

Influence of a Mindfulness Meditation-Based Stress Reduction Intervention on Rates of Skin Clearing in Patients With Moderate to Severe Psoriasis Undergoing Phototherapy (UVB) and Photochemotherapy (PUVA)

JON KABAT-ZINN, PhD, ELIZABETH WHEELER, PhD, TIMOTHY LIGHT, MD, ANNE SKILLINGS, MS, MARK J. SCHARF, MD, THOMAS G. CROPLEY, MD, DAVID HOSMER, PhD, AND JEFFREY D. BERNHARD, MD

Objective: This study tests the hypothesis that stress reduction methods based on mindfulness meditation can positively influence the rate at which psoriasis clears in patients undergoing phototherapy or photochemotherapy treatment. **Methods:** Thirty-seven patients with psoriasis about to undergo ultraviolet phototherapy (UVB) or photochemotherapy (PUVA) were randomly assigned to one of two conditions: a mindfulness meditation-based stress reduction intervention guided by audiotaped instructions during light treatments, or a control condition consisting of the light treatments alone with no taped instructions. Psoriasis status was assessed in three ways: direct inspection by unblinded clinic nurses; direct inspection by physicians blinded to the patient's study condition (tape or no-tape); and blinded physician evaluation of photographs of psoriasis lesions. Four sequential indicators of skin status were monitored during the study: a First Response Point, a Turning Point, a Halfway Point, and a Clearing Point. **Results:** Cox-proportional hazards regression analysis showed that subjects in the tape groups reached the Halfway Point ($p = .013$) and the Clearing Point ($p = .033$) significantly more rapidly than those in the no-tape condition, for both UVB and PUVA treatments. **Conclusions:** A brief mindfulness meditation-based stress reduction intervention delivered by audiotape during ultraviolet light therapy can increase the rate of resolution of psoriatic lesions in patients with psoriasis. **Key words:** psoriasis, phototherapy, photochemotherapy, meditation, mindfulness, relaxation.

PROC PHREG = SAS package procedure to fit the proportional hazards model.

INTRODUCTION

The skin has long been known as an organ system that responds to emotional stress and to psychological influences with both short- and long-lasting effects (1, 2). Over the years, occasional observational and experimental studies (3) have reported a range of skin responses to hypnotic suggestion and other psychological interventions, including the disappearance of warts. Although the elucidation of psychological and biological mediating pathways by which the skin might respond to such interventions and to stress and other emotional factors has remained obscure, there is recent evidence connecting psychological stress (in caregivers of relatives with Alzheimer's Disease), rates of wound healing, and levels of the cytokine, interleukin 1 β , a potential immunological mediator of wound healing (4). The present study sought to investigate the possible effect of a stress reduction intervention on rates of skin clearing in patients with psoriasis undergoing phototherapy as a potential model system for the study of psychological factors related to an observable healing process.

Psoriasis vulgaris is a common skin disease with an estimated prevalence of between 1% and 3% of the world's population (5). In moderate to severe cases, psoriatic lesions can be uncomfortable, itchy, and disfiguring. Although the precise pathophysiology of psoriasis is unknown, an abnormal cutaneous immunologic/inflammatory response, associated

with epidermal hyperproliferation and abnormal differentiation seems to be involved (6). Over-expression of the gene for the keratinocyte mitogen, transforming growth factor- α , has been implicated in psoriatic epidermis (7, 8), as has overexpression of the Bcl-x gene product (9), the latter suggesting that dysregulation of normal apoptotic processes in the terminal differentiation of epidermal keratinocytes may play a role in the disease. Other studies have noted changes in neuropeptides such as substance P and vasointestinal peptide (VIP) in psoriatic skin cells (10), and some investigators (11) have suggested that the former may play a significant role, through effects on lymphocytes, mast cells, neutrophils, and macrophages, on the early inflammatory events giving rise to psoriatic lesions. Neuropeptides are known to be affected by emotional stress (12). However, to date, there is no clear evidence for a specific pathophysiological mechanism linking psychological factors with the appearance of psoriatic lesions (10).

Treatment of psoriasis is directed toward alteration of epidermal differentiation, reducing the inflammatory response, and/or slowing the growth of involved skin cells. The extent and severity of the disease typically determine the therapeutic approach. Patients with extensive disease or who have proven resistant to topical agents may be candidates for phototherapy, which uses ultraviolet B irradiation (UVB), or photochemotherapy, which uses psoralen (methoxsalen) in combination with ultraviolet A irradiation (PUVA) (13). Both procedures are palliative rather than curative, aimed at retarding proliferative growth (14, 15). Other light-sensitive mechanisms may also play a role (16).

Psychological stress has long been implicated in the onset and severity of psoriatic flare-ups (10, 17, 18). Positive correlations between psychological distress and severity of psoriasis have been reported in 32–70% of patients in retrospective (19–21) and prospective studies (22, 23). Case reports have described positive responses with hypnosis (24), thermal biofeedback (25), meditation coupled with imagery (25a), and psychotherapy (26), and some investigators (20, 27, 28) have recommended relaxation and stress reduction methods as treatment adjuncts. However, few prospective randomized clinical trials have studied the efficacy of such treatments for psoriasis (22, 29, 30) and none has explored a psycholog-

From the Stress Reduction Clinic, Center for Mindfulness in Medicine, Health Care, and Society, Division of Preventive and Behavioral Medicine, Department of Medicine (J.K.Z., E.W., T.L., A.S.) and the Division of Dermatology, Department of Medicine (M.J.S., T.G.C., J.D.B.), University of Massachusetts Medical Center, Worcester, Massachusetts; and the Department of Epidemiology and Biostatistics, School of Public Health and Health Sciences, University of Massachusetts (D.H.), Amherst, Massachusetts.

