

WVU IACUC Guidelines: Humane Care of Aging Animals

Purpose

There may be circumstances in which geriatric animals are maintained across campus. The IACUC recognizes that as animals age they may become prone to a variety of age-related morbidities that would require additional oversight to ensure appropriate animal welfare is maintained. The purpose of this document is to provide recommendations for monitoring, supportive care, and humane endpoints related to aging animals across campus.

Definitions

Aging- Process of growing old; characterized by progressive declines in organ systems and increased propensity to develop neoplastic disease and chronic degenerative diseases.

Geriatric- Animals which have completed 80% of their anticipated lifespan.

Frailty- High state of vulnerability to poor health outcomes among animals of the same age.

Quality of Life- Standard of overall animal well-being that can be used to assist with euthanasia decisions.

Humane Endpoint- The point at which pain and distress in an experimental animal is prevented, terminated, or relieved.

Guidelines

- 1) Geriatric animals may be required as part of a research protocol, or animals could be maintained for an extended period as part of a research or teaching protocol.
- 2) Lifespan of each species should be considered when evaluating and developing long-term veterinary care plans for animals on campus. (*see Appendix 3*)
- 3) Working with geriatric animals may require additional considerations, such as more frequent monitoring and treatment of age-related morbidity.
- 4) Every effort should be made to determine clear, species-appropriate humane endpoints, quality of life assessments (depending on circumstances) and euthanasia plans for these animals/colonies.
- 5) **Rodent Aging Studies-** Studies that require the maintenance of aged animals to meet research objectives.
 - a. Aged rodents may present with clinical signs commonly associated with illness in younger animals (hunched, unkempt coat, less active, rounded appearance), but can be typical in aged animals. These clinical signs should be considered in the context of the animal's overall appearance and condition to avoid removing animals early from study due to non-terminal conditions.

- b. There may be occasions when animals (due to age) do not present with consistent clinical signs to allow for an established humane endpoint prior to reaching a moribund state.

End of life signs include:

- non-responsiveness to being touched
- cold body temperature to the touch
- slow or labored respiration

Animals **must** be culled if these conditions are noted, but every effort should be made to euthanize prior to this point unless scientifically justified and necessary.

- c. Most common age-related conditions in rodents (veterinary staff **must** be consulted for treatment recommendations):

- RECTAL PROLAPSE

Recommended endpoints: prolapse > 7 mm diameter and/or > 4 mm of protrusion, or if prolapsed tissue is ulcerated, dry, necrotic (dark), or is bleeding.

- ALOPECIA AND DERMATITIS

Recommended endpoints: single lesion > 2 cm in diameter, or multiple lesions reaching a total diameter of > 2 cm. Animals will also be euthanized if a lesion is present that impairs eating, drinking, or locomotion.

- OCULAR LESIONS

Recommended endpoint: Animals with apparently painful or irritating conditions that do not resolve with treatment.

- MASSES

See IACUC Policy: Tumor Development Endpoints for Euthanasia in Rodents

- d. Monitoring

- Animals should be monitored at a frequency necessary to maintain animal welfare and allow for euthanasia prior to sudden death. Office of Laboratory Animal Resources (OLAR) husbandry staff changes cage every 1-2 weeks. Aged animals may require more frequent monitoring during this interim period. Contact animal care staff in your housing area regarding any forms to submit (e.g. Special Care) or record keeping necessary.
- Monitoring frequency is based on animals' condition, age, and risk of adverse outcomes. As the age increases, monitoring frequency should increase respectively to reduce incidence of finding animals moribund or dead.
- Monitoring should include:
 - a) Overall condition (hunched, unkept, urine stained)
 - b) Behavior (alert, active, not isolated)
 - c) Signs of illness
 - d) Body Weight (endpoint > 20% weight loss from baseline)
 - e) Hydration assessment (endpoint: chronic dehydration that does not respond to medical intervention)

f) Body Condition Score (BCS) (endpoint < 2/5) *See IACUC Policy: Pain and Distress Recognition – Humane Endpoints, for a mouse BCS chart*

- The Clinical Frailty Index can be used to determine need for increased monitoring and impending mortality. A decrease in body weight and body surface temperature have been observed during the week leading up to death. (*see Appendices 1 and 2*)

e. Supportive Care

- Nutritional support is recommended for animals on aged studies. This can be initiated by laboratory or veterinary staff.
 - a) Soft Chow (rodent diet mixed with water)
 - b) Diet Gel (Clear H2O®)
 - c) Bacon Softies (Bio-Serv®)
 - d) Liquid Rodent Diet (Bio-Serv®)
- Fluid Support
 - a) Administration described in protocol or based on veterinary recommendations.
 - b) Nutritional support that provides oral rehydration (soft chow, diet gel, liquid diet).
- Soft Bedding
- Food on the cage floor or in crock

6) **Teaching or research protocols that maintain animals for extended periods of time** (animals may reach advanced age during study, but age is not a component of the research or teaching goals).

a. As animals approach advanced age, a group that includes veterinarians, husbandry staff, and research staff should meet and develop a monitoring and management plan for these animals.

b. The plan should consider:

- Ongoing health concerns and how those will be monitored and managed.
- Quality of life assessment: including parameters that can be used to determine if there is a change in well-being. This should be based on knowledge of the species and individual animals baseline behavior.
 - a) Normal intake/output
 - b) Activity
 - c) Social Interaction
 - d) Mental wellbeing (signs of stress, depressed/quiet)
- Supportive care that should be initiated.
- Frequency and parameters to monitor.

