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Lifetime prevalence and characteristics of the 'sun-allergy' polymorphic light eruption in Europe

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Abstract

Although polymorphic light eruption (PLE) is the most common idiopathic photodermatosis, epidemiological data are sparse. Former investigations led to the assumption that there is a latitudinal gradient in the prevalence of PLE, i.e. decreasing toward the equator. We performed a survey to evaluate the latitudinal impact on prevalence, the frequency of eruption in springtime and during sunny holidays, and further characteristics of PLE in Europe.

The study was conducted by 6 dermatology centres from Finland, Germany, the Netherlands, the United Kingdom, France and Greece (61-38° northern latitude). Data were obtained largely from indoor working hospital staff, using standardised questionnaires.

Eighteen percent of the 6,895 participants reported experiencing an itching rash/abnormal skin reaction after sun exposure that was distinct from sunburn. Women were nearly three times more often affected than men, i.e. 23% vs 9%, but large differences were found between Athens (Greece), 26% vs 15%, and Turku (Finland), 14 % vs 2%. PLE rashes were reported to occur in springtime in 7-10% of the interviewees in each country, without any indication of a latitudinal gradient (highest frequencies in Finland and Greece). The frequency of PLE during sunny holidays was very low among participants from Finland (9%) in comparison to other countries (14-20%). One out of 3 people with skin type I had experienced PLE, and this fraction dropped to 1 out of 10 with skin types IV-VI. Skin type distributions were similar between countries.

Apparently, photodermatoses are highly prevalent in Europeans and deserve greater recognition. There is no evidence of increasing prevalence toward higher latitudes, i.e. with greater seasonal modulation of ambient UV radiation. Strikingly, prevalence is highest in Greece, the most southern country. Our data show that gender, skin type and behavioural factors, namely exposure during sunny holidays, are of paramount importance to PLE prevalence.

Introduction

Sun-provoked skin reactions (photodermatoses) constitute one of the most prevalent forms of skin disease and have a medical and socio-economic impact on the lives of millions of people. The most common idiopathic photodermatosis is polymorphic light eruption (PLE or PMLE) which is currently poorly investigated, and largely neglected as a public health problem. There is evidence to suggest that PLE has an underlying immune aetiology¹, with a strong genetic influence.² The disorder is characterized by recurrent pruritic papules, vesicles and plaques. The type of skin lesion varies between patients, hence the term polymorphic. However, in each patient, a single morphology predominates and reoccurs. The rash appears with a delay of several minutes to hours after ultraviolet (UV) radiation exposure and it persists for a few days up to a couple of weeks. The rash subsides completely in the absence of further UV exposure, without scar formation. The V of chest, neck, and the upper and lower extremities are most commonly involved. Most patients suffer from this susceptibility to UV radiation for many years.^{3;4}

Although PLE is a common skin disease, published epidemiological data are sparse. From interviews conducted among 550 visitors of shopping malls in Perth and Ballarat (Australia) and in London (UK) the prevalence of PLE was estimated to be 5.2%, 3.6% and 14.8%, respectively.⁵ In a survey among 397 employees of a Swedish pharmaceutical company, symptoms of PLE were reported to occur by 21%.⁶ Finally, a study of 271 subjects conducted in Boston (USA) reported a prevalence of 11%.⁷ These investigations led to the assumption that the prevalence of PLE is lower in countries nearer to the equator. However, reliable data concerning this hypothesis are lacking as well as data on characteristics and treatment of PLE. In the present large-scale cross-sectional study, we performed a standardized survey on prevalence, symptoms and treatment of PLE in five European countries at different geographical latitudes.

Methods

Study design and participants

Ethical approval for the study was gained at each participating institution. The study was designed as a multi-centre observational study with in-person interviews in a sample of the adult population. We agreed that each centre would include at least 1000 subjects. One or at most two researchers at each site conducted the interviews. All studied subjects were indoor workers, mainly hospital staff of the participating centres including nurses, cleaning staff, craftsmen and kitchen staff. A group of factory workers (mainly males) was included in the data from Heidelberg. The participating centres were dermatological departments of the Universities in Athens (Greece), Besançon (France), Heidelberg (Germany), Leiden (the Netherlands), Manchester (United Kingdom) and Turku (Finland). The

northernmost city was Turku with a geographical latitude of 60.5°, followed by Manchester with 53.5°, Leiden 52°, Heidelberg 49.5°, Besançon 47° and Athens 38°.

