DOI: 10.1111/jdv.16119 JEADV

ORIGINAL ARTICLE

The role of exposome in acne: results from an international patient survey

B. Dreno,[1,*] J. Shourick,[2] D. Kerob,[3] A. Bouloc,[4] C. Taïeb[5,6]

[1]Department of Dermato-Cancerology, CHU Nantes-Hôtel-Dieu CRCINA, Inserm 1232, CIC 1413, University of Nantes, Nantes, France
[2]Bio Informatics/statistics, University of Paris Sud, Paris, France
[3]Vichy Laboratoire Internationale, Levallois-Perret, France
[4]Private Practice, Paris, France
[5]EMMA, Fontenay-sous-Bois, France
[6]Santé Publique, CHU Necker-Enfants malades, Paris, France
*Correspondence: B. Dreno. E-mail: brigitte.dreno@atlanmed.fr

Abstract

Background Acne severity and its response to treatment may be influenced by internal and external factors: the exposome.

Objectives The aim of this international real-life survey was to assess the most involved exposome factors in acne.

Methods Eleven thousand individuals, aged between 15 and 39 years, with clinically confirmed acne or without acne, defined by age, gender and prevalence, were invited to participate in an Internet survey of 63 questions in order to assess the frequency of identified acne exposome factors.

Results Data from 6679 questionnaires were used for statistical analysis purposes: 2826 from the acne group and 3853 from the control group. Nibbling, consumption of dairy products, sweets, alcohol or whey proteins, as well as exposure to pollution, stress, certain mechanical factors and humid or hot weather or sun exposure, were significantly (all $P \leq 0.05$) more frequently reported for the acne group than for the control group. This was not the case for tobacco consumption. Data regarding the impact of cannabis consumption were insufficient for drawing any conclusions.

Conclusions Data from this international, anonymized Internet questionnaire conducted with more than almost 6700 participants add new arguments to assumptions made that certain exposome factors have an impact on acne. Nutrition, pollution, stress and harsh skincare, as well as climate and sun exposure may be considered the most frequent factors related to acne.

Received: 17 October 2019; Accepted: 13 November 2019

Conflict of interest

The authors have no conflict of interest to disclose.

Funding source

The study was financially supported by Vichy Laboratoire, France.

Introduction

Acne is inflammatory disease of the pilosebaceous follicle occurring commonly in adolescents and sometimes in adults. It is associated with hyperseborrhoea altering the epithelium of the follicle with formation of comedones, a modification of the microbiote called dysbiosis targeting mainly *Propionibacterium acnes* (*P. acnes*) causing an activation of the innate immunity and thus inflammation.[1]

Skin is one of the major interfaces between the body and the external environment and is one of the main routes for the penetration of pathogens into the body.[2] The primary role of the skin is to serve as a physical barrier, protecting our body from potential assault from foreign organisms, toxic substances or any other external physical, chemical or organic factors.[2,3]

The term 'exposome' describes the sum of environmental and internal exposures to which an individual is subjected from conception to death.[4] The definition of exposome has varied over time.[4–8] In 2017, a study evaluated the impact of exposome on skin ageing for the first time and proposed the following exposome categories: sun radiation [ultraviolet (UV) radiation, visible light and infrared radiation], air pollution, tobacco smoke, nutrition, a number of less well studied, miscellaneous factors, as well as cosmetic products and aesthetic procedures.[9]

In 2018, Dréno *et al.*[10] analysed the potential role of exposome in acne by means of a literature review. According to the literature studied, nutrition, medication, occupational factors, pollutants, weather factors as well as psychosocial and lifestyle factors impact the course and severity of the disease and treatment efficacy. Moreover, the authors pointed out that external exposome factors act on the natural skin barrier and on the skin microbiota, resulting in increased sebum production, hyperkeratinisation, modification of the microbiote and activation of the innate immunity, resulting in the exacerbation of acne.[11,12] They concluded that identifying the most frequent exposome factors that trigger acne and reducing their impact is mandatory for adequate acne management.

