

of Clinical Pathology, The Melbourne Medical School, The University of Melbourne, Australia^a; Melbourne Australia and Precision Medicine, School of Clinical Sciences at Monash Health, Monash University, Melbourne, Australia^b; and Cancer Epidemiology Division, Cancer Council Victoria, Victoria, Australia.ⁱ

Drs Lodge and Dharmage contributed equally to this article.

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Correspondence to: Adrian John Lowe, PhD, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, 207 Bouverie St, Carlton, Victoria 3052, Australia

E-mail: lowea@unimelb.edu.au

REFERENCES

1. Flohr C, England K, Radulovic S, et al. Filaggrin loss-of-function mutations are associated with early-onset eczema, eczema severity and transepidermal water loss at 3 months of age. *Br J Dermatol*. 2010;163:1333-1336.
2. Schuttelaar ML, Kerkhof M, Jonkman MF, et al. Filaggrin mutations in the onset of eczema, sensitization, asthma, hay fever and the interaction with cat exposure. *Allergy*. 2009;64:1758-1765.
3. Berg ND, Husemoen LL, Thuesen BH, et al. Interaction between filaggrin null mutations and tobacco smoking in relation to asthma. *J Allergy Clin Immunol*. 2012;129:374-380, 380.e1-e2.
4. Brown SJ, Relton CL, Liao H, et al. Filaggrin null mutations and childhood atopic eczema: a population-based case-control study. *J Allergy Clin Immunol*. 2008;121:940-946.e3.
5. Lowe AJ, Lodge CJ, Allen KJ, et al. Cohort profile: Melbourne Atopy Cohort Study (MACS). *Int J Epidemiol*. 2017;46:25-26.

Characteristics of postinflammatory hyper- and hypopigmentation in patients with psoriasis: A survey study



To the Editor: Although psoriasis is commonly associated with postinflammatory hyper- and hypopigmentation, their description remains limited. Postinflammatory hyperpigmentation appears to be more frequent than hypopigmentation.^{1,2} Interestingly, a pattern of hyperpigmentation called lentiginous hyperpigmentation has been described in areas of previously affected skin after various topical or systemic treatments.^{3,4} However, the literature remains speculative regarding the clinical factors associated with this phenomenon.

The aim of this monocentric study was to describe the prevalence of hyper- and hypopigmentation in patients with psoriasis and their association with their demographic and clinical features (see "Patients and Methods" in the Supplemental Appendix 1; available via Mendeley at <https://doi.org/10.17632/r5dxjnn8fc.1>). The study included 459 patients: 287 men and 172 women (Table 1). The mean age was 49.9 years ($\sigma = 16.2$ years). The mean duration of psoriasis was 19.8 years ($\sigma = 18.2$). A total of 81.5% of patients had psoriasis vulgaris (Supplemental Appendix 2; available via Mendeley at <https://doi.org/10.17632/r5dxjnn8fc.1>). The prevalence of skin hyper- and hypopigmentation was 23.7%. Overall, 63 (13.7%) and 46 (10.0%) patients developed skin hyperpigmentation or hypopigmentation, respectively. Hyper- and hypopigmentation were observed only in areas previously affected by psoriasis. Hypopigmented lesions showed a homogeneous pattern with a sharp border and the presence of residual pigmentation confirmed by Wood's lamp examination (Fig 1, A-D). Two clinical patterns of hyperpigmentation were observed: (1) the lentiginous or nevus spilus-like pattern, characterized by the presence of multiple lentigines on a hyperpigmented background (Fig 1, C), and (2) a homogeneous pattern with well-defined borders (Fig 1, D). Hyperpigmentation was significantly associated with darker Fitzpatrick skin phototype (\geq IV) (odds ratio [OR], 3.99; 95% confidence interval [CI], 1.60-10.00). In contrast, no significant association was found between hypopigmentation and skin phototype. Hypopigmentation was significantly observed with younger age (OR, 0.96; 95% CI, 0.93-0.99). No significant association was found between other clinical features including BMI, cardiovascular risk factors, and hyper- and hypopigmentation (Supplemental Appendix 2). Although univariate analyses showed no significant

