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Standard Operating Procedures for Management of Ulcerative Dermatitis in Mice

1.0 Purpose:

This SOP authorizes and outlines objective scoring and various treatment options of mice with ulcerative dermatitis by veterinary staff, investigative personnel and animal care technicians and provides criteria for determining euthanasia in severe intractable cases of ulcerative dermatitis.

2.0 Background

2.1 Etiology: The cause of ulcerative dermatitis syndrome is unknown but is likely multifactorial with an epigenetic component. Risk factors include high fat diet and certain genotypes such as E or P selectin and inducible nitric oxide synthase knockouts. Ulcerative dermatitis may be spontaneous or may occur secondary to a break in the skin, such as fight wounds or ear tags. There is no definitive cure for ulcerative dermatitis but mild cases can be managed with long-term therapeutic intervention.

2.2 Incidence: Ulcerative dermatitis is common in C57BL/6 mice or strains with C57BL/6 background. Most genetically modified mice have C57BL/6 as part of their genetic background.


2.3 Potential impact on Research: Mice with ulcerative dermatitis develop focal dermal ulcers with a mixed inflammatory cell infiltrate consisting of neutrophils, macrophages, mast cells, and occasional lymphocytes. [1,2]. Acute and chronic dermal inflammation and secondary bacterial infections directly alter immune system parameters and behavior and indirectly alter mobility, reproductive capacity, food intake, and multiple other physiological indices. Long-term treatment with antibiotics, steroids and dietary alterations can also change physiological indices and research results.

3.0 Materials:

- 3.1: Vetericyn Plus Ophthalmic Gel® (Hypochlorous Acid (0.010%))
- 3.2: Triple antibiotic ointment (bacitracin zinc, neomycin sulfate, polymyxin B sulfate)+/- pramoxine
- 3.3: Green Clay (montmorillonite)
- 3.3: TriCalm®: Aluminum acetate (0.2%) Hydrogel
- 3.4: Chlorhexidine 2% ointment or solution
- 3.5: Silver Sulfadiazine cream 1%
- 3.6: Carprofen 5-20 mg/kg SQ or PO in drinking water
- 3.7: Enrofloxacin 5-10 mg/kg SQ or PO in drinking water
- 3.8: Maropitant citrate

4.0 Procedures:

4.1 Identification and Treatments

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4.1.1 Common Clinical signs:

Alopecia, pruritus, ulceration, crusting and exudation of the skin. Common location of lesions are the dorsum, cervical area, between the scapulae, and head. Chronic conditions can cause ulcerated areas, scarring and contracture of the skin that leads to restriction of movement.

4.1.2 Treatment options (See Appendix 1): (early treatment of mild cases have been shown to be more effective)


- a. **Trimming of rear toenails** every 10-14 days. This has been shown to be very effective in the treatment of mild UD. A restraint device is strongly recommended to help facilitate proper handling of the mice for the nail trim.
- b. **Topical treatment options:**
 - i. Daily: Apply any of the topical medications (except Green Clay) listed above once daily for 1-7 days based on PI preference. Vet Services first choice will be Vetericyn Plus Ophthalmic Gel® if the PI has no preference. The lesion should resolve within 7-10 days, if it is non-responsive, CVS will consult with PI on long term plan.
 - ii. Every 3-4 days: Green clay is mixed fresh with water until forms a thick paste, let stand for 5 minutes. Clean the affected area with dilute chlorhexidine and let dry. Apply clay poultice to a thickness of 5mm every 3-4 days
 - iii. All topical treatments must be noted on the Vet Card with the initials of the person, date, and treatment abbreviations as listed above in bold.
- c. **Housing:** Separating affected animals can prevent worsening of clinical signs due to aggressive behavior of cage mates.

4.2 Notification

Personnel identifying the condition must notify the principal investigator (or his/her designee) prior to initiating treatment, unless prior approval for treatment has been given. All animals identified with UD must be entered on the OCV Animal Health database for case tracking.

4.3 Flagging of Cage:

The cage should be flagged with a WSU OCV Vet Services Card: (see picture of card below) with the ASAF/PI, animal ID, date flagged, mark UD on the card, mark if the PI has been notified and initials of person setting up the case.

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4.4 Documentation and Scoring:


- 4.4.1 To initiate treatment documentation, use the back side of the green card. The card provides enough space to document 1 week of daily treatment. Once the case exceeds one week, the veterinary staff will assess treatment efficacy and develop a follow up care plan if needed or will resolve the case. If further treatment is necessary, the documentation will move to a paper medical record. When the case has resolved, either returned to normal limits, euthanasia or transferred to long term care, write the date on the front of the card.
- 4.4.2 A number score should be given to each UD case and documented in the treatment section: (1) Mild; (2) Moderate (3) Severe. See Appendix 1 for details on scoring.