The aim of the present large international real-life survey was to confirm from a patient prospect, the influence of the most frequent internal and external exposome factors involved in acne described by Dreno *et al.*[10]

Methodology

This international, anonymized survey was conducted between December 2018 and January 2019 via Internet in France, Germany, Italy, Brazil, Canada and Russia, with 11 000 participants with clinically confirmed acne or without acne (control group) and who agreed to participate in Internet surveys. The acne group was defined as the individuals with clinically diagnosed acne through auto-questioning: subjects had to confirm that their acne was clinically confirmed by a physician. Moreover, individuals had to confirm that they used a prescribed acne treatment or a recommended acne care at the time the questionnaire was completed.

The survey was conducted by means of local databases of Internet users who agreed to participate in surveys. It complied with local data protection laws and did not require independent review board or independent ethics committee approvals. Participants did not provide written informed consent for participation. The survey was comprised of 63 questions and was compiled by the authors, based on the article by Dréno *et al.*[10] It assessed age, gender, socio-economic features, skin types, presence of acne and current acne treatment, as well as 6 internal and external exposome factors (nutrition and nutritional supplements, occupational factors, medications, pollutants, psychosocial and modern lifestyle factors, weather conditions) as defined by Dréno *et al.*[10]; the different chapters of the survey are presented in Table 1. A modified version of a previously used algorithm to define the two study groups was applied.[13] Briefly, a polling institute (H. Chevalier Conseil, Paris France, supported by Quantar Health Care, Paris, France, both specialized in the conduct of health-related surveys) conducted the survey. A sample of the target study population aged 15–39 years in both groups was recruited using the stratified random sampling method. Based on local databases of Internet users, fixed quotas of subjects fulfilling predefined criteria were recruited. Drawing on national population data, these quotas were based on the following aspects: age, gender and acne prevalence, thereby ensuring the accurate representation of the sample population and the same representation in the acne and control groups.

Table 1 Survey structure

1	Introduction
2	Screening
3	Quotas et socio-economic information
4	Phototype
5	Nutrition and nutritional supplements
6	Occupational factors: cosmetics and mechanical factors
7	Medications: contraception, anabolic steroids testosterone
8	Pollutants: industrial and air pollutants, tobacco, cannabis and alcohol consumption
9	Psychosocial and modern lifestyle factors: stress, emotions, sleep deprivation, socio-economic pressures, excessive artificial light exposure (tablets, smartphones, computers)
10	Weather conditions: heat, humidity, ultraviolet radiation

Statistical analyses were performed using R software version 3.5.1 (The R Project for Statistical Computing, The R Foundation, Vienna, Austria).

Data concerning individuals between 15 and 39 years of age were extracted from the survey database. Quantitative variables were expressed as means and standard deviations. Qualitative variables were expressed as frequencies and percentages. Comparisons between both groups were performed using the Wilcoxon test in the case of quantitative variables; for categorical variables, intergroup comparisons were carried out with the chi-squared test. The level of significance was set at 5%. Each variable was evaluated in a univariate analysis adjusted for age, in order to identify factors associated with acne. Then, all variables associated with acne at a probability threshold of 0.1 were entered into a multiple logistic regression analysis. With this model, variables were retained in a stepwise manner in order to determine those variables that were independently associated with acne at a probability threshold of 0.05. Odds ratios (OR) were consequently generated.

Results

Demographic and socio-economic data

In total, 11 000 individuals participated in the survey and data from 6679 were usable for statistical analysis purposes: 2826 (42.3%) in the acne group and 3853 (57.7%) in the control group. The remaining 4321 questionnaires were incomplete, started, but not validated, or were completed but not validated by the users. Mean age, gender distribution and phototype were similar in both groups; the body mass index (BMI) was significantly higher ($P < 0.001$) in participants with acne (24.90) than in those without acne (23.99). Details regarding patient demographics are provided in Table 2.

