

ILAR Journal Review 2009

Issues 2008, Vol 49 (1-4)

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May 7, 2009

49(1) Noninvasive Bioimaging of Laboratory Animals

1. What special health screening must occur for staff working in an imaging facility with an MRI? What is the recommended magnetic field limit for these people?
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1. Answer: People with cardiac pacemakers, cochlear implants, drug pumps, or other metallic implants such as shrapnel should not work in close proximity to magnets. Pp. 12
The FDA recommended limit for magnet exposure for these at risk people is 5 Gauss.
-

49 (1)

2. What types of gasses are used in cooling magnets? What special considerations should be made for accommodating their use in the imaging facility?
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49 (1)

2. Answer:

Liquid helium and liquid nitrogen

Facility accommodation:

- storage space
 - sensors for temperature, humidity and oxygen (due to potential asphyxiation from the inert gases)
-

49 (1)

3. Give the name of the following abbreviations: SPECT, MRI, PET, CT

3. Answer: pp. 17

- SPECT: single photon emission computed tomography
 - CT: computed tomography
 - PET: Position emission tomography
 - MRI: magnetic resonance imaging
-

49 (1)

4. Name some factors in preparing an animal for imaging that can affect the study outcome.
-

4. Answer:

- Strain
 - Gender
 - Fed vs. Fasted
 - Circadian Rhythm
 - Anesthetic
-

49 (1)

5. Define gating.

49 (1)

6. Answer:

Gating is a process that enables the capture of images at time points triggered by specific events, thus eliminating motion artifacts (cardiac and respiratory cycles). Pp. 13 and 22, 28

49(1)

7. What is the resting heart rate of a mouse? Rat?

49(1)

7. Answer:

Rat: 300 per minute

Mouse: 500 per minute

49(1)

8. What are the three ultrasound imaging modes?

49(1)

8. Answer

B mode

M mode

Doppler

49(1)

9. What type of energy is used for the following imaging modalities:

- Ultrasound
 - MicroCT
 - MRI
-

49(1)

9. Answer

- Ultrasound: sound waves
 - MicroCT: ionizing radiation
 - MRI: radiofrequency pulse
-

49(1)

10. What is 4-D imaging?

49(1)

10. Answer:

4-D imaging is 3-D images that change over time (i.e.. A beating heart)

pp. 27

49(1)

11. MRM? What are two methods that are used to minimize signal to noise ratio in this methodology?

49(1)

11. Answer:

- Magnetic Resonance Microscopy
 - Methods to overcome SNR:
 - Optimization of the RF (radio frequency) coil
 - longer image acquisition times
-

49(1)

12. Briefly describe the principles of PET imaging.

49(1)

12. Answer:

PET imaging systems detect the 511-kiloelectron volt annihilation photons generated as a result of positron decay by unstable proton-rich radionuclides. Such nuclei achieve stability either by electron capture or by emission of a positron. Positrons emitted in this decay process are released with kinetic energy that follows a distribution that is characteristic of each radionuclide.

49(1)

13.

- What are the principles of multiphoton microscopy?
 - What are the advantages to using this imaging modality over other imaging methodologies?
-

49(1)

13. Answer:

- This technique depends on the simultaneous absorption of two infrared photons by a fluorophore, resulting in spatially localized fluorescence excitation, is capable of collecting high-resolution (0.4 micron) fluorescence images hundreds of microns into the tissue.
-

49(1)

- This methodology is limited to surface imaging. Multiphoton microscopy provides in vivo images in living animals with subcellular resolution (much higher than other imaging modalities). It is often applied after surgical alteration for tissue exposure. In vivo systems can be examined with this technique.
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49(1)

14. Describe the difference between bioluminescent and fluorescent imaging systems.

(49)1

14. Answer:

Bioluminescent markers are typically luciferase genes coupled with luciferin substrates as reporters. The light is emitted by the luciferase marker. **Fluorescence** based imaging requires an external light to stimulate the emission of the light from the probe. Pp. 79

49(1)

15. List some routine applications for bioluminescence technologies in biomedical research.
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49(1)

15. Answer:

- Cancer: tumor location, growth
 - Gene therapy: targeting vectors
 - Cell therapy: migration of adoptively transferred cells
 - Infection: Clearance of pathogens
-

49(2)

16. What 4 major viral pathogens form the basis for an SPF macaque colony? What other organism is typically considered in an SPF colony?