Address reprint requests to: Dr. Jon Kabat-Zinn, Center for Mindfulness, Shaw Bldg., University of Massachusetts Medical Center, Worcester, MA 01655-0267. E-mail: jon.kabat-zinn@banyan.ummed.edu

Received for publication May 9, 1997; revision received January 13, 1998.

ical intervention delivered while the patient is undergoing phototherapy sessions. Yet, the readily observable extent and severity of this disease, its association with psychological stress, and the controlled environment of the light booth in which phototherapy is delivered combine to present a unique opportunity to investigate the possible additive therapeutic effect of a psychological stress reduction exercise employed by the patient in conjunction with a traditional medical treatment. We hypothesized that the focused attention characteristic of a mindfulness meditation-based stress reduction exercise (see Methods) would enhance relaxation and a sense of participatory agency on the part of the patients during their treatments, and might result in the reduction or reversal of possible stress-related emotional and cognitive factors contributing to the exacerbation of the subject's condition.

We were encouraged by the results of a small preliminary study in which patients who practiced mindfulness meditation while receiving either phototherapy or photochemotherapy demonstrated a significantly faster mean rate of skin clearing than did subjects receiving standard phototherapy or photochemotherapy treatment alone (31). On the basis of that preliminary finding, we initiated the trial reported here.

METHODS

Subjects

Subjects were 37 patients (20 women, 17 men) presenting with moderate to severe psoriasis and scheduled to begin phototherapy ($N = 21$) or photochemotherapy ($N = 16$). Moderate to severe psoriasis was defined as involving 15% or more of the body surface area, and sufficiently severe to warrant treatment with UVB or PUVA rather than topical agents. The determination of mode of treatment (UVB or PUVA) was made by the patient's dermatologist in each case. UVB is typically employed first; PUVA is used when subjects have not responded to UVB or in cases where the disease is extremely severe. Patients were excluded if they had had phototherapy treatment during the previous month, systemic treatments such as corticosteroids, methotrexate, or retinoids during the previous 2 weeks, or were under 18 years of age. While in the study, patients were instructed to avoid any oral or topical psoriasis treatments not specifically prescribed by the physician, except emollients and 1% hydrocortisone cream for skinfold areas not exposed to the light, and this was reinforced by the clinic nurses throughout the study period. Study subjects were permitted to use antipsoriatic shampoos and topical steroid preparations for the scalp.

The study was described to prospective subjects as a test of the efficacy of relaxation tapes in making the experience of treatment more pleasant. Nothing was said to create expectations of a therapeutic effect from use of the tapes. After informed consent was obtained, subjects were assigned randomly to a stress-reduction audiotape condition or to a usual treatment (no-tape) condition. UVB and PUVA cohorts were randomized separately. The study included subjects undergoing both forms of treatment because patients in both conditions responded positively in the preliminary study (31).

Seventy patients were recruited by referring dermatologists between October 1991 and October 1994. Thirty declined participation, citing reluctance to be part of a research protocol. Two subjects were dropped from the study because they received treatment at another site, and another because she had enrolled in the study twice. The remaining 37 subjects averaged 43 ± 15 years of age, and had had psoriasis for an average of 11.2 ± 8.9 years.

Baseline descriptive data obtained on all subjects included age, gender, education, years with psoriasis, degree of body surface involvement, and prior experience with formal meditation and relaxation methods. Psychological status was assessed pre-intervention and post-intervention using the SCL-90-R (32) and the State-Trait Anxiety Inventory (STAI) (33). Other questionnaires assessing

psychological response to the intervention were administered periodically to monitor indicators such as how relaxed subjects felt in the past week, how stressed they felt in the past week, how "positive" they felt about today's session, how relaxed they felt after today's session, how tense they felt at the start of today's session, and to what extent they felt that the treatment was helping them. Responses were rated on a 1 to 10 scale.

Phototherapy and Photochemotherapy Protocols

Subjects were treated three times per week according to standard phototherapy and photochemotherapy treatment protocols (5, 6). During treatment sessions, the patient stood naked, with eyes shielded, in a cylindrical light booth (diameter approximately 4 feet). UV dosage (in millijoules for UVB and joules for PUVA) was increased linearly from session to session (by approximately 15% increments for UVB and one-half joule increments for PUVA). Increasing dosage resulted in corresponding increases in exposure times. Dosage increases were delayed only if there were signs of burning. Exposure times increased from approximately 30 seconds in the first treatment session to approximately 10 minutes (UVB) and 13.5 minutes (PUVA) as maximal exposure times by the later stages of treatment.

The study period was open-ended, although it was typically completed by 40 treatment sessions (approximately 13 weeks, ie, 91 days). Patients were kept in the study until they cleared or until they dropped out. The protocol called for dropping patients from the study if the dermatologist radically changed the phototherapy prescription. Skin status throughout the study was assessed both by clinic nurses and by dermatologists, as described below.

All 37 subjects who began treatment were included in the analysis, including 12 dropouts and 2 subjects who were dropped from the study (at 26 and 80 days respectively) because their treatment protocol was changed at those times to include steroids.

