Clinical Perspectives of Digital Dermatitis in Dairy and Beef Cattle

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KEYWORDS

• Digital dermatitis • Treponema • Bovine • Lameness

KEY POINTS

- Digital dermatitis (DD) is a common disease process of the skin of both dairy and beef cattle.
- Advanced lesions are associated with clinical lameness, whereas early lesions cause local skin disease with minimal lameness.
- Topical treatment with oxytetracycline is the common therapy for advanced lesions but has a high rate of recrudescence.
- An integrated management plan that relies on a combination of topical treatment of advanced lesions coupled with footbathing to control progression of earlier lesions is the most effective strategy.

INTRODUCTION

Description of Digital Dermatitis

The first article to describe the macroscopic appearance of a large number of DD lesions was done on 10 California dairies by Read and Walker in 1998.[1] A majority of the lesions were circumscribed, erosive to papillomatous, and surrounded by a ridge of hyperkeratotic skin bearing hypertrophied hairs. These lesions were typically circular to oval, raised above the surrounding skin, and 2 cm to 6 cm in diameter. Lesions were more likely to involve the rear legs (82%) and a majority (83%) were located on the proximal border of the interdigital space. The macroscopic differences in DD lesion morphology have been described with several novel scoring systems primarily used in research settings.[2–4] The "M" scoring system and the Iowa DD scoring system both describe the macroscopic changes that take place between a normal bovine foot and an end-stage DD lesion. Although each system describes lesions slightly differently, both describe lesions in preclinical and clinical states, with lameness

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only associated with certain stages. It has also been shown that there can be dynamic macroscopic changes between these stages in as few as 7 days.[5,6]

The histopathologic changes associated with DD have been described in numerous publications,[4,7–17] with several of these studies summarizing the histopathologic changes associated with a large set of DD lesions.[4,11] DD lesions were described as having a highly proliferative epidermis, pronounced rete ridge formation, hyperplastic stratum corneum, and acanthotic stratum spinosum. Additional descriptions include lesions having zones of acute degeneration, necrosis, and focal thinning of the stratum corneum with inflammatory cell infiltration. A consistent finding is the microscopic observation of spirochetes within the lesions through the use of silver staining.

Pathophysiology and Etiology

Bovine DD was first morphologically described in 1974 at the 8th International Meeting on Diseases of Cattle in Milan, Italy,[18] but despite more than 40 years of research, the fulfillment of Koch's postulates[19] in identification of an etiologic agent has yet to be achieved. The first report of a spirochete-like, filamentous organism within DD lesions was described by Blowey and Sharp in 1988.[16] It was soon found that these organisms belong to the species *Treponema* and that became the first bacterial species cultivated and implicated in the etiology of bovine DD.[20] Even from the original report, which described 2 unique bacterial morphologies that belonged to the *Treponema* spp, the identification of multiple *Treponema* spp through visual, biochemical, immunologic, and molecular techniques has been a consistent finding.

Treponema spp have been implicated as the causative agent in DD due to their identification in DD lesions by cultivation,[21–23] fluorescence in situ hybridization (FISH),[8,22,24–30] polymerase chain reaction (PCR),[21,31–33] and metagenomics.[3,25,34,35] The nomenclature for the different types of *Treponema* spp has been constantly undergoing changes based on many of the phylotypes having yet to be cultivated. At this point, there are 4 clusters—cluster 1 (*T denticola*/*T pedis*–like), cluster 2 (*T phagedenis*–like), cluster 3 (*T refringens*–like), and cluster 4 (*T medium*/*T vincentii*–like) — that have been reported in the majority of the literature as having clinical relevance to DD.[26] Studies of DD-associated *Treponema* spp have also identified them as having the ability to cause disease by impairing the innate immune and wound repair functions of bovine macrophages.[36] Multiple immunologic studies have also found an increase in antibodies to *Treponema* spp in herds and individual cows with DD.[37,38] Despite all the evidence for *Treponema* spp as the causative agent for DD, Koch's postulates have yet to be fulfilled. Attempts to induce DD lesions with pure cultures of *Treponema* spp have largely failed to consistently induce disease with the characteristic size and severity of naturally occurring DD lesions.[39,40] Additionally, vaccinations against DD-associated *Treponema* spp have failed to decrease the incidence or severity of disease.[41] There is not enough evidence currently available to differentiate *Treponema* spp from a causative organism or merely an organism associated with clinical DD lesions.

For these reasons, numerous other organisms have been studied to determine each one's significance in causing disease. Various *Campylobacter* species as well as *Dichelobacter nodosus* have been cultured from DD lesions and from normal bovine skin.[24] Several researchers[26] have used FISH to determine the level of tissue invasion of various potential pathogens. *D nodosus* was found in 27% and 51% of DD lesions and *Fusobacterium necrophorum* was identified in DD lesions but was found to have minimal invasion in any of the DD tissues evaluated. PCR detection using species-specific primers found *D nodosus* in 100% of DD lesions but also in 60% of normal

skin. Similarly, a study in beef cattle using species-specific PCR found *F necrophorum* in 44% of DD lesions but also found that 32% of healthy feet were positive for *F necrophorum*.[42] In an evaluation of the immune response of cattle and herds with and without a history of DD and found no statistical difference in reactive antibodies to *F necrophorum*[43] between cows or across herds with or without a history of DD. Conversely, cows within herds with DD were more likely to have an immune response to *Bacteroides* spp and *Porphyromonas* spp.[23,43] Viral etiologies, such as *Bovine papillomavirus*, have been proposed as a potential pathogen, but several studies have found no evidence of viral involvement.[14,33]

The use of culture-independent metagenomic techniques has provided the ability to determine the relative abundance of all bacteria within DD lesions without looking for specific targets. In a comparison of DD lesions to normal bovine skin, Yano and colleagues[34] found high numbers of *Treponema* spp and *Bacteroides* spp in DD lesions versus the normal microbiota of bovine skin consisting of *Moraxella* and *Corynebacterium*. Krull and colleagues[3] followed a series of cows for several years and obtained biopsies from DD lesions as they developed from normal skin to DD lesions; 11 families were identified as composing at least 5% of the microbiota at the various stages of lesion development. The Spirochaetaceae family increased dramatically from only 1.3% in control feet and to 69.7% in clinical lesions. As lesions developed from normal to diseased feet, an increase in several previously implicated bacterial families was noted, which included the Mycoplasmataceae, Porphyromonadaceae, and Campylobacteraceae families. In a closer look at the Spirochaetaceae family, there was found a change in the *Treponema* spp in preclinical lesions versus clinical lesions; 4 *Treponema* spp that were previously in very low numbers (<3%) in preclinical lesions (*T* PT8, *T denticola*, *T pedis*, and *T medium*) were found to comprise greater than 65% of the *Treponema* population in clinical lesions. Accompanying this increase in the population of these 4 species was a rapid decline in 4 of the 5 highly abundant *Treponema* spp identified in preclinical lesion, which then comprised less than 1% of the *Treponema* population in clinical lesions.