Table 2 Demographic and socio-economic data

	Without acne *n* = 3853		With acne *n* = 2826		*P*-value
Gender (*n*, %)					
Female (*n*, %)	2436	63.22	1746	61.78	0.26
Male (*n*, %)	1417	36.78	1080	38.22	
Age (years ± SD)	25.73 ± 7.26		25.47 ± 7.42		NS
Distribution according to age					
15–19 years (*n*, %)	705	24.9%	1127	29.2%	<0.001
20–24 years (*n*, %)	863	30.5%	1127	29.2%	
25–39 years (*n*, %)	1258	44.5%	1599	41.5%	
Weight (kg)	67.93 ± 18.32		69.21 ± 16.02		NS
Body Mass Index	24.90		23.99		<0.001
Socio-economic category					
Upper category (*n*, %)	969	34.3%	1021	26.5%	<0.001
Lower category (*n*, %)	1181	41.8%	1659	43.1%	
Unemployed (*n*, %)	676	23.9%	1173	30.4%	
Residence (*n*, %)					
Urban (*n*, %)	1668	59.0%	1874	48.6%	<0.001
Suburban. mid-size town (*n*, %)	691	24.5%	957	24.8%	
Countryside, small-size town (*n*, %)	467	16.5%	1022	26.5%	

NS, not significant.

Nutrition and nutritional supplements

The data analysis regarding nutrition and nutritional supplements showed that significantly more ($P < 0.001$) individuals with acne (48.2%, 1362/2826) consumed dairy products on a daily basis compared to individuals who did not (38.8%, 1494/3853). The difference was also statistically significant (all $P < 0.001$) for soft drinks, fruit juices or syrups, pastry, chocolate and sweets.

Significantly more ($P < 0.001$) participants in the acne group (61.9%, 1748/2826) than in the non-acne group (43.2%, 1665/3853) reported frequent and regular nibbling during the 12 months preceding the survey and significantly more ($P < 0.001$) individuals in the acne (11.0%, 311/2826) than in the acne-free group (7.3%, 281/3853) reported the regular consumption of whey proteins during the 12 months preceding the survey.

Probiotic consumption was significantly ($P < 0.001$) higher in individuals with acne (16.4%, 464/2826) than in acne-free individuals (5.2%, 202/3853).

Detailed results including OR are provided in Fig. 1.

Medication

The use of contraceptives was significantly higher ($P < 0.001$) in individuals with acne (39.0%, 677/1746) than in acne-free individuals (30.5%, 743/2436). Oral contraceptives were perceived as reducing acne in 42.7% (286/677) of individuals with acne, while 26.5% (247/677) declared that they had no influence on their acne. 20.8% (141/677) declared that they increased their acne.

In acne-free individuals, a large majority (79.5%) declared that their contraception had no influence on their skin.

Three times more individuals with acne (12.0%, 338/2826) than acne-free individuals (3.8%, 122/3853) declared the regular use of anabolic drugs during the 12 months preceding the survey, the difference was statistically significant ($P < 0.001$).

Significantly more ($P < 0.001$) individuals with acne than without reported the intake of anti-depressants, anti-epileptics or corticoids.

Table 3 provides detailed results.

Occupational factors

More than one-third of individuals with acne (35.4%, 999/2826) compared to 16.7% (645/3 853) without used an electric brush to clean their face ($P < 0.001$; the OR was: 0.44, CI 95%: (0.39; 0.48), $P < 0.0001$].

Significantly more ($P < 0.001$) individuals with acne (56.5%, 1596/2826) than those without (36.3%, 1397/3853) applied essential or plant oils to their face and 71.05% (2008/2826) of the first group compared to 43.2% (1664/3853) of the latter declared using scrubs [OR: 4.99, CI 95%: (4.28; 5.81), $P < 0.0001$] or peelings [57.8%, 1633/2826 vs 33.1%, 1275/3853; OR: 3.35, CI 95%: (2.95; 3.81), $P < 0.0001$] at least or even daily on their face. Differences were all statistically significant ($P < 0.001$).

