# Digital dermatitis in cattle
# Part II: Treatment, prevention and link with other treponemal diseases

*Digitale dermatitis bij rundvee*
*Deel II: Behandeling, preventie en de link met andere treponemale ziekten*

**A. Vermeersch, G. Opsomer**

Department of Reproduction, Obstetrics and Herd Health
Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B-9820 Merelbeke, Belgium.

annesofie.vermeersch@ugent.be

## ABSTRACT

**Digital dermatitis is the most common cause of lameness worldwide in dairy cattle. In this final part of a twin paper, treatment options and strategies to prevent digital dermatitis are reviewed. There is a wide range of different treatments available but none of them can completely cure the animal. Footbaths and applying high standards for hygiene are ways to keep this disease under control.**

**Moreover, the link to other (human and non-human) treponemal diseases will be discussed. In humans, treponemes are involved in periodontal disease, syphilis and many other illnesses. The dermatological manifestation of some of these human diseases such as yaws have a similar appearance like acute digital dermatitis. Digital dermatitis-like lesions have been described in goats, sheep and elks. The typically isolated *Treponema* spp. can also be found in equine proliferative pododermatitis affected feet. Besides in digital dermatitis, these bacteria can be found in bovine ulcerative mammary dermatitis and badly healing lesions in cattle.**

## SAMENVATTING

Digitale dermatitis is wereldwijd de belangrijkste oorzaak van kreupelheid bij melkvee. In dit laatste deel van het tweedelige artikel wordt een overzicht gegeven van de behandelings- en preventiestrategieën. Er zijn verschillende behandelingen beschikbaar maar geen enkele kan het dier volledig doen genezen. Voetbaden en een hoge hygiënestandaard toepassen zijn manieren om de ziekte onder controle te houden.

Bovendien wordt de link met andere (humane en niet-humane) treponemale ziekten besproken. Bij de mens zijn treponemen betrokken bij periodontitis, syfilis en vele andere ziekten. De dermatologische manifestatie van humane treponemale ziekten, zoals “yaws”, hebben een gelijkaardig voorkomen als acute digitale dermatitis. Digitale dermatitisachtige letsels werden reeds beschreven bij geiten, schapen en wapiti’s. De typisch geïsoleerde *Treponema* spp. kunnen ook gevonden worden bij het paard, op voeten aangetast door proliferatieve pododermatitis. Deze bacteriën kunnen niet alleen bij digitale dermatitis maar eveneens bij boviene ulceratieve mammaire dermatitis en slecht helende letsels aangetroffen worden bij rundvee.

## ANALOGIES WITH HUMAN TREPONEMAL DISEASES

### Human treponemal skin diseases

In humans, treponemes are the cause of venereal syphilis (*T. pallidum* subsp. *pallidum*) and the endemic treponematoses called yaws (*T. pallidum* subsp. *pertenue*), bejel (*T. pallidum* subsp. *endemicum*) and pinta (*T. carateum*), which are mainly characterized by typical skin lesions (Perine et al., 1984; Giacani and Lukehart, 2014; Marks et al., 2014). According to the unitarian hypothesis, these diseases are caused by one and the same pathogen but with subtle genomic differences (Hudson, 1963). Disease development and outcome are considered to be geographically region-specific. Other species like rabbits and hamsters have shown to be susceptible to develop lesions after experimental infection with human syphilis strains (Cumberland and Turner, 1949; Kajdacsy-Balla et al., 1987; Norris et al., 2001). The pathogenesis and clinical manifestation are strikingly comparable, as these diseases can all enter into a latent stage caused by the host immune response (Giacani and Lukehart, 2014). The cardiovascular, neurological and ophtalmological complications seen in venereal syphilis are not commonly seen in the other treponematoses (Perine et al., 1984). Skin-to-skin contact between children is an important mode of transmission for the endemic treponemal diseases (Perine et al., 1984; Giacani and Lukehart, 2014). A compromised skin integrity facilitates the entry of yaws-associated treponemes. Despite the important role flies play in the transmission of yaws, DD-associated treponemes have not been detected in flies on dairy farms yet (Evans et al., 2012b). Yaws, which causes berry-like skin lesions, is linked to a hot and humid climate combined with inadequate hygiene (Perine et al., 1984; Marks et al., 2014) (Figure 1). In contrast, bejel is primarily seen in dry surroundings whereas the prevalence of DD in cattle has been noticed to be higher in winter and when moist conditions are present (Perine et al., 1984; Read and Walker, 1998). Similar to DD, yaws lesions are often found on the distal extremities. Pinta is considered to be one of the mildest treponematoses because it does not spread further beyond the skin (Perine et al., 1984; Giacani and Lukehart, 2014; Marks et al., 2014).