Psychological Intervention

Mindfulness-based stress reduction (34–36) was employed as the principal psychological intervention because: a) it is effective in reducing symptoms and enhancing relaxation in patients with chronic pain (37–39) and with generalized anxiety (40, 41); b) its unique attentional stance can readily direct sustained awareness to the envelope of the skin and to sensations associated with light treatment; c) it can be practiced standing; d) it can be effectively delivered through audiotapes; and e) it allows readily for the inclusion of situation-appropriate imagery.

Three audiotapes were used to guide patients in the meditation technique. For the first three treatment sessions, all subjects in the tape groups (UVB and PUVA) listened to the same introductory tape (approximately 5 minutes in length) sitting on a chair *before* entering the light booth. Once in the light booth, they listened to a tape made specifically for their treatment condition (UVB or PUVA). They listened to the same tape in every treatment session but heard more of it with increased time in the light booth.

The meditation tapes were designed to accommodate increasing light exposure through longer listening times as the phototherapy treatments progressed. The sound of a bell punctuated the meditation instructions at 1.5- to 3.5-minute intervals to signal appropriate stopping points. The patients were instructed to remain in the light booth after the lights turned off and continue to practice the meditation according to the instructions they were hearing until the next bell was heard. Thus, with increasing length of light exposure, subjects were exposed to increasingly longer segments of the tapes.

The UVB and PUVA tapes differed slightly in the rate at which the different components of the meditation instructions were introduced. Due to the higher energy and biological efficacy of UVB radiation, UVB treatments tended to be shorter than PUVA treatments.

Meditation instructions on the tapes included guidance in mindfulness (moment-to-moment, non-judgmental awareness) of breath-

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ing, followed by mindfulness of body sensations (including warmth from the lights and air currents on the skin), ambient sounds, thoughts, and feelings. At later stages of the tapes, subjects were instructed to visualize the UV light (and the orally consumed psoralen in the case of patients undergoing PUVA) slowing down the growth and division of skin cells.

After subjects in the tape groups had completed 20 treatment sessions with their guided meditation tape, they were given the option in each subsequent session either to use the meditation tape or to practice the meditation and visualization on their own while listening to a tape of harp music.¹ The music was intended to support subjects' attempts to practice the meditation and visualization without guidance to reduce possible fatigue and resistance from over-utilization of the instructional tapes. Most subjects in the tape condition opted to use the music tape at least once. Music was not offered to the regular treatment (no-tape) groups.

Subjects in the tape groups were not asked to meditate outside of the light therapy sessions, and were not permitted to take the tapes home. No data were gathered on whether subjects in the tape groups practiced the meditation outside of treatment sessions.

Clinical Assessment of Skin Status:

Two target lesions (the most extensive and severe plaques, one on the trunk and one on an extremity when possible) were identified by the clinic nurses at the initial clinic visit. Polaroid photographs were then taken of each target lesion on each subject at that visit, and every five treatment sessions after until the patient cleared, dropped out of the study, or was dropped from the study due to a change in treatment prescription. A dermatological Polaroid camera (Lester Dine Corp, Palm Beach Gardens, FL) with a fixed focal length of one foot was used.

Skin status was also assessed by visual inspection, using a measure designed specifically for this study. Trained clinic nurses observed the overall skin status of each patient before each treatment session and recorded if and when each patient, treated as a single unit, had attained each of four clinical end points: a "First Response Point" (FRP), a "Turning Point" (TP), a "Halfway Point" (HP), and a "Clearing Point" (CP). The terms were defined as follows: FRP: the point at which morphological changes in scaling, erythema, or thickness were first noted in the target lesions; TP: the point at which psoriasis plaques began to decrease in area; HP: the point at which it was estimated that the patient had half the original amount of skin surface area involvement; and CP: the point at which less than about 5% of the original amount of psoriasis remained. Visual inspection was global and included assessment of all body lesions including the two target lesions used for the subsequent photographic analysis. As the nurses were not blinded to the study condition of the patients, their assessments of the most well-defined end point, the CP, were independently checked in two ways: first, by reviewing the blinded physicians' standardized clinic progress notes written at the time of direct examination of the patient. These clinical examinations took place every 4 weeks during the study and within 1 week of when the nurses judged the patient as having cleared; second, by blinded analysis of the photographs of the target lesions. An independent photographic confirmation of the TP was included as well.

After the data collection period for the entire study, all photographs were assessed independently by two dermatologists blinded to the subjects' identity and intervention status (tape or no-tape). Several training sessions were held to ensure uniform evaluation standards. The photographs for each subject were given to each evaluator in chronological order. Two tasks were required: first, to identify the Turning Point, and second, to rate the final photograph of each target lesion in terms of extent of clearing. Ratings were based on a 0 to 3 scale, where 0 signified "definitely not clear," 1 "possibly

clear but doubtful," 2 "probably clear," and 3 "clear without a shadow of doubt." If the rating was a 2 or a 3, the subject was considered to have cleared. If it was a 0 or 1, the subject was rated as not having cleared.

A total of 19 subjects achieved clearing. In 17 cases, there was complete agreement between the nurses' assessments of clearing and the physician assessments (through clinic progress notes and blinded photographic ratings). In two subjects, there was disagreement between nurse and physician assessment of the clearing point. In these two cases, the physician-determined clearing times, which extended 25 and 45 days beyond when the nurses had rated them as cleared, were used in the analysis.