Although there is a consistent presence of multiple *Treponema* spp in DD lesions,[16,25–27,29,31–35,44–46] 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.[39] Additionally, the clinical use of vaccines focused against spirochetes provides limited protection against the disease process.[41] Although the consistent clinical response to antibiotic therapy suggests a bacterial agent involved in the etiology of the DD,[9,10,47–58] the fulfillment of Koch's postulates in identifying the key bacterial constituent necessary to produce disease has yet to be proved. The association of DD lesions with a variety of bacterial agents, the response of the lesions to antibiotics, and the failure to induce or protect from the disease using monovalent vaccines strongly suggest that DD is a polymicrobial disease process.[41,59,60]

Similarities to Other Polymicrobial Treponema-associated Diseases

Several research teams have recognized that the bacterial community composition of DD has notable similarities to that of human periodontal disease. Given that human periodontal disease has had significantly greater investments of research time and money, it is prudent to evaluate the similarities between it and DD to gain insights into these complex polymicrobial communities. The bacterial progression of periodontal disease has been extensively studied and develops with successive waves of bacterial colonization.[59,61–65] These waves are consistent in their bacterial composition and are largely driven by the ability of each stage to set up a favorable

ecologic environment (in terms of available nutrient sources, oxygen tension, and so forth) for the colonization and growth of the following wave of bacterial agents. Several key themes emerge from this comparison that are helpful in better understanding DD.

First, the 2 disease processes share significant similarities in bacterial populations at the family and genus levels. Early colonizers of periodontal disease include the gram-positive cocci, followed by a wave of gram-positive and gram-negative rods and finally the anaerobic gram-negative rods. The early and midstage colonizers share notable overlap with organisms that are routinely isolated from DD lesions, including *Campylobacter* spp, *Bacteroiodes* spp, and *Fusobacterium* spp. As these organisms colonize they start to push the microenvironment away from a purely aerobic environment toward a more anaerobic niche at the microscopic scale. This process is critical to the development of disease given that the later bacterial colonizers are largely microaerophilic or anaerobic and do not readily grow in the initial aerobic environment of the oral cavity of humans or the skin of cattle. Additionally, as these organisms transition the microenvironment to an anaerobic one, they also transition the overall metabolic profiles of the bacterial community from largely saccharolytic (use glucose and sugars for energy) to one that relies more heavily on proteolytic metabolism of proteins.[66] This transition in local metabolism is believed critical in providing an environment for the colonization of the later colonizers of both disease processes that include the *Treponema* spp and *Porphyromonas* spp that exclusively utilize volatile fatty acids (VFAs) as an energy source as opposed to sugars. The transitions of microbial populations over disease progression described for DD[3] share remarkable similarities with the well-described changes in periodontal disease, which makes biological sense when considering the need for the final-stage organisms (namely the *Treponema* spp and *Porphyromonas* spp) to have an environment conducive to their growth.

Second, an improved understanding of the role that this sequential bacterial colonization process plays in the establishment of a conducive growth environment for the subsequent organism provides insights into explaining how an anaerobic organism, such as the *Treponema* spp, can colonize an aerobic environment like the surface of the skin. In summary, the early colonizers (largely aerobic saccharolytic organisms) set up a favorable microenvironment for the midstage colonizers (facultative anaerobes that shift metabolism sugars to produce VFAs) that then allow for the final colonization of the late-stage organisms that cannot colonize the initial aerobic environment with minimal concentrations of the VFAs that they require for growth.[66]

Finally, there is a significant body of literature on the periodontal communities to demonstrate that the late-stage colonizers, *T denticola* and *Porphyromonas gingivalis*, not only communicate with each other but also actually have direct contact between the cells.[62–64,67,68] This interaction has been demonstrated as critical to the virulence and pathogenicity of these organisms and is the focus of much of the ongoing research in this field. Based on the similarities of these 2 disease processes and that these organisms share significant genetic similarity to the specific species isolated from DD lesions, it seems prudent to consider that similar cross-species interactions are occurring and important in DD. As such, consideration of the *Treponema* spp as part of a larger bacterial community that plays a role in the progressive development and manifestation of DD lesions seems biologically prudent.

Epidemiology of Digital Dermatitis

DD has been found to have the greatest impact on welfare of all bovine lameness disorders due to high incidence and long duration.[69] With lame cows having proved difficult to identify and vastly underestimated by producers,[70] the use of lameness as an

estimate for DD prevalence has also been shown unreliable, with only 39% of cows with severe DD lesions showing signs of lameness.[71] Estimates of prevalence have been published across multiple countries[7,11,24,72–78] and range from 1.4% in 14 Norwegian herds to 39% in 5 Danish herds. The large range of prevalence reported from these studies was highly variable based on location, management system, and prevention measures used. For herds in free-stall barns, most estimates suggest a prevalence of 20% to 25% of animals affected. These estimates are based on the prevalence of clinical DD lesions that have been described as having the typical characteristics of end-stage DD lesions.

Several longitudinal studies have attempted to report the rate at which DD lesions develop. Three unique studies in 3 different countries (United States, United Kingdom, and France) found the rate of DD lesion development approximately 4 cases per 100 cow foot–months in the absence of preventative measures,[79–81] with the average time for a lesion to develop from normal skin to a DD lesion between 133 days and 146 days.[79,81] Additionally, lameness is always associated with a macroscopically clinical DD lesion and not any of the preclinical DD morphologies. Krull and colleagues found that the average time from the development of a clinical DD lesion to the onset of lameness was 161 days. This is similar to a study by Frankena and colleagues[71] that found only 39% of cows with clinical lesions were considered lame.

Economic Impact of Digital Dermatitis

Bovine DD is a leading cause of lameness in dairy cattle in the United States[82] but has also been reported at various levels in beef cattle.[11,42,83] In the most recent National Animal Health Monitoring System survey of US dairy farms, DD accounted for 61.8% of the lameness in bred heifers and 49.1% of the lameness in cows.[82] DD was determined the most costly of all foot disorders ($95 per case) in a stochastic simulation model when an estimated prevalence of 20% for clinical DD was used.[84] When milk production losses associated with treatment, decreased reproductive performance, and treatment were incorporated, the losses were estimated at $126 to $133 for every clinical case of DD.[85,86] The total economic losses to the dairy industry has been calculated at $190 million per year in the United States.[87] The estimated economic impact in the United States was based on the 17% prevalence from 1996 National Animal Health Monitoring System (NAHMS) report. The 2007 NAHAMS report estimates the current prevalence at 28%,[82] which suggests the $190 million per year estimate vastly underestimates the economic impact in the United States.