General comment:

The 49(2) is full of general health information for primates. I recommend being soundly familiar with primate quarantine, OHS practices, viral diseases and zoonosis of primates. The following questions are my interpretation of the value or new material in the articles.

49(2)

16. Answer:

- Simian Type D Retrovirus (SRV)
 - Simian Immunodeficiency Virus (SIV)
 - Simian T Cell
Lymphotropic/Leukemia Virus (STLV)
 - Cercopithecine Herpesvirus 1* (CHV-1)
 - Mycobacterium tuberculosis pp. 137*
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49(2)

17. What are two newer assays used to augment the skin TB test? What is the most effective testing regimen to ensure colonies are *M. tb* free?

49(2)

1. Answer:
 2. Whole blood in vitro interferon gamma assay
 3. Rapid lateral flow test consisting of a combination of *M. tb* specific proteins
-
- The most effective testing regimen
 - Routine TB testing
 - New assays
 - Traditional diagnostics (thoracic radiographs, gastric aspirate, BAL culture)

49(2)

18. What testing strategy should be applied once an macaque has been potentially exposed to SRV?

49(2)

18. Answer:

Animals should be tested 6-8 weeks after possible exposure b/c a measurable immune response is mounted within 6 weeks of exposure.

pp. 138

49(2)

19. Why is it important for SRV screening programs to incorporate both serology and direct virus testing?

49(2)

19. Answer:

Because there are low-antibody, high virus load animals that would be missed by serology alone.

49(2)

20. Describe the health screens that should be included in a primary quarantine program for NHP.

49(2)

20. Answer:

- 3 consecutive negative TB skin tests at 2 week intervals (5 if with positive or suspicious animals in quarantine)
- Isolation of arriving animals for 31 days with daily obs
- PE
- Baseline blood values
- Parasitology exam
- Rectal culture

pp. 152

49(2)

21. What are the two most common methodologies used for serologic screening for disease? How are they different? What test(s) are usually used for confirmation of results?

49(2)

21. Answer:

Screening: ELISA (enzyme-linked immunosorbent assay) and MFIA (multiplexed fluorometric immunoassay)

ELISA is singleplexed. MFIA is multiplexed.

Confirmation: IFA, Western Blot, PCR
pp. 159

49(2)

22. Label A-F

		Infection status		
		Infected	Uninfected	
Test status	Positive	A	B	Positive predictive value E
	Negative	C	D	Negative predictive value F
		Diagnostic sensitivity $DSn = \frac{TP}{TP + FN}$	Diagnostic specificity $DSp = \frac{TN}{TN + FP}$	

49(2)

		Infection status		
		Infected	Uninfected	
Test status	Positive	A TP	B FP	Positive predictive value E $PPV = \frac{TP}{TP + FP}$
	Negative	C FN	D TN	Negative predictive value F $NPV = \frac{TN}{FN + TN}$
		Diagnostic sensitivity $DSn = \frac{TP}{TP + FN}$	Diagnostic specificity $DSp = \frac{TN}{TN + FP}$	

49(2)

23.

_____ is a measure of the agreement between a measured test value and the expected or “true” status of any individual serum sample.

_____ is a measure of the reproducibility of a serodiagnostic test result and often is used as an indicator of the amount of random error in the system

49(2)

23. Answer:

Accuracy

Precision

pp. 163

49(2)

24. Describe the proper application and evaluation of the tuberculin skin test.

49(2)

24. Answer:

- Injection of .1 ml of mammalian old tuberculin at the eyelid or a demarcated site on the abdomen
- Reactions measured at 24, 48, 72 hours
- Scoring system: 0-5 with 0,1,2 considered negative, 3 considered suspect and 4, 5 considered positive

pp. 171

49(2)

25. What species of macaque is the natural host for SIV? What is the significance of this virus in animal housing paradigms?

