Observations of Psoriasis in the Absence of Therapeutic Intervention Identifies Two Unappreciated Morphologic Variants, Thin-Plaque and Thick-Plaque Psoriasis, and their Associated Phenotypes

Tanya E. Christensen[1], Kristina P. Callis[1], Jason Papenfuss[1,2], Matthew S. Hoffman[1], Christopher B. Hansen[1,3], Bob Wong[1], Jacqueline M. Panko[1] and Gerald G. Krueger[1]

Psoriatic plaque thickness is a clinical measure of psoriasis severity. We have observed that patients tend to revert to a baseline thickness of psoriatic plaques when in an untreated state, and hypothesized that other features of psoriasis could associate with this trait. Data prospectively collected on 500 participants in the Utah Psoriasis Initiative were used for the study. In response to a question assessing plaque thickness when disease was at its worst, 144 (28.8%) reported thick plaques, 123 (24.6%) reported thin plaques, and 233 (46.6%) reported intermediate thickness. For patients with "worst-ever" disease at enrollment ($n=122$), there was significant correlation of thickness between assessment by the patient and the physician ($r=0.448$, P-value 0.01). Thick plaques associated with male gender, increased body mass index, nail disease, psoriatic arthritis, larger plaques, more body sites, and greater total body surface area affected. Thin plaques associated with eczema, guttate psoriasis, and skin cancer. We suggest that this is preliminary evidence that plaque thickness is an easily measured trait that associates with other clinical features of psoriasis, and that stratification on this phenotype may be useful in further defining the genetic basis of this disease.

Journal of Investigative Dermatology (2006) **126,** 2397–2403. doi:10.1038/sj.jid.5700489; published online 20 July 2006

INTRODUCTION

Psoriasis is a common, multifactorial skin disorder that affects approximately 2–3% of the United States population. The search for the psoriasis gene or genes continues; although linkage to several loci have been proposed, none have a linkage to the pathogenesis of this disorder(Capon *et al.*, 2004; Griffiths, 2004; Sagoo *et al.*, 2004). The difficulty in linking psoriasis to a single gene has magnified the necessity of defining and stratifying psoriasis into phenotypic variants. It is generally presumed that genes control subtypes or features of psoriasis; that is, genotype predicts phenotype. Historically, the classic subtypes of psoriasis have been described as erythrodermic, guttate, pustular, palmar/plantar, and plaque type. However, it is probable that plaque-type psoriasis, the most common subtype of psoriasis, is composed of a variety of subtypes (Christophers, 2003; Griffiths, 2004). Different arrays of characteristics such as plaque location, concurrent nail disease, psoriatic arthritis, plaque appearance (size, thickness, shape, erythema, scale), response to environment or treatment, and course of disease may represent distinct clinical entities under the umbrella of ''psoriasis''.

The Utah Psoriasis Initiative (UPI) was established to study and classify subtypes of psoriasis based upon observable and patient-reported characteristics to facilitate the correlation of psoriasis phenotypes with genotype. In clinics specializing in the care and management of psoriasis, the senior authors (GGK and KPC) have repeatedly observed that patients with plaque-type psoriasis vulgaris tend to have a baseline (defined as no therapeutic intervention) plaque appearance, with a usual thickness and size that is characteristic for them. It is readily acknowledged that while time and treatment may clear or improve disease, we hypothesize that psoriatic plaques have a baseline appearance in an untreated state. In this study, we classified patients based on plaque thickness in

[1]*Department of Dermatology, University of Utah School of Medicine, Salt Lake City, Utah, USA*

[2]*Current address: Department of Dermatology, Medical University of South Carolina, Charleston, South Carolina, USA.*

[3]*Current address: Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, Texas, USA.*

Correspondence: Dr Gerald G. Krueger, Department of Dermatology, University of Utah Health Sciences Center, 4B454 School of Medicine, 30 North 1900 East, Salt Lake City, Utah 84132-2409, USA. E-mail: krueger@derm.med.utah.edu

Abbreviations: BSA, body surface area; NPF, National Psoriasis Foundation; PASI, psoriasis assessment scales; UPI, Utah psoriasis initiative

Received 31 August 2005; revised 10 April 2006; accepted 9 May 2006; published online 20 July 2006

the untreated (worst-ever) state and to describe the associated phenotypic features of patients with three different levels of thickness, thin, intermediate, and thick. To our knowledge, this is the first description of the associated phenotypic features of thin *versus* thick-plaque psoriasis. This distinction may be important in future studies performed to associate genotype and phenotype.

