Treatment of vitiligo
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CHAPTER 3.5

Association of the Koebner phenomenon with disease activity and therapeutic responsiveness in vitiligo vulgaris

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ABSTRACT

Objective: To investigate the association between experimentally induced Koebner phenomenon (KP-e) and the Koebner phenomenon by history (KP-h), disease activity, and therapeutic responsiveness in vitiligo vulgaris.

Design: Cohort study.

Setting: An outpatient clinic.

Patients: Sixty-one consecutive patients with vitiligo vulgaris.

Intervention: Three months after a standardized epidermodermal injury was induced, the KP-e was evaluated. For one year, narrowband UV-B therapy or topical fluticasone propionate with UV-A therapy (FP plus UV-A) was given, depending on the severity of depigmentation.

Main Outcome Measures:
The presence or absence of the KP-e, and the KP-h, disease activity as scored on a 6-point scale from -1 to +4 (Vitiligo Disease Activity [VIDA] score), and therapy induced repigmentation grade.

Results: Nineteen (31%) patients had a positive KP-h whereas 37 (61%) showed a positive KP-e (p<0.001). The VIDA score did not always predict a positive KP-e, although patients with a positive KP-e had a higher mean VIDA score (VIDA score of 1.6) than did patients with a negative KP-e (VIDA score of 0.5) (p<0.001). The responsiveness to narrowband UV-B therapy among KP-e-positive or KP-e-negative patients was not significantly different (p=0.66). However, KP-e-positive patients who were treated with FP plus UV-A therapy, showed a better response than did KP-e-negative cases (p=0.01). Among patients responding to both therapies, the VIDA scores were found to be significantly decreased (p < 0.001) when compared with VIDA scores before therapy.

Conclusion: The KP-e may function well as a clinical factor to assess present disease activity and may also predict the responsiveness to FP plus UV-A therapy, but not to narrowband UV-B therapy.
INTRODUCTION

Vitiligo is an acquired pigmentary skin disorder affecting approximately 0.5% of the world population. There are several clinical types of vitiligo. The most common type is vitiligo vulgaris that is clinically characterized by symmetrically distributed depigmented macules that usually expand in size and number during the natural course of the disease. Treatment in vitiligo is aimed at stopping the disease progress and restoring the loss of melanocytes in the lesions. Although a variety of therapeutic modalities have been applied, there is still no universally effective and safe therapy available. The currently most practiced therapies are photo(chemo)therapy, corticosteroids and transplantation of autologous melanocytes.

In order to make a reasonable choice of therapy with the highest probability of success for an individual patient, it is important to identify disease characteristics that help predict the outcome of therapy. Besides age, duration of disease, localization, and extent of the depigmentation current disease activity should also be taken into consideration during clinical decision making. This is especially essential for patients with vitiligo vulgaris because in this type, disease activity may fluctuate at a given time. Although medical therapies may be equally effective in active and stable disease, surgical methods are found to be suitable only for those with stabilized disease.

At present, disease activity is mainly assessed by the medical history. Information on disease activity can also be obtained by physical examination. Usually, the size together with the number of lesion and the grade of repigmentation during follow-up visits are recorded using photographic material. In contrast to other skin disorders such as atopic eczema, no other physical signs, e.g., redness, scaling or pruritus, have been found to be associated with disease activity in vitiligo.

To date, the role of certain “vitiligo-associated skin manifestations” in the onset or progression of vitiligo is not well documented. One of these skin manifestations is the “Koebner phenomenon” (KP), which is defined as “the development of vitiligo at sites of aspecifically traumatized skin”. Results of several independent epidemiological studies show that the KP occurs in most of the patients with vitiligo. Its clinical relevance is not yet established, although it has been frequently postulated that the KP may indicate active disease. However, no further data have been obtained to support this hypothesis. Moreover, it is unclear whether patients with a positive KP have a different prognosis than patients with a negative KP.

