (selamectin, fipronil and amitraz) in succession and was completed in February of 2007. After 12 months of intensive follow-up treatment, we are now able to declare that the treatment was effective and that the WCMC colony is again mite free.

We have also confirmed that our sentinel program is highly effective in detecting mites as they are transferred to sentinels during weekly soiled bedding transfer. Animals from known mite-infested colonies and animals identified during quarantine to be mite-infested are being rederived using a combination of anthelmintic treatment and cross-fostering of neonates. Neonates are resistant to mite infestation until they develop hair at 3-4 days of age.

*Be on the lookout for
the 2008*

*Year of the Rat
RARC User's Guide*



Research Animal Resource Center



User's Guide

March & April
Investigator
Training
Seminars

All are
welcomed to
attend!

UPCOMING SEMINARS

WHY MURINE QUARANTINE MATTERS!

Speaker: Joseph Scott, VMD, Associate Director,
Rockefeller University, CBC

Place: Rockefeller University

Date: Wednesday, March 19

Time: 2:00 - 3:30 PM

Place: Rm. 110, ROCKEFELLER RESEARCH
BUILDING, Rockefeller University campus

**COMMON MURINE PATHOGENS AND THEIR
POTENTIAL EFFECTS ON RESEARCH**

Speaker: Julie S. White, DVM, DACVP,
Comparative Pathologist, Laboratory of
Comparative Pathology & Genetically Engineered
Mouse Phenotyping Service

Date: Wednesday, April 16

Time: 2:00 - 3:30 PM

Please visit us on the WCMC intranet -

<http://intranet.med.cornell.edu/research/rarc/index.html>

About our department-

Office of the Director: (646) 888-2400

Office of the Manager: (212) 746-1023

Administration & Information Services: (646) 888-2406

Biosecurity: (646) 888-2403

Education & Quality Assurance: (212) 746-1077

Husbandry & Operations: (646) 888-2413

Laboratory of Comparative Pathology: (646) 888-2422

Veterinary Services: (212) 746-1167

EMERGENCY: (212) 746-1022

