New developments in digital dermatitis control

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Abstract

Recent work has provided a greater understanding of the etiopathogenesis of digital dermatitis (DD) infection within cattle populations. With enhanced lesion scoring and an understanding of the transitioning between lesion stages, coupled with improved data-gathering systems, we now understand the significance of the chronic stages of the disease in herd-infection dynamics. Herd control of DD must begin during the heifer-rearing period. Breeding resistant animals and use of in-feed organic trace mineral supplements are coupled with active surveillance for early acute stages of the disease. Combined with strategic foot bathing and hoof-trimming, when fully implemented on a farm, these strategies can reduce the incidence of the disease and provide a sustainable solution to this troublesome problem.

Key words: cattle, digital dermatitis, footbath

Résumé

Des travaux récents ont permis une meilleure compréhension de l'etiopathogenesis de dermatite numérique (DD), l'infection au sein de la population de bovins. Avec lésion amélioré la notation et une compréhension de la transition entre les stades de la lésion, conjuguée à l'amélioration des systèmes de collecte de données, nous comprennent maintenant l'importance du stade de la maladie chronique dans le troupeau dynamique de l'infection. Troupeau de DD de contrôle doit commencer au cours de la période d'élevage des génisses. Reproduction, l'utilisation d'animaux résistants dans les aliments Suppléments minéraux traces organiques, associée à une surveillance active pour le début des stades aigus de la maladie en combinaison avec footbathing stratégique et le sabot-fraisage, lorsqu'il sera entièrement mis en oeuvre à la ferme, peut réduire l'incidence de la maladie et fournir une solution durable à ce problème ennuyeux.

Introduction

Digital Dermatitis (DD) is the most common infectious cause of lameness in dairy cattle worldwide and it has proven a challenging disease to control. Despite our efforts, DD has continued to spread globally since it was first recognized in 1974, to the point where it is difficult to find a country with a developed dairy industry without the disease. Within herds, lesions commonly affect 20% of the cows at any one time.[30] Given the ubiquity of the condition, it is likely that DD deserves the title of being the most infectious disease present on modern dairy operations. Indeed, the condition is not confined to the dairy industry. Beef producers express growing concern over the prevalence of DD in their operations also.

Typical strategies to control DD in a herd involve topical treatment of cows at routine hoof-trimming or identified lame with a DD lesion, and routine use of a foot bath using an antimicrobial agent at regular intervals. When implemented aggressively, this strategy has been somewhat successful, but it has proven costly, both financially to the producer and environmentally, as farms have been challenged to safely dispose of chemicals such as copper sulfate, which carry environmental contamination concerns.

Our claw health team led by Dr. Dörte Döpfer developed a 5-year plan to investigate the etiopathogenesis of DD in dairy herds. The work focused on a prospective longitudinal study of DD in youngstock and led to some revelations that provide us with new tools and ideas to combat the disease. In this article, I will summarize the main findings of these studies and other recent work by others in the field.

Etiology

DD is a multifactorial disease with a strong bacterial component.[29,32] Various *Treponema* spp have been identified as the bacteria essential for development of active DD lesions with *T. denticola, maltophilum, medium, putidum, phagedenis* and *paraluiscuniculi* being the most commonly found in the US.[40] These spirochetal bacteria are strict anaerobes and are difficult to handle in the laboratory. However, using refined PCR techniques, they have been found to be common in the rumen and feces of cattle. While other bacteria such as *Candidatus Amoebophilus asiaticus* may be involved in the disease,[40] we believe that for DD to occur, treponemes are essential for 3 main reasons. Firstly, *Treponema* spp are found ubiquitously in DD lesions.[2,13,15,22] Secondly, an initial attempt to reproduce the disease from a pure culture using an isolate of *Treponema vincentii* was able to replicate an early DD lesion,[15] confirmed at the histological (immuno-histochemistry, hematoxylin–eosin and Steiner silver stains) and molecular level (polymerase chain reaction). Third, in contrast to what was found in DD lesions, T*reponema* spp were never found in control samples of healthy skin, and significant immune responses were not observed in animals without clinical signs of the disease.[5,15,23,27]

