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Deciphering Digital Dermatitis

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Deciphering Digital Dermatitis

Abstract

Bovine digital dermatitis (DD) is a leading cause of lameness in dairy cattle throughout the world. Despite more than 40 years of research, the definitive etiologic agent associated with the disease process is still unknown. Previous studies have demonstrated that multiple bacterial species are associated with lesions, with spirochetes being the most reliably identified organism.

According to the most recent National Animal Health Monitoring System survey of U.S. dairy farms, lameness is the second most common health problem identified in dairy cattle. DD was found to be the primary cause of lameness within the study herds, accounting for 61.8% of the lameness in bred heifers and 49.1% of the lameness in cows. Recently, the condition has become increasingly common in feedyard cattle as well, particularly in heavy cattle nearing slaughter weights, although it can be seen in cow-calf operations as well.

Disciplines

Large or Food Animal and Equine Medicine | Veterinary Microbiology and Immunobiology | Veterinary Preventive Medicine, Epidemiology, and Public Health

Comments

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DECIPHERING DIGITAL DERMATITIS

Research implicates multiple pathogens, with etiology changing through stages of disease progression.

BY PAUL J. PLUMMER, DVM, PH.D.; JAN K. SHEARER, DVM, M.S., COLLEGE OF VETERINARY MEDICINE, IOWA STATE UNIVERSITY

Bovine digital dermatitis (DD) is a leading cause of lameness in dairy cattle throughout the world. Despite more than 40 years of research, the definitive etiologic agent associated with the disease process is still unknown. Previous studies have demonstrated that multiple bacterial species are associated with lesions, with spirochetes being the most reliably identified organism.

According to the most recent National Animal Health Monitoring System survey of U.S. dairy farms, lameness is the second most common health problem identified in dairy cattle. DD was found to be the primary cause of lameness within the study herds, accounting for 61.8% of the lameness in bred heifers and 49.1% of the lameness in cows. Recently, the condition has become increasingly common in feedyard cattle as well, particularly in heavy cattle nearing slaughter weights, although it can be seen in cow-calf operations as well.

A PROMINENT BUT ELUSIVE DISEASE

Our research team at Iowa State University (ISU) has conducted a series of studies on the pathogens, disease processes and effects of DD in dairy and beef cattle, which have led to some key insights on the disease including:

- DD is a progressive, polybacterial disease process, and spirochetes of the *Treponema* genus, which are commonly associated with DD, typically are not predominant pathogens in early stage DD lesions.
- A DD scoring system can be useful in evaluating and monitoring disease progression and the success of interventions in a herd, and in decision making regarding treatment and control strategies.
- Lameness incidence, measured by locomotion scoring, is not necessarily a reliable indicator of the overall incidence of DD in a herd. Many lesions are locally painful to the touch but result in minimal change in locomotion score.



PHOTO: IOWA STATE UNIVERSITY

The Iowa State University lameness team includes, from left: Drs. John Coatney, Jan Shearer, Paul Plummer and Adam Krull. Members not pictured include Patrick Gorden and Vicki Cooper.

Bovine DD was first described in 1974. The first morphological description of DD as an ulcerative disease of the bovine coronary band occurred at the 8th International Meeting on Diseases of Cattle in Milan, Italy. The first etiologic descriptions of the disease were published in 1992 and were soon followed by a report describing the isolation and identification of an anaerobic spirochete, believed to be a *Treponema* spp., in the lesions.

Since that time, a number of additional papers have been published demonstrating the association of the lesions with additional bacteria, including *Bacteroides* spp. (now called *Porphyromonas* spp.), *Campylobacter* spp. and *Borrelia* spp., as well as viral etiologies. While there is a consistent presence of several *Treponema* phylotypes in DD lesions, attempts to induce disease by skin inoculation with pure cultures of these microorganisms have largely failed to result in significant disease in a majority of the animals inoculated. Furthermore, there is evidence to suggest that the clinical use of vaccines against spirochetes provides limited protection against the disease process.



150 mg/mL ANTIMICROBIAL
NADA 141-328, Approved by FDA
For subcutaneous injection in beef and non-lactating dairy cattle only. Not for use in female dairy cattle 20 months of age or older or in calves to be processed for veal.

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.
READ ENTIRE BROCHURE CAREFULLY BEFORE USING THIS PRODUCT.