RESULTS

Of the 539 participants, 500 (93%) enrolled in the UPI were included in the analysis. Of the 39 that were excluded, 24 did not have plaque-type psoriasis (most reported isolated palmar/plantar disease), and for 15 the exam registry forms were not completed. Of the 500 participants analyzed, 144/500 (28.8%) reported thick plaques when psoriasis thickness was at its worst, 123/500 (24.6%) reported thin plaques, and 233/500 (46.6%) reported intermediate.

Comparison of physician and patient thickness groups

Two separate comparisons measures were completed to verify the patient-reported worst psoriasis plaque thickness (Figure 1). First, a comparison between the physician induration score and patient-reported worst psoriasis plaque thickness was made. The analysis used only patients who were at least 80% of their ''worst-ever psoriasis'' at enrollment (patient global assessment) score 4 or 5) ($n=122$, 24.4%). The mean physician induration score for patients in this worst ever at enrollment cohort who rated their plaques as ''thick'' was 2.8 ± 0.2 SEM, for ''thin'' was 1.3 ± 0.1 SEM, and for ''intermediate'' was 2.0 ± 0.1 SEM. The mean scores demonstrated significant differences ($P<0.0001$). Pearson's bivariate correlation between patient and physician scores was 0.448 ($P=0.01$). Second, a retrospective chart review on those patients in the UPI who had participated in a prior clinical study was performed to determine if reported plaque thickness was similar to physician determined plaque induration scores from previous years. Both National Psoriasis Foundation (NPF) induration card scores and the induration component of the psoriasis assessment scales (PASI) score were compared to patient-reported thickness. Of the 500 participants, 34 (6.8%) of the UPI had been part of a previous clinical drug study, which recorded NPF induration scores at baseline. The mean score for thick ($n=19$), 2.6 ± 0.2 SEM, was significantly different than the mean score for intermediate ($n=14$), 1.9 ± 0.5 SEM ($P=0.024$), but not from the mean score for thin ($n=1$), 1.0 ± 0.0 SEM ($P=0.067$). 58/500 (11.6%) UPI participants had been part of a previous clinical study which recorded PASI scores at baseline. The mean PASI induration score for thick, 2.5 ± 0.1 SEM, was significantly different than the mean score for thin 1.7 ± 0.2 SEM ($P=0.027$), and also significantly different than the mean score for those intermediate, 2.3 ± 0.1 SEM ($P=0.023$).

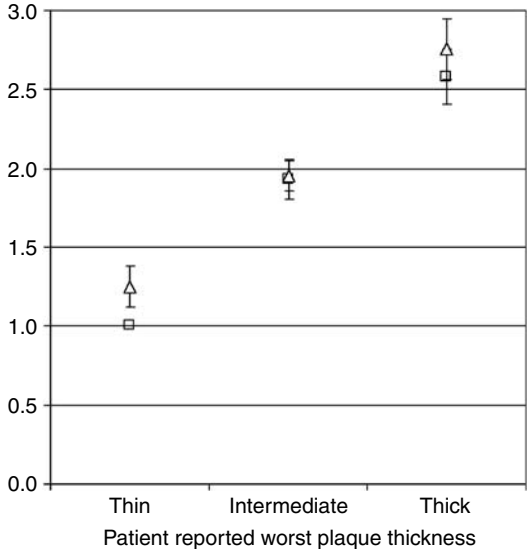

Figure 1. Validation of patient-reported plaque thickness: each marker represents the mean ± SEM NPF induration score. △, Mean physician recorded NPF induration card scores *versus* patient-reported psoriasis plaque thickness when at its worst for only those participants who reported a patient global assessment of 4 (80% of worst ever) or 5 (100% of worst ever) upon study entry ($n=122/500$). Analysis of variance ($F=15.0$, $P<0.0001$) showed significant differences between thick–thin ($P<0.0001$) and thick–intermediate ($P=0.0001$). □, Mean NPF induration card score from chart review of baseline visits from clinical trials from 2001 to 2003. Analysis of variance for NPF ($F=5.8$, $P=0.007$). Thin–thick differences ($P=0.067$); thick–intermediate ($P=0.024$), and thin–intermediate ($P=0.376$).

Phenotypic differences between thickness groups

Demographic and disease differences between thick, thin, and intermediate groups are in Table 1. No significant difference was found between groups in ethnicity, age at enrollment, age of onset, disease duration, positive family history, treatment status at enrollment, smoking, alcohol use, or reported Koebner phenomenon. There was also no association between thickness and other psoriasis diagnoses, except for guttate psoriasis, which was more commonly reported in the thin (16.3%) and intermediate (18.5%) groups than in the thick group (7.6%) ($P=0.014$).