For infection to occur, the microenvironment must be such that it allows for contamination of the skin with the bacterial inoculum, and the surface layer of the epidermis must be macerated with constant exposure to moisture.[15] It is proposed DD results from penetration of the 3 defense

layers of the epidermis. Moisture erodes the inter-cellular cement between the surface epidermal skin squames, allowing the bacteria to penetrate through the zone 1 skin barrier. Continued penetration into the deeper layers of the epidermis is facilitated by a breakdown in the connections between the epidermal cell columns in zone 2, with destruction of the gap junctions and disruption of intercellular communication. Finally, the massive tissue destruction and loss of zone 1 and 2 barriers allows for the penetration of *Treponema* into the dermis due to damage to the integrity of the basement membrane (Döpfer and Mülling, personal communication).

Hydropic maceration of the skin is commonplace in confinement-housed dairy systems, as the cow is kept in intimate contact with her manure 24/7, significantly contributing to the spread of this disease in conjunction with the intensification of the dairy industry around the world.

Lesion Stages and Treatment

The industry has been focused on the treatment of DD without consideration of the stage of the disease for several decades. Attempts to treat chronic stages of DD – often referred to as hairy heel warts – prove futile, and do not improve our ability to control DD in a herd. There are a number of reasons for this apparent treatment failure.

First, cows afflicted with DD are generally singled out to receive individual treatment based on the presence of lameness. Frankena et al,[14] however, reported that only 26.3% and 39.5% of the animals with slight or severe DD lesions, respectively, showed an identifiable lameness. Therefore, the true prevalence of DD on farms is likely underestimated and only the most severely affected animals receive treatment. Second, *Treponema* spp organisms are known to migrate into deep layers of the skin shortly after infection. Gomez et al[15] reported invasion of the dermis by *Treponema* spp organisms within a period of 7 days after experimental infection. Even in these early cases, bacterial clearance in deep layers of the skin after topical treatment was incomplete.[10] Third, *Treponema* spp organisms share with other spirochetal bacteria such as *Borrelia* spp the ability to evolve to cystic forms (so-called "round bodies") under stress and the impact of antimicrobials, chemicals, and extreme pH values.[4,33] In this regard, Döpfer et al[11] described changes in the morphology of 3 *Treponema* spp in vitro, showing the presence of spiral and cystic forms, suggesting encystation as 1 of the reasons why persistent infections could lead to recurrent lesions. Fourth, dyskeratotic skin is a common finding in chronic DD lesions[9,29,34] in the form of scaly, mass-like, and filamentous proliferations. Progressive hyperkeratosis and proliferation on the skin of untreated lesions could prevent penetration of antimicrobials into deeper (epi-) dermal layers and therefore lead to an incomplete elimination of treponemes and subsequent recurrence of DD.

For accurate assessment of DD, the lesion must be classified. DD transitions through 4 lesion stages using the so-called "M-stage" classification system.[9] M1 lesions are small, less than 20 mm, and may spontaneously resolve or expand into acute M2 lesions – the typical painful strawberry type lesion, >20 mm, on the plantar aspect of the interdigital space. If left untreated, M2 lesions expand and may become proliferative with long projections or pili developing due to uncontrolled skin proliferation, eventually becoming chronic M4 lesions with little hope for cure with topical therapy. However, if treated effectively, M2 lesions will pass through an M3 scab stage before resolving. M4 lesions may frequently recrudesce, developing small M1 lesions within the chronic lesion—we refer to these as M4.1 lesions. These lesions may transition back to M2 stages, causing pain and lameness.