Despite numerous attempts to develop a vaccine against syphilis, there is no vaccine available yet. A preliminary study by Lithgow et al. (2017) showed noteworthy results with a surface Tp0751 lipoprotein vaccine in rabbits. The Tp0751 sequence is conserved in all sequenced *T. pallidum* strains. Even though the experimental vaccine did not fully protect the animals, the lesions were less severe, the immune response was stronger and the degree of organ spreading diminished considerably. In the future, a multicompound vaccine containing Tp0751 and TprK could be used in immunization trials.

### Human periodontal disease

Periodontal disease compromises the integrity of the periodontium (gingiva, periodontal ligament and alveolar bone), going from gingivitis to bony destruction and loss of teeth (Edwards et al., 2003). Treponemes are strongly involved in active human periodontal disease, forming 'the Red Complex' together with other key bacteria, such as *Porphyromonas gingivalis* and *Tannerella forsythia* (Socransky et al., 1998; Dashper et al., 2011). The best characterized oral treponeme is *T. denticola*, a species that has also been detected in bovine DD lesions (Socransky et al., 1998; Dashper et al., 2011; Döpfer et al., 2012). A whole array of different *Treponema* species, like *T. parvum* and *T. medium*, can be isolated from the mouths of the affected patients (Umemoto et al., 1997; Wyss et al., 2001). Just like DD, human periodontitis is considered to be a multifactorial disease whereby the moist environment, host factors (e.g. obesity, insulin resistance, hygiene), local immune response and synergistic pathogenic bacteria are of great importance (Perlstein and Bissada, 1977; Al-Zahrani et al., 2003; Abusleme et al., 2013; Landzberg et al., 2015; Hajishengallis, 2015; Lertpimonchai et al., 2017). *T. denticola* is able to evade multiple immune-mediated killing mechanisms, and concurrently enhances inflammation (Miller et al., 2012; Shin et al., 2013). In affected oral tissue, levels of mediators like IL-8 and RANTES are elevated, as in bovine fibroblasts when confronted with DD-associated sonicated treponemal material (Silva et al., 2007; Evans et al., 2014).

Obesity increases the odds for developing periodontal disease, presumably through the secretion of adipocytokines like TNF-$\alpha$ by the macrophages and adipocytes in fatty tissues, a phenomenon that has recently been shown to occur in obese dairy cows (Perlstein and Bissada, 1977; Saito and Shimazaki, 2007; Depreester et al., 2018) (Figure 2). This puts the obese individual in a pro-inflammatory state, also known as 'metaflammation' (Depreester et al., 2018). Moreover, TNF-$\alpha$ has been shown to be associated with insulin resistance in humans (Hotamisligil et al., 1995; Uysal et al., 1997; Saito and Shimazaki, 2007).

## EMERGING DIGITAL DERMATITIS-LIKE LESIONS

### Cross-species digital dermatitis-like appearance

Currently, DD-resembling disease manifestations among different species are emerging and are often linked to the treponemes isolated from bovine DD (Clegg et al., 2015; 2016d; Sullivan et al., 2015). In a population of wild North-American elks (*cervus elaphus*), similar treponeme phylotypes have been found

**Figure 1. A primary yaws lesion on the arm of a young boy in Papua New Guinea, 2009. (Mitjà et al., 2011).**

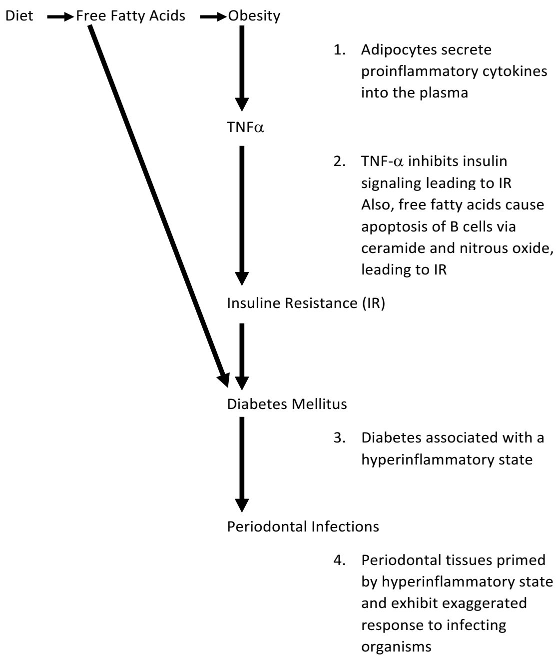



**Figure 2. This scheme is a model proposed by Genco et al. (2005), linking obesity to metabolic dysregulation in humans. In human medicine, a bi-directional relationship between diabetes mellitus and treponeme-associated periodontitis has been proposed (Saito and Shimazaki, 2007). Furthermore, obesity is a risk factor for both diseases (Saito and Shimazaki, 2007).**