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In this study, we induced an experimental Koebner phenomenon (KP-e), by performing an epidermodermal injury to the clinically uninvolved skin. Subsequently, we investigated the association between the KP-e, with the Koebner phenomenon by history (KP-h), disease activity by history (vitiligo disease activity [VIDA] score), and the responsiveness to therapy in 61 patients with vitiligo vulgaris.

**PATIENTS AND METHODS**

**PATIENTS**

In total, 61 consecutive patients with vitiligo vulgaris were selected. Included were both male and female patients with ages between 12 and 65 years old, who had not received any topical or systemic medication for treatment of vitiligo in the previous 6 months.

A routine history was taken, with special attention to the presence of the KP-h, the duration of the disease and the patient’s own opinion of the present disease activity. The latter was scored on the 6-point VIDA scale (Table 1).

By physical examination, the type of vitiligo was noted and the percentage depigmentation in relation to the total body surface was estimated, using the “handpalm-rule” i.e., a lesion with the size of the patient’s handpalm equals 1% of the total body surface.

**Table 1. Vitiligo disease activity score (VIDA-score) on a 6-point scale** *

<table>
<thead>
<tr>
<th>Disease activity †</th>
<th>VIDA-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active, in the past 6 weeks</td>
<td>+4</td>
</tr>
<tr>
<td>Active, in the past 3 months</td>
<td>+3</td>
</tr>
<tr>
<td>Active, in the past 6 months</td>
<td>+2</td>
</tr>
<tr>
<td>Active, in the past year</td>
<td>+1</td>
</tr>
<tr>
<td>Stable, for at least 1 year</td>
<td>0</td>
</tr>
<tr>
<td>Stable, for at least 1 year and spontaneous repigmenting</td>
<td>-1</td>
</tr>
</tbody>
</table>

* Consists of scoring of the patient’s own opinion of the present disease activity within the times indicated in the first column.

† Active refers to expansion of existing lesions and/or appearance of new lesions; stable, condition when these symptoms are not present.
Informed consent was obtained from all the patients: the study was approved by the Medical Ethical Committee of the Academic Medical Center, Amsterdam, The Netherlands.

THE KP-e

Four 2-mm punch epidermal grafts using biopsy punches (Stiefel, Maidenhead, United Kingdom) were removed from a normally pigmented area, mostly the hip or the buttocks, with no vitiligo lesions present within a radius of 15 cm. The grafts were cut horizontally from the base, using ophthalmologic scissors and tweezers. One of us (M.D.N.) consistently punched the skin with a constant pressure to a standard depth (± 2 mm) to induce an experimental epidermodermal injury.

After 3 months, 2 independent observers (M.D.N and W.W.) evaluated the outcome of the KP-e. When there was a disagreement, a third observer (P.K.D.) was consulted. The KP-e was scored negative when the wound healed without depigmentation and positive when depigmentation of the biopsy scar or even depigmentation beyond the biopsy margins occurred. In doubtful cases, a dermatoscope (Heine Delta 10, Heine Optotechnik, 8036 Herrsching), was used. Subsequently, photographs were taken of the biopsy sites.

THERAPY

The following therapeutic regimens were applied, according to the severity of depigmentation; (1) narrowband UV-B (311 nm) therapy twice weekly for patients with more than 5% depigmentation and (2) fluticasone propionate cream applied once daily combined with UV-A (10 J/cm²) (FP plus UV-A) twice weekly for patients with 5% or less depigmentation.

Follow-up took place every 3 months. After 1 year, the relationship between the response to each therapy and the presence or absence of the KP-e performed was studied, and the VIDA score was determined again for each patient.

For all patients, the degree of repigmentation was scored visually against the photographs obtained at the first visit for enrollment in the study and after 12 months of therapy. For the patients in the group receiving (total body) UV-B radiation therapy, the overall repigmentation grade was noted, whereas for the patients in the group receiving FP plus UV-A therapy, the repigmentation grade of only the treated lesions was calculated. Patients were considered “good responders” when the therapy resulted in 50% or more repigmentation of the lesions and as “poor-responders” when less than 50% repigmentation was achieved.
Response to therapy and VIDA scores were evaluated independently in a masked manner by two observers (M.D.N and W.W.). When there was a disagreement, a third observer was consulted (P.K.D).