The questionnaire

A standardized, simple and short one-sided questionnaire was developed by dermatologists with special expertise in photodermatology and dermatoepidemiology. In the first part of this questionnaire the questions regarding skin type, age and sex were asked. The main question of this first part was whether participants had developed an itching rash/abnormal skin after sun exposure, which they did not regard as sunburn (a so-called 'sun allergy'). If interviewees had not developed such a rash in their history, further interviewing was terminated. If they replied with 'yes' or 'do not know' they were asked to continue with another 13 questions which formed the second part of the questionnaire, including questions whether a photodermatosis has been diagnosed by a physician; questions on previous treatment of this photodermatosis; occurrence in springtime and during sunny holidays; the presence of itch; other family members afflicted; course of the disease; quality of life; age at first appearance of the rash; time of appearance after sun exposure; duration of the rash. Answers of the first part of the questionnaire were used to describe the study population and to calculate the prevalence. Analysis of the clinical features and treatment of PLE was performed using answers obtained from the second part of the questionnaire. All participants were personally asked whether they agreed to fill in a short anonymous questionnaire about sun allergies. In each centre the response rate was > 90%.

Statistics

To establish the accuracy of the findings, sample size estimations were performed. To estimate a prevalence of 10% with an accuracy of $\pm 2\%$, a sample size of about $n = 1000$ was needed. All data were collected between March 2003 and May 2004. Excel (Microsoft, Redmond, WA, USA) was used for data filing. All statistical analyses were performed in Heidelberg using SASTM 9.1 Win (Cary, NC, USA). Categorical data were summarised by means of absolute and relative frequencies (number of counts and percents). The distribution of quantitative data was inspected by means of the following summary statistics: the number of observations, the arithmetic mean, and standard deviation, minimum, median and maximum. The observed prevalences were standardised by age and sex to take into account the difference between the samples and the population structure.

Results

Overall 6,895 subjects were included. Most of the subjects were women (4,163; 62.8%) and a smaller proportion were men (2,471; 37.2%). 261 answers on gender were missing. The mean age of the study participants was 37.5 ± 12.1

(standard deviation) years. This ranged from 28.9 ± 12.4 years in Besançon (F) to 42.9 ± 11.0 years in Turku (FI). Specified data per country are given in more detail in tables 1 and 2A and 2B.

Lifetime prevalence

Total cohort

As shown in table 2, out of the total of 6,836 (59 missing due to incomplete questionnaires) included subjects, 1,235 gave a history consistent with the diagnosis of PLE. On the basis of these data, the suspected lifetime prevalence of PLE was 18.0% in the study population and 18.2% after age and sex standardisation.

Prevalence at individual centres

After standardising for age and sex, we found similar prevalences among centres ranging between 17 and 19.5%, apart from a low prevalence of 13.6% in Turku (FI), see table 2A (crude percentages ranged from 16.1 to 22.8, with a low of 12% in Turku).

PLE rashes during springtime were reported to occur (always or sometimes) by equal proportions of the total interviewed population per country (between 7 and 10%), without any indication of a latitudinal gradient (with the highest frequencies of 10% in Finland and Greece). The frequency of PLE during sunny holidays was strikingly low among Finnish participants (9%), compared to people from other countries, where it ranged between 14 and 20% (see table 2A). This explained the overall low prevalence of PLE in Finland. Among people with PLE, most (76 to 93%) suffered from the rashes during sunny holidays.

Gender

The life time prevalence of PLE among women, standardized for age, was 22.2% (crude prevalence 23.3%) which was more than double the 9.8% (9.2%) found in men. An exceptionally low prevalence among females was found in Turku (FI) (15.0%). The prevalence of PLE among men was exceptionally high in Athens (GR) (16.6%). This resulted in a relatively low female/male ratio (1.3) in Athens, compared to other countries (see table 2A).