in DD-like foot lesions (Clegg et al., 2015 ). Elks tend to have a large territorial range, and while travelling, they might graze on pastures where infected sheep and cattle have been before (Clegg et al., 2015). The mode of transmission is yet unknown but the presence of a digital dermatitis-like disease in wild animals raises questions regarding host specificity, transmissibility and the possibly opportunistic properties of treponemes. Contagious ovine digital dermatitis (CODD) in sheep and goats shows analogies with bovine DD based on bacterial involvement and histopathology, even though the clinical presentation is slightly different (Angell et al., 2015; Sullivan et al., 2015). An inflammatory process is observed dorsally at the level of the coronary band and frequently, there is a progressive separation of the claw horn capsule leading to claw avulsion in severe cases (Sullivan et al., 2014b; Duncan et al., 2018). Phylogenetically identical treponemes have been found in these lesions, as well as in erosive lesions on the tail, ear and flank skin of pigs (Sullivan et al., 2015; Clegg et al., 2016d). In a recent study by Wilson-Welder et al. (2018), in 14 out of 16 ovine feet infected with bovine DD material, DD-like lesions developed. These findings give rise to concerns about potential cross-species transmissibility. Digital dermatitis-associated treponemes have been detected in equine hoof canker samples (Sykora et al., 2014). Hoof canker is a proliferative pododermatitis of the sole, usually the frog region, causing abnormal horn formation. It is often misdiagnosed as thrush due to its visual resemblance (Oosterlinck et al., 2011). The occurrence of treponemes in multiple species and in different localizations points towards a rather opportunistic nature.

### Digital dermatitis-associated treponemes in other lesions in cattle

In a study by Evans et al. (2011a), DD-associated treponemes were found in most of the samples of non-healing toe necrosis, white line disease and sole ulcers. These diseases are characterized by a granulation tissue-like appearance that is refractory to standard treatment. Similar treponeme phylotypes have been found in bovine ischemic teat necrosis, open hock lesions and pressure sores (Clegg et al., 2016abc). Digital dermatitis-associated treponemes were isolated even from pressure sores of animals without DD. Stamm et al. (2009) found DD-like treponemes in ulcerative mammary dermatitis biopsies. Nevertheless, Evans et al. (2010) could not find convincing evidence of a possible link with DD. Surprisingly, DD-associated treponemes could not be identified in heel horn erosion samples despite the frequent concurrent presence of DD and heel horn erosions (Evans et al., 2011a; Gomez et al., 2015a; Smits et al., 2015). Spirochaetes hypothetically exacerbate prior tissue damage and prevent tissue repair processes, resulting in further bacterial colonization (Zuerner et al., 2007; Dashper et al., 2011). As a presumed opportunistic invader, they might play a role in lesion development and impair healing.

## TREATMENT OF DIGITAL DERMATITIS

Despite the fact that DD has been acknowledged as a prevalent foot problem for over a couple of decades, this complex disease can rarely be eliminated once it has been introduced into a farm (Berry et al., 2012; Evans et al., 2016). The persistence of this disease generates the requirement to repeat treatment, which is time- and money-consuming (Laven and Logue, 2006; Berry et al., 2012). Antibiotics like tetracyclines can rapidly but temporarily resolve the lesions, which suggests bacteria play an important but not a unique role in the pathogenesis (Berry et al., 2010; Wilson-Welder et al., 2015). In a study by Beninger et al. (2018), viable treponemes were found in healing lesions five days after oxytetracycline treatment. Treatment of the acute M2 stage typically involves claw trimming and consecutively, the topical application of a (non-) antibiotic substance under a bandage (Britt et al., 1999; Laven and Logue, 2006; Berry et al., 2010; Toholj et al., 2012). Up till now, there is no protocol that successfully eliminates DD from an affected herd (Evans et al., 2016). However, some measures can be taken in order to reduce the incidence. The implementation of routine foot bathing of all animals in combination with preventive claw trimming should be considered as part of the prevention program in an at-risk dairy farm (Toussaint Raven, 1985; Mahendran and Bell, 2015; Cook, 2017; Solano et al., 2017a). A reliable and affordable standard diagnostic laboratory test has not been developed yet, making clinical diagnosis in the trimming chute the gold standard (Solano et al., 2017b).