In 17 of the 18 subjects assessed by the nurses as not having cleared by the end of the study, both physician assessment methods confirmed the "not clear" status. In the remaining case, no physician progress note was available and the patient was counted as "not clear." In a single anomalous case, the final photographs of one subject were taken of non-target lesions and no physician note was available. In accordance with standard statistical convention, the subject was treated as "not clear." In two instances, the two physicians' photographic assessments of the CP were not in agreement. A third dermatologist made an independent assessment to resolve the disagreement. In both cases, the third physician's judgment was found post hoc to be consistent with physician progress notes.

Statistical Analysis

Univariate comparisons of each patient characteristic across the four treatment groups (tape, no-tape, PUVA, UVB) were done with one-way analyses of variance. Gender frequencies were compared with a chi square contingency table analysis (Table 1).

Each of the four end points (FRP, TP, HP, CP) was determined (in days) for each patient if and when they attained that end point. For subjects not attaining a given end point, their maximum follow-up time was used and considered as a right-censored value. Kaplan-Meier estimates of unadjusted response time distribution were used to obtain estimated quartiles for each of the various end points (see Table 2). The log-rank test was used to compare the response time distribution for each end point.

The Cox-proportional hazards regression model (PROC PHREG) was used to identify and adjust for confounding factors (Table 3). As noted above, data from all 37 starting subjects were included in the proportional hazards analysis. The dropouts were evenly distributed between the four comparison groups. No significant differences in dropout/censoring times between groups were observed (Kruskal-Wallis One Way ANOVA, $p = 0.14$).

Estimated response time-to-clearance curves (Figure 1, A and B) were computed from the fitted Cox-proportional hazards regression model for each of the four treatment groups (42, 43) to provide a graphical representation of the probability of clearing as a function of time. Median values of 0.2 for the initial SCL-90-R score and 11 for years with psoriasis were used.

RESULTS

Patient Characteristics

There were no statistically significant differences in baseline patient characteristics between subjects either in light treatment group or in the groups with or without guided meditation tapes (Table 1).

Of the 37 subjects in the study, 19 attained clearing (Table 2). Four subjects did not attain clearing, and 14 subjects prematurely discontinued treatment.

Table 2 shows the unadjusted estimates of the response time distribution for each end point. The log-rank test used to compare tape vs. no-tape within light groups was significant or marginally significant for FRP, TP, and HP within UVB ($p = .08, .005$, and $.002$, respectively) and marginally signif-

¹ *Birds of Paradise*, composed and played by Georgia Kelly, 211 1980 Heru Records, Sonoma, CA 95476.

TABLE 1. Patient Characteristics within the Four Treatment Conditions

Variable	PUVA		UVB		All Subjects N = 37	p from ANOVA
	No Tape Group N = 8 Mean \pm SD	Tape Group N = 8 Mean \pm SD	No Tape Group N = 10 Mean \pm SD	Tape Group N = 11 Mean \pm SD		
Age	38.3 \pm 16.6	40.8 \pm 19.0	49.4 \pm 13.0	42.1 \pm 12.5	42.9 \pm 15.1	0.44
Education	13.0 \pm 2.7	13.1 \pm 2.6	12.7 \pm 2.6	13.8 \pm 1.9	13.2 \pm 2.4	0.76
Years with psoriasis	14.4 \pm 11.0	9.4 \pm 5.5	6.3 \pm 5.7	14.4 \pm 10.3	11.2 \pm 8.9	0.17
Body surface involvement	3.4 \pm 1.1	3.2 \pm 1.1	3.3 \pm 0.8	3.3 \pm 0.9	3.3 \pm .9	0.98
SCL-90-R score	0.56 \pm 0.85	0.50 \pm 0.62	0.73 \pm 1.0	0.43 \pm 0.39	0.55 \pm 0.72	0.82
STAI score	36.0 \pm 13.9	37.0 \pm 9.6	44.8 \pm 16.6	32.0 \pm 9.5	37.4 \pm 13.2	0.16
% Female	50%	25%	70%	64%	54%	.28 ^a

Body surface involvement scores ranged from 0–6. Zero corresponded to <1% of estimated body surface involved; 6 corresponded to >76% of estimated body surface area involved. ^a Chi-square test *p* value.

TABLE 2. Unadjusted Estimates of the Response Time Distribution for Each End Point

Group				First Response		Turning Point		Half-Way Point		Clearing Point	
Light	(N)	Tape	Quartile	Days	# of Events	Days	# of Events	Days	# of Events	Days	# of Events
UVB	10	NO	25	18.0	9	40.0	6	51.0	5	97.0	4
			50	23.0		56.0		68.0		98.0	
			75	30.0		60.0		100.0		121.0	
UVB	11	YES	25	10.0	11	19.0	10	42.0	10	82.0	5
			50	12.0		33.0		47.0		84.0	
			75	23.0		39.0		51.0		—	
PUVA	8	NO	25	4.5	7	11.5	7	19.5	7	51.0	5
			50	8.0		20.5		37.0		95.0	
			75	11.5		26.0		58.0		112.0	
PUVA	8	YES	25	7.0	6	21.0	6	23.0	6	35.0	5
			50	9.0		21.5		30.0		45.5	
			75	9.0		23.0		37.0		78.0	
Log Rank Test (<i>p</i> values)			UVB	0.08		0.005		0.002		0.83	
Tape vs. no-tape			PUVA	0.98		0.36		0.24		0.06	