STATISTICAL ANALYSIS

Statistical analysis was performed using the 2 tailed Student t test, Wilcoxon matched pairs rank sum test, chi-square test and the Pearson correlation test. Significance level was set at p < 0.05.

RESULTS

PATIENTS

Table 2 presents the patient’s characteristics according to VIDA scores. In most patients (48%) disease activity was scored as +1. There was no significant correlation between the VIDA score and sex, age, percentage of depigmentation or duration of disease (chi-square test 2 X 6 table [p=0.55] and Pearson correlation coefficients of 0.10 [p=0.42], 0.07 [p=0.60] and -0.06 [p=0.58] respectively). There were no significant differences between patients with active disease (VIDA scores of +4 to +1) and those with stable disease (VIDA scores of 0 to -1) regarding sex (chi square test, p=0.90), age ( t test, p=0.09), % depigmentation ( t test, p=0.27) and duration of disease ( t test, p=0.14). The two patients with the highest VIDA score, +4, showed a significantly shorter duration of

<table>
<thead>
<tr>
<th>VIDA score</th>
<th>Patients, No. (%)</th>
<th>Sex, No.</th>
<th>Age Mean ± SD, years</th>
<th>Depigmentation Mean ± SD, %</th>
<th>Duration of vitiligo Mean ± SD, years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>M</td>
<td>F</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+4</td>
<td>2 (3)</td>
<td>0</td>
<td>2</td>
<td>20.0 ± 8.0</td>
<td>2.0 ± 1.0</td>
</tr>
<tr>
<td>+3</td>
<td>5 (8)</td>
<td>3</td>
<td>2</td>
<td>44.0 ± 12.5</td>
<td>7.4 ± 4.1</td>
</tr>
<tr>
<td>+2</td>
<td>11 (18)</td>
<td>5</td>
<td>6</td>
<td>34.9 ± 9.7</td>
<td>13.0 ± 14.1</td>
</tr>
<tr>
<td>+1</td>
<td>29 (47)</td>
<td>13</td>
<td>16</td>
<td>38.1 ± 11.3</td>
<td>8.3 ± 9.1</td>
</tr>
<tr>
<td>0</td>
<td>12 (20)</td>
<td>6</td>
<td>6</td>
<td>30.9 ± 13.8</td>
<td>6.8 ± 8.0</td>
</tr>
<tr>
<td>-1</td>
<td>2 (3)</td>
<td>0</td>
<td>2</td>
<td>24.5 ± 2.5</td>
<td>2.5 ± 1.5</td>
</tr>
<tr>
<td>Total</td>
<td>61 (100)</td>
<td>27</td>
<td>34</td>
<td>35.6 ± 12.6</td>
<td>8.4 ± 9.9</td>
</tr>
</tbody>
</table>

* VIDA indicates vitiligo disease activity
disease ($t$ test, $p < 0.001$) and a lesser percentage of depigmentation than did the remaining 59 patients (with VIDA scores +3 to -1), whereas the variables sex and age were not significantly different between these 2 groups (chi-square test, $p=0.19$, and $t$ test, $p=0.28$, respectively).

Left, Repigmentation (negative experimentally induced Koebner phenomenon [KP-e]) of the biopsy wound in stable vitiligo (VIDA score of 0).

Right, Depigmentation the biopsy wound (positive KP-e) in a patient with active disease (VIDA score of +3)

**RELATION BETWEEN THE KP-h AND THE KP-e**

By history, 19 patients (31%) were able to recall the experience of a KP-h occurring after burns, wounds or scratches. They also showed 1 or more lesions. The remaining 42 patients could not recall the occurrence of such events that had resulted in a vitiligo lesion.

In 24 cases, the injured skin healed with repigmentation (=negative KP-e) (Figure 1, left). In the remaining 37 patients (61%), a positive KP-e was observed (Figure 1, right). In 2 patients (with VIDA score of +4) depigmentation beyond the biopsy margins was noted.