However, Frössling et al. (2018) developed an antibody enzyme-linked immunosorbent assay (ELISA) utilizing bovine serum and milk in order to assess the digital dermatitis status of a herd. The ELISA showed some promising results; however, there are some concerns regarding the use of just a few proteins of *Treponema phagedenis*. Treponemes may change their proteinexpression in order to evade attacks from the immune system. Due to the presence of different *Treponema* spp. in the lesions, the sensitivity of the test could be improved by including proteins of the most abundant species. Moreover, the protein cross-reactivity and the cross-sectional nature of the test are reasons for concern. Scoring lesions during milking without washing the feet makes the farmer miss 24% of DD cases on average (Oliveira et al., 2017a). This could be improved by washing the feet and by using a mirror and a headlamp during feet health assessment (Relun et al., 2011). Using locomotion scores as a parameter for diagnosing lameness is not always reliable (Frankena et al., 2009; Krull et al., 2016). In a study by Frankena et al. (2009), merely 22% of light DD cases to 43% of cattle severely affected by DD showed lameness in cubicle housing. It has been hypothesized that skin hyperalgia is aggravated by an increase of vanilloid receptor TRPV1 fibers in the affected skin (Bonacin et al., 2017). Strangely enough, a significant increase in these fibers in the M4 stage has been documented, whereas the most painful DD stage on palpation is M2 (Bonacin et al., 2017).

## Topical treatment

Acute lesions are commonly treated with a direct, topical application of (non-) antibiotic drugs (Laven and Logue, 2006). There is no standard treatment protocol available as there is no treatment that stands out regarding efficacy (Laven and Logue, 2006; Evans et al., 2016). It has been proven that bandaging combined with topical tetracycline or activated copper and zinc-chelate gel application is beneficial for the healing process and results in less chronically affected cows (Klawitter et al., 2017). In some studies, topical application of thiamphenicol, salicylic acid or polyurethane adhesive significantly improved M2 lesions to a higher extent than oxytetracycline (Fiedler et al., 2015; Holzhauer et al., 2017). Research has shown that the habitually used antibiotics are not the most efficacious substances in in vitro tests. A panel of eight antibiotic substances has been evaluated in an in vitro susceptibility test against DD-associated treponemes (Evans et al., 2009). Erythromycin and penicillin turned out to be the best substances considering they had the lowest minimum inhibitory concentration (MIC) and minimal bactericidal concentration (MBC). A more recent in vitro antibiotic susceptibility test for another battery of antibiotics, indicated amoxicillin, azithromycin and gamithromycin as the antibiotics with the lowest MIC and MBC (Evans et al., 2012a). Azithromycin is one of the alternative treatment options for human treponemal diseases such as syphilis, besides benzanthin penicillin G as the drug of choice (Perine et al., 1984; Riedner et al., 2005; Marks et al., 2014). Systemic use of these drugs implicates a milk withhold period for dairy cattle. Nevertheless, these results should be interpreted with caution because in vitro susceptibility tests do not always bring forth equal in vivo results.

The emergence of antibiotic resistance and the increase in organic dairy farming have led to a growing interest in alternative treatments that do not require antibiotic substances (Laven and Logue, 2006). Moreover, antibiotics and copper sulfate possibly contaminate the soil and there is a risk for antibiotic residues in bovine products (Laven and Logue, 2006). In a trial performed by Cramer et al. (2018), individual milk samples of cows that were topically treated with oxytetracycline did not show a violation of the (USA) tolerance limit (300 ppb). However, in 11% of the individual milk samples, oxytetracycline concentrations between 100 and 300 ppb were found eight hours post-treatment. The estimated milk withdrawal interval on cow-level ranged between 0 and 34 hours when using a tolerance limit of 300 ng/mL, whereas this interval ranged from 0 to 70 hours taking 100 ng/mL as the limit value. Tetracycline was detected in 22% of the blood samples. After topical treatment, tetracycline could be found in the teat skin of all cows through direct contact with the feet or contamination with tetracycline containing milk. However, in a trial performed by Britt et al. (1999), milk samples of cows topically treated with oxytetracycline did not show a violation of the tolerance limit (300 ppb).

A substance that could be interesting in particular for organic farms is cornflower honey. In a study by Oelschlaegel et al. (2012), lesions (especially when 'fresh') significantly healed faster when 10 g cornflower honey was applied under a bandage than the lesions in the control group, which did not receive any specific treatment besides standard hoof trimming. Honey has been used for various purposes since ancient times and contains a mixture of natural substances with antibacterial, anti-inflammatory, anti-oxidative, hyperosmotic, acidic and debriding capacities (Olaitan et al., 2007). It also promotes the release of tissue growth factors. Some types of honey (e.g. Manuka honey) have been reported to be able to inhibit methicillin-resistant *Staphylococcus aureus* (MRSA) (George and Cutting, 2007). Moreover, another bee product called propolis has shown to be beneficial for the treatment of calf diarrhea and bovine mastitis (Madras-Majewska et al., 2015). A crucial requirement for using honey for medical purposes is the validation and testing before application due to potential contamina-