CLINICAL CORRELATION

Dairy

In dairy cattle operations, lesions are most commonly identified in the plantar aspect of the interdigital cleft of the rear feet of lactating cows. Larger lesions may extend into the interdigital space in some cows. Rarely, lesions form on the dorsal aspect of the rear feet. Although less common, lesions occasionally occur on the front feet where they most commonly are located on the dorsal surface of the foot. The reason for the higher incidence on the palmar aspect of the rear feet is unclear; however, several hypotheses have been raised. Some investigators have speculated that the rear feet are at higher risk for exposure and lesion development due to those feet having more exposure to manure slurry, remaining more moist in many tie-stall and free-stall type situations, and their having shorter heels due to a lower hoof angle. Additionally, the plantar aspect of the rear feet has the potential to have more exposure and trauma to the stall mats when an animal is laying in a normal position, in contrast to

the forelimbs, which have more exposure to the stall mats on the dorsal aspect of the claw. Lesions in younger animals and dry animals are reportedly less commonly observed by producers but are known to occur and may have a high prevalence in some herds. In many cases, the softer bedding (bedded pack vs free stall), lower body weight, and lower requirement for walking significant distances to be milked may result in a decreased ability to identify these lesions in younger animals or may delay recognition of lesions until the animal freshens and enters the lactating pen.

DD has been considered a leading cause of lameness in the dairy cattle industry for the past several decades; however, its role in beef cattle lameness has more recently emerged as a concern. Based on that fact, the first US clinical descriptions of lesions consistent with what is now called DD were identified in beef cattle.[88,89] Despite these early descriptions in beef cattle, disease identification and control efforts have been largely focused on dairy cattle management, where the lesions have historically caused the most problems. Given the high farm-level prevalence of the disease (finding a negative farm is rare), most dairy operations have been forced to development management protocols that control the animal-level incidence and severity of disease. These protocols typically revolve around a combination of approaches (discussed later) but often focus on the use of intermittent footbathing in combination with targeted treatment of lesions associated with lameness. Within-herd prevalence varies considerably, with some herds maintaining infection rates relatively low using control methods and good biosecurity and other herds having very high incidence of lesions.

Lesions develop over a series of stages that have morphologic differences that can be observed on physical examination (**Fig. 1**). This has led to the development of a variety of lesion staging systems that can be applied based on lesion appearance. The application of lesion staging in clinical medicine has potential benefits regarding treatment decision-making and monitoring treatment success. The decision of which scoring system provides the most information for a clinician should be driven by the needs and desired outcomes of the monitoring. In research settings, more complex systems with a higher number of stages might be useful for monitoring progress of therapy in higher resolution, whereas in many field situations a simpler staging system (for example a system based on description of the lesion — early or advanced) may provide the needed information while making it easier to train employees and get consistent observations. More advanced lesions are the ones associated with clinical lameness and likely shed massive numbers of infectious bacteria into the environment, so accurate diagnosis of those is potentially beneficial in terms of identifying lesions at high risk for causing lameness and treatment to lesson environmental pathogen load. Earlier lesions, although less likely to induce clinical disease, are key targets for management interventions to prevent their progression to more advanced lesions associated with clinical disease and potentially lameness. The period over which lesions develop from normal skin to advanced clinical lesions has also been studied by several groups. In a 3-year prospective observational study of cattle that received no blanket DD prevention measures, the authors showed that the average time from the first evidence of skin changes to the development of a classic clinical lesion (score = M2 or Iowa stage 3) averaged 133 days (range = 38–315 d, median = 105 d).[79] These results were similar to a multifarm study of 4000 cows in France, where the investigators found an average period of 146 days.[81] Both of these studies relied on observations of the feet while each individual was restrained in a trimming chute for detailed assessment of the skin. In many field situations, where observations are made simply by observing animals standing in stalls or in the milk parlor, it is likely that very early lesions may be missed, making the period of development seem shorter. It is also critical to realize that these progression periods are in the absence of

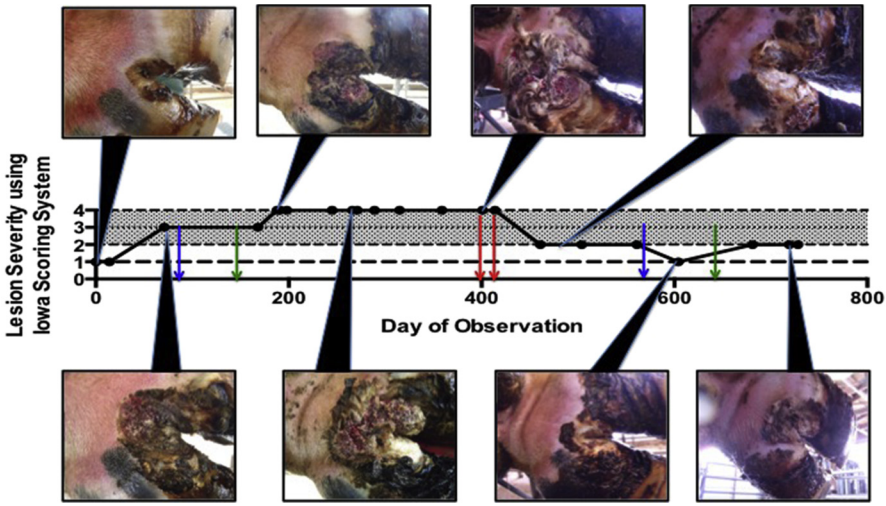

Fig. 1. A representative progression of a digital dermatitis lesion observed over a 2-year period. All pictures are of the same left rear foot of a Holstein dairy cow that was not exposed to any footbaths or management procedures other than routine hoof trimming. Blue arrows denote dry-off of the cow, green arrows denote freshening, and red arrows denote topical treatment with oxytetracycline due to significant lameness (locomotion score of >3 on 5-point scale). The lesion severity is recorded in the center timeline of the image using the linear Iowa DD scoring system.[3,79] The gray shaded area denotes lesions considered advanced lesions (stages 3–4) and the white area denotes preclinical lesions (stages 1–2). Several points are illustrated by these data. (1) In the absence of footbaths and treatment, the lesions are chronic in nature and progress very slowly. (2) This animal was regularly monitored during this 2-year period and treated with topical oxytetracycline when a locomotion score greater than 3/5 was observed (*red arrows*). Thus, despite having an obvious lesion for the entirety of this 2-year period, there were only a handful of days where this animal demonstrated significant lameness. (3) After 2 sequential topical treatments with oxytetracycline, the lesion decreases to a lower severity score but remains present as a lower severity for the full 200 days remaining in the observation period. (4) After both freshening dates (*green arrows*), the lesion on this foot increased severity score; however, this trend is not consistent across all cows observed and is likely influenced by a variety of other factors, including weather, genetics, and concurrent disease. (5) After treatment, lesions that do not heal develop a morphologic appearance similar to early lesions and contain a bacterial community identical to that of the early lesions. (*Adapted from* Krull AC, Shearer JK, Gorden PJ, et al. Deep sequencing analysis reveals temporal microbiota changes associated with development of bovine digital dermatitis. Infect Immun 2014;82:3359–73; and Krull AC, Shearer JK, Gorden PJ, et al. Digital dermatitis: Natural lesion progression and regression in Holstein dairy cattle over 3 years. J Dairy Sci 2016;99:3718–31, with permission.)

any prevention or treatment measures. Therefore, the dynamics of lesion changes are likely to occur differently in the face of routine management or therapeutic interventions.