The goal of control is to treat and cure the M2 lesions as soon as they occur. This cannot be done with a program that identifies lesions in lame cows and cows at routine trims. We have to treat the lesion when the cows are not yet lame, and this requires frequent organized surveillance. We recommend once-a-week checks either in the parlor or along the lockups in the pen, so that fresh M2 lesions can be identified and the cows topically treated with powdered or liquid oxytetracycline, with or without a light wrap. Good cure rates can be achieved with this approach. Any strategy relying on curing M4 lesions will likely ultimately fail due to very high relapse rates.[1] Following implementation of this early detection approach in a heifer pen over a 2-year period in the absence of footbath use, we saw a reduction in total M2 lesions over time, but also a striking reduction in the proportion of M2 lesions with proliferation—suggesting that this type of presentation in both M2 and M4 lesions is a measure of the timeline of infection and representative of the degree of tissue destruction that has occurred prior to identification.

The role of the footbath should not be to treat the cows with lesions, but to hold the chronic M4 affected cows in check, so that they do not recrudesce and revert back to new M2 lesions. In combination with an organized surveillance

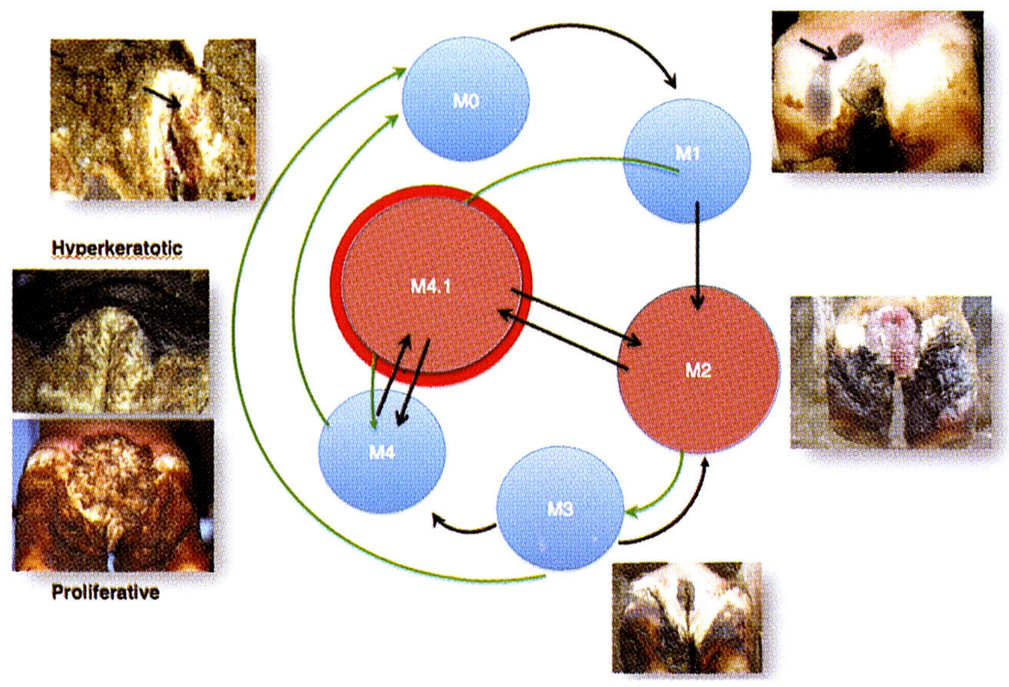

Figure 1. The M-Stage Classification for Digital Dermatitis Lesions (from Döpfer et al[9]; Berry et al[1]).

and treatment plan, we can reduce the frequency of footbathing and utilize products that have fewer safety concerns than formalin, and are less troublesome in the environment than copper sulfate. Without a plan to identify early M2 lesions, herds become too reliant on the frequent use of footbaths, and often times, chemical costs can rival the cost of all other pharmaceuticals for the dairy.

