*Original Research*

# Comparison of 3 Topical Treatments against Ulcerative Dermatitis in Mice with a C57BL/6 Background

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Ulcerative dermatitis (UD) is a common condition in C57BL/6 mice and strains with this background. The etiology of UD is unclear but appears to have a genetic component associated with the C57BL/6 strain and has been reported as secondary to a variety of conditions. Treatment is unrewarding, resulting in euthanasia in many cases. In the present study we compared 3 topical treatments against spontaneous UD in mice with a C57BL/6 background. In total, 301 mice of both sexes were included in this study, and the tested treatments comprised bacitracin–neomycin sulfate–polymixin B sulfate ointment twice daily, 10% povidone–iodine ointment plus 1% silver sulfadiazine cream once daily, and 0.005% sodium hypochlorite once daily. Lesion healing was defined as complete skin reepithelialization with or without hair regrowth. Sex, age, lesion location, and type and length of treatment were analyzed by using univariate and multivariate logistic regression. Of the 79 mice treated with triple-antibiotic ointment, 27 (34%) healed, compared with 43 of the 125 (34%) treated with povidone–iodine and sulfadiazine and 69 of the 97 (71%) treated with hypochlorite. Lesion size and treatment with 0.005% sodium hypochlorite were the only significant predictors of healing; all other variables were not statistically significant in multivariate analysis. We conclude that 0.005% sodium hypochlorite is an effective topical treatment alternative for UD in C57BL/6 mice and strains on this background, and a favorable prognosis depends on the early identification and treatment of those lesions.

**Abbreviations:** B6, C57BL/6; UD, ulcerative dermatitis

Ulcerative dermatitis (UD) is a common condition in C57BL/6 (B6) mice and strains with a B6 background.[1,21] Early lesions are characterized by small skin erosions that can affect any part of the body but are typically found between the scapulae. Usually these lesions rapidly progress to form large, irregular areas of ulcerated skin.[1] The condition can be very pruritic, resulting in self-mutilation, skin degloving, and exposure of the subcutaneous tissues and, in some cases, musculature.[1] Common sequelae in mice that recover from this disease are marked lymphadenopathy and splenomegaly due to reactive immune modulation or activation, which can confound research results.[21,31] When UD affects extensive areas and then heals, contracture and scarring of the skin cause tension that alters normal posture and ambulation.[1]

Primary (idiopathic) UD is diagnosed by ruling out other conditions that cause dermatitis (secondary) in laboratory mice, such as allergy to fur mites,[8,18] fight wounds, staphylococcal skin infections,[20,32] phenotype,[19,21,31] and experimental manipulation.[13,22,33] The exact etiology of UD remains undetermined but seems to be multifactorial.[9] Proposed etiologies include behavioral,[10,11,34,35] immune-complex–induced vasculitis,[1] cellular oxidative injury,[21] and vitamin A toxicity.[31] Calorie-restricted diets, providing 60% of the average calorie intake of the respective unrestricted group, seem to reduce ulcerative dermatitis,[28] whereas high-fat diets (35% crude fat) appear to exacerbate the condition.[27] UD has been reported to affect more female than male mice, with the highest incidence in mice older than 1 y, but UD can also occur in young mice.[1,19,31] Although UD occurs throughout the year, some authors report a peak incidence during spring and fall, whereas others note increased case numbers during the summer months.[19,31]

Attempts to find a cure for UD have not found a treatment that is completely effective. Treatment typically is unrewarding, resulting in euthanasia in many cases.[21] Dietary supplementation with vitamin E reportedly has some efficacy favoring skin reepithelization in mice with UD.[21] However, a recent study using vitamin E as a diet supplement to prevent the occurrence of UD yielded contradictory results.[24] In that study, mice fed a vitamin-E–fortified diet since weaning were more likely to develop UD than were mice fed a regular diet. However, to achieve the desire amount of vitamin E, the fat content of the diet had to be increased; high dietary fat is known to exacerbate UD.[24,27] Other studies have shown systemic administration of maropitant citrate reduces the size of UD lesions in mice by decreasing scratching,[35] and the oral administration of ibuprofen appears to help speed the healing of skin lesions by reducing inflammation and pain.[11] Topical and systemic antibiotics, corticosteroids, antihistamines, and lidocaine are poorly effective in the treatment of UD.[1,19,21,31] Among topical treatments, caladryl lotion, chlorhexidine, and

cyclosporine appear to be the most effective in treating UD.[7,12,23] Toenail trimming has been reported as effective at reducing self-trauma due to scratching in UD, thus helping to speed healing.[26,29]

In the present study, we compared 3 topical treatments against spontaneous UD in mice with a B6 background.