Beef

Over the past decade, identification and interest in DD lesions in beef cattle have increased considerably. The most common clinical presentation in the feedlot situation involves development of lameness in heavy cattle that are close to marketing.

This timing of lameness development presents significant challenges for effected feedlots, because there are significant concerns associated with residues that may be incurred due to lesions treatment and due to concerns transporting lame cattle to slaughter. At present, it is unclear exactly when and how the lesions develop in feedlots, and more work is currently under way to investigate these issues. Based on anecdotal observations, a portion of cattle enter the feedlot with early lesions that have started development prior to arrival. The number of cattle that fall into this category is likely influenced by a variety of factors, including the number of sources of cattle (commingled vs single source), prevalence of DD on farms of origin, breed/genetics, and age of the cattle. It seems likely that these cattle are more prone to developing lesions earlier during the feeding period than those that enter with no lesions. The authors also hypothesize that many cattle that enter the feedlot without lesions develop new lesions associated with exposure to either infected animals in the pen (discussed previously) or due to a contaminated pen environment. In feedlots that do not practice routine DD management strategies, lameness associated with heavy cattle is consistent with a similar timeline for lesion progression of dairy cattle in the absence of management interventions, at approximately 4 months.[79]

Nontypical Lesions (White Line, Sole Ulcer, and So Forth)

In recent years, there has been increasing reports of other claw horn lesions of cattle that seem to not be healing after routine therapy.[90] Specific examples include sole ulcers that fail to heal after therapeutic trimming and wooden block placement or white line lesions that fail to heal after appropriate trimming. There are some data to suggest that in some of these cases the corium that is exposed in these lesions has become infected with DD-associated organisms. Once infected, these lesions become significantly more difficult to heal and additional therapy focused on bacterial infections may be necessary in addition to routine trimming.

OTHER BOVINE LESIONS ASSOCIATED WITH DIGITAL DERMATITIS TREPONEMES

There is a growing body of evidence to demonstrate that a large variety of bovine skin lesions of the limbs and udder contain similar bacterial organisms to those of DD. Although full comparisons of the microbial compositions of many of these lesions are lacking, focus has been on identifying similar treponemal organisms to those observed in DD. These organisms have been identified in bovine ulcerative mammary dermatitis,[91,92] bovine teat ischemic necrosis,[93] toe necrosis,[94,95] and hock skin lesions.[96] The identification of these same organisms over a wide variety of bovine skin-related diseases suggest that these organisms have found a favorable niche for colonization in open wounds of cattle skin, although to date there is no evidence that this association has proved causation.

TREATMENT

Patient Evaluation Overview

Treatment or management interventions are likely to take 2 basic forms: individual focused therapeutic interventions of cattle with clinical lameness or obvious advanced lesions and herd-based prevention strategies designed to minimize the progression of lesions to advanced stages associated with clinical disease. Successful programs generally need to use a comprehensive variety to interventions to control the disease once it is endemic. Based on present-day clinical experience, eradication of DD from herds that are infected is not likely to be accomplished and management of the process to minimize clinical disease should be the goal. As with most herd health

programs, monitoring of lesion prevalence and clinical disease assists clinicians in identifying gaps in the management program and allows for continual process improvement. A variety of helpful tools ranging from lesions scoring systems to record-keeping software packages have been developed and may be considered for application in management strategies[97] (Zinpro Corporation, Eden Prairie, Minnesota; Supervisor Systems, Dresser, Wisconsin).

Treatment of individual cows with DD lesions is usually based on 1 of 2 mechanisms. First, during routine foot trimming, cows with DD lesions should be identified and treated. Although there are few data regarding the cost benefit of this type of treatment, it is generally regarded as beneficial and important to DD management. In most cases, all identified lesions are treated regardless of the clinical stage of lesion development. Observation and recording of lesion prevalence and lesion severity are beneficial in monitoring disease status in the herd and modifying management strategies based on outcome. In addition, most individual animal treatment systems incorporate treatment of DD lesions that are identified in cattle exhibiting clinical lameness. Most DD lesions are painful to the touch, but a majority of DD lesions are not associated with lameness.[79] DD may also occur concurrent to other hoof lesions in cattle, so a complete physical examination and hoof evaluation should be conducted. Clinical lameness associated with DD is confined to animals with advanced lesions.[79] As such, identification of early lesions in cattle with significant lameness should warrant further investigation for another cause of the lameness. Treatment of DD in such cases, along with appropriate treatment of any additional cause of lameness, is warranted. Additionally, in cases of other claw horn lesions that result in exposure of corium, the possibility of a concurrent bacterial infection of the corium associated with DD organisms that could delay or prevent appropriate healing should be considered.

Pharmacologic Treatment Options

Pharamacologic treatment of DD generally focuses on a single application of a topical antimicrobial applied directly to the lesion. The most commonly used products include oxytetracycline soluble powder or tetracycline powder. Few data are available regarding appropriate dosing, and many clinicians and professional hoof trimmers empirically report a dose of between 2 g and 25 g of powder applied topically to the lesion. There is no evidence that the higher dose provides improved treatment outcomes over lower doses, whereas using lower doses decreases the use of antibiotics. Clinicians are directed to consult the Food Animal Residue Avoidance Databank for withdrawal recommendations; however, it has been suggested that there is likely minimal risk of milk residues with the lower doses when the number of cows treated at one time in the herd is limited.[98] Although the dose is commonly applied and held in place with a light bandage, there is no evidence that this practice leads to improved outcomes and it has been speculated to actually be counterproductive due to trapping debris, footbath solution, and manure against the lesion for a prolonged period of time.[99] Furthermore, topical treatment with a paste made from the oxytetracycline powder has been shown as effective as applying the dose with a wrap.[48,98] Dosing of 2 g of oxytetracycline paste applied in a paste made of 3:1 glycol to water has been recommended.[98] If a clinician does elect to use a wrap, it is recommended that the wrap be minimal in nature and designed to fall off or be removed after several days.

In cases of treatment applied to a cow with clinical lameness associated with the DD lesion, the lameness generally improves 1 to 2 locomotion scores within a couple-day period after treatment. The lesions typically turn blackish in color and develop a thick

scab after oxytetracycline treatment. Although many people assume that these lesions are healing, the data suggest that in many cases infection remains below the scab and the lesions recrudesce once the scab falls off or is removed. Evaluation of 43 cows that were observed for a minimum of 50 days after therapy revealed that although a majority (93%) of them had an improvement in lesion score after treatment, only 9% of them returned to normal skin.[79] These data demonstrate that single-application therapy for topical oxytetracycline is likely to aid in improving acute lameness and reduce the severity of the lesion; however, it is unlikely to resolve the infection. In addition, approximately half of those animals that did not have the skin completely healed had lesion regression over the following year, and many of them required retreatment.[79] These findings suggest that clinicians need to be cautious when stating that animals that are repeatedly treated for DD are getting reinfected (as is commonly stated in the literature). It is more likely that these animals were never completely cured and are simply having a recrudescence of disease.