**Table 1. Overview of topical treatments as mentioned in the literature. This list is indicative, not limitative.**

| Treatment | Administration | Effect | Reference |
|---|---|---|---|
| **Oxytetracycline** | 3 consecutive days | 75% M2→M0/M4 | Holzhauer et al. (2017) |
| **Chlortetracycline** | 3 consecutive days,<br>2x/day with 30 seconds in between applications | 58% M2→M0/M4 | Holzhauer et al. (2011) |
| **Lincomycin** | 10 g topical paste + bandage | Reduction of lesion size and pain score | Berry et al. (2012) |
| | 25 mL topical solution (0.6 mg/mL), 2x, q48h | 6/15 lesions were healed after 14 days | Laven et al. (2001) |
| | 10 g topical + bandage | 9 cows with M2 → 7 days after treatment: 8 M3, 1 M1 | Chiba et al. (2017) |
| **Thiamphenicol** | 3 consecutive days | 89% M2→M0/M4 | Holzhauer et al. (2017) |
| **Valnemulin** | 25 mL topical solution (100 mg/mL), 2x, q48h | 5/18 lesions were healed after 14 days | Laven et al. (2001) |
| **Non-antimicrobial cream (soluble copper, cationic agent and peroxide)** | 20 mL topical cream + bandage | Reduction of lesion size (but less than lincomycin) and pain score | Moore et al. (2001) |
| **Allyl isothiocyanate** | 3 g (15% solution) + bandage | As effective as lincomycin<br>15 cows with M2 → 7 days after treatment: 2 M4, 11 M3, 1 M1, 1 M2 and lower lameness scores | Chiba et al. (2017) |
| **Salicylic acid** | 10 g + bandage | Keratolytic, anti-inflammatory, bactericidal, antiseptic | Capion et al. (2018) |
| **Calcium hydroxide** | topical + bandage | No improvement | Chiba et al. (2017) |
| **Sodium alginate** | topical + bandage | No improvement | Chiba et al. (2017) |
| **Hydrochloric acid** | 36% solution topical | 3/6 lesions M2 → M3 within 21 days | Read and walker (1998) |
| ***Stryphnodendron adstringens*** **(Martius)**<br>**Coville extract** | Postoperative treatment (metallic iodine, iron, perchlorate, methyl salicylate, oxytetracycline + 7 days later a single brush application of coville extract | Clinical recovery rate 80-93.3% in comparison to no extract (20-27%) | Silva et al. (2015) |
| **Honey** | 10 g + bandage | Faster healing | Oelschlaegel et al. (2012) |
| **Activated copper and zinc chelate gel** | 5 g on days 1, 3 and 7<br>Bandage for 3 days | 92% M2 → M0/M4 | Holzhauer et al. (2011) |
| **Copper and zinc chelate spray** | Application on day 0, 3 and 7<br>Bandage for 3 days | 86.7% clinical improvement (M2 → M0/M1/M3/M4) | Dotinga et al. (2017) |
| **Water + 0.2% soap solution (high pressure)** | Automatic washing after milking for 2 months | Reduced DD prevalence 28.6% → 10.9%<br>(control leg: 29.6% → 18.6%) | Thomsen et al. (2012) |
| **Protexin hoof care (organic acids, salts, essential oils)** | After application standing in dry surroundings for 30 minutes | Improvement: better epithelialization, decrease lameness and pain<br>Comparable to topical tetracycline treatment | Kofler et al. (2004) |

tion with microorganisms like *Proteus* spp., *Clostridium* spp. and *Bacillus* spp. (Olaitan et al., 2007; Carnwath et al., 2014). More and properly designed clinical trials are needed regarding the use of honey in bovine wound management. Another alternative that is being applied in both human and veterinary medicine, is antimicrobial photodynamic therapy (APDT), in which a photosensitizer (e.g. methylene blue) is irradiated to form reactive oxygen species (ROS) when oxygen is present. In a conference paper by Sellera et al. (2017), the outcome of this treatment (twice, q14 days) was positive but not significantly different from topical oxytetracycline treatment (twice, q14 days). Debridement is used by some veterinarians and farmers but the lesions have a high recurrence rate (Read and Walker, 1998; Toholj et al., 2012). In a study by

