

# Efficacy of non-antibiotic Repiderma spray for treatment of digital dermatitis in cows

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## Abstract

Digital dermatitis is a very painful multifactorial claw disease which can cause major economic loss and welfare problems. Therefore, it is of great importance there are treatments available which are low in costs and high in efficacy. In view of the resistance to antibiotics and any residues in milk or meat, non-antibiotic treatment is preferred.

In this article a clinical trial is described with the aim of testing non-antibiotic spray to cure bovine digital dermatitis lesions. The trial is performed at seven Dutch dairy farms between October and December 2013. Repiderma-spray® (Copper, zinc, aloe vera, alcohol, IntraCare BV, Netherlands) was used as non-antibiotic spray and chlortetracycline-spray, CTC® (chlorinetetracyclinehydrochloride®, Eurovet Animal Health BV, Netherlands), which is officially registered, as positive control.

Claws were alternately treated with Repiderma® or CTC® following the manufacturer's protocol and photographed and scored at day 0 and day 10. If there was no longer an M2 lesion at day 10, the claw was defined cured.

The average cure rate of claws treated with Repiderma®-spray at day 10 was 89.15%.

## 1. Introduction

In this article, the cure rate of Repiderma® spray will be examined. Besides that, a clinical trial is explained with the aim to investigate the ability to heal digital dermatitis lesions with two different treatments. The data collected for this clinical trial are used to examine the cure rate of Repiderma® spray.

### 1.1 Clinical trial

In the clinical trial, the efficacy of chlortetracycline-spray (CTC®) and Repiderma®-spray are compared. Both sprays were used to treat typical M2 (explained in table 1) lesions of digital dermatitis on cows. It is assumed that the claw of the cow is cured, if there is no longer a M2 lesion.

Four students of Utrecht University, faculty of veterinary medicine, gather data used for a registration study.

### 1.2 Dermatitis digitalis

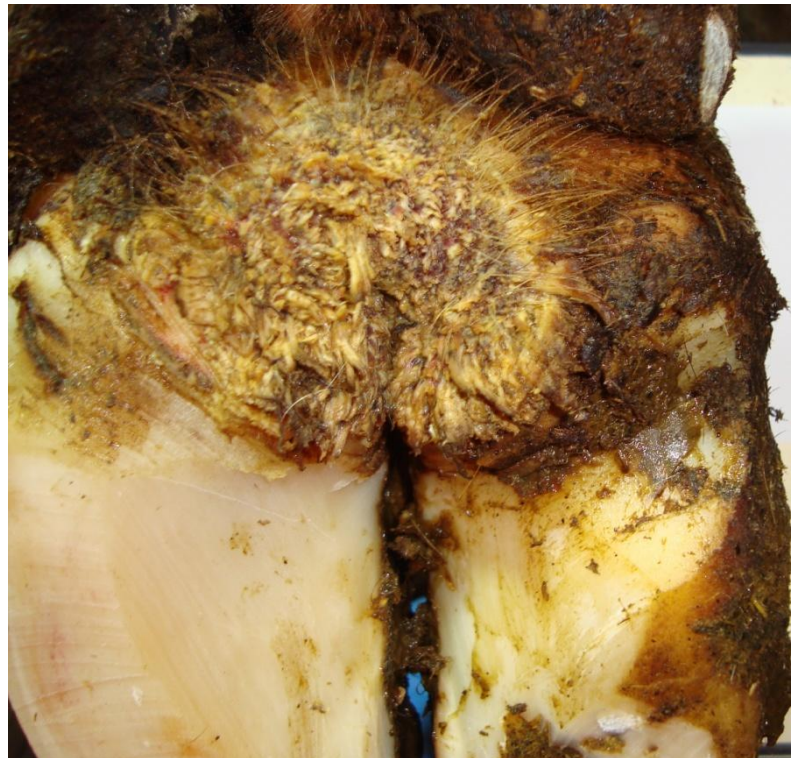
Dermatitis digitalis (digital dermatitis, DD) is a contagious disease of the skin of the claw of cows, mostly found on the planetary side of the hindclaw<sup>1-4, 14, 17, 18</sup>. These lesions can be classified from M0 to M4 to indicate seriousness, first described by Döpfer *et al.* (1997)<sup>4-6</sup>. Some examples are shown in table 1<sup>5, 7</sup>. There are two characteristic forms of the lesion, an erosive one, which is associated with an acute lesion and a papillomatous/proliferative, granular form which can be associated with later stages of disease<sup>3, 5, 8, 9</sup>. Nevertheless, both forms have the same histopathology<sup>8, 10</sup>. Examples are figure 1 and 2. Besides this typical appearance, the most