## Materials and Methods

**Animals.** The mouse colony was maintained in an AAALAC-accredited barrier facility as part of several experimental protocols approved by the National Institute of Allergy and Infectious Diseases (NIAID) Animal Care and Use Committee. All procedures and use of animals was in accordance with the *Guide for the Care and Use of Laboratory Animals*,[17] Animal Welfare Regulations,[3,4] and IACUC-approved standard operating procedures. The animals were housed in ventilated, autoclaved microisolation caging (Thoren Caging Systems, Hazleton, PA, and Lab Products, Seaford, DE) with autoclaved hardwood bedding (Sani-Chip, Harlan Teklad, Madison, WI). Mice had unrestricted access to food (Rodent NIH-31 Autoclavable NA, Zeigler Brothers, Gardners, PA), and acidified water (pH 2.8 to 3.0). Room temperature was maintained between 20.0 °C and 23.3 °C, relative humidity was between 30% to 50%, and the photoperiod was a 14:10-h light:dark cycle. All mice were maintained in the same animal facility but not necessarily in the same room, and all had the same health status. Colony sentinels are tested quarterly and were considered free of the following agents: mouse hepatitis virus, pneumonia virus of mice, Sendai virus, Theiler murine encephalomyelitis virus, mouse rotavirus, lymphocytic choriomeningitis virus, ectromelia virus, mouse cytomegalovirus, minute virus of mice, polyoma virus, reovirus 3, mouse adenovirus, rodent parvoviruses, *Mycoplasma pulmonis*, and cilia-associated respiratory bacillus. Hantavirus testing is performed once a year. The research colony is also considered free of *Salmonella* spp., *Campylobacter* spp., *Citrobacter rodentium*, *Clostridium piliforme*, *Corynebacterium kutscheri*, and *Streptobacillus moniliformis*, according to testing performed by the NIH-approved commercial vendors that supply animals to our program and on the basis of results of sporadic testing of culled research mice. Endoparasite and ectoparasite examination was performed every 6 wk in sentinel animals and throughout the year on culled research animals. Mouse norovirus (MNV) and *Helicobacter* spp. were not excluded agents from the animal colony, therefore all mice were considered potentially infected with these agents. When tested, sentinel mice were routinely positive to MNV, but individual colony and experimental mice were not tested. Euthanasia, when necessary, was performed with $CO_2$ overdose according to the AVMA's *Guidelines for the Euthanasia of Animals*.[2] Necropsies of clinical cases were performed as part of the routine colony health surveillance program.

**Experimental design.** The mice in this study consisted of a large number of genetically engineered mice and unidentifiable strains on a B6 background with spontaneous UD and randomly assigned to 1 of 3 different topical treatments. The first group of mice was treated topically with bacitracin–neomycin sulfate–polymixin B sulfate ointment (Perrigo, Allegan, MI) applied by using a sterile swab to thinly cover the entire affected area twice daily. Mice in the second group were treated with 10% povidone–iodine ointment (Qualitest Pharmaceuticals, Huntsville, AL) plus 1% silver sulfadiazine cream (Dr Reddy's Laboratories, Shreveport, LA) applied by using a sterile swab to thinly cover the entire affected area once daily. The remaining mice were treated with

0.005% sodium hypochlorite (0.125% Dakin solution, Century Pharmaceuticals, Indianapolis) once each day. Stock Dakin solution (0.125% active sodium hypochlorite) was diluted with sterile distilled water to a final concentration of 0.005% and stored in a labeled closed dark container. A new solution was prepared weekly. A sterile cotton swab soaked with the 0.005% sodium hypochlorite solution was used to apply it until the wound was covered with the solution. In all treatment groups, if mice were noted to scratch the skin lesion, 5% lidocaine ointment (E Fougera, Melville, NY) was added to the topical treatment. All procedures and treatments were approved by the NIAID Animal Care and Use Committee. Skin lesions were examined daily by the animal health technician and at least once weekly by the attending veterinarian and the findings noted in the animal's clinical record. Selected cases were submitted for necropsy and histologic examination according to routine procedures. Complete skin lesion repair was defined as the complete reepithelialization of the lesion with or without hair regrowth.