The application of systemic antibiotic therapy for the control of DD has been recently reviewed elsewhere in detail.[100] Although in vitro sensitivity testing has been described, there are no validated methods for this procedure that are approved by international laboratory testing authorities and there are no confirmed set points for Minimum Inhibitory Concentration (MIC) classification. As a consequence, results from these studies need to be interpreted with caution. With that in mind, in vitro sensitivity testing suggests that the DD-associated treponemes have only intermediate sensitivity to lincomycin, spectinomycin, oxytetracycline, ceftiofur, and gentamicin. In contrast, those treponemes had higher levels of sensitivity to penicillin, penicillin derivatives, and the macrolides.[49,54,101] Given the polymicrobial and polytreponemal nature of DD, clinicians should be cautious in making blanket assessments of drug susceptibility based on single-organism testing; however, these results suggest that many of the most commonly used antibiotics in dairy cattle of the United States (tetracyclines and cephalosporins) may have poor efficacy against the most prevalent bacteria in these lesions. This observation is supported by clinical data that demonstrate that concurrent therapy with these commonly used antibiotics had no significant impact on DD lesion severity.[79] In vitro sensitivities to penicillin were better for the treponemes, and there are data to suggest that systemic penicillin (aqueous procaine penicillin G; intramuscularly; 3 days; 18,000 U/kg; twice daily) does improve clinical lesions[1]; such a treatment regimen would not be clinically applied in most US dairy systems due to milk residues and the time associated with twice-daily application of antibiotics to the large number of animals commonly infected in US dairies.

Nonpharmacologic Treatment Options

In recent years there has been significant interest in the importance of macro and micro mineral nutrition in hoof health and lameness. At present, there is 1 commercial mineral mix that includes higher than typically recommended levels of organic trace minerals and iodine marketed for aid in maintaining appropriate hoof health. This mineral mix was specifically tested under research conditions for its ability to reduce the incidence of experimentally induced DD lesions.[102] Although the investigators were able to demonstrate a trend toward a decrease incidence of lesion formation and overall size of the lesion, neither result reached the level of statistical significance. Mineral nutrition, however, is beneficial in general hoof health and lameness; therefore, clinicians are encouraged to consider these issues and assure appropriate mineral nutrition in farms with significant lameness problems.

There is also a diverse range of commercially available therapies marketed for the control of DD. In almost all cases there are few to no evidence-based medicine trials

to suggest improved therapeutic efficacy and control. Many products cite anecdotal reports or the results of poorly controlled studies; however, clinicians should consider these reports in light of the standard evidence-based medicine principles. There is a significant need for additional work comparing the efficacy of these products to the current gold standard–type therapies using strong unbiased research approaches that allow for direct comparison of treatment efficacy. Another commonly encountered problem in these types of trials is the use of inappropriate outcomes or comparisons. For instance, many companies try to use resolution of clinical lameness or lameness prevalence as a measure of treatment efficacy. Given that only a small percentage of animals with DD experiences clinical lameness, however, use of this measure as a proxy for lesion prevalence is risky and generally misleading.

Treatment Resistance/Complications

As discussed previously, there is a high rate of treatment failure after the single application of topical oxytetracycline when animals are monitored for periods of time sufficient for the initial scab formed by the treatment to fall off. Several shorter-term studies that followed animals for 14 days to 30 days post-treatment with a single dose of topical tetracycline have reported moderate to good cure rates, ranging from 68% to 87%, although 1 showed cure rates of only 14%.[2,55,103] Given that the scab that forms looks smooth, dry, and less painful, it is fairly easy to see why these lesions are considered healed. In contrast, when following these animals for longer periods of time that allow for the scab to fall off, a different picture emerges. When animals were followed a minimum of 50 days with an average of 289 days, only 9% returned to normal skin; 40 of the 43 animals had improvement of at least 1 score after treatment; however, only 4 went to normal skin and 17 of the others demonstrated an increased lesion severity during the follow-up period.[79]

An additional complication is the secondary invasion of these organisms in any other claw horn lesions that result in exposure of the corium. When cattle with sole ulcers, white line lesions, or toe necrosis fail to heal as expected, the potential for concurrent infection with DD-associated organisms in these lesions should be considered.

MANAGEMENT/PREVENTION

Management of DD in dairies or feedlots requires an integrated multifaceted approach that relies on a variety of tools and interventions. Key to this process is monitoring the disease prevalence and treatment success, and these measures should be emphasized at all levels of management. Record keeping of lameness, etiology of lameness, treatment success, eventual outcome, and footbath usage should be emphasized and required.

Most effective management approaches rely on a combination of individual animal treatment of advanced lesions and footbathing to assist in controlling the progression of early lesions to clinical disease. For a more detailed discussion of footbathing, see Nigel B. Cook's article, "A Review of the Design and Management of Footbaths for Dairy Cattle," in this issue. Footbaths require management and monitoring and, therefore, time, cost, and energy. In feedlots, use of footbaths is increasingly common. As opposed to the single-lane footbaths that are routinely used in dairies, these feedlots often install wider and longer baths that allow larger loads of animals to walk through as a group. Although there is no consensus at present on when and how often to footbath feedlot cattle, common times include entry into the feedlot and perhaps several times during the feeding period (ie, at reimplant and so forth). In terms of biosecurity,

moving animals through the footbath on arrival may provide some additional benefit for control of animals entering with the disease, especially animals with early lesions.