INDICATIONS

ZACTRAN is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis* in beef and non-lactating dairy cattle. ZACTRAN is also indicated for the control of respiratory disease in beef and non-lactating dairy cattle at high risk of developing BRD associated with *Mannheimia haemolytica* and *Pasteurella multocida*.

CONTRAINDICATIONS

As with all drugs, the use of ZACTRAN is contraindicated in animals previously found to be hypersensitive to this drug.

WARNING: FOR USE IN CATTLE ONLY. NOT FOR USE IN HUMANS. KEEP THIS AND ALL DRUGS OUT OF REACH OF CHILDREN. NOT FOR USE IN CHICKENS OR TURKEYS.

The material safety data sheet (MSDS) contains more detailed occupational safety information. To report adverse effects, obtain an MSDS or for assistance, contact Merial at 1-888-637-4251.

RESIDUE WARNINGS: Do not treat cattle within 35 days of slaughter. Because a discard time in milk has not been established, do not use in female dairy cattle 20 months of age or older. A withdrawal period has not been established for this product in pre-ruminant calves. Do not use in calves to be processed for veal.

PRECAUTIONS

The effects of ZACTRAN on bovine reproductive performance, pregnancy, and lactation have not been determined. Subcutaneous injection of ZACTRAN may cause a transient local tissue reaction in some cattle that may result in trim loss of edible tissues at slaughter.

ADVERSE REACTIONS

Transient animal discomfort and mild to moderate injection site swelling may be seen in cattle treated with ZACTRAN.

EFFECTIVENESS

The effectiveness of ZACTRAN for the treatment of BRD associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* was demonstrated in a field study conducted at four geographic locations in the United States. A total of 497 cattle exhibiting clinical signs of BRD were enrolled in the study. Cattle were administered ZACTRAN (6 mg/kg BW) or an equivalent volume of sterile saline as a subcutaneous injection once on Day 0. Cattle were observed daily for clinical signs of BRD and were evaluated for clinical success on Day 10. The percentage of successes in cattle treated with ZACTRAN (58%) was statistically significantly higher ($p < 0.05$) than the percentage of successes in the cattle treated with saline (19%).

The effectiveness of ZACTRAN for the treatment of BRD associated with *M. bovis* was demonstrated independently at two U.S. study sites. A total of 502 cattle exhibiting clinical signs of BRD were enrolled in the studies. Cattle were administered ZACTRAN (6 mg/kg BW) or an equivalent volume of sterile saline as a subcutaneous injection once on Day 0. At each site, the percentage of successes in cattle treated with ZACTRAN on Day 10 was statistically significantly higher than the percentage of successes in the cattle treated with saline (74.4% vs. 24% [$p < 0.001$], and 67.4% vs. 46.2% [$p = 0.002$]). In addition, in the group of calves treated with gamithromycin that were confirmed positive for *M. bovis* (pre-treatment nasopharyngeal swabs), there were more calves at each site (45 of 57 calves, and 5 of 6 calves) classified as successes than as failures.

The effectiveness of ZACTRAN for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica* and *Pasteurella multocida* was demonstrated in two independent studies conducted in the United States. A total of 467 crossbred beef cattle at high risk of developing BRD were enrolled in the study. ZACTRAN (6 mg/kg BW) or an equivalent volume of sterile saline was administered as a single subcutaneous injection within one day after arrival. Cattle were observed daily for clinical signs of BRD and were evaluated for clinical success on Day 10 post-treatment. In each of the two studies, the percentage of successes in the cattle treated with ZACTRAN (86% and 78%) was statistically significantly higher ($p = 0.0019$ and $p = 0.0016$) than the percentage of successes in the cattle treated with saline (36% and 58%).

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The use of lameness in herds as a proxy for the prevalence of DD would underestimate the number of cows affected with DD, as we observed that the majority of clinical lesions fail to induce lameness.

Our team recently reported a study detailing the deep sequencing-based metagenomic evaluation of 48 staged DD biopsy specimens collected during a three-year longitudinal study of disease progression. Over 175 million sequences were evaluated by utilizing both shotgun and 16S metagenomic techniques.

Based on the shotgun sequencing results, there was no evidence of a fungal or DNA viral etiology. The bacterial microbiota of biopsy specimens progresses through a systematic series of changes that correlate with the novel morphological lesion-scoring system developed as part of this project. This scoring system was validated, as the microbiota of each stage was statistically significantly different from those of other stages ($P < 0.001$). The microbiota of control biopsy specimens were the most diverse and became less diverse as lesions developed.