important symptom is walking on the tip of the toe. Other symptoms mostly seen are less milk production and less fertility. In short: major economic loss<sup>2, 4, 10</sup>.



**Figure 1: Erosive form of digital dermatitis**


**Figure 2: Papillomatous form of digital dermatitis**



The disease is influenced by many factors such as parity, breed, stadium of lactation and housing system. For example, the Holstein-Friesian breed, first-parity, lactating (compared to dry cows), rough and wet floors and hoof trimmers who also visit other farms are considered a risk factor <sup>2,10</sup>. These influences can be divided in cow factors, management factors and environmental factors <sup>2,7,10</sup>. The etiology of the disease is not entirely understood, although presence of *Treponema*-like spirochetes believed to be the main casual factor <sup>2,3,9,10,17</sup>.

Digital dermatitis is a multifactorial disease and therefore it is difficult to treat <sup>7</sup>. At this moment, chlortetracycline-spray (chlorinetetracyclinehydrochloride®, Eurovet Animal Health BV, Netherlands), Ceffect (Cefquinome®, EMDOKA bvba, Belgium) and Intra Hoof-fit gel (Copper, zinc, aloe vera, alcohol, IntraCare BV, Netherlands) are registered for treating digital dermatitis in the Netherlands <sup>11</sup>. CTC®-spray and violet aerosol spray (Dichlorphen®, Triclosan®, Agrapharm, Netherlands) are known as the most effective treatment. In case of prevention, a footbath with copper solution or formalin can be helpful. If used wrong, increase the amount of digital dermatitis lesions is possible <sup>2,3,12</sup>. Footbaths containing antibiotics (oxytetracycline, erythromycin, lincomycin) are prohibited in the Netherlands since 1998, because of resistance problems <sup>3,13,14</sup>.

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Classification and explanation	Picture
M1 (first stadium). The lesion is 0-2 centimetres in size, red and very painful.	



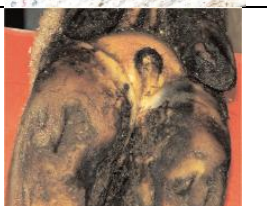
<p>M2 (second stadium). This lesion is much bigger than M1 lesions, 2-4 centimetres. It is more painful and the skin is swollen and ulcerated.</p>		
<p>M3 (third stadium). This lesion is less painful than the M2 lesion. The skin is less swollen and covered by a black crust.</p>		
<p>M4 (fourth stadium). This stadium is also called 'chronic'. It is characterized by dyskeratosis and not painful.</p>		

Table 1: Classification of digital dermatitis lesions <sup>5,7</sup>

### 1.3 Repiderma® spray

Due to the fact that IntraCare, the company that produces Hoof fit products, doesn't reveal the ingredients and active substances of Hoof fit spray (also called Repiderma®) at the moment, except from 'chelated zinc and copper', Hoof fit gel® is taken as an example. It is assumed that the composition of Hoof fit spray is the same as Hoof fit gel®. The excipients may differ but at least the active components of the medicine are comparable. Both substances are meant to treat individual animals <sup>15</sup>.