Biosecurity of the farm is also a consideration. Care should be taken to not purchase and introduce animals into the housing facility from herds known to have DD. This is especially important for dairies and feedlots that currently have minimal issues with the disease. When possible, animals should be purchased from trusted sources in which the risk of DD can be adequately assessed prior to purchase. In addition, there is a documented increased risk of having significant DD problems in farms that use professional traveling foot trimmers. As such, training and implementation of in-house foot care teams provide significant benefits in limiting biosecurity risk. DD-associated organisms have been identified on foot-trimming equipment, and these instruments should be regularly disinfected after use on animals with DD lesions when feasible.[92,104]

REFERENCES

1. Read DH, Walker RL. Papillomatous digital dermatitis (footwarts) in California dairy cattle: clinical and gross pathologic findings. J Vet Diagn Invest 1998; 10:67–76.
2. Manske T, Hultgren J, Bergsten C. Topical treatment of digital dermatitis associated with severe heel-horn erosion in a Swedish dairy herd. Prev Vet Med 2002;53:215–31.
3. Krull AC, Shearer JK, Gorden PJ, et al. Deep sequencing analysis reveals temporal microbiota changes associated with development of bovine digital dermatitis. Infect Immun 2014;82:3359–73.
4. Dopfer D, ter Huurne AAHM, Cornelisse JL, et al. Histological and bacteriological evaluation of digital dermatitis in cattle, with special reference to spirochaetes and Campylobacter faecalis. Vet Rec 1997;140:620–3.
5. Nielsen BH, Thomsen PT, Green LE, et al. A study of the dynamics of digital dermatitis in 742 lactating dairy cows. Prev Vet Med 2012;104:44–52.
6. Dopfer D, Holzhauer M, Boven M. The dynamics of digital dermatitis in populations of dairy cattle: model-based estimates of transition rates and implications for control. Vet J 2012;193:648–53.
7. van Amstel SR, van Vuuren S, Tutt CL. Digital dermatitis: report of an outbreak. J S Afr Vet Assoc 1995;66:177–81.
8. Capion N, Boye M, Ekstrom CT, et al. Infection dynamics of digital dermatitis in first-lactation Holstein cows in an infected herd. J Dairy Sci 2012;95:6457–64.
9. Berry SL, Read DH, Famula TR, et al. Long-term observations on the dynamics of bovine digital dermatitis lesions on a California dairy after topical treatment with lincomycin HCl. Vet J 2012;193:654–8.
10. Berry SL, Read DH, Walker RL, et al. Clinical, histologic, and bacteriologic findings in dairy cows with digital dermatitis (footwarts) one month after topical treatment with lincomycin hydrochloride or oxytetracycline hydrochloride. J Am Vet Med Assoc 2010;237:555–60.
11. Brown CC, Kilgo PD, Jacobsen KL. Prevalence of papillomatous digital dermatitis among culled adult cattle in the southeastern United States. Am J Vet Res 2000;61:928–30.
12. Milinovich GJ, Turner SA, McLennan MW, et al. Survey for papillomatous digital dermatitis in Australian dairy cattle. Aust Vet J 2004;82:223–7.
13. Shibahara T, Ohya T, Ishii R, et al. Concurrent spirochaetal infections of the feet and colon of cattle in Japan. Aust Vet J 2002;80:497–502.

14. Rebhun WC, Payne RM, King JM, et al. Interdigital papillomatosis in dairy cattle. J Am Vet Med Assoc 1980;177:437–40.
15. Bassett HF, Monaghan ML, Lenhan P, et al. Bovine digital dermatitis. Vet Rec 1990;126:164–5.
16. Blowey RW, Sharp MW. Digital dermatitis in dairy cattle. Vet Rec 1988;122:505–8.
17. Blowey RW, Done SH, Cooley W. Observation on the pathogenesis of digital dermatitis in cattle. Vet Rec 1994;135:115–7.
18. Cheli R, Mortellaro CM. Digital dermatitis in cattle. In: 8th International Meeting on Diseases of Cattle. Piacenza (Italy), 1974. p. 208–13.
19. Untersuchungen über Bakterien: V. Die Ätiologie der Milzbrand-Krankheit, begründet auf die Entwicklungsgeschichte des Bacillus anthracis. Investigations into bacteria: V. The etiology of anthrax, based on the ontogenesis of Bacillus anthracis. Cohns Beitrage zur Biologie der Pflanzen (in German) 1876;2(2):277–310.
20. Walker RL, Read DH, Loretz KJ, et al. Spirochetes isolated from dairy cattle with papillomatous digital dermatitis and interdigital dermatitis. Vet Microbiol 1995;47:343–55.
21. Demirkan I, Carter SD, Hart CA, et al. Isolation and cultivation of a spirochaete from bovine digital dermatitis. Vet Rec 1999;145:497–8.
22. Schrank K, Choi BK, Grund S, et al. Treponema brennaborense sp. nov., a novel spirochaete isolated from a dairy cow suffering from digital dermatitis. Int J Syst Bacteriol 1999;49(Pt 1):43–50.
23. Trott DJ, Moeller MR, Zuerner RL, et al. Characterization of Treponema phagedenis-like spirochetes isolated from papillomatous digital dermatitis lesions in dairy cattle. J Clin Microbiol 2003;41:2522–9.
24. Knappe-Poindecker M, Gilhuus M, Jensen TK, et al. Interdigital dermatitis, heel horn erosion, and digital dermatitis in 14 Norwegian dairy herds. J Dairy Sci 2013;96:7617–29.
25. Klitgaard K, Boye M, Capion N, et al. Evidence of multiple Treponema phylotypes involved in bovine digital dermatitis as shown by 16S rRNA gene analysis and fluorescence in situ hybridization. J Clin Microbiol 2008;46:3012–20.
26. Rasmussen M, Capion N, Klitgaard K, et al. Bovine digital dermatitis: possible pathogenic consortium consisting of Dichelobacter nodosus and multiple Treponema species. Vet Microbiol 2012;160:151–61.
27. Choi BK, Nattermann H, Grund S, et al. Spirochetes from digital dermatitis lesions in cattle are closely related to treponemes associated with human periodontitis. Int J Syst Bacteriol 1997;47:175–81.
28. Moter A, Leist G, Rudolph R, et al. Fluorescence in situ hybridization shows spatial distribution of as yet uncultured treponemes in biopsies from digital dermatitis lesions. Microbiology 1998;144(Pt 9):2459–67.
29. Nordhoff M, Moter A, Schrank K, et al. High prevalence of treponemes in bovine digital dermatitis-a molecular epidemiology. Vet Microbiol 2008;131:293–300.
30. Schlafer S, Nordhoff M, Wyss C, et al. Involvement of Guggenheimella bovis in digital dermatitis lesions of dairy cows. Vet Microbiol 2008;128:118–25.
31. Rijpkema SG, David GP, Hughes SL, et al. Partial identification of spirochaetes from two dairy cows with digital dermatitis by polymerase chain reaction analysis of the 16S ribosomal RNA gene. Vet Rec 1997;140:257–9.
32. Collighan RJ, Woodward MJ. Spirochaetes and other bacterial species associated with bovine digital dermatitis. FEMS Microbiol Lett 1997;156:37–41.

