

ORIGINAL ARTICLE

Dermatological future of european patients with atopic dermatitis

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Abstract

Background The dermatological becoming of children presenting with atopic dermatitis (AD) is not well known.**Objective** We performed a study on the presence of AD and other dermatological diseases in subjects with a previous history of AD.**Methods** An opinion poll was conducted in eight countries through a telephone interview: Belgium, France, Germany, Greece, Italy, Portugal, Spain and Switzerland.**Results** Among 4369 interviewees, 12.25% declared a history of AD in infancy and 12.4% declared to suffer from a dermatological disease (27% of patients had a history of AD and 10.3% did not have it). Current declared cases of atopic eczema or contact eczema were more frequent in patients with previous history of AD (39.3% vs. 21.5%), whereas these patients appeared less affected by rosacea (2.9% vs. 7.9%). Some differences were observed between different countries.**Conclusion** The main interests of this study are the large number of subjects, originating from eight different countries, and its focus on the dermatological future of patients with AD, which is not limited to AD itself.

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Keywords

atopic dermatitis, epidemiology, Europe, natural history

Conflicts of interest

Sami Boussetta, Pierre Shoonemann and Charles Taieb are employees of the Pierre Fabre Group. Laurent Misery is consultant for Abbott, Astellas, Cogniz, Galderma, Johnson & Johnson, Leo, Pierre Fabre, Schering-Plough, Stiefel, UCB, Wyeth.

Introduction

Atopic dermatitis (AD) is the inflammatory skin disorder associated with atopy.¹ Although it is very frequent, and easily diagnosed, diagnostic criteria are currently the subject of debate.² Its prevalence is increasing.³ In 1935, Hill and Sulzberger reported a natural history of the recently defined 'atopic dermatitis', with a continuum from infancy to adult ages.⁴ Incidence and severity of AD decrease with the advancing age of the patient.⁵

The burden of AD is heavy and its impact on the quality of life of patients and their surroundings could be severe.⁶ However, it is believed that 40% of adolescents⁷ may still suffer from their childhood AD, and 50% of adults who had AD may continue to experience recurrences,⁸ although new cases of AD remain very rare. These data are interesting, but are extracted from small

numbers of studied patients. In addition, there is only one cohort study to our knowledge to have evaluated the natural history of patients with AD from 1958 to 1998.⁹ This impressive study was conducted in the United Kingdom, focusing on the British population, and was restricted to the prevalence of AD. In other studies,^{10,11} relations between asthma or allergic rhinitis and prior or current AD have been clearly demonstrated since they are other manifestations of atopy, a collection of common inflammatory disorders characterized by a Th2-polarized cytokine profile and type 1 antigen hypersensitivity.

However, despite high levels of co-morbidity, relatively low levels of genomic co-incidence have been observed between atopic triad disorders. Conversely, current mapping data reveal a striking co-localization pattern between AD disease loci and those mapped using other chronic dermatological diseases, like psoriasis,¹⁰ whereas polymorphisms or mutations of *filaggrin*^{12,13} or *beta-adrenergic receptor*¹⁴ genes suggest comorbidity of AD with ichthyosis^{12,13,15} or stress-aggravated inflammatory skin diseases.¹⁴

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Table 1 Questionnaire

Question 1: Do you think that you have very sensitive skin, sensitive skin, slightly sensitive skin or no sensitive skin?
Question 2: Your last consultation with a dermatologist was: the last month? between 1 month and 1 year? between 1 and 2 years? more than 2 years? never?
Question 3: Today, are you suffering from a dermatological disease? yes? no?
Question 4: If yes, which one? acne? contact eczema? atopic dermatitis? rosacea/couperosis? psoriasis? vitiligo? seborrheic dermatitis? other? (several answers are possible)
Question 5: How is your skin? dry? normal? greasy?
Question 6: When you were a child, did you suffer from eczema or atopic dermatitis? yes? no?
Question 7: Among the following sentences, which is the most adequate to your skin?
1. Light skin, freckles, blond or red hairs, no tanning (or few), constant sunburns
2. Light skin, blond or brown hairs, few tanning, frequent sunburns
3. Matt skin, brown or dark hairs, usual tanning, rare sunburns
Other questions:
§ Age
§ Job of the headhouse
§ Job of the interviewee
§ Area
§ Size of the town

These data suggest that people with a history of AD could suffer from other skin diseases (especially inflammatory dermatoses).