Unadjusted estimates of the quartiles of the response time distribution for each end point are shown, along with *p* values for the log-rank tests of tape vs. no-tape conditions within light treatment type. The number of events represents the number of subjects who achieved the indicated end points in each of the four study conditions.

icant for CP within PUVA ($p = .06$). The median values as well as first and third quartiles shown in Table 2 support these results. In general, the UVB no-tape cohort took the longest time to respond, whereas the PUVA tape group responded most rapidly. Because the log-rank test was not statistically significant ($p = 0.83$) for the UVB clearing point, the difference between the medians of the tape (98 days) versus no-tape (84 days) subjects receiving UVB treatment (14 days) was not significant, whereas for the PUVA clearing point, the difference between the medians of the tape (95 days) and no-tape (45.5 days) subjects (49.5 days) was nearly significant ($p = .06$).

Table 3 presents the adjusted estimated hazards ratios obtained from proportional hazards regression analysis of time to the four end points. All models included years with psoriasis and initial SCL-90-R score. Hazard ratios and

confidence intervals are shown for group (tape or no-tape) and light (UVB or PUVA). At both the HP and the CP, there is a statistically significant difference between the tape group and the no-tape group, the rate of attainment being about 3.8 times more likely in the tape group at both time points. There also is a trend toward an increased rate of attainment at the First Response Point with a hazard ratio of about 2. Strong differences due to light are also in evidence at all four time points, due to the well-known difference in potency between UVB and PUVA, with hazard ratios ranging from 4.4 to 6.2.

The differences in the estimated adjusted time-to-clearance distribution response between tape and no-tape groups are seen in Figure 1, A and B. These curves were obtained from SAS using the estimated Cox proportional hazards model and median values for years with psoriasis and SCL-90-R score. They represent the estimated probability of clearing for each

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TABLE 3. Estimated Cox Proportional Hazard Ratios and 95% Confidence Intervals for the Effect of Tape Group and Light in the Treatment of Psoriasis

Outcome	Variables	Estimated Hazard Ratio	95% Confidence Interval	<i>p</i>
First response	Group	2.16	(0.90, 5.17)	0.083
	Light	5.53	(2.08, 14.69)	0.001
Turning point	Group	2.02	(0.80, 5.12)	0.139
	Light	6.21	(2.18, 17.64)	0.001
Halfway point	Group	3.88	(1.34, 11.25)	0.013
	Light	4.71	(1.73, 12.81)	0.002
Clearing point	Group	3.75	(1.11, 12.65)	0.033
	Light	4.42	(1.37, 14.21)	0.013

p Values are given for the effect of Group (tape or no tape) and Light (UVB or PUVA) on the four treatment response end points. Estimates are adjusted for number of years with psoriasis and SCL-90-R score.

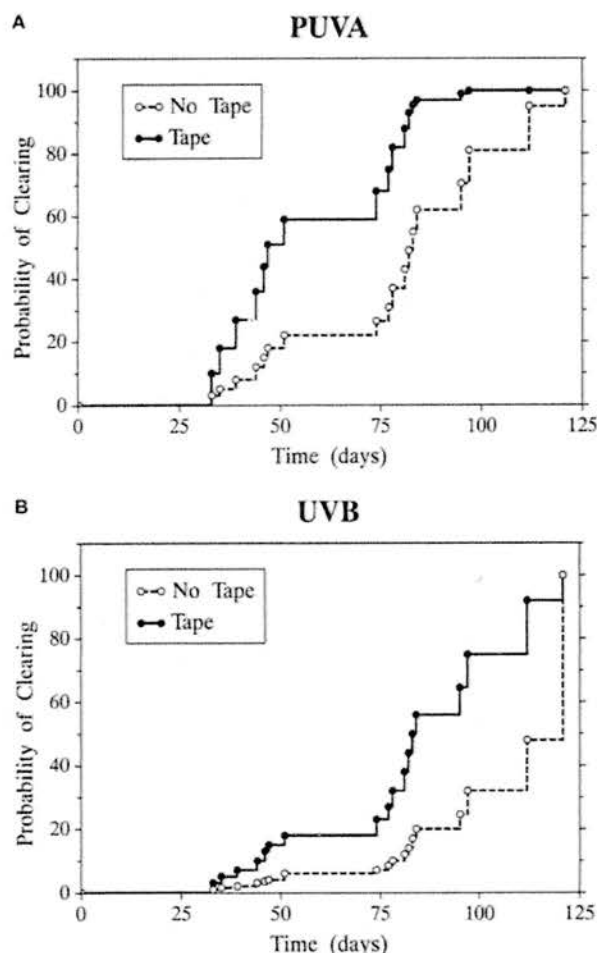


Figure 1. Estimated probability of clearing as a function of time for subjects in the tape (guided stress reduction/meditation condition) and no tape (conventional UVB or PUVA treatment) conditions. A, PUVA; B, UVB. The curves are based on the estimated proportional hazards model in Table 3 and are adjusted to median values for years with psoriasis and SCL-90-R score.

value of time used in the analysis of the CP, regardless of whether it was a censored or non-censored value.