33. Brandt S, Apprich V, Hackl V, et al. Prevalence of bovine papillomavirus and Treponema DNA in bovine digital dermatitis lesions. Vet Microbiol 2011;148:161–7.
34. Yano T, Moe KK, Yamazaki K, et al. Identification of candidate pathogens of papillomatous digital dermatitis in dairy cattle from quantitative 16S rRNA clonal analysis. Vet Microbiol 2010;143:352–62.
35. Klitgaard K, Foix Breto A, Boye M, et al. Targeting the treponemal microbiome of digital dermatitis infections by high-resolution phylogenetic analyses and comparison with fluorescent in situ hybridization. J Clin Microbiol 2013;51:2212–9.
36. Zuerner RL, Heidari M, Elliott MK, et al. Papillomatous digital dermatitis spirochetes suppress the bovine macrophage innate immune response. Vet Microbiol 2007;125:256–64.
37. Walker RL, Read DH, Loretz KJ, et al. Humoral response of dairy cattle to spirochetes isolated from papillomatous digital dermatitis lesions. Am J Vet Res 1997;58:744–8.
38. Demirkan I, Walker RL, Murray RD, et al. Serological evidence of spirochaetal infections associated with digital dermatitis in dairy cattle. Vet J 1999;157:69–77.
39. Gomez A, Cook NB, Bernardoni ND, et al. An experimental infection model to induce digital dermatitis infection in cattle. J Dairy Sci 2012;95:1821–30.
40. Krull AC, Cooper VL, Coatney JW, et al. A Highly Effective Protocol for the Rapid and Consistent Induction of Digital Dermatitis in Holstein Calves. PLoS One 2016;11:e0154481.
41. Berry SL, Ertze RA, Read DH, et al. Field evaluation of Prophylactic And Therapeutic Effects of a Vaccine Against (Papillomatous) Digital Dermatitis of Dairy Cattle in Two California Dairies. In: 13th International Symposium on Ruminant Lameness. Slovenija (Maribor). February 11–15, 2004.
42. Sullivan LE, Evans NJ, Blowey RW, et al. A molecular epidemiology of treponemes in beef cattle digital dermatitis lesions and comparative analyses with sheep contagious ovine digital dermatitis and dairy cattle digital dermatitis lesions. Vet Microbiol 2015;178(1–2):77–87.
43. Moe KK, Yano T, Misumi K, et al. Detection of antibodies against Fusobacterium necrophorum and Porphyromonas levii-like species in dairy cattle with papillomatous digital dermatitis. Microbiol Immunol 2010;54:338–46.
44. Evans NJ, Brown JM, Demirkan I, et al. Three unique groups of spirochetes isolated from digital dermatitis lesions in UK cattle. Vet Microbiol 2008;130:141–50.
45. Evans NJ, Brown JM, Demirkan I, et al. Association of unique, isolated treponemes with bovine digital dermatitis lesions. J Clin Microbiol 2009;47:689–96.
46. Klitgaard K, Nielsen MW, Ingerslev HC, et al. Discovery of bovine digital dermatitis-associated Treponema spp. in the dairy herd environment by a targeted deep-sequencing approach. Appl Environ Microbiol 2014;80:4427–32.
47. Apley MD. Clinical evidence for individual animal therapy for papillomatous digital dermatitis (hairy heel wart) and infectious bovine pododermatitis (foot rot). Vet Clin North Am Food Anim Pract 2015;31:81–95, vi.
48. Cutler JH, Cramer G, Walter JJ, et al. Randomized clinical trial of tetracycline hydrochloride bandage and paste treatments for resolution of lesions and pain associated with digital dermatitis in dairy cattle. J Dairy Sci 2013;96:7550–7.
49. Evans NJ, Brown JM, Demirkan I, et al. In vitro susceptibility of bovine digital dermatitis associated spirochaetes to antimicrobial agents. Vet Microbiol 2009;136:115–20.

50. Hernandez J, Shearer JK. Efficacy of oxytetracycline for treatment of papillomatous digital dermatitis lesions on various anatomic locations in dairy cows. J Am Vet Med Assoc 2000;216:1288–90.
51. Laven RA, Hunt H. Comparison of valnemulin and lincomycin in the treatment of digital dermatitis by individually applied topical spray. Vet Rec 2001;149:302–3.
52. Loureiro MG, Rodrigues CA, Nascimento ES, et al. Efficacy of topical and systemic treatments with oxytetracycline for papillomatous digital dermatitis in cows. Arquivo Brasileiro de Medicina Veterinária e Zootecnia 2010;62:13–22.
53. Shearer JK, Hernandez J. Efficacy of two modified nonantibiotic formulations (Victory) for treatment of papillomatous digital dermatitis in dairy cows. J Dairy Sci 2000;83:741–5.
54. Yano T, Moe KK, Chuma T, et al. Antimicrobial susceptibility of Treponema phagedenis-like spirochetes isolated from dairy cattle with papillomatous digital dermatitis lesions in Japan. J Vet Med Sci 2010;72:379–82.
55. Nishikawa A, Taguchi K. Healing of digital dermatitis after a single treatment with topical oxytetracycline in 89 dairy cows. Vet Rec 2008;163:574–6.
56. Silva LA, Silva CA, Borges JR, et al. A clinical trial to assess the use of sodium hypochlorite and oxytetracycline on the healing of digital dermatitis lesions in cattle. Can Vet J 2005;46:345–8.
57. Ando T, Fujiwara H, Kohiruimaki M, et al. Peripheral blood leukocyte subpopulation of dairy cows with digital dermatitis and effect of hoof trimming with antibiotic treatment. J Vet Med Sci 2009;71:391–5.
58. Laven RA. Efficacy of systemic cefquinome and erythromycin against digital dermatitis in cattle. Vet Rec 2006;159:19–20.
59. Edwards AM, Dymock D, Jenkinson HF. From tooth to hoof: treponemes in tissue-destructive diseases. J Appl Microbiol 2003;94:767–80.
60. Logue DN, Offer JE, Laven RA, et al. Digital dermatitis–the aetiological soup. Vet J 2005;170:12–3.
61. Diaz PI, Hoare A, Hong BY. Subgingival microbiome shifts and community dynamics in periodontal diseases. J Calif Dent Assoc 2016;44:421–35.
62. Grenier D. Nutritional interactions between two suspected periodontopathogens, Treponema denticola and Porphyromonas gingivalis. Infect Immun 1992;60:5298–301.
63. Ito R, Ishihara K, Shoji M, et al. Hemagglutinin/Adhesin domains of Porphyromonas gingivalis play key roles in coaggregation with Treponema denticola. FEMS Immunol Med Microbiol 2010;60:251–60.
64. Nilius AM, Spencer SC, Simonson LG. Stimulation of in vitro growth of Treponema denticola by extracellular growth factors produced by Porphyromonas gingivalis. J Dental Res 1993;72:1027–31.
65. Socransky SS, Haffajee AD, Cugini MA, et al. Microbial complexes in subgingival plaque. J Clin Periodontol 1998;25:134–44.
66. Takahashi N. Oral microbiome metabolism: from "Who Are They?" to "What Are They Doing?". J Dent Res 2015;94:1628–37.
67. Simonson LG, McMahon KT, Childers DW, et al. Bacterial synergy of Treponema denticola and Porphyromonas gingivalis in a multinational population. Oral Microbiol Immunol 1992;7:111–2.
68. Yao ES, Lamont RJ, Leu SP, et al. Interbacterial binding among strains of pathogenic and commensal oral bacterial species. Oral Microbiol Immunol 1996;11:35–41.