We performed a study on the presence of AD and other dermatological diseases in subjects from eight European countries with a previous history of AD to evaluate the presence of AD nowadays in adults who suffered from this disease in infancy, and to search for comorbidity of other common dermatological diseases with past or current AD.

Methods

An opinion poll was conducted by CSA-Santé, which is a poll company, in eight European countries in their respective languages: Belgium (French, Flamish), France (French), Germany (German), Greece (Greek), Italy (Italian), Portugal (Portuguese), Spain (Spanish) and Switzerland (German, French, Italian). About 500 persons were interviewed in each country. This sample (4506 persons) was drawn from a representative sample of the European population aged 15 years or older. Poll subjects were interviewed by telephone and selected according to the quota method (gender, age, occupation of the head of the household, type of geographical area and region). Interview checks were performed by calling back 20% of the interviewees. If this procedure had revealed an abnormal finding in a single questionnaire, all the interviews conducted by the interviewer in question would have been checked. No such abnormal finding was observed.

Table 2 Current dermatological condition according to the presence of an AD history

Dermatosis	Total		AD history		No AD history	
	n	%	n	%	n	%
No dermatosis	3862	88.40%				
Acne	111	2.54%	26	18.57	85	23.16
Contact eczema	103	2.36%	43	30.71	60	16.35
Atopic dermatitis	31	0.71%	12	8.57	19	5.18
Rosacea	33	0.76%	4	2.86	29	7.90
Psoriasis	62	1.42%	17	12.14	45	12.26
Vitiligo	6	0.14%	1	0.71	5	1.36
Seborrheic dermatitis	29	0.66%	7	5.00	22	5.99
Other dermatoses	132	3.02%	30	21.43	102	27.79
Total	4369	100.00%	140	100.00	367	100.00

Interviewees answered questions (Table 1) about a previous history of AD, current dermatological disorders or skin barrier abnormalities, and their dermatological consultations over the previous year. Answers were restricted to a limited number of items.

Qualitative variables were compared using chi-squared tests or the Fisher's exact test if conditions for application were not met. Statistical analyses were performed using SAS software, version 8.2 (SAS Institute).

Results

The representativeness of the studied population was assessed by the quota method according to socio-demographic characteristics in Europe and each country. Among 4506 questionnaires, 4369 were exploitable.

Among 4369 interviewees, 12.25% (535 patients) declared a history of AD in infancy: from 6.5% in Portugal to 14.8% in Belgium ($P < 0.001$; Fig. 1). Among them, 54% were women vs. 52.1% without a history of AD, but there was no significant difference. They were younger than people without a history of AD. 10.5% of people above 55 years of age had an AD history, compared to 11.7% between the ages of 35 and 54, and 14.7% between the ages of 15 and 34 ($P = 0.002$).

Among the interviewees, 12.4% declared to suffer from a dermatological disease, of which 27% had a history of AD and 10.3% did not have this antecedent ($P < 0.001$). The most frequent reported diseases were eczema (contact eczema and AD), acne and psoriasis (Table 2). It should be noted that there was no difference in psoriasis and most dermatoses between the two groups. However, current declared cases of atopic eczema or contact eczema were more frequent in patients with a previous history of AD (39.3% vs. 21.5%, $P < 0.001$), whereas these patients appeared less affected by rosacea (2.9% vs. 7.9%, $P < 0.001$). Many differences were observed between countries (Fig. 2). Only 3.3% currently had AD and an AD history in Italy, whereas this figure rose to 31.3% in Portugal ($P < 0.001$) (Table 3). Among patients with an