49(2)

25. Answer:

- African NHPs are the natural host for SIV. Asian primates do not harbor SIV in their habitat. Infection is asymptomatic in the African animals whereas in Asian animals it induces a lentiviral inflammatory disease and immunosuppressive disease.
- The significance is in consideration of cohousing Asian and African animals.

Pp. 180

49(2)

26. What organisms are involved with MAC? What is the significance of this complex?

49(2)

26. Answer:

Mycobacterium avium complex is composed of *M. avium* and *M. intracellulare* and is the most common disseminated bacterial infection in both human and simian AIDS.

pp.198

49(2)

27. What is NOMA?

49(2)

27. Answer:

NOMA is a form of rapidly progressive necrotizing stomatitis and osteomyelitis that has been described in macaques infected with SIV and SRV. It is believed to be associated with a mixed population of anaerobes and spirochetes.

pp. 200

49(2)

28. What are the most common viral complications of immunosuppression after organ transplantation in primates?

49(2)

28. Answer:

CMV

BK polyomavirus

EBV

pp. 211

49(2)

29. What are the two most common endemic bacterial gastrointestinal pathogens in NHPs that result in disease after transplantation?

49(2)

28. Answer:

Shigella and *Campylobacter jejuni*

Other mentionables: *E. coli*,
Pseudomonas aeruginosa, *Yersinia*,
Samonella. Pp. 211

49(20)

30. What classes of virus constitute Hepatitis A-G? Which animal is susceptible to infection with Hepatitis C virus?

49(2)

30. Answer:

Hep A: Picornaviridae

Hep B: Hepadnaviridae

Hep C: Flaviviridae

Hep E: Hepeviridae

Hep G: Flaviviridae

Chimpanzee

49(3)

31. According to the survey taken by Cartier, what are the four most common viral and bacterial mouse disease?

49(3)

31. Answer:

Viral:

MPV, MVM, MHV, EDIM

Bacterial:

*P. pneumonia, Helicobacter, Staph,
Pseudomonas*

49(3)

32. What is the best tissue to submit for PCR evaluation for MPV? What other tissues harbor this infection?

49(3)

32. Answer:

The best tissue for submittal are the mesenteric lymph nodes.

The virus may also live in other lymphoid organs, and targets endothelial, lymphoid and Kupffer cells. Pp. 279

49(3)

33. What is the best method for detection of *Helicobacter* spp.? Why do the test results typically report *Helicobacter* spp. results and then speciate the helicobacters separately?

49(3)

33. Answer:

The most sensitive and specific tests are PCR based assays. A single generic test for the detection of several helicobacters is performed. Once a positive test is identified, secondary PCR test are run to identify the species of helicobacter.

pp. 280

49(3)

34. What are the histologic lesions created by MNV? What population is most vulnerable to disease?

49(3)

34. Answer:

The most vulnerable population are immune deficient animals.

The lesions found in these animals included: hepatitis, interstitial pneumonia, and peritonitis

pp. 283

49(3)

35. True/False The etiologic agent associated with Rat Respiratory Virus has been characterized and effective serologic assays have been developed for it's detection.

49(3)

35. Answer:

False. The agent is yet unidentified and the best diagnostic test is histologic identification of lesions in the lungs.