UD was defined as single or multiple areas of skin excoriation, erosion, ulceration or degloving with serosanguineous exudate or granulation tissue or adherent crusts affecting the muzzle, head, neck, dorsum, thorax, flank, lumbar or sacral areas, ear pinnae, periauricular areas, or limbs. Lesion location was noted, and the greatest length and width were measured and recorded (in $mm^2$) along with the lesion character (moist or dry, raw or scabbed, superficial or deep). Due to humane reasons, no mice were left untreated as controls. Only animals that were not currently in experiments were included in the statistical analyses. Skin lesions due to fighting or associated with ear tags and facial lesions possibly secondary to other inflammatory processes, such as excessive barbering, ocular or eyelid infections, and gingivitis, were treated but not included in the study. Severe cases of UD, covering more than 10% of the body surface area or with intense scratching, causing automutilation, were not included in the study because these mice were euthanized for humane reasons. Dermatitis associated with fur mites was ruled out by sentinel testing results, which were consistently negative in the colony for over 7 y, and by direct testing of colony mice with UD that did not respond to treatment and were submitted for pathologic evaluation. After exclusion of the mice that did not fit the described criteria, 301 mice (31 B6 mice and 270 mice with a B6 background; 190 female, 111 male) ranging from 6 to 92 wk of age were statistically analyzed for significant differences in wound healing.

**Statistical analysis.** To assess whether treatment outcome (healed or not) was associated with sex, age, lesion size, lesion location, type of treatment, and length of treatment in mice with UD, individual univariate analyses that paired each outcome variable with each covariate were performed. The Fisher exact test was used to test the association between healing and categorical variables, such as sex, lesion location, and type of treatment. The 2-sample *t* test was used to assess the correlation between healing and continuous variables, such as age, lesion size, and length of treatment. Then a multivariate logistic regression model was used to examine healing and covariates jointly. S-plus software (TIBCO Software, Boston, MA) was used for all statistical analyses. A *P* value of less than 0.05 was considered as statistically significant.

## Results

Of the 79 mice with UD treated with bacitracin–neomycin sulfate–polymixin B sulfate ointment, the lesions healed in 27 (34%),

**Table 1.** Treatment outcome according to skin lesion location in mice with UD

|  | Back | Chest or abdomen | Dorsum or shoulder | Ear | Flank | Head | Leg | Neck |
|---|---|---|---|---|---|---|---|---|
| Nonhealed | 13 | 1 | 14 | 2 | 14 | 1 | 26 | 91 |
| Healed | 10 | 0 | 19 | 5 | 4 | 1 | 21 | 79 |

compared with 43 of the 125 (34%) mice treated with 10% povidone–iodine ointment with 1% silver sulfadiazine cream and 69 of the 97 (71%) animals treated with 0.005% sodium hypochlorite.

Univariate analysis failed to reveal significant associations between treatment outcome and sex (healed: female, 89; male, 50; nonhealed: female, 101; male, 61; $P = 0.86$, Fisher exact test), between treatment outcome and lesion location (Table 1; $P = 0.17$, Fisher exact test), between treatment outcome and age (age: nonhealed, $33.8 \pm 19.0$ wk; healed, $30.2 \pm 15.5$ wk; $P = 0.077$, 2-sample $t$ test), and between treatment outcome and treatment duration (duration: nonhealed, $17.4 \pm 11.2$ d; healed, $15.4$ d $\pm 9.0$; $P = 0.085$, 2-sample $t$ test). Univariate analysis demonstrated significant association between treatment outcome and type of treatment (Table 2; $P < 0.0001$, Fisher exact test) and between treatment outcome and lesion size before treatment (size: nonhealed, $28.3 \pm 22.89$ mm$^2$; healed, $15.4$ mm$^2$ $\pm 11.1$; $P < 0.0001$, 2-sample $t$ test).