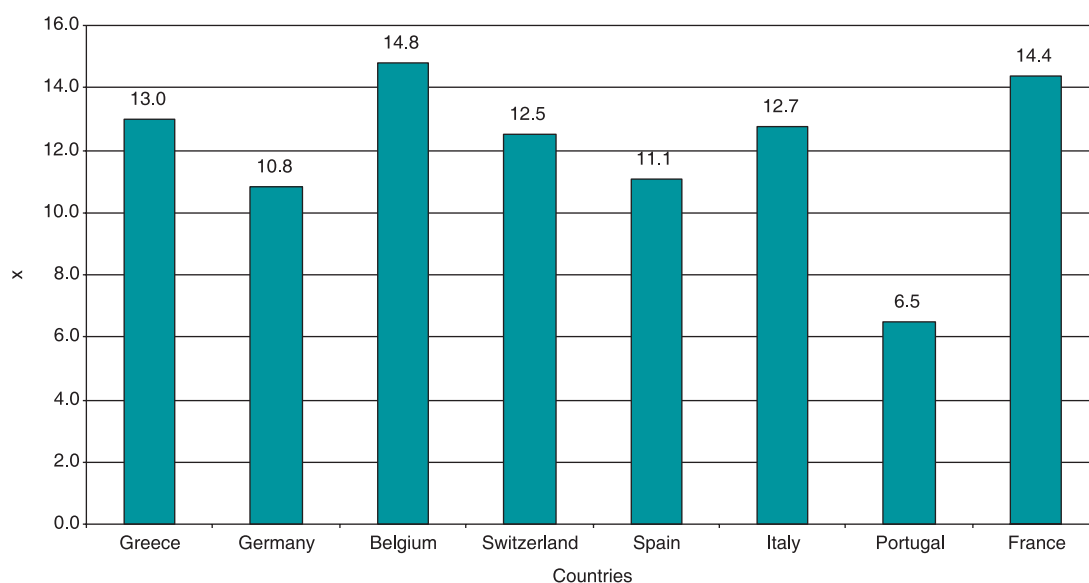


Figure 1 Patients with a history of AD in eight European countries.

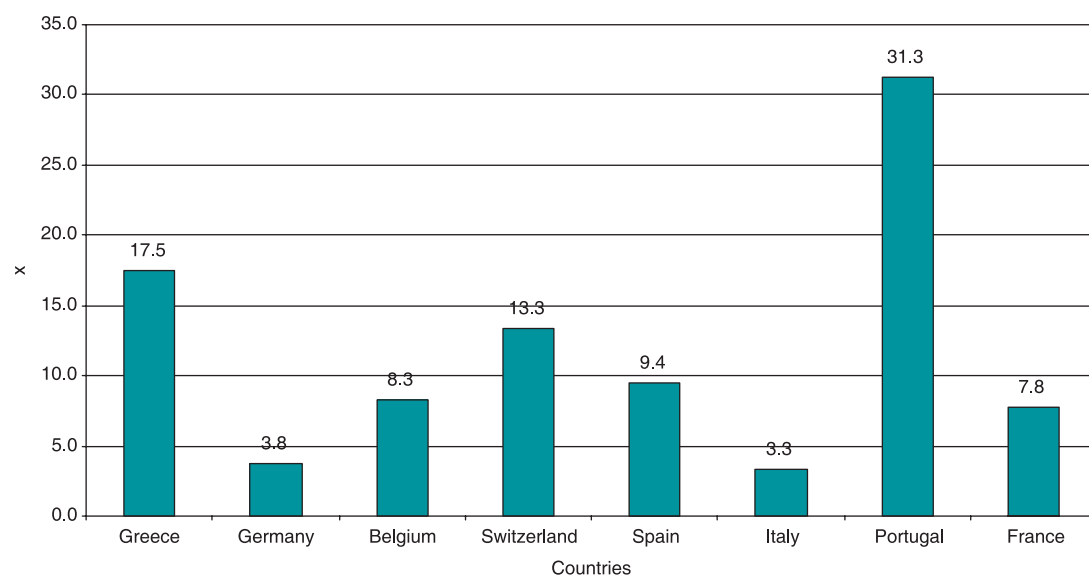


Figure 2 Patients suffering currently and previously from AD in eight European countries.