Timing of Infection

Within the dairy industry, we have recently turned our focus toward DD infection in the heifer population. It is not uncommon to find 20-30% of heifers after breeding age affected by DD in many rearing facilities, likely as a result of the same poor leg hygiene risk factors that have exacerbated the problem in mature cows. Laven and Logue[26] and Holzhauer et al[21] have demonstrated the importance of the pre-partum period in affecting DD occurrence during the following lactation.

For his PhD study, Dr. Arturo Gomez followed 640 pregnant heifers housed in freestalls on one dairy facility through first calving to the end of their first lactation. During the rearing period, we identified heifers that did not suffer DD at any time (Type I), heifers that suffered only one case of DD (Type II) and heifers that suffered more than one case of DD (Type III). All cases were treated topically as soon as they were identified as described. The incidence rates of DD in heifers during their first lactation were remarkable when compared to their infection history prepartum. The first lactation incidence of DD was 3%, 37% and 44% for Type I, II and III heifers respectively. This astonishing result suggests that control of DD at the herd level must start with the heifer or it is doomed to failure. We have submitted samples from each group of heifers for genomic testing and determined that the heritability for being a Type III heifer is 0.41-0.56, suggesting a significant genetic component to this complex disease (Döpfer, personal communication). In the future, genomic bull selection may help us to control DD with the breeding of less susceptible animals. However, in the meantime, we must look elsewhere for solutions to this problem.

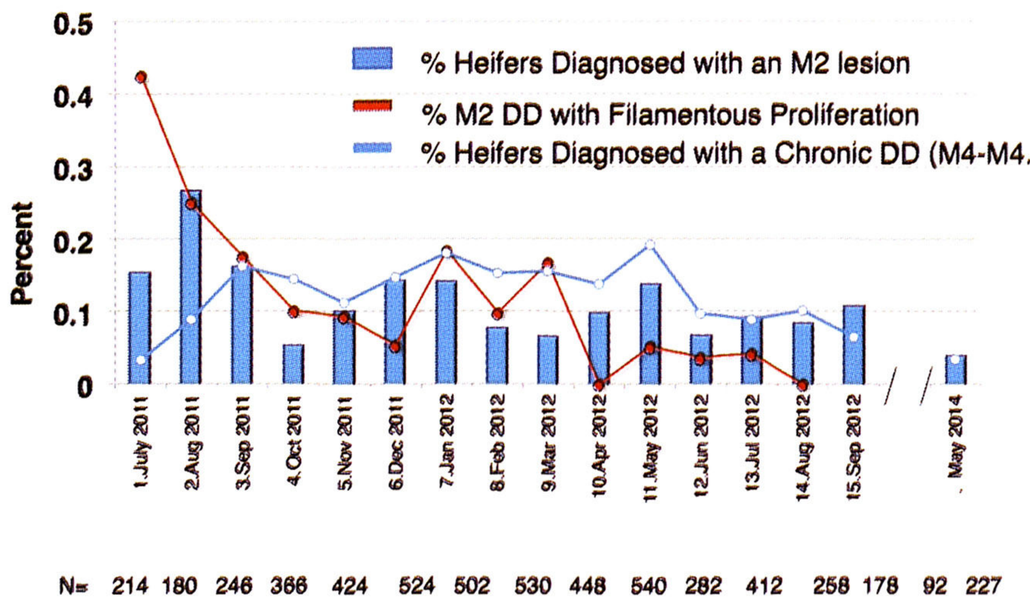

Figure 2. Implementation of active M2 surveillance in a heifer pen and impact on M2 incidence and prevalence of proliferation over a 2-year period.

Consequences of Infection

We had the opportunity to investigate the short and long-term impact of DD infection in our longitudinal study.