Although *Treponema* spp. predominated in the advanced lesions, they were in relatively low abundance in the newly described early lesions that are believed to be associated with the initiation of the disease process. The consortium of *Treponema* spp. identified at the onset of disease changes considerably as the lesions progress through the morphological stages identified.

The results of this study support the hypothesis that DD is a polybacterial disease process and provide unique insights into the temporal changes in bacterial populations throughout the development of lesions.

BACTERIAL CONNECTION

The widely observed and consistent clinical response to topical antibiotics suggests a bacterial agent as the true etiology of the disease. The association of DD lesions with a variety of bacterial agents, the response of the lesions to antibiotics and the failure to induce disease or protect against it using monovalent vaccines strongly suggest that DD is a polymicrobial disease process.

SCORING SYSTEM FOR DD

In our three-year study, the ISU team used the Iowa DD scoring system to evaluate the epidemiology of natural lesion development by digitally photographing the rear legs of a cohort of dairy cows over a three-year period. Sixty-one adult Holstein dairy cows were monitored for 1,032 cow foot-months, during which they were not exposed to any DD-control measures. The incidence rate of lesion development was four lesions per 100 cow foot-months, with the average time for a lesion to develop being 133 days.

The Iowa DD scoring system classifies lesions as:

Stage 0: Normal skin.

• **Early lesions**

Stage 1: Initial onset lesions. Stage 1 lesions are characterized as small, localized focal to multifocal lesions that have failed to coalesce into a continuous lesion that involves the majority of the plantar skin adjacent to the interdigital cleft.

Stage 2: Developing lesions. Once the lesions have coalesced to involve the majority of the plantar skin adjacent to the interdigital cleft they would be characterized as stage 2.

• **Active lesions**

Stage 3: Lesions associated with clinical disease in the acute hyperemic ulcerative form. The transition to stage 3 lesions is characterized by the presence of an ulcerated, hyperemic circular lesion that has the roughened strawberry-like appearance of a classical DD lesion.

Stage 4: Chronic hyperkeratotic form.

Additionally, stages 1 and 2 are subdivided into two subtypes, with “A” type lesions being exclusively located in the plantar interdigital cleft and having a more ulcerated appearance, and “B” type lesions having a thickened, crusted appearance diffusely spread across the heel.

Whereas 20% of the 1,678 foot observations exhibited clinical DD lesions, an additional 55% of all observations exhibited preclinical stage 1 and 2 lesions that were indicative of DD lesion development (having a different microbial population than that observed in active lesions).

Utilizing the dichotomous categorization of preclinical lesions in the Iowa DD scoring system, it was found that first-lactation heifers had a higher rate of the thickened and crusted “B” type lesions, whereas the ulcerative “A” type lesions were more likely to be identified in multiparous animals.

For clinical DD lesions that received topical treatment, scoring of the post-treatment lesions using the Iowa DD scoring system was found to be useful in prognosticating both the risk of recrudescence and the time until recrudescence.

Systemic disease, systemic antibiotic therapy and periparturient stress were not associated with an increase or decrease in DD lesion scores. Treatment with a single topical tetracycline

wrap was associated with a significant decrease (–1.17) in DD lesion score. The results of this study demonstrate that the complex morphologic changes associated with DD can be readily classified using the Iowa DD scoring system, and the scores can be used to predict and monitor the effects of treatment and prevention measures. In some clinical scenarios it is useful to simplify lesion scoring by condensing the scores down to early lesions (stages 1 and 2) and active lesions (stages 3 and 4). A critical factor in implementing and using a DD scoring system on-farm is having a good understanding of how the data will be used and what outcomes will be measured. A variety of scoring systems have been developed and have utility in the management of DD, and veterinarians and producers are encouraged to determine what scoring system best fits their needs.

Our team conducted routine locomotion scoring throughout the study to monitor for evidence and severity of lameness. Any animal that reached a locomotion score of 4 on the 5-point lameness scale, or any animal noted by caretakers as being lame, was promptly examined by the study personnel.

If lameness was determined to be associated with DD lesions, and no other cause of lameness was observed, treatment with a topical tetracycline wrap was initiated. This wrap consisted of approximately 5 g of oxytetracycline hydrochloride placed over the lesion, then covered with gauze and wrapped with a self-adherent wrap.