Table I. Demographic and psoriasis features of patients included

Features	Total	Pigmentation disorders		No pigmentation disorder
		Hyperpigmentation	Hypopigmentation	
Demographic features				
n (%)	459	63 (13.7)	46 (10)	350 (76.6)
Age, mean (σ), y	49.9 (16.2)	49.7 (17.5)*	40.6 (15.3)*	51.2 (15.7)*
Sex ratio, male/female, n (%)	287 (62.5)/ 172 (37.5)	44 (70)/19 (30)	20 (43.5)/26 (56.5)	223 (63.7)/ 127 (36.3)
BMI, kg/m ² , mean (σ)	27.2 (6.1)	27.1 (5.6)	27.2 (6.3)	27.2 (6.1)
Psoriasis features				
Years since psoriasis onset, mean (σ)	19.8 (18.2)	19.7 (22.5)	17.3 (12.1)	20.1 (18.1)
DLQI mean(σ)	4.5 (6.3)	2.7 (4.2)	5 (5.5)	4.1 (6.6)
PASI mean(σ)	4.2 (7.1)	3.8 (5.1)	3.8 (3)	4.4 (7.8)
Phototype, n (%)				
I	9	0	1 (11.1)	8 (88.1)
II	112	18 (16.1)	13 (11.6)	81 (72.3)
III	266	31 (11.6)	26 (9.7)	209 (78.6)
IV	34	9 (26.5)*	6 (17.6)	19 (55.9)*
V	3	3 (100)*	0	0*
VI	2	1 (50)*	0	1 (50)*
Autoimmune disease, n (%)				
Atopic dermatitis	8	0	1 (12.5)	7 (87.5)
Thyroiditis	10	2 (20)	2 (20)	6 (60)
Alopecia areata	1	0	0	1 (100)
Other	13	2 (15.4)	2 (15.4)	9 (70.2)
Treatment duration, mo, mean (σ)	32.1 (35.5)	26.8 (33.4)*	16.4 (27.8)*	35 (36.2)*
PASI75 after 4-8 months of treatment, n (%)	170	27 (15.9)	18 (10.6)	125 (73.5)
PASI90 after 4-8 months of treatment, n (%)	112	16 (14.3)	7 (6.3) [†]	89 (79.4) [†]
Previous or current NB-UVB therapy, n (%)	259	40 (15.4)	31 (12)	188 (75.6)
Visual numerical scale for pigmentation disorder, mean (σ)	—	1.9 (2.6)	2.1 (2.8)	—

BMI, Body mass index; DLQI, Dermatology Life Quality Index; NB-UVB, narrow-band ultraviolet B; PASI, Psoriasis Area and Severity Index; PASI75, 75% reduction in Psoriasis Area and Severity Index; PASI90, 90% reduction in Psoriasis Area and Severity Index.

* $P < .01$.

[†] $P < .05$.

association between the occurrence of hyper- and hypopigmentation and the treatment received by patients, multivariate regression analysis showed that past or current treatment with phototherapy was significantly associated with hyperpigmentation (OR, 2.21; 95% CI, 1.05-4.67). Hypopigmentation was significantly associated with a shorter course of treatment ($P = .0053$) and negatively associated with a 90% reduction in Psoriasis Area and Severity Index (OR, 0.28; 95% CI, 0.10-0.72) and age (OR, 0.96; 95% CI, 0.93-0.99). Overall, hyper- and hypopigmentation were not associated with high impact on quality of life, as assessed by the use of a visual analog scale. Although underestimated in the literature, the occurrence of hyper- and hypopigmentation appears to be frequent. These abnormalities are consistently located on areas previously affected by psoriasis. Patients with higher Fitzpatrick skin phenotype had an increased risk of developing hyperpigmented lesions. Our results suggest that hyper- and/or

hypopigmentation mostly occur independently of the treatment for psoriasis, except for phototherapy. Hypopigmentation developing shortly after the beginning of treatment suggests that it is restricted to the first months of therapy and may resolve afterward, in contrast to hyperpigmented lesions, which may persist longer. The development of hyper- and hypopigmentation could be explained by the skin inflammatory environment associated with increased production of tumor necrosis factor- α and interleukin 17, which have been shown to affect melanogenesis.⁵

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S  verine Amico, MD,^a Thomas Barnetche, PhD,^b Laure Dequidt, MD,^a Antoine Fauconneau, MD,^a Emilie G  rard, MD,^a Lucile Boursault, MD,^a Katia Boniface, PhD,^c Anne-Sophie Darri-
gade, MD,^a and Julien Seneschal, MD, PhD,^{a,c}