49(3)

36. Are the lifecycles of *A. tetraptera* and *Syphacia* the same? How are they different?

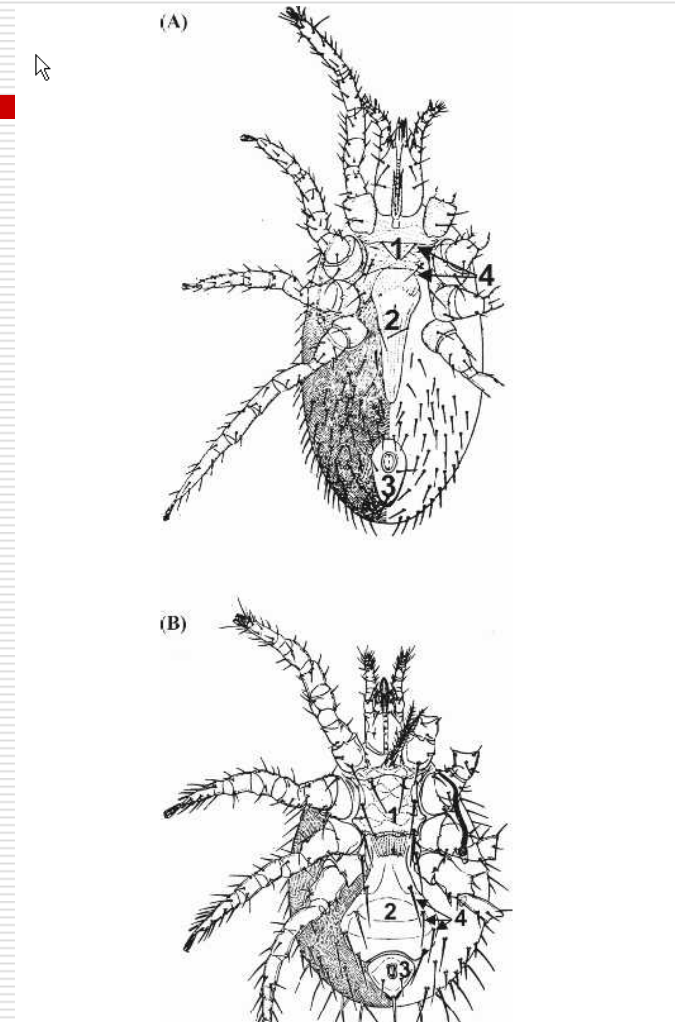
49(3)

36. Answer:

	<i>A. tetraptera</i>	<i>Syphacia</i>
Embryonate	5 d	5-20 h
Time to hatch		
in the intestine	2-6 h	2 h
# eggs laid/female	17	350-550
Life cycle	24 d	12 d (S. obveata) 7-8 d (S. muris)

49(3)