The active ingredients of the Hoof fit gel® are copper chelate (40 mg/g) and zinc chelate (40 mg/g). Copper has an antimicrobial effect, zinc furthers healing of the lesion. According to IntraCare, these chelated minerals can be easily absorbed by the skin due to the size of the particle. By using adhesive substances, they ensure that the medicine attaches to the skin for a long time. Although this gel can be easily absorbed by the skin, the chelated minerals reach the blood only in minimal concentrations <sup>15</sup>.

It is recommended to treat a digital dermatitis lesion following the protocol. This protocol is also used in the clinical trial and explained in chapter 1.1. A summary can be found in the attachment (figure 3). It is important that the bandages are removed after 3 days, otherwise the healing will be less than expected. If necessary, the treatment has to be repeated <sup>15</sup>.

The most important advantage of Repiderma® is that it's a nonantimicrobial treatment. Therefore, it is possible for hoof trimmers to treat (and wrap) the claws of lame cows, because they are not legally allowed to use antimicrobials <sup>12</sup>.

#### **1.4 Chlortetracycline® spray**

According to the Medicine Evaluation Board, CTC®-spray contains chlorinetetracyclinehydrochloride, 3.21 gram in a flask of 270 millilitres, which equates to 2.45%. In the Netherlands, it is registered as REG NL 9013 and also 'UDA', which means that it is required to have a veterinarian's prescription <sup>11, 12, 16</sup>. It is advised to spray at a 15 to 20 centimetres distance, then wait 30 seconds and spray again. This treatment has to be repeated for three days <sup>11, 16</sup>. CTC®-spray is used in the clinical trial as positive control.

#### **1.5 Hypothesis**

The hypothesis of this paper is: Repiderma® has a cure rate of 60%.

## 2. Clinical trial

### 2.1 Material and methods

Previous to the actual clinical trial, four students were trained using photographs and to perform the treatments. Prior to the clinical trial, participating farms were obliged to leave out any treatments or walk-through footbaths to cure dermatitis digitalis lesions for at least three weeks.

On day 0, all the cows were placed in a hoof trimming chute, the claws were trimmed and inspected for M2 digital dermatitis lesions <sup>5, 7</sup>. Because of higher appearance of lesions on hind feet and for practical reasons, only hind feet were used <sup>1, 14, 17, 18</sup>. If affected, the claws were cleaned with the help of blue udder paper and treated, alternately with Repiderma<sup>®</sup> or CTC<sup>®</sup>-spray. The same treatment per claw was repeated following the treatment schedule (table 2). Both sprays were used for 3 seconds from 15 to 20 centimetres distance. CTC<sup>®</sup>-spray had to dry for 30 seconds and then sprayed again. Besides that, the claws of the cows treated with Repiderma<sup>®</sup> also received a bandage (Vetrap<sup>®</sup> elastic, figure 3 in the attachment) and a bandage gauze. At day 3 this bandage is removed and the claw is only sprayed. In case of a cow with two affected claws, it would be treated with two different treatments. Treated animals were marked to recognize them the next day.

To register each individual digital dermatitis lesion, a form was filled out and a picture (before treatment) was made. On this form, score, size, location, appearance and soreness had to be filled out.

Given the instructions, table 2 is the treatment schedule.

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Repiderma	T/S/P			T/S				T/S			S/P
CTC-spray	T/S/P	T/S	T/S								S/P

Explanation table:

T = treat

S = score

P = photograph

**Table 2: Treatment and scoring schedule**

In total, seven herds were included in this clinical trial. The planning of these farms is showed in table 6 in the attachment. Farm number 6 is excluded of the clinical trial, because of the little amount of M2-lesions that were found (4 affected claws).

