

## Treating constitutional eczema with DerMel skin ointment

Drs M.W.H.M. Roovers

- Allergologist, St. Elisabeth Hospital Tilburg

Drs I. Boersma

- Dermatologist, Albert Schweitzer Hospital Zwijndrecht

### Introduction

Constitutional eczema (CE) is a chronic inflammatory disease of the skin that progresses with exacerbations and remissions. The main risk factor for developing constitutional eczema is genetic predisposition. Mutations found in patients with constitutional eczema include those in the gene encoding body substances that are important for the skin barrier and for the inflammatory response. It is hypothesised that these genetically determined abnormalities cause environmental substances (such as water and soap) and bacteria to enter the skin more easily, causing an excessive inflammatory response.<sup>1</sup> The disease often results in greatly reduced quality of life. The most prominent symptom of CE is itching; scratching leads to skin damage and exacerbation of the skin abnormalities.

In 2003, GPs were aware of an estimated 260,000 people diagnosed with constitutional eczema (prevalence: 15.2 per 1,000 men and 16.8 per 1,000 women per year). These estimates are based on GPs' registration data. In 2003, GPs saw an estimated 96,000 new patients with CE.<sup>1</sup>

The skin of people with constitutional eczema is often (extremely) dry. Due to the disturbed moisture balance, the barrier function of the skin decreases. Proper skin care for patients with CE should therefore aim at keeping the barrier function of the skin intact as far as possible and, in the event of damage, to heal it as quickly as possible. Ceramides are important building blocks for the horny layer of the skin. They contribute to an intact skin barrier and play an important role in preventing the skin from drying out. The skin of CE patients contains fewer ceramides than in non-CE patients. Partly for this reason, their skin does not retain moisture well. This leads to problems, with the skin becoming more sensitive to external influences such as bacteria and allergens, and with a greater tendency to be irritated and itch. Intact skin is of great importance to patients with CE.

Treatment of CE using base ointments and locally applied corticosteroid ointments aims at proper care for (extremely) dry skin and reduced chronic inflammation of the skin. The efficacy of locally applied corticosteroid ointments has been sufficiently demonstrated. A disadvantage of chronic use of corticosteroid ointments is that this can lead to skin atrophy, with the skin becoming even more fragile. Further, there is often parental resistance to the application of corticosteroids to children.

### Staphylococcus aureus as CE exacerbation trigger

Scientific research shows that colonisation of the skin by *Staphylococcus aureus* is significantly more common in people with CE than in those without CE. Studies show that > 90% of CE patients are colonised by *S. aureus*.<sup>2,3</sup> Skin damaged as a result of scratching easily results in skin infection and associated exacerbation. *S. aureus* also has further effects. Recent studies have shown that harmful exotoxins from *S. aureus* can serve as *superantigens*. The Staphylococci superantigens (SsAgs) penetrate the (weakened) skin barrier and contribute to CE exacerbation. This mainly involves activated T cells and monocytes in the skin.<sup>3,4</sup> The *S. aureus* superantigens are therefore increasingly seen as exacerbation triggers. Research by Lever et al. has shown that eradication of *S. aureus* leads to a statistically significant decrease in the colonisation of eczema by staphylococci, compared to a placebo, and that eczema severity decreases.<sup>5</sup> Therefore seems to be a clear rationale for the eradication of *S. aureus*, in the expectation that this will reduce the number of CE exacerbations. However, the standard application of antibiotic ointment does not seem to be an option, as an unacceptable increase in resistance is highly likely. There is therefore a clear need for a base ointment with good skin care and wound-healing properties, combined with anti-inflammatory and antibacterial effects that significantly reduce colonisation of the skin by *S. aureus*. The aim being to improve quality of life by reducing the number of CE exacerbations and potentially decrease the use of corticosteroid ointments. This article describes the properties and clinical results of an ointment that may meet these criteria. It is a skin-care base ointment supplemented with 100% natural, pure, enzyme-rich honey (DerMel).