The relation between the KP-h and the KP-e is shown in Table 3. The positive predictive
Table 3. The relation between the KP by history (KP-h) and the experimentally induced KP (KP-e) (N=61) *

<table>
<thead>
<tr>
<th></th>
<th>KP-e</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>KP-h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>17</td>
<td>19 †</td>
</tr>
<tr>
<td>-</td>
<td>20</td>
<td>42 †</td>
</tr>
<tr>
<td>Total</td>
<td>37 †</td>
<td>61</td>
</tr>
</tbody>
</table>

* KP indicates Koebner phenomenon  † Statistical analysis by Chi-square test for 2 X 2 table, p < 0.001

value of the KP-h was 89% (17/19). The negative predictive value of the KP-h was 52% (22/42). Two (11%) of the KP-h-positive cases were false-positive, whereas 48% (20/42) were false-negative cases. The differences as shown in Table 3 were statistically significant (p=0.0007) after performing the chi-square test.

RELATION BETWEEN THE KP-e AND THE VIDA SCORE

Figure 2 shows the distribution of KP-e-positive and KP-e-negative patients as a function of their VIDA scores. Patients with VIDA scores of +1 and +2 did not necessarily show a positive KP-e. However, all patients with VIDA scores of +3 and +4 showed a positive KP-e. There were also 2 patients with “stabilized disease” (VIDA score of 0) who scored a positive KP-e. The two patients with stabilized disease and spontaneous repigmentations (VIDA score of -1) showed a negative KP-e.

Table 4 shows that sex, age, percentage of depigmentation and the duration of disease

Figure 2 Distribution of experimentally induced Koebner phenomenon (KP-e)- positive and KP-e-negative patients as a function of their vitiligo disease activity (VIDA) scores (N=61)
Table 4. The relation between the KP-e and sex, age, percentage of depigmentation, duration of vitiligo and VIDA score *

<table>
<thead>
<tr>
<th>KP-e</th>
<th>Sex</th>
<th>Age, Mean ± SD, years</th>
<th>Depigmentation, Mean ± SD, %</th>
<th>Duration of vitiligo, Mean ± SD, years</th>
<th>VIDA score, Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>M</td>
<td>17</td>
<td>37.3 ± 12.0</td>
<td>9.2 ± 11.5</td>
<td>13.2 ± 9.0</td>
</tr>
<tr>
<td>-</td>
<td>F</td>
<td>20</td>
<td>33.0 ± 12.7</td>
<td>7.2 ± 6.3</td>
<td>10.8 ± 7.4</td>
</tr>
<tr>
<td>p-value</td>
<td>0.74†</td>
<td>0.20</td>
<td>0.39</td>
<td>0.27</td>
<td>&lt; 0.001‡</td>
</tr>
</tbody>
</table>

* KP-e indicates experimentally induced Koebner phenomenon; VIDA, vitiligo disease activity. Statistical analysis was done by 2-tailed Student t test except where noted. † Chi-square test for 2 X 2 contingency tables. ‡ Significant

were not significantly different for those who were KP-e-positive than for those who were KP-e-negative. However, the 37 KP-e-positive patients had significantly higher mean ± SD VIDA score (1.6 ± 1.0) than did the 24 KP-e-negative patients (0.5 ± 0.8) (Student’s t test p < 0.001).

**RELATION BETWEEN THE KP-e AND THE RESPONSE TO THERAPY**

Two patients dropped out of the study because of lack of motivation to continue therapy. Further data analysis was done with the remaining 59 patients who received either narrowband UV-B therapy (n=27) or FP plus UV-A therapy (n=32).