In this study, we categorized animals into four possible groups based on the observed outcome following a single treatment of a clinical DD lesion (stage 3 or 4) with a tetracycline wrap. These groups were followed for an average of 300 days post treatment and were classified as:

1. A lesion that did not respond to treatment (i.e., a lesion of stage 3 or 4 did not drop below a stage 3 following treatment).
2. A lesion that responded to treatment (regression to stage 2 or less) but subsequently returned to a stage 3 or 4 lesion within the time of observation,
3. A lesion that responded to treatment (regression to stage 2 or less) and remained as a stage 1 or 2 lesion without returning to normal skin or returning to a clinical lesion.
4. A lesion that responded to treatment and returned to normal skin.

These pictures illustrate the two pre-clinical digital dermatitis lesion types.



PHOTOS: IOWA STATE UNIVERSITY

More advanced clinical or active DD lesions include mature lesions (left) and a more chronic lesion (right).



PHOTOS: IOWA STATE UNIVERSITY

These four outcomes were deemed as nonresponsive to treatment, lesion recrudescence, lesion regression and treatment success, respectively. A treatment failure collectively included all of the first three categories that did not result in a lesion reverting to normal skin. Importantly, following a single application of oxytetracycline we observed an almost 90% treatment failure rate when lesions were followed for an extended period of time (i.e., the majority redeveloped lesions over the following year). The average time to lesion formation was associated with the minimum score achieved following treatment. In cases where the skin returned to normal (only about 10% of the cases), it remained normal throughout the remainder of the follow-up period, which averaged 420 days for that group.

The ability for an early lesion to progress to an advanced lesion is believed to be influenced by a variety of factors that include:

- Exposure to and colonization of the early lesion by bacterial agents necessary for this transition (i.e., the bacteria that differentiate advanced lesions from early lesions based on our prior work, described in Krull *et al.*, 2014).
- Host genetics and immunity.
- Environmental conditions.

Clinical experience would also suggest that in a small number of dairy herds the only types of DD lesions observed are early lesions (stage 1 and 2). At present, it is unclear how the various factors described above work together to limit the transition to advanced lesions, and additional research to answer this interesting question is warranted.

Several other important observations were noted over the course of the three years that have implications as to how we view the incidence of DD. The fact that 75% of observations had lesion scores greater than zero suggests that when cows are not exposed to any DD-prevention measures, the majority of feet in farms with endemic DD could develop some level of DD. With a smaller portion of those lesions being clinical lesions that would be recognized by hoof trimmers and practitioners as classic DD lesions, estimates of incidence rates and prevalence

have the potential to be greatly underestimated in the literature.

Although we did not directly measure prevalence, our calculation of prevalence was in line with other studies' estimates of 20% to 26% in freestall barns (Cramer *et al.*, 2008). Importantly, the use of lameness in herds as a proxy for the prevalence of DD would underestimate the number of cows affected, as we observed that the majority of clinical lesions fail to induce lameness. The use of locomotion score as a way to identify cows with DD was shown to be very inconsistent, with many cows maintaining clinical lesions for months to years without ever reaching a stage 4 or 5 locomotion score. This is consistent with data from Frankena *et al.* (2009), in which only 39% of cows with severe DD lesions ever showed any sign of lameness.

TREATMENT OPTIONS

Topical antibiotic applications remain the best option for controlling and treating active DD lesions. The use of footbaths also plays an important role in the control of earlier lesion stages and likely minimizes the number of animals that develop active mature lesions and become lame. While systemic therapy would be far more convenient, there are no controlled studies that support the efficacy of parenteral treatment with antibiotics routinely used in bovine practice. This is an area in need of further study to confirm the possible benefits of treatment with some of the newer long-acting antibiotics.

Medicated feed also would provide convenience, but no oral antibiotics have a claim for controlling or preventing DD, and it is illegal to use antibiotics in an extra-label manner in feed.

In short, based upon available literature and experience, the best treatments at the present time are individual treatment with topical antimicrobials, topical spray or a well-designed and managed footbath.

Future research into whether more aggressive treatment as a means to return DD lesions back to normal skin would be beneficial in lowering the recrudescence rate is warranted. Additionally, further studies evaluating the economics of treating the more prevalent preclinical lesions before developing into clinical DD lesions should be looked at to reduce lameness and production losses associated with clinical lesions. ©