### DerMel skin ointment, a skin-care base ointment with enzyme-rich honey

DerMel skin ointment is a new ointment developed in cooperation with Wageningen University and Research. The ointment contains a skin-care base ointment plus enzyme-rich honey. This skin ointment has specific antibacterial, anti-inflammatory and wound-healing properties. Medically applied honey has long been known for this triple effect.<sup>6,7,8,9</sup>

### Antibacterial effect

The antibacterial effect is influenced by the glucose oxidase (GOX) enzyme. Upon contact with water or skin moisture, GOX activates the conversion of honey sugar (glucose) to gluconic acid and hydrogen peroxide. Continuous production of a small amount of hydrogen peroxide provides a long-term antibacterial effect and gluconic acid creates an acidic environment and, thus, a poor environment for bacteria. The higher the enzyme content, the more effective the bactericidal effect. DerMel contains a high enzyme content.

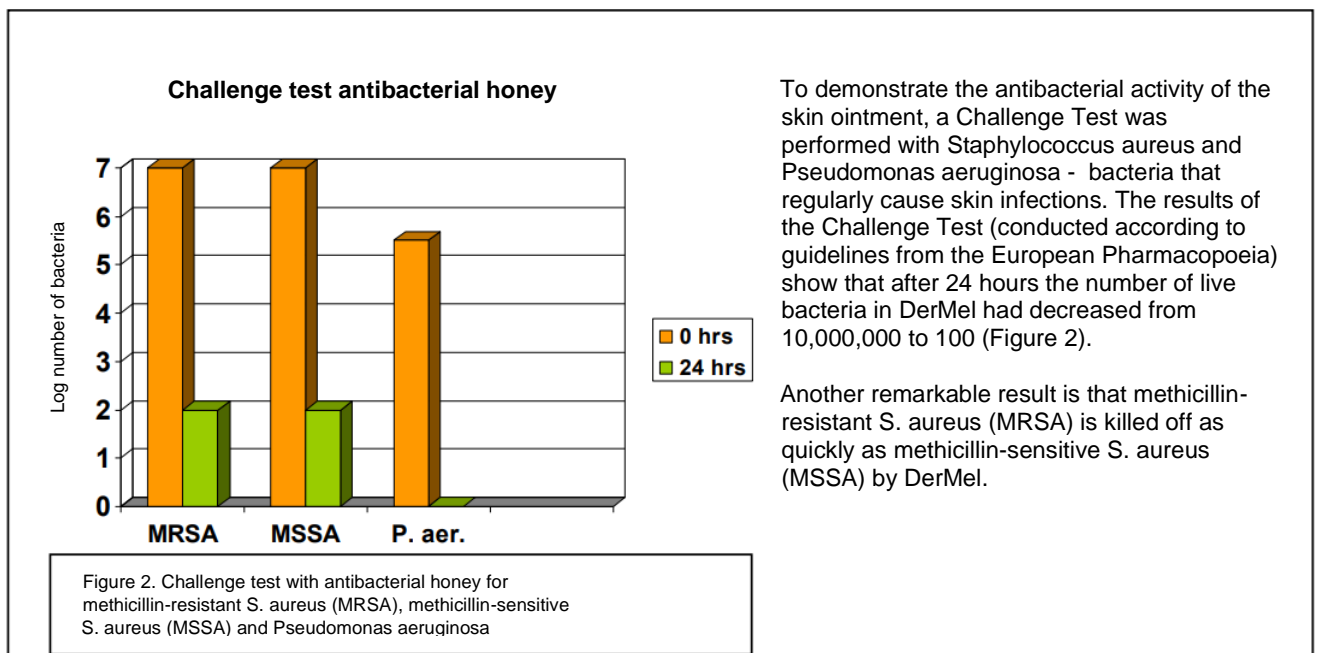
### Anti-inflammatory

The anti-inflammatory effects of honey can be partly explained by the presence of phenols and flavonoids. Phenols and flavonoids have strong antioxidant activity and trap harmful oxygen radicals. Research by Tonks et al. shows that honey induces human monocytes to produce cytokines that play a role in wound healing.<sup>10</sup> Furthermore, Tonks shows that honey significantly inhibits the production of reactive oxygen radicals by macrophages.<sup>11</sup> Subrahmanyam et al. (2003) showed that treatment of burns with honey decreases inflammation.