Skin type

People with skin type I (according to Fitzpatrick) had the highest prevalence of PLE: 33.4% in women and 28.6% in men. These percentages declined in skin type II to 30.8% in women vs 15.0% in men, in skin type III to 18.9% in women vs 7.0% for men. Subjects with skin type IV had the lowest prevalence with 11.2% in women compared to 4.0% in men. The prevalence among different skin types showed a significant trend (Cochran-Armitage Trend Test; $p < 0.001$).

Table 1. Demographic data of the total survey population

	Athens GR	Besançon F	Heidelber g	Leiden NL	Manchester UK	Turku FI	Total
Participants	1,263	980	1,634	1,034	984	1,000	6,895
Age in years	36.7 ± 11.8	28.9 ± 12.4	38.7 ± 10.6	38.1 ± 11.4	38.9 ± 11.3	42.9 ± 11.0	37.5 ± 12.1
Skin Type							
I	96 (7.7)	56 (5.8)	26 (1.7)	40 (3.9)	100 (10.8)	52 (5.2)	370 (5.5)
II	341 (27.2)	296 (30.7)	358 (22.8)	284 (27.8)	306 (32.9)	331 (33.2)	1,916 (28.4)
III	661 (52.8)	524 (54.3)	1,090	590 (57.8)	412 (44.4)	546 (54.8)	3,823 (56.8)
≥IV	155 (12.4)	89 (9.2)	98 (6.2)	106 (10.4)	111 (11.9)	67 (6.7)	626 (9.3)
missing data	10	15	62	14	55	4	160
No. of females	744 (59.1)	752 (76.7)	553 (34.8)	491 (58.4)	778 (80.6)	845 (84.5)	4,163 (62.8) ¹

Table 2. A: PLE in total survey population; B: Characteristics of PLE patients specified

A	Athens GR	Besançon F	Heidelber g	Leiden NL	Manchester UK	Turku FI	Total
Reporting PLE	273 (19.5)	169 (17.5)	256 (18.9)	201 (17.0)	217 (17.3)	119 (13.6)	1235 (18.2)
Female/male ratio	1.3	4.0	3.1	3.0	2.2	3.1	2.3
PLE in springtime²	130 (10.3%)	64 (6.5%)	109 (6.7%)	94 (9.1%)	65 (6.6%)	101 (10.1%)	563 (8.2%)
PLE during sunny	240 (19.0%)	152	232	179	201 (20.4%)	91 (9.1%)	1095 (15.9%)
B							
Diagnosed by a physician	121 (44.3)	74 (43.8)	74 (28.9)	47 (23.4)	18 (8.3)	12 (10.1)	346 (28.0)
of which by a dermatologist	87 (31.9)	46 (27.2)	41 (16.0)	10 (5.0)	3 (1.4)	5 (4.2)	192 (15.5)
Any treatment	123 (45.1)	97 (57.4)	97(37.9)	67 (33.3)	94 (43.3)	79 (66.4)	557 (45.1)
steroid creams	73 (26.7)	39 (23.1)	44 (17.2)	30 (14.9)	25 (11.5)	61 (51.2)	272 (22.0)
steroid tablets/injections	0 (0)	25 (14.8)	2 (0.8)	8 (4.0)	0 (0)	2 (1.7)	33 (2.7)
phototherapy	7 (2.6)	27 (16.0)	11 (4.3)	1 (0.5)	0 (0)	4 (3.4)	50 (4.0)
Itching during rash	231 (84.6)	154 (91.1)	233 (91.0)	184 (91.5)	188 (86.6)	115 (96.6)	1,105 (89.5)
Age of onset in years	27.9 ± 10.4	21.3 ± 11.5	26.2 ± 10.7	22.3 ± 11.2	24.1 ± 10.6	23.9 ± 12.2	24.7 ± 11.2
Reduced Quality of Life	109 (40.0)	45 (26.9)	87 (34.1)	16 (7.9)	39 (17.9)	27 (23.1)	322 (26.2)