The data presented in Table 5 show that among the KP-e-positive patients treated

Table 5. The relation between the KP-e and the response to treatment after 1 year of narrowband UV-B (UV-B nb) therapy (n=27) or topical fluticasone propionate plus local UV-A therapy (FP + UV-A) (n=32) *

<table>
<thead>
<tr>
<th>Therapy</th>
<th>KP-e</th>
<th>Good responders, No. †</th>
<th>Poor responders, No. †</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV-B nb</td>
<td>+</td>
<td>10 †</td>
<td>5 †</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>7 †</td>
<td>5 †</td>
</tr>
<tr>
<td>FP + UV-A</td>
<td>+</td>
<td>13 §</td>
<td>9 §</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>1 §</td>
<td>9 §</td>
</tr>
</tbody>
</table>

* KP-e indicates experimentally induced Koebner phenomenon. † Good responders had 50% or more repigmentation; poor responders, less than 50% repigmentation. § Chi-square test for 2 X 2 table, p = 0.66. ¶ Chi-square test for 2 X 2 table, p = 0.01

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with narrowband UV-B, 67% (10/15) showed good response whereas 33% (5/15) showed poor response. Of the KP-e-negative patients, 58% (7/12) were good responders while 42% (5/12) were poor responders. These differences in responsiveness between KP-e-positive and KP-e-negative patients were not statistically different (p=0.66). Of the KP-e-positive patients treated with FP plus UV-A therapy, 59% (13/22) showed good response whereas 41% (9/22) showed poor response. Only 1 (10%) of 10 KP-e-negative patients responded well to therapy, while in 9 of the 10 patients, no signs of repigmentation were observed. These differences in responsiveness between KP-e-positive and KP-e-negative patients to FP plus UV-A therapy were statistically significant (p=0.01).

In the narrowband UV-B treated patients, age, percentage depigmentation or duration of disease were not significantly different between good responders (n=17) and poor responders (n=10) (Table 6). In the FP plus UV-A group, age and percentage of depigmentation were also not significantly different between good responders and poor responders. However, patients with a good response to FP plus UV-A therapy (n=14), had a significantly shorter mean ± SD duration of disease (5.8 ± 5.4 years) than did the poor-responding patients (n=18) (2 tailed Student t test, p=0.003).

Table 6: Factors affecting response to therapy

<table>
<thead>
<tr>
<th>Therapy*</th>
<th>Response†</th>
<th>Age, Mean ± SD years</th>
<th>Depigmentation, Mean ± SD, %</th>
<th>Duration of vitiligo, Mean ± SD, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV-B nb</td>
<td>Good responders (n=17)</td>
<td>34.2 ± 11.0</td>
<td>14.3 ± 11.6</td>
<td>14.6 ± 8.8</td>
</tr>
<tr>
<td></td>
<td>Poor responders (n=10)</td>
<td>39.2 ± 11.5</td>
<td>17.4 ± 13.9</td>
<td>18.3 ± 9.2</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.27</td>
<td>0.56</td>
<td>0.31</td>
</tr>
<tr>
<td>FP + UV-A</td>
<td>Good responders (n=14)</td>
<td>39.4 ± 14.7</td>
<td>2.8 ± 1.4</td>
<td>5.8 ± 5.6</td>
</tr>
<tr>
<td></td>
<td>Poor responders (n=18)</td>
<td>33.1 ± 12.9</td>
<td>3.6 ± 1.4</td>
<td>12.9 ± 7.1</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.22</td>
<td>0.10</td>
<td>0.003 †</td>
</tr>
</tbody>
</table>

* UV-B nb indicates narrowband UV-B therapy; FP + UV-A, topical fluticasone propionate plus local UV-A therapy. † Good responders had 50% or more repigmentation; poor responders, less than 50% repigmentation, † Significant by Student t test (2-tailed)
THE VIDA SCORES BEFORE AND AFTER 1 YEAR OF THERAPY

Figure 3 shows that a good response to either narrowband UV-B therapy or FP plus UV-A therapy was significantly associated with lower VIDA scores after therapy compared with the VIDA scores before therapy (Wilcoxon test, p < 0.001, for both groups).

In the poor responders treated with either narrowband UV-B or FP plus UV-A, the VIDA scores were not significantly different after one year of therapy (Wilcoxon test, p > 0.05, for both groups) (results not shown).

Figure 3A. The changes of the vitiligo disease activity (VIDA) scores in the good responder group before and 1 year after narrowband UV-B therapy (n=17 patients). In 13 patients, VIDA scores were decreased after therapy; in the remaining 4 patients VIDA scores were unchanged (Wilcoxon rank sum test, p < 0.001).