**Table 2. Overview of foot bathing solutions as mentioned in the literature. This list is indicative, not limitative.**

| Treatment | Administration | Effect | Reference |
|---|---|---|---|
| **Copper sulfate** | 5% solution, weekly | Improved lesions significantly | Speijers et al. (2010) |
| **Formalin** | 5%, 2x/wk for 1 month | 17% healing rate | Teixeira et al. (2010) |
| **Peracetic acid** | Each milking for 2 weeks and then for 6 consecutive milkings every 2 weeks.<br>5 minutes contact time | Prevalence M2 33% → 15.5% after 12 weeks treatment.<br>No significant effect on severe lesions | Blowey et al. (2004) |
| **Dragonhyde** | 5%, 2x/wk for 1 month | 31% healing rate | Teixeira et al. (2010) |
| **Copper sulfate** | 10%, 2x/wk for 1 month<br>5%, for 4 consecutive milkings/ week. + pre-washing<br>2 kg/100 L water, for 1 week (daily) | 24% healing rate<br>M2 prevalence 8.8% → 3.6% (after 22 weeks)<br>Decrease in mean lesion score (3.2 → 0.9) | Teixeira et al. (2010)<br>Solano et al. (2017a)<br>Laven and Hunt (2002) |
| **Biodegradable solution containing organic acids, tea tree oil and wetting agents** | 3%, 5 days/wk for 9 weeks | DD frequency -18% in 9 weeks | Smith et al. (2014) |
| **Erythromycin** | 0.035 g/L, 2 consecutive milkings<br>2x q24 h | Less pain, lameness, redness and exudation of lesion. No reduction of DD size<br>Decrease severity of lesions | Laven and Proven (2000)<br>Laven (2006) |
| **1 % sodium hypochlorite** | 2x/day, 1 month | 73.3% recovery rate | Silva et al. (2005) |
| **Pediline (5% solution of quaternary ammonium compounds, aluminiumsulphate, coppersulphate and glutaraldehyde)** | 2x/day for 5 days and 1 week later 1x/day for 5 days | 100 % clinical recovery | Brydl et al. (2004) |
| **Quaternary ammonium compounds** | 2%, 2x/day for 2 days/wk for 8 weeks | No significant effect on healing rate | Thomsen et al. (2008) |
| **Organic acids (peracetic acid, acetic acid, hydrogen peroxide)** | 1%, 2x/day for 2 days/wk for 8 weeks | No significant effect on healing rate | Thomsen et al. (2008) |
| **Peroxide, soluble copper, cationic agent** | Daily for 5 days, then 2 days no treatment and finally daily for 3 days. | 26-56% improvement on day 28 (depends on the formulation)<br>Uncertain stability of product. | Shearer and Hernandez (2000) |
| **Glutaraldehyde** | 1.5%, 2x/day for 2 days/wk for 8 weeks | No significant effect on healing rate | Thomsen et al. (2008) |
| ***Stryphnodendron adstringens* (Martius) Coville extract** | 10%, daily for 45 days | Clinical recovery rate of 66.66-86.66% in comparison to control (20-27%) | Silva et al. (2015) |

Read and Walker (1998) six out of six removed lesions came back within seven to twelve weeks post-treatment. In the same study, cryotherapy was used for one lesion but it was deemed to be unsuccessful. Other non-antibiotic treatments include allylisothiocyanate, a natural *Brassicaceae* extract with antibacterial properties, and copper-chelate gel (Chiba et al., 2017; Dotinga et al., 2017) (Table 1).

Since treponemes are situated throughout the skin layers, the question rises if topical application of drugs is sufficient to completely eliminate persistent and deeply nested treponemes. In several studies, treponemes have been shown to remain in the skin after topical treatment, albeit in lower abundance (Berry et al., 2010; Capion et al., 2018). Topical treatment has the advantage over foot bathing that the active substance is much more concentrated and a lesser amount of the product should be used, causing a lower risk for environmental pollution (Shearer and Elliot, 1998).

## Herd foot bathing

Foot bathing should be implemented to reduce microbial transmission and to benefit claw and skin health (Cook, 2017). Solutions used in foot baths are antibiotics and/or antiseptics. It is of crucial importance that the recommended concentration is respected, so there is no under- or overdosage, reducing the efficacy of the treatment. Solutions that are too caustic, cause skin damage of the adjacent foot skin and udder (Cook, 2017). Besides the preparation of the correct dilution of the solution, foot baths are relatively easy to use (Holzhauer et al., 2004). Foot baths should be implemented to keep the infection pressure under control at herd level rather than to treat acute lesions (Solano et al., 2017a). The design and upkeep of the foot bath are of vital importance (Cook, 2017). The ideal foot bath can be cleaned thoroughly and is easily accessible for cattle. The length should be 3.0-3.7 m, which guarantees at least two hind feet passages. Ideally, the width is 0.6 m and the step-in height 0.25 m (Cook et al., 2012; Cook, 2017). The side walls are sloped and the fluid level should be at least 0.15 m (Cook, 2017).