Farm	Repiderma <sup>®</sup>	CTC <sup>®</sup>	Total	Both claws	Excluded
1	12	10	22	4	0
2	17	18	35	5	0
3	14	14	28	3	0
4	44	44	88	18	1(Repiderma <sup>®</sup> )
5	12	13	25	3	0
7	9	8	17	1	0
8	35	35	70	17	1(CTC <sup>®</sup> )
Total	142	141	283	51	2

**Table 3: Overview of treated claws per farm**



## 2.2 Results

The results of the clinical trial are shown in table 4 and 5. Of all farms, the M-scores of the lesions treated with Repiderma®-spray on the first day (day 0) were collected and compared to the M-scores of the eleventh day (day 10).

Farm number	Claws cured	Claws not cured	Total
01	11	1	12
02	13	4	17
03	12	2	14
04	41	2	43
05	11	1	12
07	8	1	9
08	33	2	35
Total	129	13	142

Table 4: Data per farm for Repiderma®-spray

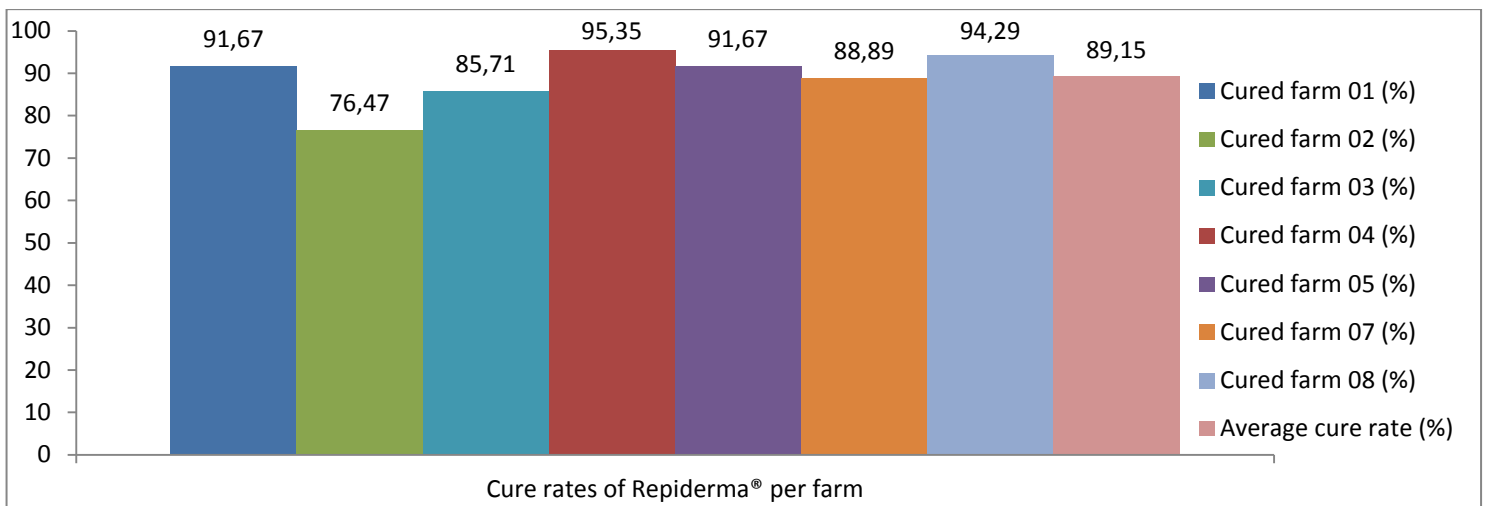


Table 5: Cure rates of Repiderma®-spray per farm

### 3. Conclusion

Risk factors as parity, stage of lactation and type of floor were not investigated.

A two-sided test is used for statistical analysis. A P-value of  $1,456 \cdot 10^{-16}$  is found at a confidence interval of 95% and thus significance level of 0.05, which means that the result of the test is statistically significant and the hypothesis will be rejected.

The average cure rate of Repiderma®-spray at these seven herds is 89.14880681%.