Data presented as N (%) or mean ± SD; ¹overall 261 missing data on gender; ²PLE reported to occur 'sometimes and always'

Medical diagnoses of PLE

To the question whether their 'sun allergy' had been diagnosed by a physician, 346 subjects (28% of the people reporting PLE) answered yes (see table 2B). The highest percentages of PLE diagnosed by physicians (> 40%) were found in Athens and Besançon, and the lowest (around 10%) in Manchester and Turku. An additional question established that often (40-70%) the consulted physician had been a dermatologist, except in Manchester and Leiden, where only around 20% of the consulted physicians were dermatologists. After standardising for age and sex, in 6.0% of the study population the diagnosis of PLE was confirmed by a physician (Athens 11.2%, Besançon 8.9%, Heidelberg 6.4%, Leiden 5.6%, Manchester 2.6%, Turku 1.7%).

Age of onset

Subjects were asked about their age at first appearance of the 'sun allergy'. The mean age of onset was 24.7 ± 11.2 years for all centres (ranging from 21.3 ± 11.5 years in Besançon (F) to 27.9 ± 10.4 in Athens (GR); see table 2B).

Treatment

Out of 1,235 subjects with suspected PLE, 272 (22.0%) had been treated with steroid creams. Topical steroids were used most frequently in Turku (FI) ($n = 61$; 51.2%). In other centres the frequency was much lower (11-27%). A majority (55%) had never applied any treatment (see table 2B).

Itching

Itching is the predominant symptom. 90% complained of itching during their 'sun allergy' with a similar distribution in all centres (see table 2B).

Global quality of life

The quality of life due to PLE was reported to be reduced between 40% in Athens (GR) and only 8% in Leiden (NL) (see table 2B).

Discussion

This study has investigated the prevalence and characteristics of PLE in 6 European countries ranging geographically from Scandinavia to the Mediterranean. We found an estimated PLE prevalence of 18% across Europe, based on interviews with 6,895 people. This finding is comparable with former although much smaller European surveys held in Stockholm (Sweden) (21%) and London (UK) (14.8%).^{5,6} 'Sun-allergy' is quite possibly the commonest skin disorder affecting Europeans, and deserves greater recognition.

Apart from the commonly occurring PLE, idiopathic photodermatoses include rare conditions associated with more severe symptoms, such as actinic prurigo, chronic

actinic dermatitis and solar urticaria.⁹ Photosensitivity can also occur in rare genetic and/or biochemical conditions,¹⁰ and can be precipitated by medication.^{11;12} In this survey we have particularly focussed on the detection of PLE, but we can not exclude that a limited number of responders were actually suffering from other photodermatoses. Questions to differentiate PLE from other photodermatoses were included (age of onset, delay to onset of rash following sun-exposure, duration of episodes, itch). In a review of photosensitivity patients seen at the specialist photodermatology unit in Athens, 65% of the patients were reported to suffer from PLE, 18% had been diagnosed with solar urticaria, while the diagnosis of other idiopathic photodermatoses was made in < 1% to 4% of subjects.¹³ Woong and Khoo examined the spectrum of photodermatoses in several photodermatology units.¹⁴ Again, it was found that the most common idiopathic photodermatosis was PLE, affecting between 38% (in Scandinavia) and 22% (in Australia) of all phototested patients,^{15;16} and this was corroborated by other centres.¹³⁻¹⁷ Considering that many people with PLE, in contrast to those with the rarer photosensitivity disorders have mild symptoms and therefore do not consult dermatologists, we conclude that the large majority of subjects in our study suffer from PLE and not from other photodermatoses.

In our study, women were two to three times more often affected than men (standardised prevalence ratio of female/male= 2.3), and this sex ratio was skin type dependent with an decreasing trend towards skin type IV. Surveys conducted in Stockholm (Sweden) and Boston (USA) presented similar results.^{6;7;18} Only Athens was an outlier with a relatively low female/male ratio (1.3) compared to other countries. Increasing skin phototype correlated with a decreased prevalence of photodermatoses and this showed a significant trend, corroborating data from smaller studies.^{5;6;19;20} An explanation for this finding is that men generally have a higher threshold for expression of the disorder, but that in sunnier countries, i.e. under conditions of higher UV exposure, their sun seeking behaviour and clinical expression of PLE approximates that of women. Genetic differences could potentially play a role.