According to multivariate logistic regression analysis of the significant variables in the univariate analysis, the estimated log odds ratio for lesion size was $-0.06738 \pm 0.01177$ ($P < 0.0001$) and the odds ratio was 0.935 (95% confidence interval, 0.91 to 0.96), meaning that lesion size was negatively correlated with healing. The estimated log odds ratio for 0.005% sodium hypochlorite compared with triple-antibiotic ointment was $1.63 \pm 0.366$ ($P < 0.0001$), with an odds ratio of 5.118 (95% confidence interval, 2.50 to 10.49). That is, mice treated with 0.005% sodium hypochlorite had a better outcome than did mice treated with triple-antibiotic ointment. In contrast, the estimated log odds ratio for 10% povidone–iodine plus silver sulfadiazine compared with triple-antibiotic ointment was $-0.05 \pm 0.36$ ($P = 0.89$), with an odds ratio of 0.95 (95% confidence interval 0.48 to 1.88), indicating there was no difference between these treatments in terms of healing. All other variables were nonsignificant in the multivariate analysis. Lesion size and treatment with 0.005% sodium hypochlorite were the only significant predictors of healing ($P < 0.0001$).

Flank lesions appeared to have the worst outcome for healing when compared with the other individual locations, but the differences were not statistically significant (Table 1). However, flank lesions were significantly different as compared with all other lesion locations combined ($P = 0.049$). The estimated log odds ratio for lesion site was $-1.488 \pm 0.6866$ ($P = 0.03$), with an odds ratio of 0.26 (95% confidence interval, 0.059 to 0.867), meaning that flank lesions had a worse outcome of healing than did all other locations combined. In addition, the estimated log odds ratio for lesion size was $-0.06971 \pm 0.01207$ ($P < 0.0001$), and the odds ratio was 0.93 (95% confidence interval, 0.91 to 0.96), such that lesion size was negatively correlated with healing. Regarding treatment type, the estimated log odds ratio for 0.005% hypochlorite compared with triple-antibiotic ointment was $1.68 \pm 0.372$ ($P < 0.0001$), with an odds ratio of 5.37 (95% confidence interval, 2.59 to 11.12), indicating that sodium hypochlorite led to healing more often than did triple-antibiotic ointment. However, there was no difference between 10% povidone–iodine ointment plus 1% silver sulfadiazine and triple antibiotic ointment in terms of healing (estimated log odds ratio, $-0.0898 \pm 0.3498$; $P = 0.7973$; odds ratio,

**Table 2.** Treatment outcome according to type of treatment in mice with UD

|  | Triple-antibiotic | 10% povidone-iodine + silver sulfadiazine | 0.005% sodium hypochlorite |
|---|---|---|---|
| Nonhealed | 52 | 82 | 28 |
| Healed | 27 | 43 | 69 |

0.91; 95% confidence interval, 0.46 to 1.81). All other variables were nonsignificant in the multivariate analysis.

In the univariate analysis, the use of lidocaine was associated with healing outcome (nonhealed: no lidocaine, 112; with lidocaine, 50; healed: no lidocaine, 114; with lidocaine, 25; $P = 0.01115$). Since the majority of the animals treated with sodium hypochlorite were not given lidocaine, when all groups were added together, we may falsely claim that the use of lidocaine hinder healing. The reason is because lidocaine efficacy was closely associated with the type of treatment applied to the skin lesions (Table 3; $P < 0.0001$, Fisher exact test). However, the effect of lidocaine use on healing was not significant in the multivariate analysis that included location (flank compared with others), size, and treatment ($P = 0.164$). The final model remained the same: skin lesion location (others compared with flank), lesion size, and treatment with 0.005% sodium hypochlorite were the only significant predictors of healing. All other variables were not statistically significant.