Pollutants

Significantly more ($P < 0.001$) individuals with acne than acne-free individuals reported living close to an airport (10.9%, 308/2826 vs 7.2%, 276/3853), to an industrial site (15.6%, 428/2826 vs 9.9%, 380/3853) or to cultivated land (21.2%, 598/2826 vs

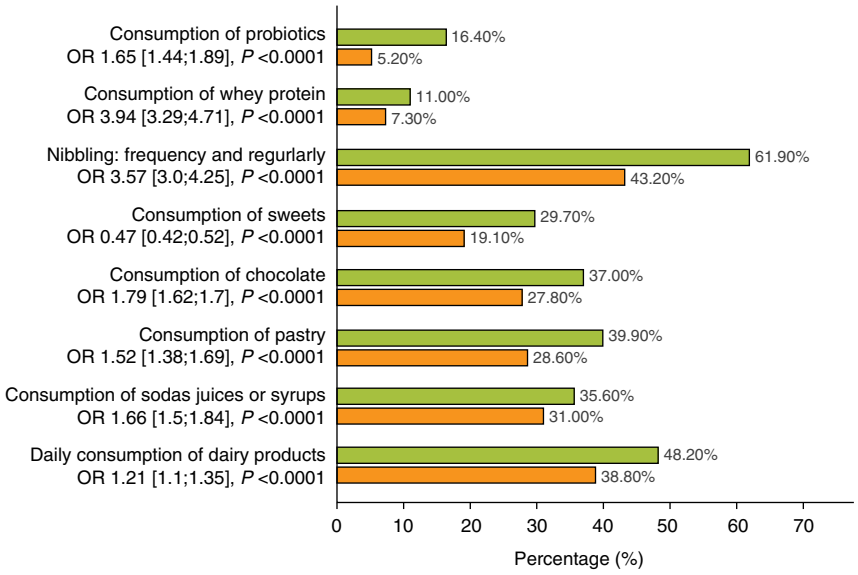

Figure 1 Impact of nutrition and nutritional supplements during the 12 months preceding the survey. OR, odds ratio, (confidence interval) 95%, *P* = *P*-value.

19.21%, 740/3853). A large majority of individuals with acne compared to those without were exposed significantly more often to tar (9.3%, 262/2826 vs 2.3%, 164/3853; $P < 0.001$), solvent emanation and crude oil (10.7%, 301/2826 vs 4.7%, 182/3853) or oil emanation (13.1%, 371/2826 vs 7.8%, 301/3853). A statistically significant difference ($P < 0.001$) for anthropic pollutants (tobacco, cannabis or alcohol consumption) between both groups was only shown for alcohol consumption: (56.5%, 1597/2826 vs 43.0%, 1656/3853). No significant difference was shown for tobacco consumption. Due to legal restrictions in certain countries concerning cannabis consumption, the available sample size of individuals consuming cannabis was insufficient for making any statistically validated observation.

Detailed results for all sub-factors including OR are provided in Table 4.

Psychosocial and modern lifestyle

When rating the level of stress on a visual analogue scale ranging from 0 (none) to 10 (very high), a significantly higher ($P < 0.001$) mean score was observed in individuals with acne (5.9 ± 2.3) compared to those without (5.0 ± 2.7).

The prevalence of individuals suffering from important and extremely high-stress levels was significantly higher ($P < 0.001$) in individuals with acne (51.0%, 1440/2826) than in acne-free individuals (29.0%, 1118/3853).

Significantly more ($P < 0.001$) individuals with acne (54.6%, 1542/2826) than without (47.6%, 1834/3853) reported lacking sleep and significantly more ($P < 0.001$) individuals without acne (52.4%, 2020/3853) than those with (50.3%, 1420/2826) reported restful sleep.

In both groups, the exposure to screens and tablets just before falling asleep was reported by a large majority of individuals with significantly more individuals ($P < 0.001$) in the acne (91.3%, 2580/2826) than in the acne-free group (85.2%, 3281/3853).

Detailed results including OR are provided in Table 5.

Weather factors

There was no significant difference in prevalence of individuals with or without acne living in temperate or cold regions. Conversely, acne was significantly more frequent in hot [24.6% (696/2826) vs 17.1% (659/3853)] or humid regions [13.0% (367/2826) vs 11.5% (442/3853); $P < 0.001$ and $P < 0.03$, respectively].

Acne was significantly ($P < 0.01$) more frequent in individuals with moderate or intensive sun exposure due to their work or daily activities [42.8% (1208/2826) vs 31.6% (1216/3853)]. Details are given in Table 6.

Discussion

Data from this international, anonymized Internet questionnaire conducted with almost 6700 participants add new arguments to assumptions made that certain exposome factors have an impact on acne.