Participants who reported thick-plaque psoriasis were more likely to be male (59% thick, *versus* 51.9% intermediate *versus* 41.5% thin, $P=0.014$). There was also a significantly increased prevalence of psoriatic arthritis ($P=0.0005$), psoriatic nail disease ($P=0.001$), and larger plaques ($P=0.001$) in participants with thicker disease.

Although there was no significant difference in age of onset overall, when segregated by gender, the age of onset for males was significantly different between groups (analysis of variance, $F=5.7$, $P=0.004$). The mean age of onset in years for males with thin-plaque psoriasis, 35.0 ± 18.5, was significantly higher than the mean age of onset for males with intermediate, 28.9 ± 15.9 ($P=0.049$), and thick, 25.9 ± 12.8 ($P=0.002$).

Figure 2 shows the differences in the median percent body surface area (BSA) affected for thin, intermediate, and thick-plaque psoriasis. Physician-reported BSA upon enrollment correlated closely with patient-reported BSA upon enrollment ($r=0.882$, $P<0.0001$). Patients with thick-plaque psoriasis had significantly more body surface affected on enrollment than thin or intermediate groups (Kruskal–Wallis, $P=0.0001$

Table 1. Demographic and disease data for patient-reported worst psoriasis plaque thickness

	Sample (*n*=500)	Thin (*n*=123)	Intermediate (*n*=233)	Thick (*n*=144)	*P*-value
Gender					0.014
Male	248 (49.6)	51 (41.5)	112 (48.1)	85 (59)	
Female	252 (50.4)	72 (58.5)	121 (51.9)	59 (41)	
Ethnicity					
White/Caucasian	465 (93)	119 (96.7)	213 (91.4)	133 (92.4)	0.068
Age at enrollment (years)	49.5±16.5 (50)	51.5±18.9 (54)	48.9±16.0 (49)	48.8±15.0 (50)	0.303
Age onset (years)	27.2±16.4 (23)	29±18.5 (23)	27±16.7 (24)	26±13.8 (23)	0.321
Male	29.1±15.6	35.0±17.3 (30)	28.9±15.9 (26.5)	25.9±12.8 (22.0)	0.004
Female	25.3±17.0	24.7±18.1 (19)	25.2±17.2 (20)	26.2 15.1 (23)	0.880
Disease duration (years)	22.3±15 (19)	22.5±15.6 (19)	21.9±14.6 (18)	22.8±15.0 (21)	0.836
BMI (kg/m^2)	29.2±7.4 (27.9)	27.3±5.4 (26.5)	29.4±7.5 (27.9)	30.6±8.2 (28.8)	0.001
Family history positive	331 (66.2)	80 (65)	162 (69.5)	89 (61.8)	0.291
Currently treated	410 (82.5)	94 (77)	194 (83.6)	122 (85.3)	0.174
Smoking	186 (37.2)	40 (32.5)	83 (35.6)	63 (43.8)	0.132
Alcohol	171 (34.2)	37 (30.1)	79 (33.9)	55 (38.2)	0.376
Koebner phenomenon	211 (42.2)	44 (35.8)	99 (42.5)	68 (47.2)	0.167
Nail disease	304 (62.2)	65 (53.7)	134 (59)	105 (74.5)	0.001
Psoriatic arthritis	136 (27.4)	19 (15.6)	64 (27.6)	53 (37.1)	0.0005
Size of plaques					
Small, scattered plaques	183 (36.7)	82 (66.7)	73 (31.3)	28 (19.6)	<0.0001
Mix of both	217 (43.5)	31 (25.2)	129 (55.4)	57 (39.9)	—
Large, geographic plaque type	99 (19.8)g	10 (8.1)	31 (13.3)	58 (40.6)	—
Other diagnoses other than plaque-type					
Erythrodermic	7 (1.4)	1 (0.8)	4 (1.7)	2 (1.4)	0.788
Guttate	74 (14.8)	20 (16.3)	43 (18.5)	11 (7.6)	0.014
Generalized pustular	12 (2.4)	2 (1.6)	8 (3.4)	2 (1.4)	0.367
Inverse	141 (28.2)	34 (27.6)	69 (29.6)	38 (26.4)	0.786
Only palmar/plantar disease	15 (3)	2 (1.6)	10 (4.3)	3 (2.1)	0.279
Palmar/plantar pustulosis (PPP)	11 (2.2)	2 (1.6)	7 (3)	2 (1.4)	0.514

ANOVA, analysis of variance; BMI, body mass index.
For categorical variables, data presented as number (%) and *P*-values calculated from χ^2 test. For continuous variables, data presented as mean±SD (median) and *P*-values calculated from ANOVA.

for patient-reported BSA, $P<0.0001$ for physician-reported BSA; Mann–Whitney test between groups, all *P*-values <0.02). Patient-reported worst-ever BSA was significantly higher for thick plaque participants (median 15%, range 1–100%) than for either intermediate (median 7%, range 1–99%) or thin (median 6%, range 1–96%) (Kruskal–Wallis $P<0.0001$; Mann–Whitney test for thin–thick, $P=0.0003$, thick–intermediate, $P<0.0001$, and thin–intermediate, $P=0.633$).