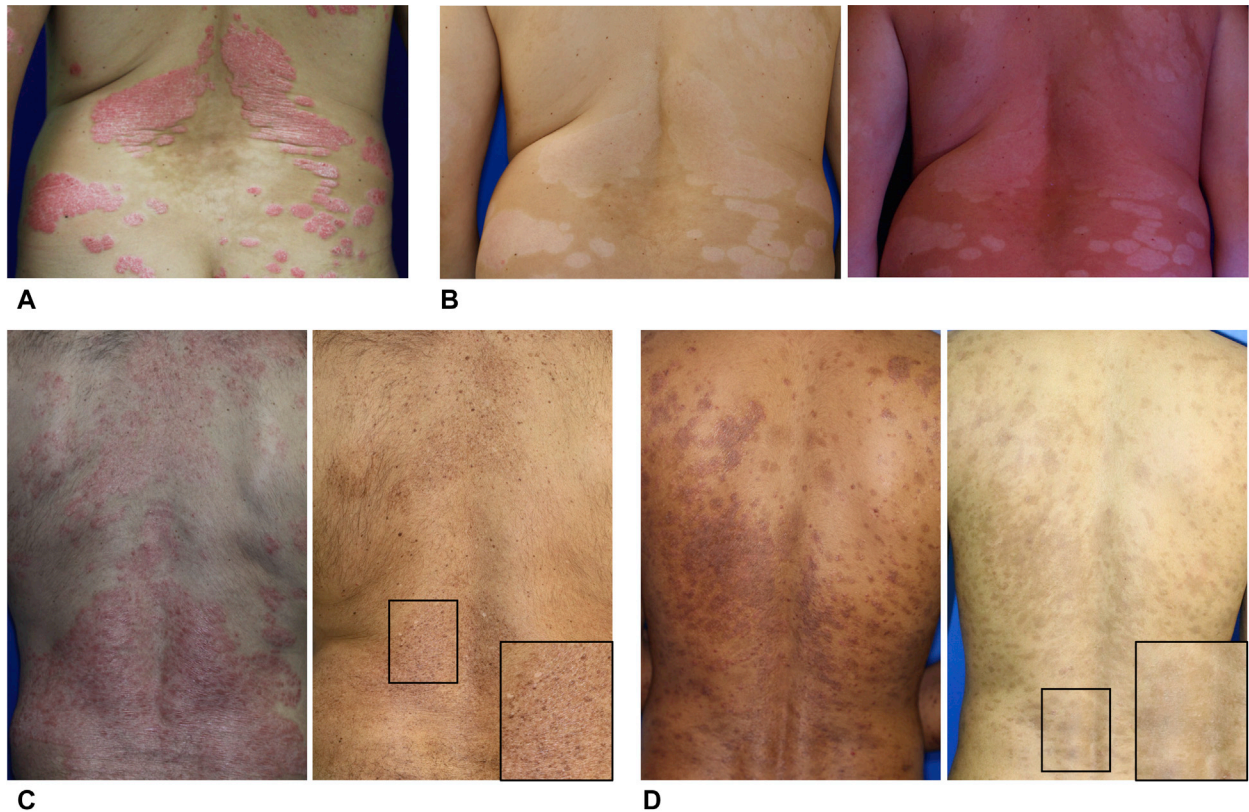


Fig 1. **A** and **B**, Hypopigmentation pattern. Lesional skin before the initiation of systemic therapy. Hypopigmented lesions shown under normal light and under UV light, observed on areas of previously affected psoriasis skin after 6 months of systemic therapy. Wood's lamp examination of hypopigmented skin showing well-defined borders of lesions. **C** and **D**, Hyperpigmentation patterns. **C**, Lentiginous hyperpigmentation pattern occurring on areas previously affected by psoriasis. **D**, Homogeneous hyperpigmented pattern occurring on areas previously affected by psoriasis.

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From the Department of Dermatology, National Reference Center for Rare Skin Disorders, Hôpital Saint-André, Centre Hospitalo-Universitaire (CHU) de Bordeaux^a; Department of Rheumatology, National Reference Center for Severe Systemic Autoimmune Diseases, Hôpital Pellegrin, CHU de Bordeaux^b; and Inserm U1035, Biothérapie des Maladies Génétiques, Inflammatoires et Cancers (BMGIC), Immunodermatology team, University of Bordeaux, Bordeaux, France.^c

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Correspondence to: Julien Seneschal, MD, PhD, Department of Dermatology, Hôpital Saint-André, CHU de Bordeaux, Bordeaux, France

E-mail: julien.seneschal@chu-bordeaux.fr

REFERENCES

1. Narumol S, Indermeet K, Suteeraporn C, Lim HW, Hamzavi I. Postinflammatory hyperpigmentation: a comprehensive overview. *J Am Acad Dermatol.* 2017;77(4):591-605.
2. Saleem MD, Oussedik E, Schoch JJ, Berger AC, Picardo M. Acquired disorders with depigmentation: a systematic approach to vitiliginoid conditions. *J Am Acad Dermatol.* 2019;80:1215-1231.
3. Micieli R, Alavi A. Eruptive lentiginosis in resolving psoriatic plaques. *JAAD Case Rep.* 2018;4(9):924-929.