## Discussion

In our facility, as in many others that house B6 mice and related strains, UD is a significant clinical problem. No treatment has been deemed 100% successful. At our institution, the standard treatment protocol comprises twice-daily topical bacitracin–neomycin sulfate–polymixin B sulfate ointment or once-daily 10% povidone–iodine ointment plus 1% silver sulfadiazine cream. In our search for alternative treatments, we found that 0.005% sodium hypochlorite reportedly is effective against atopic dermatitis and *Staphylococcus aureus* skin infections in humans.[16] This agent is also used for skin-ulcer debridement and a skin-wound disinfecting agent that does not impair the fibroblast function necessary for tissue repair and that does not induce the bacterial resistance frequently associated with prolonged use of antibiotics.[6,25] We therefore decided to use 0.005% sodium hypochlorite for treating UD, and the preliminary results prompted us to establish whether these 3 treatment protocols differed significantly.

We found 0.005% sodium hypochlorite to be more effective for treating UD in our animal facility than were our standard treatments. Specifically we saw a positive treatment response in twice as many of the cases treated with diluted Dakin solution than with the other 2 treatment protocols. Advantages of diluted sodium hypochlorite solution are that it is an inexpensive, readily available, topical disinfectant. In addition, diluted sodium hypochlorite does not cause systemic effects that might interfere with research studies or produce bacterial resistance, as might occur with prolonged use of antibiotics.[6,16,22]

**Table 3.** Treatment outcome when lidocaine was added to each treatment

|  | Triple-antibiotic | 10% povidone-iodine + silver sulfadiazine | 0.005% sodium hypochlorite |
|---|---|---|---|
| Nonhealed | 32 | 13 | 5 |
| Healed | 6 | 7 | 12 |

Sodium hypochlorite's healing properties can be explained by multiple factors. Specifically, sodium hypochlorite inhibits the excessive neutrophil oxidative burst believed to underlie some forms of autoimmune dermatitis in humans[5,15] and that might be responsible for pruritus in UD, given that B6 neutrophils produce and release histamine.[30] In mouse models, neutrophils play critical roles in various phases and diverse models of allergic skin inflammation, making them attractive targets for the development of potential treatments.[33] A recent study describes the use of topical hypochlorite to treat acute radiation dermatitis in B6 mice.[22] In that study, hypochlorite treatment induced epidermal hyperplasia and cell proliferation, maintained the normal skin architecture, and reversed markers of epidermal aging in B6 mice.[22]

Histologically, the lesion preceding overt UD skin lesions has been characterized as a leukocytoclastic vasculitis with IgG–IgM immune deposits in the lumen of small subcutaneous vessels with inflammatory cell infiltrate, thus resulting in subsequent necrosis and ulceration of the skin.[1] Early UD lesions demonstrate primary follicular dystrophy resulting in scarring dermatitis, similar to central centrifugal cicatricial alopecia in humans.[31] In all cases of UD, once the skin lesions are grossly visible, the histologic picture is one of a predominantly neutrophilic inflammatory infiltrate accompanied by lymphocytes, macrophages, and mast cells—thus prompting our interest in testing sodium hypochlorite as a topical treatment.[1,14,19,31] Sodium hypochlorite may help to prevent further tissue damage in mice with UD by inhibiting excessive neutrophilic oxidative burst, thereby allowing—and possibly hastening—tissue healing, as studies in humans and mice suggest.[5,15,22]

We conclude that regardless of treatment protocol, a favorable prognosis depends on the early identification and treatment of UD lesions. In addition, once-daily topical treatment with 0.005% sodium hypochlorite was more effective for UD in B6 mice and strains on this background than were our previous treatment protocols. Therefore, we propose the use of diluted Dakin solution as a novel approach for the treatment of UD in B6 mice and related strains.