As can be seen in Figure 1, A and B, there is a strong separation between the curves describing the tape and no-tape

conditions. For UVB, the estimated time to achieve a 50% probability of clearing is 83 days for the tape group and 113 days for the no-tape group. For PUVA, the results are 48.5 days for the tape group and 85 days for the no-tape group respectively. The estimated adjusted time differences for achieving 50% probability of clearing in the tape versus no-tape conditions are 30 and 40 days respectively for UVB and PUVA. These values differ from the unadjusted differences of 14 days and 49.5 days shown in Table 2, and reflect the averaging over patients that takes place in the modeling process.

Similar statistically significant separations in the kinetics of clearing in the comparison groups were seen when the data were subjected to a Kaplan-Meier analysis, and when the analyses were performed as a function of increasing energy exposure (in millijoules for UVB and joules for PUVA) rather than as a function of time (data not shown).

Psychological Outcomes:

Data acquired on the 22 subjects who completed the entire protocol, who were assessed before treatment and at the conclusion of the protocol on the General Severity Index of the SCL-90-R showed no change in mean GSI (0.296 pre; 0.290 post) for those subjects in the no-tape condition ($N = 11$) and a 35% reduction in the mean GSI for those subjects with complete pre/post data ($N = 11$) in the tape group (0.360 pre; 0.233 post). Although the latter finding did not reach statistical significance in the univariate *t* test ($p = 0.18$), it is similar in magnitude to reductions routinely observed on this index in the stress reduction clinic and reported in a number of studies (37–39). No change in STAI was observed in either cohort.

Data from periodically administered rating scales of subjective response to treatment showed nonstatistically significant trends suggesting that subjects in the tape groups: a) increased in "positivity about today's session" compared with no tape subjects (14% mean percent increase from the start of treatment to the midpoint ($N = 14$), compared with -3% ($N = 14$)); b) increased in "degree of relaxation after today's session" compared with no tape subjects (6% ($N = 14$) vs. 1% ($N = 14$)); and c) increased in "the extent to which you think the treatment is helping" (29% ($N = 12$) vs. 14% ($N = 11$)).

DISCUSSION

The results suggest that the rate of skin clearing in patients with moderate to severe psoriasis can be accelerated when subjects engage in an audiotape-guided, meditative stress

reduction exercise during their UVB or PUVA treatment sessions. This phenomenon has now been observed in two separate studies – the original pilot (31), and the present study, which includes two blinded, independent confirmations of each subject's skin status. In both studies, a pronounced effect was observed in spite of a small study size, suggesting that the effect is robust and attainable in a significant number of psoriasis patients practicing the stress reduction exercises. These results must be interpreted cautiously, however, in light of the small numbers of patients. This finding is, however, consistent with anecdotal reports (25a, 45) and other studies suggesting that stress reduction methods including relaxation, hypnosis, and imagery may positively affect symptoms in psoriasis in the absence of phototherapy (46, 47) or as a complement to it (48). Moreover, as noted in Methods, the present results cannot be explained by a differential dropout rate between groups.

The psychological outcome data, taken as a whole, suggest that the tape intervention resulted in reduced distress and increased well-being. With small numbers of subjects, it is difficult to achieve statistical significance with outcome measures like the SCL-90-R, which typically show high variability. We saw no change in state anxiety on the STAI between preintervention and postintervention in either the controls or the experimental subjects. A comprehensive assessment of the type and degree of psychological change resulting under these study conditions requires further investigation.

The increased rate of skin clearing and the concomitant reduction in number of sessions necessary to achieve clearing in patients who made use of the psychological intervention during treatment may have two important clinical implications: a) a possible reduction in the risk of skin cancers associated with exposure to phototherapy and photochemotherapy (49–51); b) the potential to significantly reduce the cost of treatment by reducing the total number of treatments necessary to achieve clearing.

It should be noted that, although it seems from Figure 1, A and B that 100% of patients cleared by the end of the study, this is not the case. As noted in Methods, 12 subjects dropped out of the study before their treatments were completed and 2 were censored due to prescription changes. The curves show only that, had all subjects remained in the protocol for 121 days, the *probability* of their clearing would have approached 100%. The figures represent predictions from the estimated model using the observed data and are not plots of the observational data themselves.

The attribution of the results of this study to elements of the stress reduction intervention should be considered preliminary and tentative. Until further studies are performed to control for additional variables, we cannot rule out the possibility that expectancy effects (ie, enthusiasm and/or disappointment about tape group assignment) may have played a role in the observed differences, inasmuch as the control group did not make use of placebo instructional or music audiotapes. Nevertheless, the findings of this study suggest an important psychological influence on the rate of skin clearing related to assignment to the meditation tape or no-tape condition. A conclusive attribution of the observed acceleration in rate of skin clearing to specific psychological factors, such as elements of the meditation practice and the guided imagery awaits further research.

Our present findings suggest that this experimental design

is well-suited for studying the role of belief, expectation, and psychological conditioning in the resolution of a specific and readily observable disease process that psoriasis represents. Placebo (non-therapeutic) wavelengths of light could be used to differentiate effects due to light from effects due to psychological factors. The system could also be used in future studies to differentiate between therapeutic effects attributable to the meditation versus those attributable to the visualization component of the present intervention, to investigate the specificity of the meditation instructions through use of "pseudo-meditation" instructions, to study the interaction between individual patient characteristics and response to specific psychological interventions, and to assess the long-term efficacy of such interventions in preventing or slowing recurrence after treatment.

It is interesting to note that the dimension of social support, thought to be highly important in other studies of psychological interventions exerting a potentially mitigating effect on disease progression (52–54), is minimal in this experimental design because each subject undergoes the combined light treatment and psychological intervention in isolation.