### Wound healing

Due to its high sugar concentration, honey has a strong hydrophilic effect. This creates a moist wound environment that stimulates tissue regeneration and causes the wound to heal quickly.

The enzyme-rich honey in DerMel skin ointment is produced under controlled conditions, which gives it a highly consistent composition and high bioactivity.<sup>7,8</sup> The antibacterial effect of this honey on skin flora has been demonstrated in a clinical study conducted at the AMC hospital.<sup>6</sup> This study showed that application of this honey over a period of two days decreased skin colonisation by a factor of 100.



### Experience study

An experience study with DerMel skin ointment was conducted in two different hospitals using the Three Item Severity (T.I.S.) score.<sup>12</sup> Twenty-four patients participated in the study, sourced from the St. Elisabeth Hospital in Tilburg and the Albert Schweitzer Hospital in Zwijndrecht. The age of the patients ranged from 8 months to 57 years. All patients had atopic eczema, almost all with symptoms on both the face and other parts of the body. The medication used at the start of the experience study was continued in all cases (corticosteroid cream and/or antimycotic cream). Treatment with an indifferent base ointment (leniens FNA, vaseline-cetomacrogol cream, paraffin/silicone cream, Locobase Repair, coconut oil, lanette cream FNA, vaseline/lanette cream, cetomacrogol cream) was stopped and replaced by treatment with DerMel skin ointment after the first consultation. Patients then returned to the doctor after an average of 2.5 weeks (2<sup>nd</sup> consultation) and 5 weeks (3<sup>rd</sup> consultation). The scores for objective symptoms (erythema, oedema and excoriations) and subjective symptoms (itching, insomnia) were noted by the doctor at each consultation. At the third consultation, the patient's experiences were also scored, on a 0-10 scale.

## Experience study results

### Objective symptoms

Treatment with DerMel skin ointment led to a decrease in erythema and excoriations in eighteen out of twenty-four patients (Figure 4a). Two to three weeks after starting treatment with the skin ointment, erythema and excoriations symptoms decreased from moderate to mild (Figure 4b). In one patient, erythema worsened during the first two weeks and treatment was stopped. In eighteen patients, moderate to mild oedema was observed at the first consultation. Treatment with DerMel skin ointment resulted in reduction of symptoms in seven patients. The most significant reduction of complaints as a result of treatment with DerMel skin ointment was achieved after only 2-3 weeks.

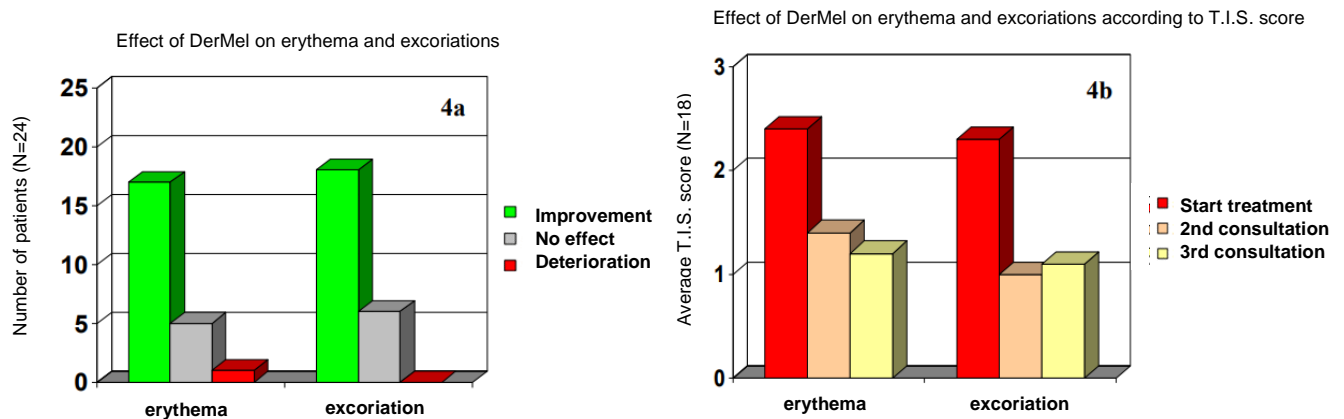


Figure 4. The effect of DerMel skin ointment on erythema and excoriations.  
 4a: The number of patients with/without improvement or worsening of symptoms.  
 4b: T.I.S. score (0=none, 1=mild, 2=moderate, 3=severe) for patients who responded positively to treatment with DerMel skin ointment.