Association with other conditions

Table 2 lists 16 other medical conditions with a prevalence >5% within the sample. Eczema had a marginally significant *P*-value (0.014) with a greater frequency in thin plaque (17.1%) than in either intermediate (7.3%) or thick (13.9%). Skin cancer was reported significantly more frequently in participants with thin-plaque psoriasis (19.5%) than in those with intermediate (9.4%) or thick (4.9%) ($P=0.0004$). The rest of the disease listed in Table 2 either had nonsignificant *P*-values for differences between thickness groups or the sample size was to small to assess an effect.

DISCUSSION

Classification of the clinical features of psoriasis has been a controversial subject among investigators. Defining presence or absence of psoriatic arthritis, nail disease, what constitutes ''early onset'' of disease, and even certainty of the diagnosis of psoriasis are challenging tasks for the clinician when

findings are subtle. It has been our belief that classification of phenotypic features such as plaque thickness is possible and may lead to genetic associations and better understanding of psoriasis. Stratification by phenotype has already led to the identification of susceptibility loci in numerous studies (Samuelsson *et al.*, 1999; Allen *et al.*, 2005; Karason *et al.*, 2005).

In this study, we present data suggesting that plaque psoriasis can be classified by its thickness, that patient self-report of thickness correlates with physician induration scores, and that some phenotypic features of psoriasis associate with plaque thickness. Subjects with thick-plaque psoriasis have significantly more nail disease, psoriatic arthritis, larger plaques, more BSA affected, and are more likely to be male than are their counterparts with thin-plaque psoriasis. Although plaque induration is a part of most PASI (NPF Psoriasis Score), to our knowledge, there are no previous studies comparing inherent phenotypic differences across plaque thickness.

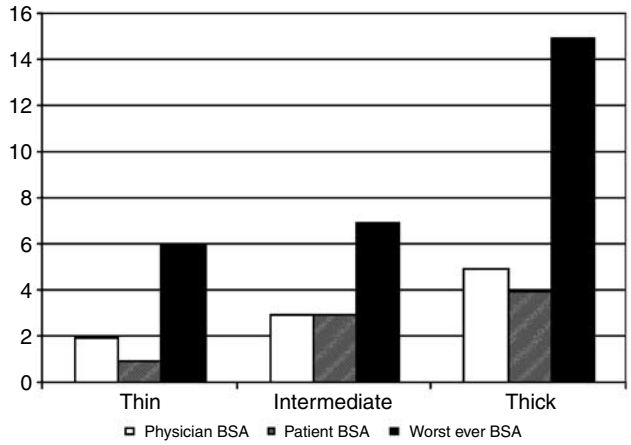

Figure 2. Comparison of median percent total BSA between patient-reported worst psoriasis plaque thicknesses. Significant differences between groups by Kruskal–Wallis for worst-ever BSA ($P=0.0001$), physician BSA ($P<0.0001$), and patient BSA ($P<0.0001$). Physician BSA = physician-reported total BSA affected at the time of examination; patient BSA = patient-reported total BSA affected at the time of examination; worst-ever BSA = patient-reported worst-ever total body surface affected.

Thickness validity

A chronic challenge has been designing a sensitive tool to detect and segregate phenotypic differences within psoriasis. The question posed to our patients asking them to describe the thickness of their plaques when at their worst is an attempt to capture a reasonably accurate description of a disease process at a single point in time. Participants were in varying states of disease flare or remission upon enrollment. Our data are therefore subject to significant recall bias. To assess appearance of psoriasis plaques when at their worst, we relied on patient report with assistive measures including the NPF induration card and standard photos, which also have limitations. Determination of induration, even by investigators trained to do psoriasis assessments for clinical trials, is an inexact science in the absence of an objective measure. Use of the NPF induration card was therefore instituted to assist with the induration assessments. This card is consistently used as part of the NPF Psoriasis Score, which has been validated against PASI in clinical trials where both scoring systems were used as end points. Although the card has not been validated against biopsies or ultrasound, in one

Table 2. Disease prevalence by thickness for diseases with a prevalence >5% in the sample