37. Name these mites.

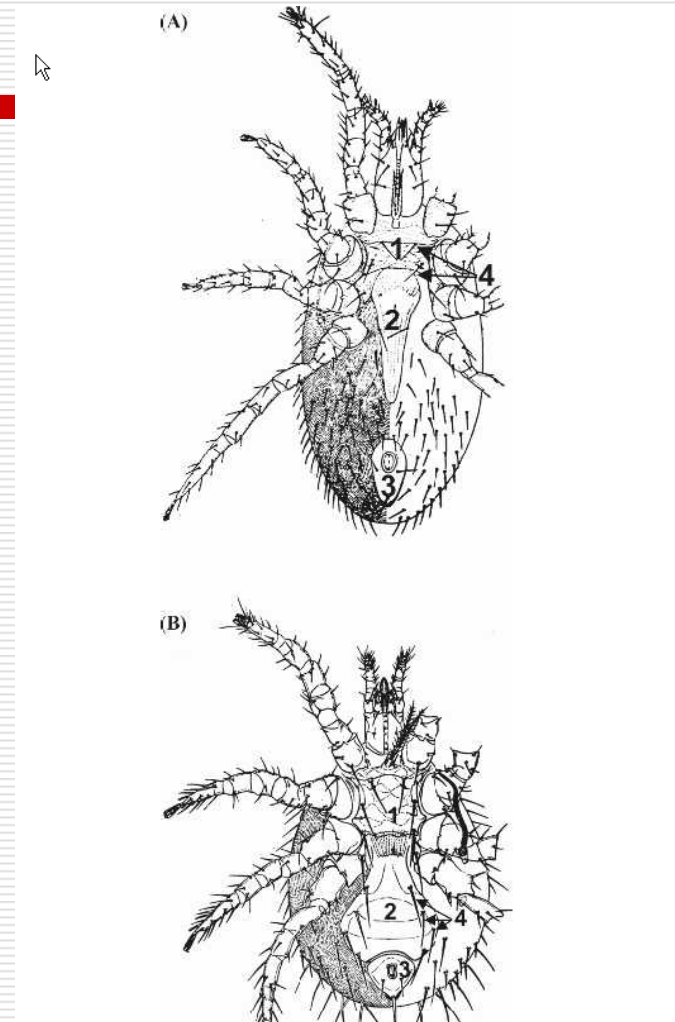


49(3)

37. Answer:

A. *Ornithonyssus bacoti*

B. *Laelaps echidnina*



49(3)

38. What type of mouse is most appropriate as a sentinel animal?

49(3)

38. Answer:

Outbred stocks

- less expensive
- susceptible to infection but resistant to disease (early, robust seroconversion)

Note:

- C57Bl resistant to MPV
- DBA/2 lethal infection with Sendi prior to seroconversion

pp. 319

49(3)

39. What considerations should be made to age and replacement of sentinels?

49(3)

39. Answer:

Animals should arrive early enough to be sensitive to MPV and mouse rotovirus. Pp. 319

49(3)

40. Name some biologics that are potential sources of rodent pathogens.

49(3)

40. Answer:

Stem cells

Hybridomas

Cancer cell lines

Bacteria

Serum

Basement membrane
matrix

Hormones

Growth factors

Antibodies

DNA/RNA

Mouse gametes

You name it.....

49(4)

41. What would be signs of a weak AV?

49(4)

41. Answer:

- AV rarely on site
- Inadequate review of proposed animal activities that are on the agenda for discussion
- Investigator maintained animal colonies
- Persistent physical plant problems
- High morbidity and mortality
- Poor sanitation practices

Pp. 376

49(4)

42. What would be indications of an overzealous IACUC?

49(4)

42. Answer:

- Ignoring the AV during protocol review
 - Overriding the veterinarian's recommendations or suggestions about drug doses or choices
 - Justification for a physical method of euthanasia w/o anesthesia or sedation
 - Need for asepsis during a proposed procedure
 - Proposed justification for not recommended forms of husbandry
 - Dictatorial chairperson
-

49(4)

43. What four critical leadership qualities does the IO bring to the position?

49(4)

43. Answer:

1. Vision
2. A commitment to quality and integrity
3. Strong planning and resource development
4. Accountability

Pp. 379

49(4)

45. In what way does a well-designed and efficiently run post approval monitoring program contribute or benefit research?

49(4)

45. Answer:

- the *institution and administration*, by minimizing the possibility of noncompliance, which can negatively affect the research enterprise
- the *researcher*, by helping them avoid noncompliance, which can drain time, energy and resources from their primary responsibilities
- the *animals*, which receive better treatment during all phase of research
- the *science*, which will be more consistent and of higher quality

Pp. 394

49(4)

46. What is the most frequent concern expressed by USDA inspectors about animal care activities?

49(4)

46. Answer:

Inadequate post approval compliance
monitoring

49(4)

47. List 10 characteristics of a successful post approval compliance monitoring program (PAM).
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49(4)

47. Answer

1. The institutional leadership, regulatory agencies and funding agencies have confidence in the institution's self-management.
 2. The IACUC provides clear guidance and directions for PAM.
 3. The PAM program has the support of the institutional official and IACUC.
 4. The PAM program focus is on evidence of good performance with praise for such performance when found.
 5. 5. The PAM program identifies problems while they are small and facilitates correction.
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49(4) continued answer...

6. The PAM staff are viewed as partners
 7. The PAM staff are known as good observers, fair, and consistent.
 8. The PAM staff foster communication between the IACUC and research community
 9. The research and husbandry staff self-report animal incidences.
 10. Corrective actions are viewed as positive educational opportunities.
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