The survey showed that significantly more individuals with acne live in an urban area have an upper socio-economic category and a significantly higher BMI (all $P < 0.001$).

Nibbling and the consumption of dairy products, sweets, alcohol or whey proteins were reported significantly more often

Table 3 Impact of medication

	Without acne ***n*** **= 2436**		**With acne** ***n*** **= 1746**		***P*-value**
Use of oral contraceptive (*n*, %)	743	30.5	677	39.0	<0.001
The oral contraceptive	*n* = 187		*n* = 677		
Increased acne (*n*, %)	0	0	141	20.8	
Reduced acne (*n*, %)	0	0	289	42.7	
Impact (*n*, %)	187	4.6	247	36.5	
The contraceptive had an impact on the skin	*n* = 741		*n* = 430		
Yes (*n*, %)	150	20.2	141	20.8	
No (*n*, %)	591	79.5	289	42.7	
Intake of a hormonal treatment based on steroids or testosterone during the last 12 months (*n*, %)	*n* = 3853 122	3.2	*n* = 2826 338	12.0	<0.001
OR	3.03				
CI 95%	(2.27; 4.03)				
P-value	<0.0001				
Intake during the last 12 months of (*n*, %)					
An antidepressant	338	8.8	472	16.7	<0.001
OR	0.35				
CI 95%	(0.3; 0.42)				
P-value	<0.0001				
An antiepileptic	71	1.8	153	5.4	<0.001
OR	3.93				
CI 95%	(3.17; 4.88)				
P-value	<0.0001				
Oral or IV Corticodes	120	3.1	319	11.3	<0.001
OR	4.9				
CI 95%	(3.54; 6.79)				
P-value	<0.0001				

CI, confidence interval; IV, intravenous; OR, odd ratio.

(all $P \leq 0.05$) by individuals with acne and confirmed observations previously made.[14–36] Not surprisingly, the intake of probiotics was significantly ($P < 0.001$) higher in individuals with acne. This may be due to the fact that probiotics are becoming more and more popular and that their use is encouraged more and more via social networks and Internet blogs than by dermatologists or other physicians, even though promising study results exist.[37,38]

The survey further confirms that individuals with acne consider that oral contraception significantly reduces their acne ($P < 0.001$). Despite this, almost 21% of individuals in this group reported that they consider that their contraception had worsened their acne. This observation may be explained by the use of 1st or 2nd generation contraceptive pills, a phenomenon already described in 2016 by Leclerc-Mercier *et al.*[39] and who also reported that the use of 3rd or 4th generation contraceptive pills improve acne as these contraceptives contain the most often low or non-androgenic progestin (desogestrel, gestodene) not activating the androgen receptors of sebaceous glands and even blocking this receptor for certain HCPs. However, we were not able to confirm this allegation using the data collected. Moreover, three times more individuals with acne regularly used anabolic steroids, indirectly confirming scientific data suggesting an acne-stimulating action of these molecules.[40–42] Use of certain other medications, such as anti-depressants, anti-epileptics or corticoids, was more frequently observed in individuals with acne, confirming their role in the induction of acne-like lesions, according to Dréno *et al.*[10]

According to the participants, hot and humid climates, as well as sun exposure, play a significant role in acne. These findings confirm observations made in the past and also very recently by Narang *et al.*[43–47] One of the lipids produced by human sebaceous glands on the face and torso is squalene. This unsaturated fatty acid represents ~10–15% of sebum and is readily oxidized by ozone, long UV rays and tobacco smoke.[48] These oxidized sebum lipids cause keratinocyte hyperproliferation and inflammatory cytokine release, leading ultimately to the onset or worsening of acne. However, in acne, the association between sebum oxidation and comedogenesis has not been investigated thoroughly.[49]

The survey also confirmed that exposure to pollution or to stress and to certain mechanical factors, such as the use of a dermo-roller or harsh cleansing of the face, is more frequently