	Sample (n=500)	Thin (n=123)	Intermediate (n=233)	Thick (n=144)	P-value*	P_c-value**
Arthritis	169 (33.8)	40 (32.5)	76 (32.6)	53 (36.8)	0.665	NS
High blood pressure	141 (28.2)	36 (29.3)	59 (25.3)	46 (31.9)	0.364	NS
Depression	110 (22)	28 (22.8)	51 (21.9)	31 (21.5)	0.969	NS
High cholesterol	101 (20.2)	20 (16.3)	51 (21.9)	30 (20.8)	0.442	NS
Migraine headaches	70 (14)	20 (16.3)	35 (15)	15 (10.4)	0.323	NS
Eczema	58 (11.6)	21 (17.1)	17 (7.3)	20 (13.9)	0.014	NS
Diabetes	53 (10.6)	7 (5.7)	25 (10.7)	21 (14.6)	0.063	NS
Skin cancer	53 (10.6)	24 (19.5)	22 (9.4)	7 (4.9)	0.0004	0.013
Anemia	49 (9.8)	9 (7.3)	21 (9)	19 (13.2)	0.235	NS
Asthma	43 (8.6)	9 (7.3)	21 (9)	13 (9)	0.843	NS
Irritable bowel disease	43 (8.6)	10 (8.1)	21 (9)	12 (8.3)	0.952	NS
Thyroid disease	41 (8.2)	13 (10.6)	18 (7.7)	10 (6.9)	0.525	NS
Seborrheic dermatitis	37 (7.4)	11 (8.9)	20 (8.6)	6 (4.2)	0.212	NS
Recurrent strep throat	35 (7)	11 (8.9)	16 (6.9)	8 (5.6)	0.554	NS
Cancer	28 (5.6)	8 (6.5)	16 (6.9)	4 (2.8)	0.216	NS

NS, nonsignificant.
*P-value from χ^2 test.
**P_c: corrected P-value for 32 multiple comparisons.

pilot study at three centers, we demonstrated a trend toward improved intra-observer reliability when investigators used the card.[1]

Regardless, our data show that the patient's assessment of plaque thickness at UPI enrollment is comparable to the PASI and NPF induration assessments at enrollment of clinical trials in the past when the patient had typically not been treated for 2–4 weeks during a ''wash-out'' period. In addition, for those patients who were at their worst at enrollment, the physician-recorded mean NPF score correlated significantly with patient report.

Association of plaque thickness with clinical phenotypes

The associations that we found between thick plaques and clinical features of psoriasis including nail disease, psoriatic arthritis, and male gender are corroborated by previously described phenotypic variants. Nail disease and psoriatic arthritis have been shown to be markers for more severe psoriasis, and they have also been shown to occur in association with one another (Williamson *et al.*, 2004). Males have also been shown to have psoriatic arthritis at a ratio of 1.3:1 to females (Taylor, 2002). Changes in epidermal thickness correlate with disease improvement as measured by PASI (Gottlieb, 2003).

The argument can be made that thick-plaque psoriasis is simply a marker of more severe disease. However, disease severity remains difficult to classify and is most often used in clinical trials as measures of improvement, or in the clinic to determine appropriate aggressiveness of therapy and often in conjunction with insurance definitions. Studies that have stratified patients on psoriatic arthritis and nail disease have yielded new minor genetic susceptibility loci (Samuelsson *et al.*, 1999; Karason *et al.*, 2005). We propose that the classification of plaque thickness and its relationship to psoriatic arthritis and nail disease requires further genome-based investigation.

Our findings show that thin-plaque psoriasis was associated with a reported history of guttate psoriasis, with a reported history of eczema, and with an increased prevalence of skin cancer when compared with those with thick-plaque psoriasis. These associations are subject to recall bias and potential past misdiagnosis of conditions such as guttate psoriasis or eczema that is inherent and cannot be readily eliminated. The association of thin plaque disease with guttate psoriasis is very interesting as it is known that guttate psoriasis has a high association with the major genetic psoriasis susceptibility locus, HLA-Cw6 (Asumalahti *et al.*, 2003). Atopic dermatitis is associated with numerous loci in common with psoriasis (Bowcock and Cookson, 2004). Our observation of thin plaque disease associating with atopic diatheses needs to be replicated and assessed in a cohort that is to be followed longitudinally. With this in hand a more complete association analysis can be carried out to determine if the genes/gene-sets that give rise to the aptopic diathesis also have a role in the presentation of thin plaque disease.