4. Dogan S, Atakan N. Multiple lentiginos confined to psoriatic plaques induced by biologic agents in psoriasis therapy: a case and review of the literature. *Cutan Ocul Toxicol.* 2015;34(3): 262-264.
5. Wang CQ, Akalu YT, Suárez-Fariñas M, et al. IL-17 and TNF synergistically modulate cytokine expression while suppressing melanogenesis: potential relevance to psoriasis. *J Invest Dermatol.* 2013;133(12):2741-2752.

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Temporal trends in primary and secondary skin cancer prevention in the United States



To the Editor: Skin cancer incidence is rising in the United States despite public health efforts encouraging skin cancer prevention.¹ We analyzed temporal trends of skin-cancer related primary (concerned with disease prevention) and secondary (concerned with early disease detection) preventive behaviors to look for potential areas for improvement.

The National Health Information Survey (NHIS) was examined over a 10-year period from 2005 to 2015.² The NHIS conducts representative population-based annual interviewing of the adult US population and had response rates of 70.1% to 80.7% during the examined period.² Our outcomes of interest were use of sun-protective measures

(including sun avoidance, protective clothing, and sunscreen use), lifetime history of full-body skin examination by a physician, and histories in the past year of indoor tanning and 2 or more sunburns. Specifically, use of sun-protective measures were defined as use always or most of the time when outside for more than 1 hour on a warm, sunny day. Protective clothing included at least 1 of the following: long pants, hat, or long-sleeved shirt. A small percentage of individuals answered the sun protection questions by stating that they don't go out in the sun.² These individuals and those with unknown or missing responses were excluded from the analysis.²

Multivariable logistic regression analyses were used to assess the association between time period and weighted prevalence of sun-protective behaviors, adjusting for sex, region, health insurance, alcohol use, smoking status, education, personal and family histories of skin cancer, income, race, and skin reaction to the sun. *P* values were adjusted for multiple comparisons. Because of substantial missing data for income, NHIS imputed data were used.²

The unweighted study included a total of 67,471 individuals. From 2005 to 2015, the unadjusted and adjusted prevalence of most skin cancer—preventive behaviors rose, including sun avoidance, sunscreen use, and full-body skin examination, with the

Table I. Unadjusted and adjusted prevalence of sun protective behaviors by survey year

	Year, unadjusted prevalence, % (95% CI)			Adjusted		Year, adjusted prevalence, % (95% CI)			Adjusted	
	2005	2010	2015	<i>P</i> _{trend} value*	<i>P</i> _{2015 vs 2005} value†	2005	2010	2015	<i>P</i> _{trend} value*,‡	<i>P</i> _{2015 vs 2005} value†
Sun avoidance	31.1 (30.2-32)	35.4 (34.5-36.3)	37.5 (36.5-38.4)	<.001	<.001	31.7 (30.9-32.6)	35.5 (34.7-36.4)	36.8 (35.9-37.6)	<.001	<.001
Protective clothing	35.5 (34.7-36.3)	38.5 (37.5-39.4)	37.5 (36.6-38.4)	<.001	.006	35.9 (35.1-36.7)	38.4 (37.5-39.2)	37.2 (36.3-38.1)	<.001	.098
Sunscreen ASE	30.6 (29.8-31.3)	32.7 (31.7-33.6)	35.5 (34.7-36.4)	<.001	<.001	31.5 (30.7-32.2)	33.1 (32.2-34)	34.3 (33.5-35.1)	<.001	<.001
Full body skin exam	18.1 (17.4-18.7)	22 (21.2-22.8)	23.6 (22.9-24.4)	<.001	<.001	19.0 (18.4-19.6)	22.4 (21.7-23.1)	22.4 (21.7-23)	<.001	<.001
Indoor tanning	14.8 (14.1-15.5)	6.2 (5.7-6.7)	3.9 (3.5-4.3)	<.001	<.001	14.1 (13.5-14.8)	6.2 (5.7-6.7)	4.1 (3.8-4.5)	<.001	<.001
Sunburn	18.7 (18.1-19.3)	21.0 (20.2-21.7)	19.6 (18.8-20.4)	<.001	.198	18.2 (17.7-18.8)	21.1 (20.4-21.8)	19.9 (19.2-20.7)	<.001	.001

Adjusting covariates include sex, census region, health insurance coverage, alcohol use, smoking status, education level, personal history of skin cancer, family history of skin cancer, income, race, and skin reaction to the sun. Bold *P* values are statistically significant at the .05 level.

*Wald tests based on the logistic regression were performed to test for any change in log odds over 2005, 2010, and 2015.

†Pairwise Wald tests based on the logistic regression were performed to test for change in log odds in any two time points. *P* values were adjusted for multiple comparisons using Benjamini & Hochberg (1995).⁵

‡Median *P* rule was used to obtain the final adjusted *P* values due to multiple imputation for income.