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## References

1. **Andrews AG, Dysko RC, Spilman SC, Kunkel RG, Brammer DW, Johnson KJ.** 1994. Immune complex vasculitis with secondary ulcerative dermatitis in aged C57BL/6NNia mice. Vet Pathol **31:**293–300.
2. **American Veterinary Medical Association.** Guidelines for the euthanasia of animals. 2013 edition.
3. **Animal Welfare Act as Amended**. 2008. 7 USC § 2131-2156.
4. **Animal Welfare Regulations**. 2008. 9 CFR § 3.129.
5. **Carlson JA.** 2010. The histological assessment of cutaneous vasculitis. Histopathology **56:**3–23.
6. **Coetzee E, Whitelaw A, Kahn D, Rode H.** 2012. The use of topical, un-buffered sodium hypochlorite in the management of burn wound infection. Burns **38:**529–533.
7. **Crowley ME, Delano ML, Kirchain SM.** 2008. Successful treatment of C57BL/6 ulcerative dermatitis with Caladryl lotion. Abstract presented at the 59th AALAS National Meeting, Indianapolis, Indiana, Nov. 9–13, 2008. J Am Assoc Lab Anim Sci 47:109-110.
8. **Dawson DV, Whitmore SP, Bresnahan JF.** 1986. Genetic control of susceptibility to mite-associated ulcerative dermatitis. Lab Anim Sci **36:**262–267.
9. **Duarte-Vogel SM, Lawson GW.** 2011. Association between hair-induced oronasal inflammation and ulcerative dermatitis in C57BL/6 mice. Comp Med **61:**13–19.
10. **Dufour BD, Adeola O, Cheng HW, Donkin SS, Klein JD, Pajor EA, Garner JP.** 2010. Nutritional up-regulation of serotonin paradoxically induces compulsive behavior. Nutr Neurosci **13:**256–264.
11. **Ezell PC, Papa L, Lawson GW.** 2012. Palatability and treatment efficacy of various ibuprofen formulations in C57BL/6 mice with ulcerative dermatitis. J Am Assoc Lab Anim Sci **51:**609–615.
12. **Feldman SH, McVay L, Kessler MJ.** 2006. Resolution of ulcerative dermatitis of mice by treatment with topical 0.2% cyclosporine. Abstract presented at the 57th AALAS National Meeting, Salt Lake City, Utah, Oct. 15–19, 2006. J Am Assoc Lab Anim Sci 45:92-93.
13. **Forlow SB, White EJ, Thomas KL, Bagby GJ, Foley PL, Ley K.** 2002. T cell requirement for development of chronic ulcerative dermatitis in E- and P-selectin-deficient mice. J Immunol **169:**4797–4804.
14. **Hampton AL, Hish GA, Aslam MN, Rothman ED, Bergin IL, Patterson KA, Naik M, Paruchuri T, Varani J, Rush HG.** 2012. Progression of ulcerative dermatitis lesions in C57BL/6Crl mice and the development of a scoring system for dermatitis lesions. J Am Assoc Lab Anim Sci **51:**586–593.
15. **Hansbrough JF, Zapata-Sirvent RL, Cooper ML.** 1991. Effects of topical antimicrobial agents on the human neutrophil respiratory burst. Arch Surg **126:**603–608.
16. **Huang JT, Abrams M, Tlougan B, Rademaker A, Paller AS.** 2009. Treatment of *Staphylococcus aureus* colonization in atopic dermatitis decreases disease severity. Pediatrics **123:**e808–e814.
17. **Institute for Laboratory Animal Research.** 2011. Guide for the care and use of laboratory animals, 8th ed. Washington (DC): National Academies Press.
18. **Jungmann P, Guenet JL, Cazenave PA, Coutinho A, Huerre M.** 1996. Murine acariasis: I. Pathological and clinical evidence suggesting cutaneous allergy and wasting syndrome in BALB/c mouse. Res Immunol **147:**27–38.
19. **Kastenmayer RJ, Fain MA, Perdue KA.** 2006. A retrospective study of idiopathic ulcerative dermatitis in mice with a C57BL/6 background. J Am Assoc Lab Anim Sci **45:**8–12.
20. **Krugner-Higby L, Brown R, Rassette M, Behr M, Okwumabua O, Cook M, Bell C, Flowers MT, Ntambi J, Gendron A.** 2012. Ulcerative dermatitis in C57BL/6 mice lacking stearoyl CoA desaturase 1. Comp Med **62:**257–263.
21. **Lawson GW, Sato A, Fairbanks LA, Lawson PT.** 2005. Vitamin E as a treatment for ulcerative dermatitis in C57BL/6 mice and strains with a C57BL/6 background. Contemp Top Lab Anim Sci **44:**18–21.
22. **Leung TH, Zhang LF, Wang J, Ning S, Knox SJ, Kim SK.** 2013. Topical hypochlorite ameliorates NF-κB-mediated skin diseases in mice. J Clin Invest **123:**5361–5370.
23. **Lumpkins KC, Swing S, Emerson C, Ali F, Van Andel R.** 2006. Efficacy of topical chlorhexidine for treatment of ulcerative dermatitis in C57BL/6 mice. Abstract presented at the 57th AALAS National Meeting, Salt Lake City, Utah, Oct. 15–19, 2006. J Am Assoc Lab Anim Sci **45:**94–95.
24. **Mader JR, Mason MA, Bale LK, Gades NM, Conover CA.** 2010. The Association of Early Dietary Supplementation with Vitamin E with the Incidence of Ulcerative Dermatitis in Mice on a C57BL/6