Table 3 Patients suffering currently and previously from AD

Current AD in patients with AD history	Total		Greece		Germany		Belgium		Switzerland		Spain		Italy		Portugal		France	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
No	480	89.72	52	82.54	51	96.23	66	91.67	52	86.67	48	90.57	58	96.67	22	68.75	131	92.25
Yes	55	10.28	11	17.46	2	3.77	6	8.33	8	13.33	5	9.43	2	3.33	10	31.25	11	7.75
Total	535	100.00	63	100.00	53	100.00	72	100.00	60	100.00	53	100.00	60	100.00	32	100.00	142	100.00

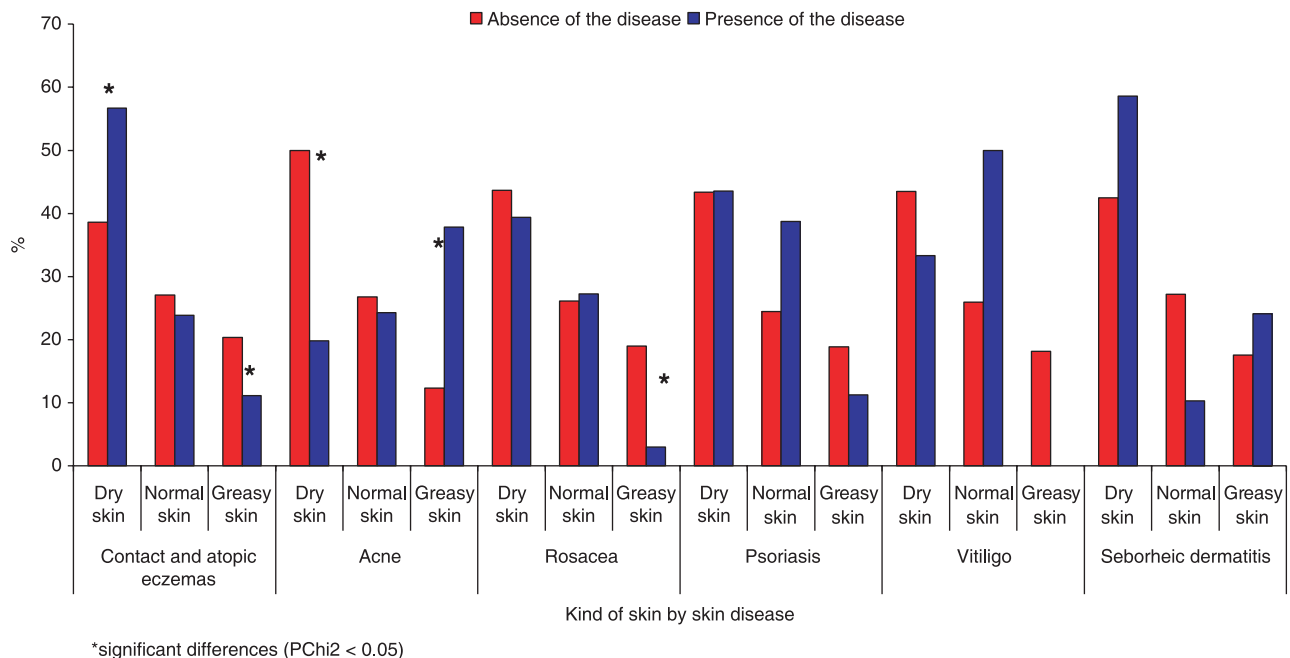


Figure 3 Types of skin and skin diseases.

AD history, 12.4% of those currently suffering from AD were aged between 15 and 34, 9% were aged between 35 and 54, and 9% were aged over 55 ($P = 0.44$).

There were no significant differences in phototypes between patients with or without an AD history, but many of the cosmetological properties of skin differed (Fig. 3). Dry skin was more frequent in patients suffering from contact or atopic eczema (56.7% of patients with eczema suffered from dry skin vs. 38.6% of patients suffering from another skin disease). Greasy skin was more frequent in patients suffering from acne or rosacea (37.8% of patients with acne suffered from greasy skin vs. 12.4% of patients suffering from another skin disease and 3.0% of patients with rosacea suffered from greasy skin vs. 19% of patients suffering from another skin disease; Fig. 3). Skin reactivity (skin sensitivity) was more frequent in subjects with an AD history ($P < 0.001$), and these people effectively reported more unexplained incidences of skin flushes or redness ($P = 0.002$). Emotions did not significantly induce more redness ($P > 0.1$), but cosmetics did induce skin irritation more frequently ($P < 0.001$).