Appendix 1. Mouse Frailty Assessment Form[©] (see References, #4)

Date: _____

Mouse #: _____ Date of Birth: _____ Sex: F M
 Body weight (g): _____ Body surface temperature (°C): _____

Rating: 0 = absent 0.5 = mild 1 = severe

➤ Integument:				NOTES:
❖ Alopecia	0	0.5	1	_____
❖ Loss of fur colour	0	0.5	1	_____
❖ Dermatitis	0	0.5	1	_____
❖ Loss of whiskers	0	0.5	1	_____
❖ Coat condition	0	0.5	1	_____
➤ Physical/Musculoskeletal:				
❖ Tumours	0	0.5	1	_____
❖ Distended abdomen	0	0.5	1	_____
❖ Kyphosis	0	0.5	1	_____
❖ Tail stiffening	0	0.5	1	_____
❖ Gait disorders	0	0.5	1	_____
❖ Tremor	0	0.5	1	_____
❖ Forelimb grip strength	0	0.5	1	_____
❖ Body condition score	0	0.5	1	_____
➤ Vestibulocochlear/Auditory:				
❖ Vestibular disturbance	0	0.5	1	_____
❖ Hearing loss	0	0.5	1	_____
➤ Ocular/Nasal:				
❖ Cataracts	0	0.5	1	_____
❖ Corneal opacity	0	0.5	1	_____
❖ Eye discharge/swelling	0	0.5	1	_____
❖ Microphthalmia	0	0.5	1	_____
❖ Vision loss	0	0.5	1	_____
❖ Menace reflex	0	0.5	1	_____
❖ Nasal discharge	0	0.5	1	_____
➤ Digestive/Urogenital:				
❖ Malocclusions	0	0.5	1	_____
❖ Rectal prolapse	0	0.5	1	_____
❖ Vaginal/uterine/penile prolapse	0	0.5	1	_____
❖ Diarrhoea	0	0.5	1	_____
➤ Respiratory system:				
❖ Breathing rate/depth	0	0.5	1	_____
➤ Discomfort:				
❖ Mouse Grimace Scale	0	0.5	1	_____
❖ Piloerection	0	0.5	1	_____
❖ Temperature score: _____				
❖ Body weight score: _____				

Total Score/ Max Score: _____

© Susan E. Howlett, 2013

Appendix 2. Clinical signs of Aging in Mice (*see References #4*)

System	Parameter	Potential Deficits
Integument		
	Alopecia	Hair loss due to age-related balding and/or barbering (fur trimming)
	Loss of fur colour	Change in fur colour from black to grey or brown
	Dermatitis	Inflammation, overgrooming, barbering or scratching causing skin erosion. Can result in open sores anywhere on the body
	Loss of whiskers	Loss of vibrissae (whiskers) due to aging and/or whisker trimming
	Coat condition	Ruffled fur and/or matted fur. Ungroomed appearance. Coat does not look smooth, sleek, and shiny
Physical/ musculoskeletal		
	Tumors	Development of tumors or masses anywhere on the body
	Distended abdomen	Enlarged abdomen. May be due to tumor growth, organ enlargement, or intraperitoneal fluid accumulation
	Kyphosis	Exaggerated outward curvature of the lower cervical/thoracic vertebral column. Hunched back or posture
	Tail stiffening	Tail appears stiff, even when animal is moving in the cage. Tail does not wrap freely when stroked
	Gait disorders	Lack of coordination in movement including hopping, wobbling, or uncoordinated gait. Wide stance. Circling or weakness
	Tremor	Involuntary shaking at rest or during movement
	Forelimb grip strength	A decline in forelimb grip strength
	Body condition score	Visual signs of muscle wasting or obesity based on the amount of flesh covering bony protuberances
Vestibulocochlear/ auditory		
	Vestibular disturbance	Disruption in the ability to perceive motion and gravity. Reflected in problems with balance, orientation, and acceleration
	Hearing loss	Failure to respond to sudden sound (e.g., clicker) indicative of hearing loss or impairment
Ocular/nasal		
	Cataracts	Clouding of the lens of the eye. An opaque spot in the center of the eye
	Corneal opacity	Development of white spots on the cornea. Cloudy cornea
	Eye discharge/ swelling	Eyes are swollen or bulging (exophthalmia). They may exhibit abnormal secretions and/or crusting
	Microphthalmia	Eyes are small and/or sunken. May involve one or both eyes
	Vision loss	Vision loss, indicated by failure to reach toward the ground when lowered by the tail
	Menace reflex	Rapid eye blink and closure of the palpebral fissure in response to a nontactile visual threat to the eye. Measures the integrity of the entire visual pathway including cortical components
	Nasal discharge	Signs of abnormal discharge from the nares
Digestive/urogenital		
	Malocclusions	Incisor teeth are uneven or overgrown. Top teeth grow back into the roof of the mouth or bottom teeth are long and easily seen
	Rectal prolapse	Protrusion of the rectum just below the tail
	Vaginal/uterine/ penile prolapse	Vagina or uterus protrudes through the vagina and vulva. Penis cannot reenter the penile sheath
	Diarrhea	Feces on the walls of the home cage. Bedding adheres to feces in cage. Feces, blood, or bedding around the rectum
Respiratory		
	Breathing rate/depth	Difficulty breathing (dyspnea), pulmonary congestion (rales), and/or rapid breathing (tachypnea)
Discomfort		
	Mouse Grimace Scale	Measure of pain/discomfort based on facial expression. Assessment of five facial features: orbital tightening, nose bulge, cheek bulge, ear position (drawn back), or whisker change (either backward or forward)
	Piloerection	Involuntary bristling of the fur due to sympathetic nervous system activation
Other		
	Temperature	Increase or decrease in body temperature
	Weight	Increase or decrease in body weight