Background: Diet and Ulcerative Dermatitis in Mice. Scand J Lab Anim Sci **37:**253–259.

25. **McKenna PJ, Lehr GS, Leist P, Welling RE.** 1991. Antiseptic effectiveness with fibroblast preservation. Ann Plast Surg **27:**265–268.

26. **Mufford T, Richardson L.** 2009. Nail trim versus the previous standard of care for treatment of mice with ulcerative dermatitis. Abstract presented at the 60th AALAS National Meeting, Denver, Colorado, Nov. 8–12, 2009. J Am Assoc Lab Anim Sci **48:**546.

27. **Neuhaus B, Niessen CM, Mesaros A, Withers DJ, Krieg T, Partridge L.** 2012. Experimental analysis of risk factors for ulcerative dermatitis in mice. Exp Dermatol **21:**712–713.

28. **Perkins SN, Hursting SD, Phang JM, Haines DC.** 1998. Calorie restriction reduces ulcerative dermatitis and infection-related mortality in p53-deficient and wild-type mice. J Invest Dermatol **111:**292–296.

29. **Seta S.** 2009. A simplified method for the treatment of mouse dermatitis. Abstract presented at the 60th AALAS National Meeting, Denver, Colorado, Nov. 8–12, 2009. J Am Assoc Lab Anim Sci **48:**548.

30. **Smuda C, Wechsler JB, Bryce PJ.** 2011. TLR-induced activation of neutrophils promotes histamine production via a PI3 kinase dependent mechanism. Immunol Lett **141:**102–108.

31. **Sundberg JP, Taylor D, Lorch G, Miller J, Silva KA, Sundberg BA, Roopenian D, Sperling L, Ong D, King LE, Everts H.** 2010. Primary follicular dystrophy with scarring dermatitis in C57BL/6 mouse substrains resembles central centrifugal cicatricial alopecia in humans. Vet Pathol **48:**513–524.

32. **Tamura H, Kuwamizu I, Tajima M, Shimizu A, Kimura S, Niki R, Maejima K, Sato G.** 1985. [[An outbreak of staphylococcal dermatitis in laboratory mice]] Jikken Dobutsu **34:**147–154 [[Article in Japanese]].

33. **Weber FC, Németh T, Csepregi JZ, Dudeck A, Roers A, Ozsvári B, Oswald E, Puskás LG, Jakob T, Mócsai A, Martin SF.** 2014. Neutrophils are required for both the sensitization and elicitation phase of contact hypersensitivity. J Exp Med **212:**15–22.

34. **Williams LK, Csaki LS, Cantor RM, Reue K, Lawson GW.** 2012. Ulcerative dermatitis in C57BL/6 mice exhibits an oxidative stress response consistent with normal wound healing. Comp Med **62:**166–171.

35. **Williams-Fritze MJ, Carlson Scholz JA, Zeiss C, Deng Y, Wilson SR, Franklin R, Smith PC.** 2011. Maropitant citrate for treatment of ulcerative dermatitis in mice with a C57BL/6 background. J Am Assoc Lab Anim Sci **50:**221–226.