Table 4 Impact of pollution factors

	Without acne *n* = 3853		With acne *n* = 2826		*P*-value
Lives close to					
An airport (*n*, %)	276	7.2	308	11.0	<0.001
OR (CI 95%) *P*-value	0.37 (0.33; 0.41) <0.0001				
An industry facility (*n*, %)	380	9.9	428	15.2	<0.001
OR (CI 95%) *P*-value	1.58 (1.33; 1.87) <0.0001				
Cultivated land (*n*, %)	740	19.2	598	21.2	<0.001
OR (CI 95%) *P*-value	1.63 (1.4; 1.89) <0.0001				
Exposure during work to					
Tar (*n*, %)	164	4.3	262	9.3	<0.001
OR (CI 95%) *P*-value	1.44 (1.31; 1.59) <0.0001				
Solvent emanations, crude oil (*n*, %)	182	4.7	301	10.7	<0.001
OR (CI 95%) *P*-value	2.29 (1.87; 2.81) <0.0001				
Oil emanations (*n*, %)	301	7.8	371	13.1	<0.001
OR (CI 95%) *P*-value	2.39 (1.97; 2.89) <0.0001				
Tobacco consumption					
Does not smoke (*n*, %)	2722	70.7	2033	71.9	<0.001
Smokes occasionally or daily (*n*, %)	1131	29.4	793	28.1	
OR (CI 95%) *P*-value	4.14 (3.35; 5.13) <0.0001				
Alcohol consumption (*n*, %)	*N* = 3853		*N* = 2826		
	1656	43.0	1597	56.5	<0.001
OR (CI 95%) *P*-value	1.34 (1.05; 1.7) <0.0001				
Cannabis consumption (*n*, %)	*N* = 1016		*N* = 740		
	169	16.6	156	21.1	NS

CI, confidence interval; NS, not significant; OR, odd ratio.

Table 5 Impact of psychosocial and modern lifestyle factors

	Without acne *n* = 3853		With acne *n* = 2826		*P*-value
Stress felt					
Score expressed on VAS (mean±SD)	5	2.7	5.9	2.3	<0.001
OR (CI 95%) *P*-value	1.78 (1.52; 2.09) <0.0001				
Stress felt					
No or moderate stress (*n*, %)	2735	18.9	1386	12.1	<0.001
Important or extreme stress (*n*, %)	1118	29.0	1440	51.0	
OR (CI 95%) *P*-value	1.15 (1.12; 1.17) <0.0001				
Lacking sleep (*n*, %)	1834	47.6	1542	54.6	<0.001
OR (CI 95%) *P*-value	1.79 (1.62–1.98) <0.0001				
Repairing sleep (*n*, %)					
Yes	2020	52.4	1420	50.3	<0.001
No	1833	47.6	1406	49.8	
OR (CI 95%) *P*-value	1.33 (1.21–1.47) <0.0001				
Looking at a screen/tablet the hour before falling asleep					
Several times per week or every evening (*n*, %)	3281	85.2	2580	91.3	<0.001
Rarely or never (*n*, %)	572	14.9	246	8.7	
OR (CI 95%) *P*-value	1.83 (1.56–2.14) <0.0001				

CI, confidence interval; OR, odd ratio; VAS, visual analogue scale (0–10).

observed in individuals with acne.[48,50–58] It did not confirm the link between acne and tobacco, thereby endorsing the data of the literature with divergent results reported in a recent paper with by Wolkenstein *et al.*[13,59]

Due to legal constraints concerning the consumption of cannabis in certain countries, we were unable to assess the link of cannabis consumption in a sufficiently large study population, thereby not providing any conclusions.

Table 6 Impact of weather factors and sun exposure

	Without acne $n = 3853$		With acne $n = 2826$		*P*-value
Do you or have you lived during the last 12 months in a region or country with					
Temperate weather	1989	51.62%	1428	50.53%	NS
Particularly hot weather	659	17.10%	696	24.63%	<0.001
Particularly cold weather	581	15.08%	446	15.78%	NS
Particularly humid weather	442	11.47%	367	12.99%	0.03
Due to your job or your daily activities or exposure to sun light is					
Intense or moderate	1216	31.56%	1208	42.75%	<0.001
Low or none	2637	68.44%	1618	57.25%	

NS, not significant.