The experimental design used in the present study also might prove useful in investigating the role of potential biological mediating variables in skin clearing and their interaction with a range of psychological factors and practices. One candidate for study is the cellular titer and activity of different lymphocyte populations and cytokines involved in the dermal inflammatory response and wound healing (4) as well as in psoriasis (7). Other important areas of investigation include possible differential gene expression in the case of transforming growth factor (TGF- α), as well as the reported over-expression of the Bcl-x protein in keratinocytes. As noted in the Introduction, both of these factors have been implicated in psoriasis (8, 9). Such investigations have the potential to inform our understanding of how psychological factors might interact with disruptions of apoptosis, giving rise to uncontrolled cellular proliferation. This process may be relevant to malignancies in which anti-apoptotic factors are expressed, such as basal cell carcinoma (9), as well as to psoriasis itself.

Thus, the experimental design described in the present study may provide an opportunity to investigate elements of an observable healing process ranging from gene expression and cell proliferation to attitudes, expectations, and the use of specific psychological methods such as meditation and visualization.

This work was supported in part by the Fetzer Institute, Kalamazoo, Michigan. We wish to thank Elizabeth Kabachenski, LPN, for her dedicated and outstanding contribution to organizing the phototherapy clinic to perform the study protocol described in this paper and the earlier one. We also wish to thank Joan Goyette, LPN, and Carolyn Appel, LPN, for their important contributions in the execution of this study. We also wish to thank Drs. James Hebert, Tom Hurley, and Bernard Fox for their statistical input and advice, and Drs. James Hebert, Michael Bratt, Robert Ader, David Eisenberg, Albert Stunkard, Robert Woodland, Ira Ockene, Peter Quesenberry, and Zindel Segal for their suggestions for improving the manuscript.