Figure 3B. The changes of the vitiligo disease activity (VIDA) scores in the good responder group before and 1 year after topical fluticasone propionate plus UV-A therapy (n=14 patients). In 12 patients, VIDA scores were decreased after therapy; in the remaining 2 patients VIDA scores were unchanged. (Wilcoxon rank sum test, p < 0.001).

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COMMENT

There seems to be no consensus regarding the clinical evaluation of disease activity in vitiligo. The definitions for either active or stable vitiligo seem to be different for different clinicians. According to Moellmann et al. 17, active vitiligo is the clinical stage “when lesions are enlarging in the 6 weeks” prior to examination, whereas according to Cui et al. 18, active vitiligo is “the development of new lesions or extension of old lesions in the 3 months before the first consultation. Other clinicians, such as Uda et al. 19, define active vitiligo when the lesions are reported to “spread without regression within the last half year”. On the other hand, “stable vitiligo” is defined by Falabella et al. 6 as “a condition that has not been progressing for at least 2 years”, whereas Kumar et al. 20 consider the disease as being stable when “no progression is observed for at least one year before admission of the patient”. Boersma et al. 21 define stable vitiligo when “neither spread of existing lesions nor development of new lesions have appeared in the previous 6 months”. It is obvious that using such different “cutoff points”, the disease activity of some patients will be either underestimated or overestimated. Furthermore, from the clinical standpoint, there can only be two possible outcomes, whether the disease is active or the disease is stable. Therefore it is essential to establish a better and rational approach to determine clinical disease activity. In this study, disease activity was scored by history taking on a 6-point scale, the VIDA score (Table 1). The VIDA score is a simple scoring system for classifying the ongoing disease activity in relation to time, as assessed by the patient. In addition, the changes in the VIDA score, as assessed in this study before and after 1 year follow up, also correlated well with the response to therapy (Figure 3). However, because disease activity tends to be unpredictable and capricious in vitiligo, it is possible that patients not receiving treatment have different VIDA score at different time points of evaluation. It would be interesting to investigate this aspect prospectively in future studies. The VIDA score does not provide us with information regarding the exact rate of pigment loss. Therefore, photographic documentation of the lesions remains important to monitor both changes in the extent of depigmentation as well as grade of repigmentation. Perhaps in future, computer-aided designs may reflect these changes more accurately 22.

Our results suggest that the presence or absence of the KP-h should be confirmed by inducing the KP-e, because the KP-e seems to occur more frequently than the KP-h. We assume that the KP-h may not always be accurate. The recollection for occurrence of a
KP-h may be false-negative or false-positive. Table 3 shows that a high percentage of the cases (48% [20/42]) were false-negative. It is possible that some patients did not recognize or notice the appearance of a white lesion after a skin injury. It is also possible that some patients never had skin trauma at all. In addition, it has been previously postulated that the KP only occurs when a certain “threshold value” is exceeded or that a certain depth of trauma is induced to the skin. Gopinathan observed depigmentation of the healthy-looking skin in 69% (9/13) of the patients with vitiligo studied, after performing “scarification” procedures. In contrast, “tape stripping” did not produce depigmentation in any of these patients. He concluded that the KP only occurred after epidermodermal trauma and not after (superficial) epidermal trauma of the skin. However, the KP has been reported to occur after all sorts of “trauma” to the skin. It has also been hypothesized that even superficial but constant “friction or pressure” to the skin may lead to depigmentation in susceptible individuals. In the cases reported, no direct evidence has been given to support this hypothesis; therefore any relationship between superficial trauma and the development of vitiligo should be regarded as highly speculative.

On the other hand, there were only 2 false-positive cases (11%). Interestingly, these two patients referred the KP-h to a surgical scar that had existed for many years. At the time of performance of the KP-e, they both stated the disease had stabilized (VIDA score of 0).