Discussion

The main interests of this study are the large number of subjects, originating from eight different countries, and its focus on the dermatological future of patients with AD, which is not limited to AD itself. The representativeness of the studied population was assessed by the quota method, according to socio-demographic characteristics in Europe and each country. The use of surveys appears suitable as a method for conducting an epidemiological

study on dermatological diseases. The use of a representative sample of the population is useful for producing extrapolative results about dermatological diseases,^{16–18} although this study does not claim to have an epidemiological value with respect to dermatological diseases as all data were declared in interviews; some data could be overestimated or underestimated,¹⁸ and some people may have had diagnosis difficulties, i.e. distinguishing between AD and contact eczema (or acne and rosacea).

The number of people who declared having a history of AD in infancy (12.3%) is similar to that in other studies,^{3,19,20} which confirms that our methodology adequately evaluated the frequency of dermatological diseases. The higher frequency of an AD history in young interviewees confirms that there is an increasing incidence of AD.²⁰ The prevalence of AD has doubled or tripled in industrialized countries over the past three decades, underlying the importance of epidemiological studies conducted at a population level to gain a more balanced understanding of the enigma of AD.²¹ A study²² performed from 1992 to 2001 showed that the increase in prevalence of asthma and hay fever in 5- to 7-year-old children living in Switzerland may have ceased. However, symptoms of AD may still be on the rise, especially among girls.

Regarding current dermatological diseases, there is a very important difference in frequency between people with or without an AD history, which is mainly related to the high frequency of contact and atopic eczemas in those having had AD in infancy. Current occurrences of AD decrease with age, as previously described.^{19,20} Our results are consistent with a previous study that was made by conducting a poll in France.¹⁸ Numerous studies

have been performed about the epidemiology of atopy in Europe,^{3,20,23} and our main aim was to evaluate the frequency of non-eczematous dermatological diseases in patients with atopy.

The hypothesis of a link between psoriasis and atopy¹⁰ is not confirmed. Atopy seems to protect against acne or rosacea. The skin dryness of atopic patients, which is confirmed in our study, probably explains this. A previous study²⁴ did not find skin dryness, measured by *trans*-epidermal water loss (TEWL), or AD characteristics in 75 patients with rosacea. On the contrary, TEWL and the characteristics of an atopic diathesis were significantly greater in 75 patients with perioral dermatitis, suggesting that this is a different disease and that it could be associated with the use of topical steroids in patients with AD. The incidence of perioral dermatitis was not specifically studied in our study.

Many differences were observed between countries. It is interesting to remark that there are differences in the frequency of this antecedent according to different countries: Portugal appears to be 'protected' against AD in infancy; yet, the persistence of AD in adults is very frequent. This suggests that AD is more probably related to genetic causes than the environment in this country.

There were no significant differences in phototypes between patients with or without an AD history, which runs counter to the idea that AD may be more frequent in people with pale skins. Skin sensitivity was more frequent in subjects with an AD history, and these people effectively reported more incidences of skin flushes or redness for no apparent reason or after applying cosmetics. We have published these results about skin sensitivity and atopy in another paper about skin sensitivity.²⁵ In immunological phrasing, it is better to use 'skin reactivity' rather than 'skin sensitivity' as it is defined as the onset of erythema and/or prickling, burning, or tingling sensations (possibly pain or pruritus) due to various factors, which may be physical (ultraviolet radiation, heat, cold, wind), chemical (cosmetics, soap, water, pollution), psychological (stress) or hormonal (menstrual cycle).²⁶ There is no immunological mechanism but there are disorders in epidermal sensory receptors and skin innervation.²⁷

Diverging opinions about AD distinguish an IgE-associated form of AD (extrinsic AD) from a non-IgE-associated form (intrinsic AD)^{28,29} or not.³⁰ Epidemiological studies about associations between atopy and cosmetological and dermatological disorders, like ours, may help improve understanding. As there is no previous large epidemiological study about these associations, to our knowledge, the main new data resulting from our study are as follows:

- Psoriasis does not appear to be associated with AD, in spite of the co-localization of susceptibility genes¹⁰
- Patients with AD history are less affected by acne
- They are less affected by rosacea.

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