A high degree of soiling of the foot bath reduces its effectiveness (Hartshorn et al., 2013). Forcing the cows to walk through a dirty manure filled bath, has the opposite effect of what the farmer is trying to achieve: a good claw health. Cleaning the claws before a foot bath passage therefore improves the foot baths efficacy (Holzhauer et al., 2004). Placing a washing foot bath before the treatment-foot bath exposes the claws better to the antiseptic or antibacterial solution, reduces the contamination and thus prolongs the usage period (Manning et al., 2016). This set-up strains the manure management system and it possibly dilutes the treatment solution. Moreover, dirty feet are not cleaned sufficiently by a single passage through water (Cook, 2011). Regularly performing a pH test to verify that the pH is between 3 and 4.5 when using an acidic solution gives an indication of the efficacy of the solution (Cook, 2017). The frequency of use depends on many factors like the number of cows on the farm, management and the claw health history. A general recommendation is to weekly foot bathe for four consecutive milkings when foot health is severely compromised and fortnightly for four consecutive milkings when the infectious foot diseases are more or less under control (Speijers et al., 2013). The frequency of foot bathing can be adjusted after a reassessment of the foot health four to six weeks after the start of the foot bathing regime (Cook, 2017). The foot bath solution should be changed approximately every two hundred cow passages, depending of the nature of the product used in the bath and the level of contamination (Cook, 2017).

Many farmers implement foot baths but there is no evidence of what product should ideally be used in the bath. Two of the most frequently used non-antibiotic solutions, formalin and copper sulfate, could potentially harm the environment and implicate animal and human health risks (Stehouwer and Roth, 2004; IARC, 2006). More importantly, the use of formalin for foot bathing is currently forbidden in Belgium, and soon, a ban on the use of copper sulfate will follow. Formalin is a potential carcinogenic substance and is notably irritating for wounds and mucosae (IARC, 2006). It easily gets inactivated by temperatures below 17°C and contamination. The major risk of using copper sulfate is environmental contamination when disposed inadequately, slowing down the soil nutrient cycle and crop growth (Stehouwer and Roth, 2004). Besides the environmental risk, it stings when applied to an acute lesion. It is possible to build a filter system in order to recuperate copper sulfate after a whole-herd foot bathing session (Müller et al., 2017). In New Zealand, a filter composed of a pump, a funnel originating from an old fertilizer spreader bin, a filter membrane and a collection tank has been described by Müller et al. (2017). They were able to recuperate 92.5% of the copper, saving 55 New Zealand dollars per foot bath. There are no antibiotic substances registered for foot bathing purposes in the EU (Laven and Proven, 2000). Besides the legal aspect, there is a lack of information regarding the efficiency and the maximum amount of cow passages before renewing (Cook, 2017). Additionally, it remains unclear how to safely dispose antibiotic solutions afterwards.

In a study by Solano et al. (2017a), the implementation of a standardized weekly 5% $CuSO_4$-foot bath in farms with a high prevalence of DD, significantly decreased the number of active lesions but no effect could be seen in farms with a low prevalence. Interestingly, shotgun metagenomic sequencing performed on skin biopsies has shown an increase in bacterial genes coding for zinc and copper resistance in active and chronic DD lesions (Zinicola et al., 2015a). Various non-antibiotic alternatives such as Coville

**Table 3. Some antibiotics, which are systemically used against digital dermatitis. It should be noted that the use of cephalosporins in cattle should be avoided because of concerns for resistance in human medicine.**

| Treatment | Administration | Effect | Reference |
|---|---|---|---|
| **Cefquinome** | 1 mg/kg IM 3-5 days | Less severe lesions | Laven (2006) |
| **Oxytetracyclin** | 10 mg/kg, IM q48 h, 4x<br>(+ 1% NaClO foot bath q12 h, 1 month) | 56.67% recovery rate<br>(86.6% recovery rate) | Silva et al. (2005) |
| **Procain penicillin G** | 18 000 units/kg IM, 2 x/day for 3 days | 9/9 lesions transitioned from M2 to M3 within 21 days | Read and Walker (1998) |
| **Ceftiofur** | 2 mg/kg IM, daily for 3 days | 41/44 lesions transitioned from M2 to M3 within 21 days | Read and Walker (1998) |

extract and thymol have been examined (Kulow et al., 2015; Silva et al., 2015) (Tables 1 and 2). Thymol, a substance found in thyme, presents low MIC and MBC values in an in vitro assay with various bacteria (e.g. *Dichelobacter nodosus*, *Fusobacterium necrophorum*, *Treponema* spp.) (Kulow et al., 2015). Most studies lack a non-treated control group due to animal welfare reasons, making it difficult to fully attribute clinical healing to the treatment effect and not to spontaneous healing. There is an urgent need for an alternative, commercial foot bathing solution that neither harms the environment, the farmers nor the livestock.

### Systemic treatment

Systemic treatment is usually based on antibiotics; however it is not often used due to the associated costs, milk- and meat withdrawal period and because its clinical effectiveness is uncertain (Read and Hunt, 1998; Laven and Logue, 2006; Laven, 2006). Also, the current worldwide policy to reduce the use of antibiotics, causes the use of this type of treatment for DD to be very limited (Table 3).