Environmental explanations may better explain the association between thin-plaque psoriasis and skin cancer. It is plausible that thin plaque participants may have been treated with more light therapies; it is known that an increased exposure to psoralen UVA increases the incidence of squamous cell carcinomas in psoriasis patients (Stern and Lunder, 1998). A second possibility is that subjects with thick-plaque psoriasis are inherently more resistant to skin cancer. A recent study showed that patients with psoriasis may have fewer actinic keratoses (Paltiel *et al.*, 2004), and hence a decreased likelihood of developing non-melanoma skin cancers. Nickoloff (2004) proposes that psoriatic plaques are resistant to developing skin cancer owing to UV light triggering senescence in keratinocytes of psoriatic plaques. As thick-plaque psoriasis patients had more BSA affected in our cohort, they are possibly less likely to develop skin cancer than thin plaque patients simply because they have more plaques inherently resistant to skin cancers.

Limitations

As discussed above, our study has limitations. A major component of the UPI database relies on patient self-report and thus has an inherent recall bias. Patient classification of plaques or BSA, even with assistive measures, as well as physician induration scores are not objective measures; however, the ''gold standard'' of biopsying and photographing every patient is impractical and is not even performed in clinical trials. Determining presence or absence of nail disease and psoriatic arthritis also are areas of controversy. We did not have a rheumatologist confirm every case of psoriatic arthritis, and although we are very certain that we have not excluded patients with psoriatic arthritis, we may have included some patients with overlap, that is, they have both an inflammatory arthritis and a degenerative arthritis, and thus it is possible that misclassification of arthritis could have skewed our results. Nevertheless, using our study physicians, we have established an incidence of psoriatic arthritis of 27.4%, which is in line with previously published studies (Farber and Nall, 1974; Stuart *et al.*, 2002).

Conclusion

As the elucidation of the genetics of psoriasis continues, the phenotypic stratification of subtypes of psoriasis becomes increasingly important. Several studies have described phenotypic differences in psoriasis based on characteristics such as early and late age of onset (Henseler and Christophers, 1985; Swanbeck *et al.*, 1995; Ferrandiz *et al.*, 2002), facial psoriasis (Young Park *et al.*, 2004), or family history (Stuart *et al.*, 2002). The association between genetics and phenotype has been studied within and near HLA-Cw6 (Henseler and Christophers, 1985; Gudjonsson *et al.*, 2002; Asumalahti *et al.*, 2003; Gudjonsson *et al.*, 2003), for large- and small-plaque psoriasis (Lew *et al.*, 2004) and for psoriatic arthritis (Gudjonsson *et al.*, 2003). Ultimately, genome-based studies will determine the validity of stratification on morphological variants, such as thin- and thick-plaque psoriasis. It is our hope that genotype–phenotype associations will not only help elucidate the genetics of psoriasis but may also help predict response to treatment and relapse probability over time.

MATERIALS AND METHODS

The UPI was designed to collect phenotypic information on psoriasis patients to stratify phenotypes for more informative genotyping. The study was approved by the University of Utah Institutional Review Board, and patients enrolled from November 2002 to July 2004 were included in this analysis. All volunteers gave written informed consent, and the study was conducted according to the Declaration of Helsinki Principles. Patients were recruited through the dermatology clinics affiliated with the University of Utah and other dermatology clinics in the greater Salt Lake City area. Only those patients with confirmed psoriasis by Drs Krueger, Callis, or a trained research fellow, Drs Hansen or Papenfuss, were enrolled. The study enrollment procedure consisted of three parts. First, patients completed an enrollment questionnaire. Next, the patient was examined and questioned by a trained physician using a structured exam registry form. Last, DNA was isolated from peripheral blood and stored for future genotype analysis.

Questions pertinent to this study in the patient enrollment questionnaire included gender, identifying information, age, ethnicity, medical history (including other medical conditions), smoking, alcohol, family history, age of onset, and diagnosis, description of psoriasis when it first appeared, factors that improve or worsen their psoriasis, history of Koebner phenomenon (developing psoriasis at sites of skin injury), and typically affected body parts. The patient was queried using descriptions and specific questions as to determine whether they had a history of guttate, erythrodermic, generalized pustular, palmar/plantar pustular, only palmar/plantar disease (defined as at any time having only their palms and/or soles affected), or inverse psoriasis (defined as having any psoriasis at any time in the body folds, including the axilla, beneath the breast, abdominal folds, inguinal folds, or gluteal folds).