Our study has several limitations. Patients reported themselves that they suffered from acne. Even though the questionnaire requested that acne had to be confirmed by a clinician prior to participation, the design of the study, using an anonymous Internet questionnaire did not allow to confirm the inclusion criteria. Thus potentially, patients with rosacea, erythema or other acne-like conditions could have participated. Moreover, products used to manage their acne might not have been described or recommended by a physician. Despite these limitations and the potential bias due to the Internet study design, our results confirm for the first time and on a large international level, assumptions made and presented by Dréno *et al.* in 2018.[10]

Our data confirm that among the questioned internal and external exposome factors, nutrition, pollution, stress, harsh skincare, temperature, humidity and sun exposure had a significant impact on acne, thereby confirming published results and allegations, our methodological approach and that a holistic approach is necessary for the efficient management of acne.

Acknowledgements

The authors acknowledge the participants of this survey and the writing and editing support of Karl Patrick Göritz, SMWS – Scientific and Medical Writing Services, France.

References

1 Dreno B. What is new in the pathophysiology of acne, an overview. *J Eur Acad Dermatol Venereol* 2017; **31**(Suppl 5): 8–12.
2 Grice EA. The skin microbiome: potential for novel diagnostic and therapeutic approaches to cutaneous disease. *Sem Cut Med Surg* 2014; **33**: 98–103.
3 Grice EA, Segre JA. The skin microbiome. *Nat Rev Microbiol* 2011; **9**: 244–253.
4 Wild CP. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomarkers Prev* 2005; **14**: 1847–1850.
5 Miller GW, Jones DP. The nature of nurture: refining the definition of the exposome. *Toxicol Sci* 2014; **137**: 1–2.
6 Buck Louis GM, Sundaram R. Exposome: time for transformative research. *Stat Med* 2012; **31**: 2569–2575.
7 Rappaport SM, Smith MT. Epidemiology. Environment and disease risks. *Science* 2010; **330**: 460–461.
8 Lippmann M. Exposure science in the 21st century: a vision and a strategy. *J Expo Sci Environ Epidemiol* 2013; **23**: 1.
9 Krutmann J, Bouloc A, Sore G, Bernard BA, Passeron T. The skin aging exposome. *J Dermatol Sci* 2017; **85**: 152–161.
10 Dreno B, Bettoli V, Araviiskaia E, Sanchez Viera M, Bouloc A. The influence of exposome on acne. *J Eur Acad Dermatol Venereol* 2018; **32**: 812–819.
11 Murillo N, Raoult D. Skin microbiota: overview and role in the skin diseases acne vulgaris and rosacea. *Future Microbiol* 2013; **8**: 209–222.
12 Wolf R, Parish LC. Effect of soaps and detergents on epidermal barrier function. *Clin Dermatol* 2012; **30**: 297–300.
13 Wolkenstein P, Misery L, Amici JM *et al.* Smoking and dietary factors associated with moderate-to-severe acne in French adolescents and young adults: results of a survey using a representative sample. *Dermatology* 2015; **230**: 34–39.
14 Melnik BC, John SM, Plewig G. Acne: risk indicator for increased body mass index and insulin resistance. *Acta Derm Venereol* 2013; **93**: 644–649.
15 Cerman AA, Aktas E, Altunay IK, Arici JE, Tulunay A, Ozturk FY. Dietary glycemic factors, insulin resistance, and adiponectin levels in acne vulgaris. *J Am Acad Dermatol* 2016; **75**: 155–162.
16 Kucharska A, Szmurlo A, Sinska B. Significance of diet in treated and untreated acne vulgaris. *Postepy Dermatol Alergol* 2016; **33**: 81–86.
17 Kwon HH, Yoon JY, Hong JS, Jung JY, Park MS, Suh DH. Clinical and histological effect of a low glycaemic load diet in treatment of acne vulgaris in Korean patients: a randomized, controlled trial. *Acta Derm Venereol* 2012; **92**: 241–246.
18 Smith RN, Braue A, Varigos GA, Mann NJ. The effect of a low glycemic load diet on acne vulgaris and the fatty acid composition of skin surface triglycerides. *J Dermatol Sci* 2008; **50**: 41–52.
19 Mahmood SN, Bowe WP. Diet and acne update: carbohydrates emerge as the main culprit. *J Drugs Dermatol* 2014; **13**: 428–435.
20 Reynolds RC, Lee S, Choi JY *et al.* Effect of the glycemic index of carbohydrates on Acne vulgaris. *Nutrients* 2010; **2**: 1060–1072.
21 Fabbrocini G, Izzo R, Faggiano A *et al.* Low glycaemic diet and metformin therapy: a new approach in male subjects with acne resistant to common treatments. *Clin Exp Dermatol* 2016; **41**: 38–42.
22 Smith R, Mann N, Makelainen H, Roper J, Braue A, Varigos G. A pilot study to determine the short-term effects of a low glycemic load diet on hormonal markers of acne: a nonrandomized, parallel, controlled feeding trial. *Mol Nutr Food Res* 2008; **52**: 718–726.
23 Kim H, Moon SY, Sohn MY, Lee WJ. Insulin-like growth factor-1 increases the expression of inflammatory biomarkers and sebum production in cultured sebocytes. *Ann Dermatol* 2017; **29**: 20–25.
24 Ben-Amitai D, Laron Z. Effect of insulin-like growth factor-1 deficiency or administration on the occurrence of acne. *J Eur Acad Dermatol Venereol* 2011; **25**: 950–954.
25 Ferdowsian HR, Levin S. Does diet really affect acne? *Skin Therapy Lett* 2010; **15**: 1–2, 5.
26 Berra B, Rizzo AM. Glycemic index, glycemic load: new evidence for a link with acne. *J Am Coll Nutr* 2009; **28**(Suppl): 450s–454s.