Appendix 3. Average lifespan of Species used in Teaching and Research

Species	Average Lifespan*	Comments
Mouse	18-36 months	After 24 months survivorship markedly drops off; 50% survivorship ~28 months of age
Rat	2.5-3.5 years	
Rabbit (New Zealand white)	5-8 years	
Pigeon	10-15 years	
Zebrafish	2-3 years	
Sheep	10-12 years	
Cattle	15-20 years	
Horse	25-30 years	
Donkey	27-40 years	
Llama	15-25 years	
Poultry	5-10 years	
Swine	15-20 years	

*Life expectancy may vary depending on stock, strain, and breed.

Appendix 4. Health Concerns in Aging Agricultural Animals (*see References, #5*)

Species	Reason for culling	Potential age-related cause
Cattle	Udder health Low fertility Low production	Immune system Loss of reproductive function
Pig	Low fertility Leg weakness	Reproductive tract pathology Osteochondrosis
Sheep	Low fertility Disease susceptibility Udder health Tooth wear and loss	Loss of reproductive function Immune system Wear and tear
Goat	Udder disorder Locomotor disorder Digestive disorder Reproductive disorder emaciation	Immune system Wear and tear Loss of reproductive function

Appendix 5. Behavioral Questions to Consider for Quality of Life Assessment

(see References, #1)

- 1) What makes this animal unique? What behaviors do you think of when you think of this animal?
- 2) How do other animals treat this animal?
- 3) Describe this animal's temperament?
- 4) Does the animal participate in training activities? How does the animal perform during training? Are they responsive and readily participate? Not interested in training?
- 5) If this animal takes medication or receives treatment, what is the normal procedure and response upon giving the medication or treatment? Does the animal readily come up to take medication or receive treatment? Do the other group members interfere during this process?
- 6) How does this animal deal with potentially stressful situations like shifting, restraint, anesthetization, isolation, and introductions back into social group or to new social partners?
- 7) What is the normal activity level of this animal?
- 8) What are the normal eating patterns and/or preferences of this animal?
- 9) How does this animal typically use its enclosure? Do they have a preferred or typical sleeping site or posture?
- 10) Does this animal display any behavioral indicators of pain (e.g. wincing, crying, discomfort while moving, trouble swallowing, etc.)?

References

- 1) Establishing 'quality of life' parameters using behavioural guidelines for humane euthanasia of captive non-human primates. *Animal Welfare*. 2013 September 1; 22(4):429–435. <https://pubmed.ncbi.nlm.nih.gov/25505822/>
- 2) Identifying and Implementing Endpoints for Geriatric Mice. *Comparative medicine*. 2018 Dec 1;68(6):439-451. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6310203/>
- 3) Practical pathology of aging mice. *Pathobiology of Aging & Age-related Diseases*. Published online 31 May 2011. <https://www.tandfonline.com/doi/full/10.3402/pba.v1i0.7202?src=>
- 4) A clinical frailty index in aging mice: comparisons with frailty index data in humans. *J Gerontol A Biol Sci Med Sci*. 2014 June;69(6):621–632. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4022099/>
- 5) A short life on the farm: aging and longevity in agricultural, large-bodied mammals. *GeroScience*. Published online 2 May 2020. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7286991/>