### 4. Discussion

At the first farm, there was some confusion about scoring the lesions. Some lesions were scored M2, which were in fact M4.1 lesions according to the supervisor of the students and D. Döpfer. A M4.1 lesion is a combination of M1 and M4, which is explained in an article of D. Döpfer <sup>19</sup>. Because of the photographs, this problem was noticed soon and resolved quickly. The scoring of lesions went well on other farms.

There was one cow of the Repiderma® group which was excluded from the clinical trial. At the second day (D1) at farm 4, students noticed a swollen foot and the bandage seemed to pinch. This bandage was removed immediately and foot rot (an interdigital inflammation) was diagnosed. This disease had to be treated by a veterinarian, which can have influence on the curing of the digital dermatitis lesion. Therefore this cow was excluded of the trial.

At the third day at farm 4, many bandages and gauzes turned out to be soaked with manure, which is logically not intended. As a result, the lesions were all weak, wet and open in contrast to other lesions (dry gauzes) which were dried and had a crust. The floor in this stable was wetter compared to other farms, which can influence curing of lesions.

It was plain to see that dry lesions were cured better than wet lesions. Therefore, a wooden cube attached under the claw due to another disease such as sole ulcer, was clearly an advantage in view of healing of lesions. That is another indication that wetness is very important in the etiology of digital dermatitis.

Finally, in this clinical trial 142 cows of seven different herds were treated with Repiderma®-spray. It is not surprising that cure rates of Repiderma® differ between farms, because of the multifactorial nature of this disease. As mentioned before, housing system, breed, stadium of lactation and parity are important factors. None of these were included in this clinical trial because the purpose of this test was to prove the healing of Repiderma®-spray, apart from predisposing factors.

## References

1. Logue, D. N., Gibert, T., Parkin, T., Thomson, S. & Taylor, D. J. A field evaluation of a footbathing solution for the control of digital dermatitis in cattle. *The Veterinary Journal* **193**, 664-668 (2012).
2. Holzhauer, M., Hardenberg, C., Bartels, C. J. M. & Frankena, K. Herd- and Cow-Level Prevalence of Digital Dermatitis in The Netherlands and Associated Risk Factors. *J. Dairy Sci.* **89**, 580-588 (2006).
3. Laven, R. A. & Logue, D. N. Treatment strategies for digital dermatitis for the UK. *The Veterinary Journal* **171**, 79-88 (2006).
4. Relun, A., Guatteo, R., Roussel, P. & Bareille, N. A simple method to score digital dermatitis in dairy cows in the milking parlor. *J. Dairy Sci.* **94**, 5424-5434 (2011).
5. Döpfer, D. *et al.* Histological and bacteriological evaluation of digital dermatitis in cattle, with special reference to spirochaetes and *Campylobacter faecalis*. *Vet. Rec.* **140**, 620-623 (1997).
6. Döpfer, D., Holzhauer, M. & Boven, M. V. The dynamics of digital dermatitis in populations of dairy cattle: Model-based estimates of transition rates and implications for control. *Vet. J.* **193**, 648-653 (2012).
7. Van Aert, M. Treatment of Mortellaro's disease. *Vlaam. Diergeneeskd. Tijdschr.* **78**, 452-456 (2009).
8. 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.* **53**, 215-231 (2002).
9. Refaai, W., Van Aert, M., Abd El-Aal, A. M., Behery, A. E. & Opsomer, G. Infectious diseases causing lameness in cattle with a main emphasis on digital dermatitis (Mortellaro disease). *Livestock Science* **156**, 53-63 (2013).
10. Holzhauer, M., Bartels, C. J. M., Döpfer, D. & van Schaik, G. Clinical course of digital dermatitis lesions in an endemically infected herd without preventive herd strategies. *Vet. J.* **177**, 222-230 (2008).
11. <http://www.cbgmeb.nl/CBG/nl/diergeneesmiddelen/diergeneesmiddeleninformatiebank/default.htm>.
12. Moore, D. A., Berry, S. L., Truscott, M. L. & Koziy, V. Efficacy of a nonantimicrobial cream administered topically for treatment of digital dermatitis in dairy cattle. *J. Am. Vet. Med. Assoc.* **219**, 1435-1438 (2001).
13. Holzhauer, M. *et al.* The effect of an acidified, ionized copper sulphate solution on digital dermatitis in dairy cows. *The Veterinary Journal* **193**, 659-663 (2012).
14. Relun, A., Lehebel, A., Bareille, N. & Guatteo, R. Effectiveness of different regimens of a collective topical treatment using a solution of copper and zinc chelates in the cure of digital dermatitis in dairy farms under field conditions. *J. Dairy Sci.* **95**, 3722-3735 (2012).