Locally, DD infection causes changes to the conformation of the foot that may increase the likelihood of prolonged infection. Previously, Laven[25] described a significant negative relationship between DD and both heel height and toe length. We had the ideal opportunity to prospectively examine conformation changes around the time of DD lesion development in heifers. DD lesions were associated with an increase in heel height, an increase in the depth of the interdigital space, a worsening of manure contamination in the interdigital space and a significant increase in the amount of heel horn erosion (HHE) that accompanied the infection. Indeed, for the most part, layered heel erosion appeared to be a consequence of DD infection and an obvious marker for a DD infection problem in the herd.[19] Holzhauer et al[22] used a cross-sectional study to estimate a DD attributable risk of 32.2% for ID/HHE and 9% for interdigital hyperplasia (corns), suggesting that these diseases could be causally associated with DD.

Proliferation of M2 lesions was also a marker of significance. The odds ratio for becoming a Type III animal was 2.1 when proliferation was present at the first M2 lesion, further emphasizing the need to treat lesions early on, while changes to tissue architecture are limited. Interestingly, following prompt effective treatment, most of the changes in the structure of the claw observed after DD lesion development were reversed upon cure.

Animals identified with M2 stages of DD had a significant immune response to *Treponema* spp as measured by a 45% increase in specific serum IgG levels.[17] After treatment, a gradual decrease of these anti-*Treponema* antibodies was observed in animals that did not relapse with the disease. However, a sustained response was observed in animals diagnosed with repeated cases of the disease. In contrast, there was a null reaction of the immune system to early and intermittent (M1, M4.1) cases of the disease, particularly in heifers chronically affected by repeated episodes of active M2 lesions. This finding has important epidemiological implications - chronic DD lesions can harbor large numbers of *Treponema* spp that under favorable conditions develop into clinically active M2 stages, therefore representing reservoirs of infection. However, the systemic reaction from such chronically affected individuals seems delayed or non-existent, likely limiting the animals' ability to cure the infection.

The economic consequences of infection have been previously examined. Relun et al[32] reported an average milk production loss of approximately 1.2 lb (0.55 kg) per day in primiparous cows and 1.43 lb (0.65 kg) per day in multiparous cows using monthly milk recordings. Cha et al,[6] taking into consideration losses to milk production having to do with

treatment, reproductive performance, and treatment costs, calculated a loss of $133 per DD case, attributing the most importance (40%) to treatment costs. Similarly, Wilshire and Bell[40] calculated a cost of $126 per DD case in the UK. However, these assessments are clouded by comparison of diseased cows with non-diseased cows, often in a single lactation. We know that DD and other causes of lameness affect higher producing animals more than lower producing ones, and we also know that the risk for repeated episodes of DD infection is higher in animals that have suffered the disease in the prior lactation.[29] We examined the losses in the first lactation between heifers uninfected during the rearing period (Type I) compared to animals repeatedly infected (Type III), controlling for early lactation milk yield, and found that Type III animals produced 740 lb (335 kg) less milk in their first lactation than Type I animals, and days open was extended by 25 days. The extent of this loss is remarkable and can be used to motivate the implementation of early prevention strategies during the rearing period.

A New Take on Control Strategies

DD control must start during the heifer-rearing period. Footbaths alone have relatively modest impact on control, with surveillance for fresh M2 lesions and prompt topical therapy being far more effective throughout the life cycle of the cow.

We have investigated the potential role for in-feed trace mineral supplementation in prevention of DD both in our experimental challenge model and in the field. A unique commercially available mix of organic trace minerals showed a strong tendency to reduce the proportion of feet affected by experimental M2 lesions (OR = 0.54 [0.18, 1.09]) compared to controls receiving traditional supplements,[18] and further field studies have confirmed the efficacy of this product on commercial dairy farms, with the likelihood that this supplement serves to enhance the zone 2 epidermal skin barrier to DD infection. As an added bonus, supplemented heifers produced 420 lb (191 kg) more milk over the first lactation compared to controls reared on traditional supplements.

Prior to first calving we recommend a hoof-trim with an expanded modeling of the axial groove area of the outer claw of the rear foot. This appears to reduce the risk for DD in lactation, likely by modifying the micro-environment between the claws and improving hygiene. Regular routine trimming is also recommended at least twice per lactation in mature cows.