### Claw trimming

In the pursuit of maintaining a healthy herd, claw trimming is an important part of the management at a modern dairy farm (Mahendran and Bell, 2015). Keeping data from each trimming session in a computerized database helps to identify issues in the herd so that appropriate measures can be taken (Kofler, 2013). Trimming of the claws helps to achieve the optimal claw shape and restores normal weight bearing, which lowers the risk of (non-)infectious claw diseases (Mahendran and Bell, 2015). By hollowing the axial upper part of the sole, the elimination of dirt becomes easier, which is important in the prevention of (inter) digital dermatitis; in addition, the risk of developing a sole ulcer decreases significantly (Mahendran and Bell, 2015). Moreover, heel horn erosions should be treated because they are considered to be a reservoir for dirt and bacteria (Manske et al., 2002). In 1985, Raven (1985) recommended to keep the dorsal wall length at a minimum of 7.5 cm; however, the dorsal wall length varies according to breed, cow size and age (Raven, 1985). Using a standard, outdated measurement holds a significant risk of overtrimming. A modern approach according to a study by Archer et al. (2015), in which the authors utilized computer tomography to visualize the bovine foot, is to trim the length to 8.5 cm (minimum) for first and second parity Holstein-Friesians and up to 9.0 cm (minimum) for older Holstein-Friesian cows. The recommended toe angle is between 45° and 52°. Minimum thickness of the sole and the wall is 5 and 8 mm, respectively. Claw trimming is furthermore considered to be beneficial for the optimization of a topical treatment (Manske et al., 2002; Holzhauer et al., 2008). It is advisable to remove projective, papillomatous skin proliferation associated with DD in order to aid the healing process and to make the lesion more accessible for topical treatment (Toholj et al., 2012).

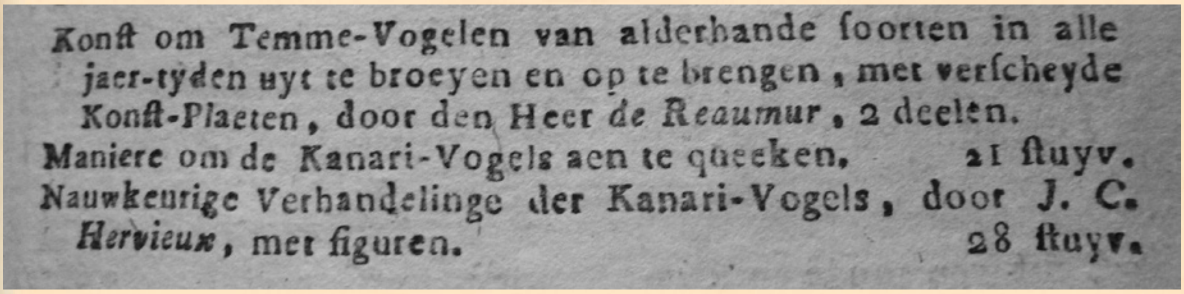
## CONCLUSION

It is clear that more research needs to be performed on all facets of digital dermatitis, especially concerning the pathogenesis. Research on the deviant inflammation and the inadequate immune response to *Treponema* spp. may lead to the discovery of possible points of action, which may be addressed in order to find an adequate treatment and prevention strategy. The initial trigger for developing digital dermatitis is still unknown. More emphasis should be put on what goes wrong at the level of the local immune response. It is possible that treponemes are able to evade the immune system; it might be that the immune system of certain cows is not able to arm itself properly against treponemes. It is important not to focus solely on the bacterial component of the pathogenesis, considering that digital dermatitis cannot be eradicated by the use of antibiotics. The interaction between the present *Treponema* spp. and other bacterial species should be examined in order to get a clear view on the infectious element of digital dermatitis. With the currently available treatments, acute lesions can temporarily be healed but digital dermatitis keeps on circulating in the herd. This implies the need for a thorough re-assessment of the commonly used (non-)antibiotic substances. Testing the in vitro efficacy of foot bathing products, additionally with manure present to mimic the in vivo situation, against *Treponema* spp. will aid in finding an appropriate mass treatment.

## LITERATURE

An extended literature list can be obtained from the authors.

**Uit het verleden**



Konſt om Temme-Vogelen van alderhande ſoorten in alle jaer-tyden uyt te broeyen en op te brengen, met verſcheyde Konſt-Plaeten, door den Heer *de Reaumur*, 2 deelen.
Maniere om de Kanari-Vogels aen te queeken. 21 ſtuyv.
Nauwkeurige Verhandelinge der Kanari-Vogels, door J. C. *Hervieux*, met figuren. 28 ſtuyv.

**Een vroege publicatie over vogels: eieren uitbroeden en kanaries kweken. In 1789 verkrijgbaar bij de boekhandel-drukkerij Gimblet op de Gentse Korenmarkt.**

**Detail uit de 'Wegwijzer der Stad Gent' van dat jaar (Stadsarchief Gent – Zwarte Doos, Gentbrugge).**