REFERENCES

1. Dunbar F: Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships 1910-1953. 4th edition. New York, Columbia, 1954, 594-631
2. Selye H: The Physiology and Pathology of Exposure to Stress. Montreal, Acta Inc., 1950, 726-741
3. Barber TX: Hypnosis, suggestions, and psychosomatic phenomena: A new look from the standpoint of recent experimental studies. *Am J Clin Hypn* 21:13-27, 1978
4. Kiecolt-Glaser J, Marucha PT, Malarkey WB et al: Slowing of wound healing by psychological stress. *Lancet* 346:1194-1196, 1995
5. Greaves MW, Weinstein GD: Treatment of psoriasis. *N Engl J Med* 332:581-588, 1995
6. Camisa C: Psoriasis. Boston, Blackwell Scientific, 1994, 3
7. Nickoloff BJ: The cytokine network in psoriasis. *Arch Dermatol* 127:871-884, 1991
8. Elder JT, Fisher GJ, Linquits PB, et al: Overexpression of transforming growth factor α in psoriatic epidermis. *Science* 243:811-814, 1989
9. Wrone-Smith T, Johnson T, Nelson B, et al: Discordant expression of Bcl-x and Bcl-2 by keratinocytes in vitro and psoriatic keratinocytes in vivo. *Am J Pathol* 146:1079-1088, 1995
10. Pincelli C, Fantini F, Magnoni C: Psoriasis and the nervous system. *Acta Derm Venereol Suppl* 186:60-61, 1994
11. Faber EM, Nickoloff BJ, Recht B, et al: Stress, symmetry, and psoriasis: Possible role of neuropeptides. *J Am Acad Dermatol* 14:305-311, 1986
12. Pert CB, Ruff MR, Weber RJ, Herkenham M: Neuropeptides and their receptors: A psychosomatic network. *J Immunol* 135(2): 820-826, 1985
13. Parrish JA, Fitzpatrick TB, Tanenbaum L, Pathak MA: Phototherapy of psoriasis with oral methoxsalen and longwave ultraviolet light. *N Engl J Med* 219:1207-1211, 1974
14. Abel EA (ed). Photochemotherapy in Dermatology. New York, Igaku-Shoin, 1992
15. Morison WL: Phototherapy and Photochemotherapy of Skin Disease. New York, Raven, 1991
16. Weiss JM, Renkl AC, Denfeld RW, et al: Low-dose UVB radiation perturbs the functional expression of B7.1 and B7.2 costimulatory molecules on human Langerhans cells. *Eur J Immunol* 25:2858-2862, 1995
17. Farber EM, Nall L: Psoriasis: A stress-related disease. *Cutis* 51:322-326, 1993
18. Van Moffaert M: Psychodermatology: an overview. *Psychother Psychosom* 58(3-4):125-136, 1992
19. Engels DW: Psychosomatic illness review: IV Dermatological Disorders. *Psychosomatics* 23:1209-1219, 1982
20. Baughman R, Sobel R: Psoriasis, stress, and strain. *Arch Dermatol* 103:599-605, 1971
21. Fava GA, Perini GI, Santanastaso P, Forsana CV: Life events and psychological distress in dermatological disorders: Psoriasis, chronic urticaria, and fungal infections. *Br J Med Psychol* 53:277-282, 1980
22. Gaston L, Crombez JC, Lassonde M et al: Psychological stress and psoriasis: Experimental and prospective correlational studies. *Acta Derm Venereol Suppl* 156:37-43, 1991
23. Gaston L, Lassonde M, Bernier-Buzzanga J et al: Psoriasis and stress: A prospective study. *J Am Acad Dermatol* 17:82-86, 1987
24. Frankel FH, Misch RC: Hypnosis in a case of long-standing psoriasis in a person with character problems. *Int J Clin Exp Hypn* 21:121-129, 1973
25. Goodman M: An hypothesis explaining the successful treatment of psoriasis with thermal biofeedback: A case report. *Biofeed Self Regul* 19(4):347-352, 1994
- 25a. Gaston L, Crombez JC, Dupuis G: An imagery and meditation technique in the treatment of psoriasis: A case study using an A-B-A design. *J Mental Imagery* 13(1):31-38, 1989
26. Tsushima WT: Current psychological treatments for stress-related skin disorders. *Cutis* 42(5): 402-404, 1988
27. Kantor SD: Stress and psoriasis. *Cutis* 46:321-322, 1990
28. Winchell SA, Watts RA: Relaxation therapies in the treatment of psoriasis and possible pathophysiologic mechanisms. *J Am Acad Dermatol* 18:101-104, 1988
29. Zachariae R, Oster H, Bjerring P, Kragballe, K: Effects of psychologic intervention on psoriasis: A preliminary report. *J Am Acad Dermatol* 34:1008-1015, 1996
30. Keinan G, Segl A, Gal U, Brenner S: Stress management for psoriasis patients: The effectiveness of biofeedback and relaxation techniques. *Stress Med* 11:235-241, 1995
31. Bernhard JD, Kristeller J, Kabat-Zinn J: Effectiveness of relaxation and visualization techniques as an adjunct to phototherapy and photochemotherapy of psoriasis. *J Am Acad Dermatol* 19:572-573, 1988
32. Derogatis LR, Rickels K, Rock AF: The SCL-90 and the MMPI: A step in the validation of a new self-report scale. *Br J Psychiatry* 128:280-289, 1976
33. Spielberger CD, Gorsuch RC, Lushene RE: Manual for the State-Trait Anxiety Inventory. Palo Alto, Consulting Psychologists, 1970
34. Kabat-Zinn J: Full Catastrophe Living. New York, Delacorte, 1990
35. Kabat-Zinn J: Mindfulness meditation: Health benefits of an ancient Buddhist practice. In Goleman D, Gurin, J (eds), *Mind/Body Medicine*. Yonkers, Consumer Reports Books, 1993
36. Thera N: The Heart of Buddhist Meditation, New York, Weiser, 1962
37. Kabat-Zinn J: An out-patient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. *Gen Hosp Psychiatry* 4:33-47, 1982
38. Kabat-Zinn J, Lipworth L, Burney, R: The clinical use of mindfulness meditation for the self-regulation of chronic pain. *J Behav Med* 8:163-190, 1985
39. Kabat-Zinn J, Lipworth L, Burney R, Sellers W: Four year follow-up of a meditation-based program for the self-regulation of chronic pain: Treatment outcomes and compliance. *Clin J Pain* 2:159-173, 1986
40. Kabat-Zinn J, Massion AO, Kristeller J et al: Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. *Am J Psychiatry* 149:936-943, 1992
41. Miller J, Fletcher K, Kabat-Zinn J: Three-year follow-up and clinical implications of a mindfulness-based stress reduction intervention in the treatment of anxiety disorders. *Gen Hosp Psychiatry* 17:192-200, 1995
42. Collett D: Modeling Survival Data in Medical Research. New York, Chapman Hall, 1994, 98-102
43. SAS. SAS Statistics Users Guide-PROC PHREG. Cary, NC, SAS Institute, 1994
44. Deleted in proof.
45. Veiga JA: Hypnotic autogenic treatment of patients with derma-

- tological disorders: Psoriasis. *Bol Psicologia (Cuba)* 7(2):135-144, 1984
46. Gaston L, Crombez JC, Joly J et al: Efficacy of imagery and meditation techniques in treating psoriasis. *Imagination Cognition Personality* 81(1):25-38, 1988
47. Price ML, Mottahedin I, Mayo PR: Can psychotherapy help patients with psoriasis? *Clin Exp Dermatol* 16:114-117, 1991
48. Boncz I, Beata F, Hunyadi J: Experiences with group hypnotherapy of psoriatic patients. *Aust J Clin Hypnother Hypn* 11(1):15-18, 1990
49. Stern RS, Laird N, Melski J, et al: Cutaneous squamous-cell carcinoma in patients treated with PUVA. *N Engl J Med* 310:1156-1161, 1984
50. Stern RS, Laird N: The carcinogenic risk of treatments for severe psoriasis: Photochemotherapy Follow-up Study. *Cancer* 73: 2759-2764, 1994
51. Stern RS, Nichols KT, Vakeva LH: Malignant melanoma in patients treated for psoriasis with methoxsalen (Psoralen) and ultraviolet A radiation (PUVA). *N Engl J Med* 336:1041- 1045, 1997
52. Spiegel D, Bloom JR, Kraemer, Gottheil E: Effect of psychosocial treatment on survival of patients with metastatic breast cancer. *Lancet* 2:888-891, 1989
53. Fawzy IF, Fawzy NW, Hyun CS et al: Malignant melanoma: Effects of an early structured psychiatric intervention, coping, and affective state on recurrence and survival 6 years later. *Arch Gen Psychiatry* 50:681-689, 1993
54. Ornish DM, Brown SE, Scherwitz LW et al: Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *Lancet* 336:129-133, 1990