15. [www.intracare.nl](http://www.intracare.nl).

16. Dechra Veterinary Products. Cyclospray 2012. (2012).

17. Holzhauer, M., Bartels, C. J., van Barneveld, M., Vulders, C. & Lam, T. Curative effect of topical treatment of digital dermatitis with a gel containing activated copper and zinc chelate. *Veterinary record* **169**, 555 (2011).

18. Relun, A., Guatteo, R., Auzanneau, M. M. & Bareille, N. Farmers' practices, motivators and barriers for adoption of treatments of digital dermatitis in dairy farms. *Animal* **7**, 1542-1550 (2013).

19. Berry, S. L., Read, D. H., Famula, T. R., Mongini, A. & Döpfer, D. Long-term observations on the dynamics of bovine digital dermatitis lesions on a California dairy after topical treatment with lincomycin HCl. *Vet. J.* **193**, 654-658 (2012).

*The pictures in this paper (except table 1) are made by students of Utrecht University, Faculty of Veterinary Medicine (P.A. De Weerd, E. Van Vliet, A.G. Dotinga and S.M. Versteegen) for sake of the clinical trial.*

## Attachment



**Intra Hoof-fit Gel**  
REG NL 109438  
Voor individuele behandeling



- 

1. Bekap de klauwen 2 tot 3 keer per jaar. Laat bij voorkeur een professionele klauwbekapper alle diersoorten bekappen.
- 

2. Maak de klauwen goed schoon. Zorg dat alle mest verwijderd is, ook in de tussenklauwspleet. Maak de klauw daarna droog.
- 

3. Smeer met bijgeleverde kwast Hooft-fit Gel op de klauw en in de tussenklauwspleet.
- 

4. Bij zeer ernstige problemen adviseren wij de klauwen in te tappen. Na max. 3 dagen de tape verwijderen en opnieuw behandelen met Hooft-fit Gel. (ditmaal zonder tape).
- 

5. Controleer de laesie op dag 7. Indien herstel niet voldoende, breng de gel nogmaals aan zonder verband.



Figure 3 15

Week	Monday		Tuesday		Wednesday		Thursday		Friday	
40 (30 sep)			1 d0		1 d1		1 d2		1 d3	
41 (7 oct)			2 d0	1 d7	2 d1		2 d2		1 d10	2 d3
42 (14 oct)			3 d0	2 d7	3 d1		3 d2		3 d3	2 d10
43 (21 oct)	4 d0		4 d1	3 d7	4 d2		4 d3		3 d10	
44 (28 oct)	4d7		5 d0		5 d1		4 d10	5 d2	5 d3	
45 (4 nov)	6 d0			5 d7					5 d10	
46 (11 nov)			7 d0		7 d1		7 d2		7 d3	
47 (18 nov)			7 d7						7 d10	
48 (25 nov)			8 d0		8 d1		8 d2		8 d3	
49 (2 dec)			8 d7						8 d10	

Table 6: Planning clinical trial

Explanation: 1d0 means farm number 1 day 0, 1d1 means farm number 1 day 1 and so on.