The observation that patients with a positive KP-e had a significantly higher mean VIDA score (VIDA score of 1.6) than did patients with a negative KP-e (VIDA score of 0.5) (Table 4) indicated that a positive KP-e is associated with active disease and a negative KP-e with stabilized disease. On the other hand, Figure 2 shows that VIDA score of 0, +1, or +2 did not always predict a positive KP-e. There were patients with VIDA scores +1 and +2 (12/61) who claimed that their disease was active while KP-e was negative. Two patients, who claimed that their disease had stabilized (VIDA score of 0) showed a positive KP-e. The patients’ impression of the disease activity might not always be accurate. In particular, fair-skinned patients report that during the summer, more white patches appeared. However, this phenomenon could also be due to an increased contrast between healthy and lesional skin caused by sun exposure. As a result, the white patches became more obvious. These patients report that the disease is active, while it could have stabilized. It is also conceivable that minor expansions of old lesions or the appearance of new but very small lesions are not always noticed by the patient, especially when these are located on sites that are less conspicuous to the patient (e.g. axillae or back). In addition, patients
with extensive vitiligo involving more than 30% of total body surface also find it difficult to assess the disease activity. Interestingly, all patients with a VIDA score +3 and higher had a positive KP-e and all patients with score -1 had a negative KP-e.

We have also performed the KP-e in patients with “vitiligo segmentalis”. In this less common type of vitiligo, the lesions tend to have a rapid spread at onset and to show a more stable course thereafter. In our experiments, KP-e was not observed in any of these patients (M.D.N., P.K.D., J.D.B. and W. W.). All these patients stated that their disease had stabilized, at the time the KP-e was performed. These findings confirmed the results found by Koga and Tango in 1988, who also did not observe the KP in the segmental form of vitiligo.

The baseline variables of sex, age, percentage of depigmentation and duration of vitiligo were not significantly different for patients with a positive KP-e or for patients with a negative KP-e. If we assume that KP-e indicates active disease, it is interesting to observe that patients with a positive KP-e do not necessarily have a more severe disease, in terms of extent of depigmentation, than do those with a negative KP-e. This finding is in contrast to patients with psoriasis, in whom a positive KP-e was positively correlated with the extent of psoriatic lesions. This allowed us to conclude that in vitiligo, the KP-e does not have a predictive value to the extent of depigmentation.

Most patients responded well to narrowband UV-B therapy, which was in concordance with the results of an earlier study performed using this radiation therapy. The response to narrowband UV-B therapy was not significantly different among KP-e-positive (67% responders) or KP-e-negative (58% responders) patients, indicating that the KP-e did not predict the outcome of narrowband UV-B therapy. This also suggests that patients in both active and stable stages of the disease may respond equally well to narrowband UV-B therapy. More research is needed to elucidate the mechanisms by which narrowband UV-B therapy leads to stabilization and repigmentation in vitiligo.

In contrast, patients with a positive KP-e responded significantly better to topical FP combined with UV-A therapy than did those with a negative KP-e, suggesting that this therapy is most effective when applied during the active stage of disease. It has been frequently proposed that in vitiligo, corticosteroids act by suppressing abnormal immune responses that are present in active spreading lesions; however substantial evidence to support this theory has not yet been provided. The combination with UV-A therapy might have further promoted the repigmentation process in these lesions, but this also remains to be proven. Patients with a good response to FP plus UV-A, also seem to have
a significantly shorter duration of disease than do those with a poor response, a finding that may also explain the difference in responsiveness to this therapy among the KP-e-positive and the KP-e-negative patients. Long-standing lesions have been previously shown to be relatively resistant to local corticosteroid treatment, probably because of the depletion of melanocyte reserves in the hair follicles.

From the results of the present study we may conclude that the KP-e may function as a valuable clinical factor to assess disease activity. The KP-e may also predict responsiveness to local corticosteroid therapy, but not to narrowband UV-B therapy. Although the data indicate that the VIDA score is appealing for clinical use, this new scoring system needs to be validated in other institutions with other patient groups.

REFERENCES

Koebner phenomenon, disease activity and therapeutic responsiveness


