McGill

STANDARD OPERATING PROCEDURE #412

HUMANE INTERVENTION POINTS FOR AGING RODENTS

1. PURPOSE

This Standard Operating Procedure (SOP) describes humane intervention points for aging rodents.

2. RESPONSIBILITY

Principal investigator (PI) and their research staff, veterinary care staff, Facility Animal Care Committee (FACC).

3. CONSIDERATIONS

Rodents older than 18 months are considered as aging animals.

Aging rodents will develop age-associated clinical manifestations that, although they may make the animal appear ill and may cause some discomfort, are not life-threatening. These may include:

- Skin lesions, alopecia, excessive barbering, ulcerative dermatitis, scarring.
- Rectal prolapse of varying severity
- Ocular lesions such as conjunctivitis, blepharitis, keratitis, opacity, retrobulbar masses, etc.
- Palpable masses, subcutaneous or internal.

Aging mice may also suffer from a combination of subclinical diseases that can be vary in their clinical presentations and should be considered as part of the progressive decline in organ function that defines aging. These include, but are not limited to, neoplasias, heart lesions, renal disease, systemic inflammation and degenerative joint and dental lesions.

Furthermore, a distinction can be made between studies where aging animals are to be kept up to a predetermined age (e.g., 24 months) and studies where aging animals are to be maintained alive as long as possible, that is, until near the end of their natural life. Justification for rodent colonies kept until near end of life must be provided to the FACC in the Animal Use Protocol (AUP).

4. PROCEDURES

4.1. Monitoring:

4.1.1. Intensive monitoring in studies involving aging rodents is critical to prevent undue suffering and distress and loss of experimental data when animals are found dead.

4.1.2. Monitoring is the responsibility of the PI and research staff.

4.1.3. Cages of aging rodents should be clearly labeled with the experimental endpoint (e.g., 24 months) or as near end of life (NEOL).

4.1.4. Animals showing clinical signs are reported to the veterinary care staff who will determine follow-up actions such as frequency of monitoring and weighing, treatments and supportive therapy, or euthanasia.

4.1.5. Frequency of monitoring:

4.1.5.1. Daily observation by animal care staff

4.1.5.2. Weekly monitoring by research staff

4.1.5.3. Animals nearing end of life, as determined by clinical signs and up to 20% weight loss are to be monitored twice per day, every day, including weekends and holidays.

4.2. Supportive Care:

4.2.1. Supportive care is an important factor in preventing a decline in functional health of aging rodents and should be provided when clinical signs are noted.

4.2.2. Supportive care may include:

4.2.2.4. Moist food in the bottom of the cage

4.2.2.5. Water bottles with long sipper tubes to ease drinking

4.2.2.6. Administration of parenteral fluids.

4.3. Recommended intervention points for aging rodents in near end of life studies:

4.3.1. To prevent unnecessary early euthanasia of animals with non-terminal diseases associated with old age, descriptive criteria for end-of-life and humane euthanasia have been determined. In order to be considered at end of life, rodents are to appear moribund and demonstrate clinical signs that suggest imminent death within 24 hours. These clinical signs may include:

4.3.1.7. No response to external stimuli

4.3.1.8. Cold body temperature to the touch

4.3.1.9. Slow or labored breathing

4.3.1.10. Hunched posture with matted coat

4.3.1.11. Failure to eat and drink, marked dehydration

4.3.1.12. Incoordination, paralysis

4.3.1.13. Body condition score less than 2

4.3.1.14. Rapid weight loss exceeding 20% of recent bodyweight

4.3.1.15. Pale eyes and/or extremities (rodents) or mucous membranes

4.3.1.16. Mass that is ulcerated, necrotic or impairing normal function (e.g., eating, drinking) or exceeding acceptable size endpoints:

4.3.1.16.1. Mice: $2cm^3$or 10% of the baseline bodyweight

4.3.1.16.2. Rats: $5cm^3$ or 5% of the baseline bodyweight

5. REFERENCES

5.1. Pettan-Brewer, C., Treuting, P.. Practical pathology of aging mice. *Pathobiology of Aging & Age-related Diseases, North America*, 1, May. 2011. http://www.pathobiologyofaging.net/index.php/pba/article/view/7202.