### Subjective symptoms

Treatment with DerMel skin ointment leads to a decrease in itching in twenty of the twenty-four patients while insomnia was reduced in eighteen patients (Figure 5a). On a scale of 0 to 10, itching decreases on average from 8 to 4 and insomnia from 3 to 1. We also see that the main decreases in itching and insomnia symptoms occur as early as 2-3 weeks after commencement of treatment with DerMel skin ointment.

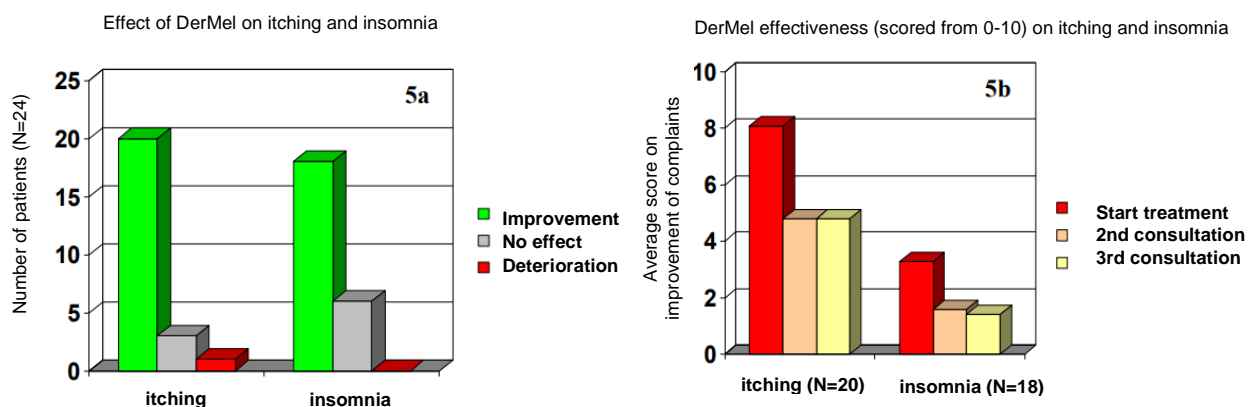
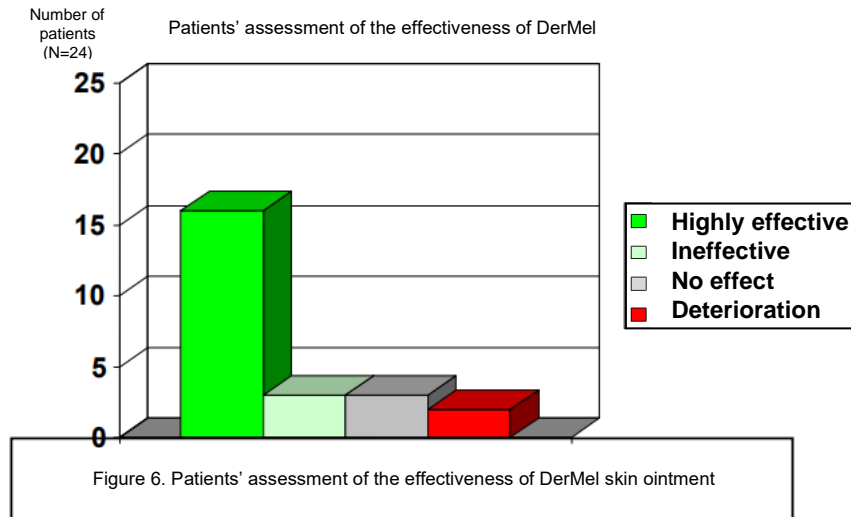


Figure 5. The effect of DerMel skin ointment on itching and insomnia due to atopic eczema.  
 5a: The number of patients with/without improvement or worsening of symptoms.  
 5b: Scores (0=none, 10=extreme complaints) of patients who responded positively to treatment with DerMel skin ointment.