Earlier surveys supported the contention that PLE is more common in temperate climates than nearer the equator. In contrast, in our larger population sample, we found the highest prevalence of photodermatoses in the most southern city, i.e. Athens (19.5%, latitude 38°), and the lowest in the most northern city, i.e. Turku (13.6%, latitude 60.5°). All Middle European centres had prevalences between 17% and 18.9%. A small survey in Australia and England found a prevalence of PLE of only 3.6% in Ballarat, Australia (latitude 37.5°), which contrasts strikingly with that of Athens although the latitude and distribution of skin types are similar.⁵ Our data therefore did not confirm the former hypothesis that prevalence of PLE reflects a higher tendency to lose skin UV adaptation during wintertime in countries with temperate climates than in tropical and subtropical climates. In contrast, an equal proportion of people from Finland and Greece reported to suffer from PLE during springtime, suggesting that the UV

radiation is equally sufficient to trigger the rashes in both countries, despite possible differences in winter-time loss of UV adaptation. Moreover, we found that PLE rashes occurred in an exceptionally low percentage in Finnish interviewees during sunny holidays. However, in this study we have not investigated whether the sunny holidays were in the patient's own country or abroad. If the sunny holidays are spent mostly in the patient's own country, the data may reflect a difference in the ratio of UVA/UVB between countries.

Generally, for those living in northern Europe, sunny holidays are holidays abroad, and they gravitate to the Mediterranean. These data suggest that behavioural factors, such as sun-seeking holidays, are more likely to affect the PLE prevalence than the intensity of ambient UV radiation per se.

We found that only 28% of all cases with PLE had been diagnosed by a physician and that of these, 55% was seen by a dermatologist. These observations suggest a wide spectrum of severity, consistent with clinical observations of the disorder.¹⁸ While many sufferers are anticipated to have a high threshold of UV sensitivity, others may have consulted a physician because their UV sensitivity severely affected their quality of life. Among centres, large differences were found in the number of patients that had consulted a dermatologist for their sun allergy. This probably reflects the differences in organisation of the local health care systems. In Athens, Besançon, and Heidelberg 16-32% of patients, had consulted a dermatologist. On the other hand, only 1-5% of all PLE suffering subjects from Manchester, Turku and Leiden had consulted a dermatologist. In the latter countries the dermatologists mostly practice in hospitals and there is not a dense network of dermatologists available for consultation, and/or a referral from a general practitioner is first needed in order to consult a medical specialist. These data also suggest that the majority had only a mild form of PLE which did not severely affect their daily lives. Analysis of answers to a global question concerning the impact of the condition on quality of life revealed that people in Athens were most severely affected and people from Leiden least. A reasonable explanation for this would be the climatological differences between Greece and the Netherlands but other factors could also play a role (e.g. psychological, social).

We conclude that photosensitivity is highly prevalent in Europe. Our study is the first large scale epidemiological study in Europe, with a consistent standardized approach, which led to novel findings supplementing previous much smaller surveys, and negating unwarranted inferences about latitudinal gradients. The majority of cases reporting 'sun-allergy' are most likely suffering from the condition PLE. There is no evidence of increasing prevalences toward higher latitudes, e.g., where more striking seasonal changes in ambient UV radiation may cause severe loss of UV adaptation. Greeks are most affected, with a high prevalence in both males and females compared to other European countries. They live in a climate that may aggravate their disease more easily. Moreover, our data suggest that sun

exposure behaviour during sunny holidays is likely to affect most strongly the overall prevalence of PLE. Future studies may focus on the precise conditions under which PLE occurs (e.g., sudden or repeated overexposure). Such data could provide clues on the mechanisms behind provocation of PLE, and the lack of 'UV adaptation' in PLE patients.

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