Psoriatic nail disease was determined by physician exam of the fingernails. Onycholysis, pitting (total of $\geqslant 5$ pits on fingernails) (Rich and Scher, 2003), subungual hyperkeratosis, and dystrophy were considered signs of nail disease. The patient was considered to have psoriatic arthritis based on the following criteria: (1) either the patient had been diagnosed as having psoriatic arthritis by a rheumatologist or (2) the patient presented with symptoms of an inflammatory arthritis and not those of degenerative arthritis and had evidence of enthesitis, morning stiffness lasting one hour or more, sacroiliac pain, characteristic joint deformities of the fingers and toes, and/or pauciarticular disease of the large joints.

BSA was determined by the palm method (the palm to the proximal interphalangeal joint, including the thumb, of the patient $\approx 1\%$ of the total BSA). The patient was asked to estimate their total BSA on enrollment and then to estimate their worst-ever BSA. The physician also assessed BSA on enrollment.

At enrollment, the physician recorded the severity of present lesions using the NPF Psoriasis Score, described elsewhere (Krueger *et al.*, 1999). Induration was scored from NPF induration score card, which has embossed elevations from 0 to 1.25 mm, where $0 = 0$ mm, $1 = 0.25$ mm, $2 = 0.50$ mm, $3 = 0.75$ mm, $4 = 1.0$ mm, and $5 \geqslant 1.25$ mm. Patient global assessment at enrollment was based on a scale of 0–5 with $0 =$ no psoriasis; $1 = 20\%$ as bad as ever; $2 = 40\%$ as bad as ever; $3 = 60\%$ as bad as ever; $4 = 80\%$ as bad as ever; and $5 =$ the worst their psoriasis has ever been. To determine the appearance of psoriasis at its worst, patients were asked to describe the typical erythema, scale, and induration of their worst untreated lesions. For this assessment, a standard set of photographs was given to the patients and the patient was asked to score their disease for erythema (0–5) and scale (0–5) based on the photograph that most closely resembled their psoriasis when at its worst. Induration of psoriasis plaques when at their worst was determined by asking the patient to describe their psoriasis at its worst as ''thick, indurated plaques with tenacious, thick scale'', ''thin plaques, light pink, with fine scale'', or ''in between the above (intermediate)''. Two analyses were performed to compare the physician induration score and patient-reported psoriasis plaque thickness. For those patients where at least 80% of their ''worst-ever psoriasis'' at enrollment (PGA score 4 or 5), a physician NPF induration score was performed at enrollment using the NPF card. The mean physician induration score was determined again for each patient thickness group; additionally, a Pearson's univariate correlation was performed between the physician and patient scores. Third, a retrospective chart review on those patients in the UPI who were in a prior clinical study where the PASI and/or NPF Psoriasis Score was performed. Prior NPF induration scores of 0–1 were considered ''thin'', 2 was considered ''intermediate'', and 3, 4, or 5 considered ''thick''; prior PASI induration scores of 0–1 considered ''thin'', 2 was considered ''intermediate'', and 3 or 4 considered ''thick''. Mean physician induration scores were again averaged for each of the three patient thickness groups and compared using analysis of variance.

Statistical analysis

Thin, intermediate, and thick groups were compared across continuous and categorical variables. Categorical variables were compared using χ^2 test. For continuous parametric variables, analysis of variance was used with the Tukey's *post hoc* comparison to determine if any significant differences existed between each of the groups. For non-parametric continuous variables, the Kruskal–Wallis and Mann–Whitney test was used. Data were presented as mean $\pm$ SD, except where specified in the results section. Pearson's correlation coefficients were calculated for the correlation analysis of BSA and for correlation analysis of patient and physician induration scores. The Cramer V correlation statistic was reported for the validation analyses (i.e., comparing thickness groups to physician-reported NPF scores and previous induration scores). *P*-values less than 0.05 were considered significant, except for the comparison of other diseases between thickness groups (see Table 2), where the Bonferoni correction was used for multiple comparisons.

CONFLICT OF INTEREST

The authors state no conflict of interest.

ACKNOWLEDGMENTS

We thank LineaGen inc. and the NPF for their support.

REFERENCES

Allen MH, Ameen H, Veal C, Evans J, Ramrakha-Jones VS, Marsland AM *et al.* (2005) The major psoriasis susceptibility locus PSORS1 is not a risk factor for late-onset psoriasis. *J Invest Dermatol* 124:103–6

Asumalahti K, Ameen M, Suomela S, Hagforsen E, Michaelsson G, Evans J *et al.* (2003) Genetic analysis of PSORS1 distinguishes guttate psoriasis and palmoplantar pustulosis. *J Invest Dermatol* 120:627–32

Bowcock AM, Cookson WO (2004) The genetics of psoriasis, psoriatic arthritis and atopic dermatitis. *Hum Mol Genet* 13(Spec No. 1):R43–55