In order to enhance our understanding of herd dynamics of infection, we are working to capture lesion stage information in hoof-trimmer databases and new apps that serve to help record DD lesion types and allow prediction of likely increases in disease incidence.

We can track proliferation in M2 and M4 lesions to fine-tune the prevention program. Proliferation in M2s is suggestive that the herd is not identifying acute lesions quickly enough, which will impact the efficacy of treatment. Proliferation in M4 lesions is indicative of skin damage likely as a result of too aggressive a footbathing regime, perhaps with a chemical with too high or too low pH. We currently recommend baths with a pH no lower than 3.0. DD lesion stages can also be recorded at routine trims – and we recommend that herds keep track of M2 and M4 lesions at a minimum.

Footbaths remain an important part of control, but they need to be operated judiciously for both heifers and cows. Copper sulfate ($CuSO_4$) stands out as the most frequently tested chemical and, corresponding to its extensive use in the field,[7] is also the chemical most frequently used as a comparison (control) group in research trials. Typically these trials confirm the efficacy of copper sulfate and formalin in footbaths, which tend to out perform other test products.[3,35,36,37,38,39] However, more recently, we have focused more on the design of the delivery system. From our research we have eliminated wash baths and recommend treatment

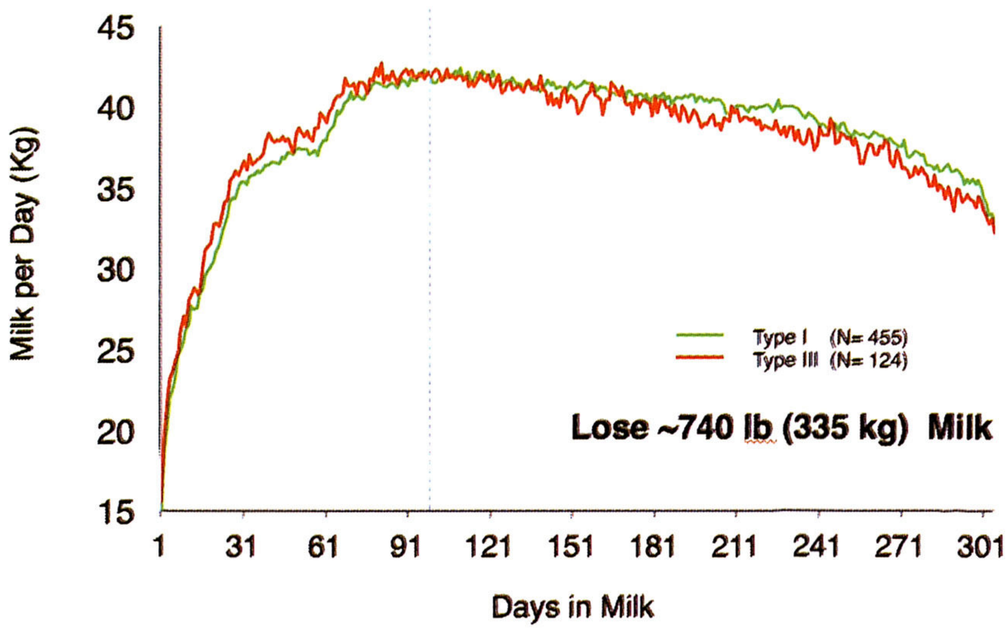

Figure 3. Comparison first lactation milk yield between heifers uninfected with DD during the rearing period (Type I) and those repeatedly infected (Type III).