## Patient experiences

Patients were predominantly very positive about the effectiveness of DerMel skin ointment. Nineteen patients found DerMel skin ointment effective. Three patients experienced no improvement in their symptoms after treatment with the skin ointment, two found the ointment 'sticky' and one patient felt a 'burning' sensation when the ointment was applied.



## Conclusions

This experience study shows that DerMel skin ointment reduces the symptoms of atopic eczema in the majority of patients. The main complaints that decrease in severity are erythema, excoriations, itching and insomnia. The ointment combines a soothing base ointment, for good moisture balance and restoration of the skin's barrier function, with special anti-inflammatory, wound-healing and antibacterial effects. The number of skin bacteria decreases significantly, reducing the release of harmful *S. aureus* exotoxins (superantigens). Given the special antimicrobial action, the occurrence of resistance is not to be expected. DerMel skin ointment can therefore be used by all patients. The skin ointment is well tolerated, can be applied to very sensitive skin and combines well with other dermatological medications. DerMel skin ointment does not contain corticosteroids and can be used by patients of all ages. In this experience study, DerMel skin ointment appears to deliver clear added value, compared to the application of indifferent base ointments. DerMel skin ointment can be seen as a 'base ointment plus' and excels in applications that support medication treatment.

A caveat to this experience study is the relatively small number of participating patients. However, the positive results justify the tentative conclusion that DerMel skin ointment can make an important contribution to improving the treatment of atopic eczema. Additional research is needed to further substantiate these conclusions.

## Literature

1. Prof. Dr C.A. Bruijnzeel-Koomen – UMCU. Nationaal Kompas Volksgezondheid, 2008. Carried out by RIVM Bilthoven.
2. Abeck D, Mempel M, - Munchen; *S.aureus* colonization in atopic dermatitis and its therapeutic implications, *Br. J. Dermatol*, 1998 Dec; 139 Suppl. 53: 13-6
3. Lin YT et al, department of Pediatrics, National Taiwan University Hospital; *Clin. Rev. Allergy Immunol*, 2007 Dec; 33(3): 167 – 177
4. R.W.A. Janssens, De rol van bacteriële superantigenen: pathobiologie en therapeutische implicaties voor de behandeling van huidziekten, *Ned. Tijdschr. Geneeskd* 1999;143:760-1
5. Lever R, Hadley K, Downey D, Mackie R. Staphylococcal colonization in atopic dermatitis and the effect of topical mupirocin therapy. *Br J Dermatol* 1988;119:189-98.
6. Kwakman PHS, Van den Akker JPC, Güçlü A, Aslami H, Binnekade J, de Boer L, Boszhard L, Paulus F, Middelhoek P, te Velde A, Vandenbroucke-Grauls CMJE, Schultz MJ, SAJ Zaat. Medical grade honey kills antibiotic-resistant bacteria in vitro and eradicates skin colonization. *Clinical Infectious Diseases* 2008;46:1677–1682
7. Creemers T, Bosma WJ, Boon ME. Enzymrijke honing: een natuurlijke remedie voor vaginale dysbalans. Jaarverslag van het Leids Cytologisch en Pathologisch laboratorium, 2005.
8. Eijk van W. en Groenhart O. Zoet na het zuur. Honinggel, een goede remedie voor wonden. 2006; *WCS Nieuws* 22(4):610
9. Molan PC. The evidence supporting the use of honey as a wound dressing. *Lower Extremity Wounds* 2006; 5(1): 40-54.
10. Tonks A, Cooper RA, Price AJ, Molan PC, Jones KP. Stimulation of TNF-alpha release in monocytes by honey. *Cytokine* 2001; 14(4): 240-242

11. *Tonks AJ, Cooper RA, Jones KP, Blair S, Parton J, Tonks A.* Honey stimulates inflammatory cytokine production from monocytes. *Cytokine* 2003; 21(5): 242-247
12. *Wolkerstorfer A, De Waard-van der Spek FB, Glazenburg EJ, Mulder PG, Oranje AP.* Scoring the severity of atopic dermatitis: three item severity score as a rough system for daily practice and as a pre-screening tool for studies. *Acta Derm Venereol* 1999; 79: 356-359.