69. Bruijnis MR, Beerda B, Hogeveen H, et al. Assessing the welfare impact of foot disorders in dairy cattle by a modeling approach. Anim Int J Anim Biosci 2012;6:962–70.
70. Fabian J, Laven RA, Whay HR. The prevalence of lameness on New Zealand dairy farms: a comparison of farmer estimate and locomotion scoring. Vet J 2014;201:31–8.
71. Frankena K, Somers JG, Schouten WG, et al. The effect of digital lesions and floor type on locomotion score in Dutch dairy cows. Prev Vet Med 2009;88:150–7.
72. Becker J, Steiner A, Kohler S, et al. Lameness and foot lesions in Swiss dairy cows: I. Prevalence. Schweiz Arch Tierheilkd 2014;156:71–8.
73. Capion N, Thamsborg SM, Enevoldsen C. Prevalence and severity of foot lesions in Danish Holstein heifers through first lactation. Vet J 2009;182:50–8.
74. Capion N, Thamsborg SM, Enevoldsen C. Prevalence of foot lesions in Danish Holstein cows. Vet Rec 2008;163:80–5.
75. Cramer G, Lissemore KD, Guard CL, et al. Herd- and cow-level prevalence of foot lesions in Ontario dairy cattle. J Dairy Sci 2008;91:3888–95.
76. Holzhauer M, Hardenberg C, Bartels CJ, et al. Herd- and cow-level prevalence of digital dermatitis in the Netherlands and associated risk factors. J Dairy Sci 2006;89:580–8.
77. Hulek M, Sommerfeld-Stur I, Kofler J. Prevalence of digital dermatitis in first lactation cows assessed at breeding cattle auctions. Vet J 2010;183:161–5.
78. van der Linde C, de Jong G, Koenen EP, et al. Claw health index for Dutch dairy cattle based on claw trimming and conformation data. J Dairy Sci 2010;93:4883–91.
79. Krull AC, Shearer JK, Gorden PJ, et al. Digital dermatitis: natural lesion progression and regression in Holstein dairy cattle over 3 years. J Dairy Sci 2016;99:3718–31.
80. Hedges J, Blowey RW, Packington AJ, et al. A longitudinal field trial of the effect of biotin on lameness in dairy cows. J Dairy Sci 2001;84:1969–75.
81. Relun A, Lehebel A, Bruggink M, et al. Estimation of the relative impact of treatment and herd management practices on prevention of digital dermatitis in French dairy herds. Prev Vet Med 2013;110:558–62.
82. USDA. Dairy 2007, part IV: reference of dairy cattle health and management practices in the United States. Fort Collins (CO): USDA: APHIS:VS, CEAH; 2009.
83. Sullivan LE, Carter SD, Blowey R, et al. Digital dermatitis in beef cattle. Vet Rec 2013;173:582.
84. Bruijnis MR, Hogeveen H, Stassen EN. Assessing economic consequences of foot disorders in dairy cattle using a dynamic stochastic simulation model. J Dairy Sci 2010;93:2419–32.
85. Cha E, Hertl JA, Bar D, et al. The cost of different types of lameness in dairy cows calculated by dynamic programming. Prev Vet Med 2010;97:1–8.
86. Wilshire JA, Bell NJ. An economic review of cattle lameness. Cattle Practice 2009;17:136–41.
87. Losinger WC. Economic impacts of reduced milk production associated with papillomatous digital dermatitis in dairy cows in the USA. J Dairy Res 2006;73:244–56.
88. Lindley WH. Malignant verrucae of bulls. Vet Med Small Anim Clin 1974;69:1547–50.
89. Barthold SW, Koller LD, Olson C, et al. Atypical warts in cattle. J Am Vet Med Assoc 1974;165:276–80.

90. Evans NJ, Blowey RW, Timofte D, et al. Association between bovine digital dermatitis treponemes and a range of 'non-healing' bovine hoof disorders. Vet Rec 2011;168(8):214.
91. Evans NJ, Timofte D, Carter SD, et al. Association of treponemes with bovine ulcerative mammary dermatitis. Vet Rec 2010;166:532–3.
92. Rock C, Krull A, Gorden P, et al. Metagenomic evaluation of the dairy farm environment and facilities for evidence of digital dermatitis associated bacteria. In: International Ruminant Lameness Conference, Valdivia (Chile). November 22–25, 2015.
93. Clegg SR, Carter SD, Stewart JP, et al. Bovine ischaemic teat necrosis: a further potential role for digital dermatitis treponemes. Vet Rec 2016;178:71.
94. Minini S, Crowhurst F, Nicolás J, et al. Toe necrosis and non-healing hoof lesions in commercial dairy herds in Argentina. In: 17th International Symposium and 9th International Conference on Lameness in Ruminants. Bristol (United Kingdom). August 11–14, 2013.
95. Acevedo J, Chesterton R, Hurtado C, et al. Bovine digital dermatitis and non-healing lesions and toe necrosis in grazing dairy herds in Chile. In: 17th International Symposium and 9th International Conference on Lameness in Ruminants. Bristol (United Kingdom). August 11–14, 2013.
96. Clegg SR, Bell J, Ainsworth S, et al. Isolation of digital dermatitis treponemes from cattle hock skin lesions. Vet Dermatol 2016;27:106–12.e29.
97. Tremblay M, Bennett T, Dopfer D. The DD check App for prevention and control of digital dermatitis in dairy herds. Prev Vet Med 2016;132:1–13.
98. Cramer G, Johnson R. Evaluation of risks of violative milk residues following extra-label topical administration of tetracycline for digital dermatitis in dairy cattle. In: American Association of Bovine Practitioners. Albuquerque (NM). September 18–20, 2014.
99. Shearer JK, Plummer PJ, Schleining J. Perspectives on the treatment of claw lesions in cattle. Vet Med Res Rep 2015;6:273–92.
100. Evans NJ, Murray RD, Carter SD. Bovine digital dermatitis: current concepts from laboratory to farm. Vet J 2016;211:3–13.
101. Evans NJ, Brown JM, Hartley C, et al. Antimicrobial susceptibility testing of bovine digital dermatitis treponemes identifies macrolides for in vivo efficacy testing. Vet Microbiol 2012;160:496–500.
102. Gomez A, Bernardoni N, Rieman J, et al. A randomized trial to evaluate the effect of a trace mineral premix on the incidence of active digital dermatitis lesions in cattle. J Dairy Sci 2014;97:6211–22.
103. Berry DB 2nd, Sullins KE. Effects of topical application of antimicrobials and bandaging on healing and granulation tissue formation in wounds of the distal aspect of the limbs in horses. Am J Vet Res 2003;64:88–92.
104. Sullivan LE, Blowey RW, Carter SD, et al. Presence of digital dermatitis treponemes on cattle and sheep hoof trimming equipment. Vet Rec 2014;175:201.