4.5 Resolution of Case

Affected animals that have been assessed and treated and have improvement of clinical signs where there is no active inflammation (hair loss may still be present) can be resolved and treatment stopped. Resolution of a case can be initiated by trained PI staff, animal care staff or Campus Vet Services (CVS) staff. Resolution date should be noted on the Vet Treatment Card or paper record. The green card should be placed behind the cage card for the life of the animal to indicate prior history and possible recurrence of the UD. If the animal is euthanized place the date of euthanasia on the card and place the card in the Index Card Holder in the room marked “CVS Cases”.

4.6 Criteria for Euthanasia

- 4.6.1 Severe UD with score of 3 that has not resolved or improved after 7-14 days with treatment,
- 4.6.2 Presence of lesions which impair normal functions such as eating or drinking, locomotion.
- 4.6.3 Depression, lethargy, loss of body condition
- 4.6.4 Every effort will be made to contact the PI and staff when animals have reached the criteria for euthanasia before the animal is euthanized.

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4.7 Campus Veterinary Service Care



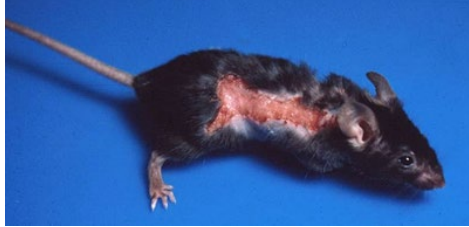
4.7.1 All affected animals will be examined by CVS staff within 4 days of notification of the issue unless the case is resolved or is euthanized before the indicated time period.


4.7.2 CVS staff will make a clinical plan for each case if there is no resolution after 7 days of treatment.

4.7.3 CVS staff will be in communication with animal care staff and PI personnel to insure adequate medical care and meet the needs of the research project.

Appendix 1.

Scoring/Treatment Ulcerative Dermatitis Cases*

1 Mild	<ul style="list-style-type: none"> Excoriations and/or punctuate crust(s) (≤ 2 mm**) Any ulcerative lesion ≤ 5 mm** in diameter on the body but not on face or extremities. Lesion is not characterized by scratching. Mild cases are the most likely to respond to treatment and may resolve naturally 		<ul style="list-style-type: none"> Trim nails Recheck in 3-5 days for worsening condition If close to parturition, do not disturb until at least 3-5 days post pupping
2 Moderate	<ul style="list-style-type: none"> A single ulcerative lesion from 0.5 to 1.5cm** in diameter. Any lesion < 3 mm** involving the face or extremities. Any lesion that is continually scratched. 		<ul style="list-style-type: none"> Trim nails Apply Vetericyn or 3abx with pain daily and notify CVS staff. Should be resolving within 3-7 days. If close to parturition, do not disturb until at least 3-5 days post pupping
3 Severe	<ul style="list-style-type: none"> Any ulcerative lesion > 1.5cm** in diameter. Multiple ulcerative lesions that add up to > 1.5 cm** in length Ulcerative lesion > 3mm** on face 		<ul style="list-style-type: none"> Contact CVS staff If animal is needed, systemic treatments with Carprofen and Enrofloxacin will be recommended by CVS staff.

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* Animal has at least one of the criteria in each category. The animal does not have to meet all the criteria.

Pictures and scoring taken from: Hampton, A.L, JAALAS Vol 51, No. 5. 2012 & <http://med.stanford.edu/news/all-news/2016/01/toenail-trim-saves-lab-mice-from-life-threatening-skin-condition.html> & <http://dora.missouri.edu/mouse/ulcerative-dermatitis-syndrome/>

** Measure the longest diameter of the largest lesion identified

References:

1. **Hampton AL et al.** 2012. Progression of ulcerative dermatitis lesions in C57BL/6CrI mice and the development of a scoring system for dermatitis lesions. *JAALAS*. 51(5): 586-593
2. **Kastenmayer RJ, Fain MA, Perdue KA.** 2006. A retrospective study of idiopathic ulcerative dermatitis in mice with a C57BL/6 background. *JAALAS*. 45:8-12.
3. **Martel, KA and Careau, C.** 2011. Green clay therapy for mice topical dermatitis. *Tech Talk* 16:2-3
4. **Mufford T, Richardson L.** 2010. Nail trims versus the previous standard of care for treatment of mice with ulcerative dermatitis. *JAALAS*. 48(5): 532-640.
5. **Neuhaus B, Niessen CM, Mesaros A, Withers DJ, Krieg T, Partridge L.** 2012. Experimental analysis of risk factors for ulcerative dermatitis. *Experimental Dermatology*. 21: 710-720.

Revision History

Version	Change	Date Replaced
1	Added Vetericyn	6/27/18
2	Refined treatment options, added systemics	3/7/20
3	Updated appendix 1 with specific treatment options for each score and the directive to not treat pregnant mice with a score of 1-2	6/3/22