Capon F, Trembath RC, Barker JN (2004) An update on the genetics of psoriasis. *Dermatol Clin* 22:339–47, vii

Christophers E (2003) Genotyping psoriasis. *J Invest Dermatol* 120:xvii

Farber EM, Nall ML (1974) The natural history of psoriasis in 5,600 patients. *Dermatologica* 148:1–18

Ferrandiz C, Pujol RM, Garcia-Patos V, Bordas X, Smandia JA (2002) Psoriasis of early and late onset: a clinical and epidemiologic study from Spain. *J Am Acad Dermatol* 46:867–73

Gottlieb AB (2003) Infliximab for psoriasis. *J Am Acad Dermatol* 49:S112–7

Griffiths CE (2004) Psoriasis: future research needs and goals for the twenty-first century. *Dermatol Clin* 22:493–9, x

Gudjonsson JE, Karason A, Antonsdottir A, Runarsdottir EH, Hauksson VB, Upmanyu R *et al.* (2003) Psoriasis patients who are homozygous for the HLA-Cw*0602 allele have a 2.5-fold increased risk of developing psoriasis compared with Cw6 heterozygotes. *Br J Dermatol* 148:233–5

Gudjonsson JE, Karason A, Antonsdottir AA, Runarsdottir EH, Gulcher JR, Stefansson K *et al.* (2002) HLA-Cw6-positive and HLA-Cw6-negative patients with Psoriasis vulgaris have distinct clinical features. *J Invest Dermatol* 118:362–5

Henseler T, Christophers E (1985) Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. *J Am Acad Dermatol* 13:450–6

Karason A, Gudjonsson JE, Jonsson HH, Hauksson VB, Runarsdottir EH, Stefansson K *et al.* (2005) Genetics of psoriasis in Iceland: evidence for linkage of subphenotypes to distinct Loci. *J Invest Dermatol* 124:1177–85

Krueger GG, Day RM, Duvic M, Elder JT (1999) New method being developed for assessing psoriasis. *Natl Psoriasis Found Prof Member Newslett* 5:4–5

Lew W, Lee E, Krueger JG (2004) Psoriasis genomics: analysis of proinflammatory (type 1) gene expression in large plaque (Western) and small plaque (Asian) psoriasis vulgaris. *Br J Dermatol* 150:668–76

Nickoloff BJ (2004) The skin cancer paradox of psoriasis: a matter of life and death decisions in the epidermis. *Arch Dermatol* 140:873–5

Paltiel O, Adler B, Herschko K, Tsukrov B, David M (2004) Are patients with psoriasis susceptible to the classic risk factors for actinic keratoses? *Arch Dermatol* 140:805–10

Rich P, Scher RK (2003) Nail psoriasis severity index: a useful tool for evaluation of nail psoriasis. *J Am Acad Dermatol* 49:206–12

Sagoo GS, Tazi-Ahnini R, Barker JW, Elder JT, Nair RP, Samuelsson L *et al.* (2004) Meta-analysis of genome-wide studies of psoriasis susceptibility reveals linkage to chromosomes 6p21 and 4q28–q31 in Caucasian and Chinese Hans population. *J Invest Dermatol* 122:1401–5

Samuelsson L, Enlund F, Torinsson A, Yhr M, Inerot A, Enerback C *et al.* (1999) A genome-wide search for genes predisposing to familial psoriasis by using a stratification approach. *Hum Genet* 105:523–9

Stern RS, Lunder EJ (1998) Risk of squamous cell carcinoma and methoxsalen (psoralen) and UV-A radiation (PUVA). A meta-analysis. *Arch Dermatol* 134:1582–5

Stuart P, Malick F, Nair RP, Henseler T, Lim HW, Jenisch S *et al.* (2002) Analysis of phenotypic variation in psoriasis as a function of age at onset and family history. *Arch Dermatol Res* 294:207–13

Swanbeck G, Inerot A, Martinsson T, Wahlstrom J, Enerback C, Enlund F *et al.* (1995) Age at onset and different types of psoriasis. *Br J Dermatol* 133:768–73

Taylor WJ (2002) Epidemiology of psoriatic arthritis. *Curr Opin Rheumatol* 14:98–103

Williamson L, Dalbeth N, Dockerty JL, Gee BC, Weatherall R, Wordsworth BP (2004) Extended report: nail disease in psoriatic arthritis – clinically important, potentially treatable and often overlooked. *Rheumatology (Oxford)* 43:790–4

Young Park J, Hyun Rim J, Beom Choe Y, Il Youn J (2004) Facial psoriasis: comparison of patients with and without facial involvement. *J Am Acad Dermatol* 50:582–4