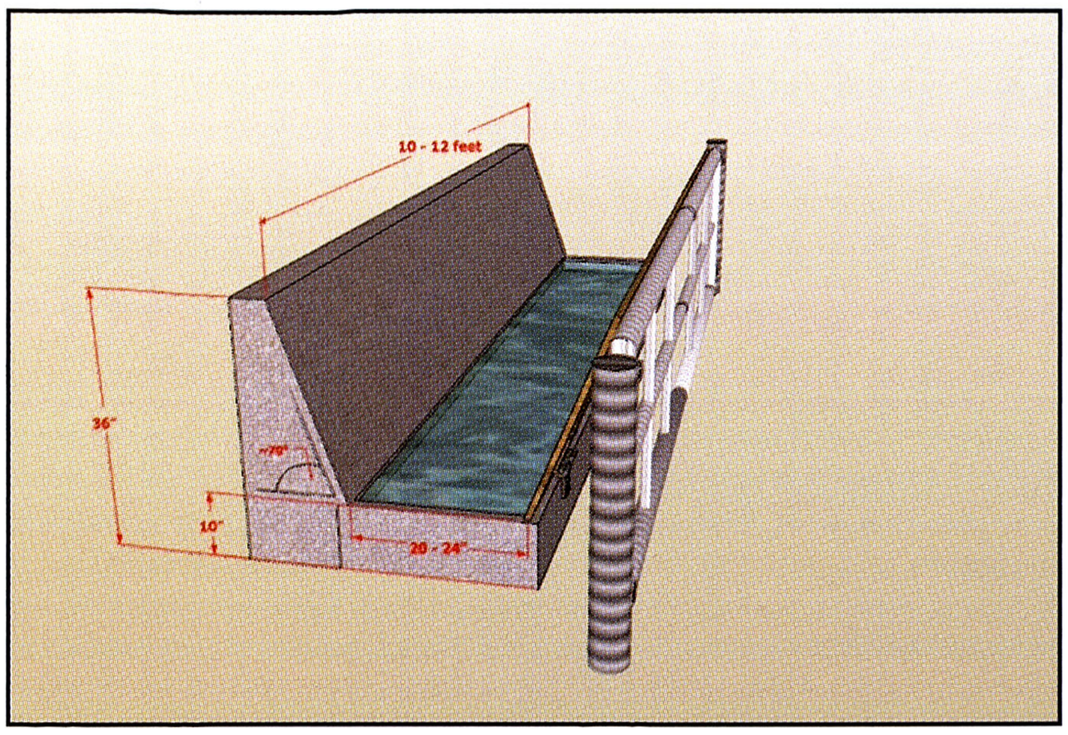

Figure 4. The 'ideal' footbath design.

baths that are 10-12' long, 24" wide at the base, with a 10" high step-in to ensure that all rear feet receive at least two immersions as cows pass through the bath.[7] These baths when filled with solution to ~3 to 4" deep will contain 50 gallons, to minimize use and cost of chemicals. The side-walls are sloped to a width of 36" at a height of 36" above the floor. Larger farms will place 2 baths in parallel to deal with the high throughput of cows, and it is essential that the entry to the bath is direct from a narrow alley that serves to funnel the cows into the bath. Using a factorial study design including two footbath products (5% copper sulfate solution vs. a proprietary new footbath agent), and two footbath dimensions (7.5' (2.3 m) and 15' (4.6 m) long), Logue et al[27] were able to clearly demonstrate the greater efficacy of longer footbaths in preventing DD occurrence (OR = 2.49 to 3.3).

Improved contact time allows us to use lower concentrations of copper sulfate (2-3% vs 5-10%), and when associated with improved M2 surveillance, frequency of use can be reduced from 3 to 5 days per week to 2 to 3 days per week, with the inclusion of chemicals such as oil of thyme, tea tree oil or other types of product in the rotation, which pose fewer challenges for handling and disposal.

Finally, improved hoof hygiene, while difficult to achieve in practice is an essential goal for DD control at all ages.

Conclusions

Our research has created some new opportunities to refocus DD control efforts on the heifer rearing period and understand the importance of lesion stage identification in the treatment and prevention of acute stages of DD. Implementation of this control plan is having a significant impact on the incidence of DD in our dairy herds, creating a more sustainable solution to control for the future.

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