27 Abulnaja KO. Changes in the hormone and lipid profile of obese adolescent Saudi females with acne vulgaris. *Braz J Med Biol Res* 2009; **42**: 501–505.
28 Agamia NF, Abdallah DM, Sorour O, Mourad B, Younan DN. Skin expression of mammalian target of rapamycin and forkhead box transcription factor O1, and serum insulin-like growth factor-1 in patients with acne vulgaris and their relationship with diet. *Br J Dermatol* 2016; **174**: 1299–1307.
29 Simonart T. Acne and whey protein supplementation among bodybuilders. *Dermatology* 2012; **225**: 256–258.
30 Melnik BC. Evidence for acne-promoting effects of milk and other insulinotropic dairy products. *Nestle Nutr Workshop Ser Pediatr Program* 2011; **67**: 131–145.
31 Adebamowo CA, Spiegelman D, Danby FW, Frazier AL, Willett WC, Holmes MD. High school dietary dairy intake and teenage acne. *J Am Acad Dermatol* 2005; **52**: 207–214.
32 Adebamowo CA, Spiegelman D, Berkey CS *et al.* Milk consumption and acne in adolescent girls. *Dermatol Online J* 2006; **12**: 1.
33 Ismail NH, Manaf ZA, Azizan NZ. High glycemic load diet, milk and ice cream consumption are related to acne vulgaris in Malaysian young adults: a case control study. *BMC Dermatol* 2012; **12**: 13.
34 Silverberg NB. Whey protein precipitating moderate to severe acne flares in 5 teenaged athletes. *Cutis* 2012; **90**: 70–72.
35 Donnarumma G, Perfetto B, Paoletti I *et al.* Analysis of the response of human keratinocytes to Malassezia globosa and restricta strains. *Arch Dermatol Res* 2014; **306**: 763–768.
36 Claudel JP, Auffret N, Leccia MT, Poli F, Dreno B. Reply to comments made by M. Donnarumma et al. Comment on "Acne and nutrition: hypotheses, myths and facts" published by our expert group in 2018. *J Eur Acad Dermatol Venereol* 2019; **33**: e420.
37 Jung GW, Tse JE, Guiha I, Rao J. Prospective, randomized, open-label trial comparing the safety, efficacy, and tolerability of an acne treatment regimen with and without a probiotic supplement and minocycline in subjects with mild to moderate acne. *J Cutan Med Surg* 2013; **17**: 114–122.
38 Fabbrocini G, Bertona M, Picazo O, Pareja-Galeano H, Monfrecola G, Emanuele E. Supplementation with Lactobacillus rhamnosus SP1 normalises skin expression of genes implicated in insulin signalling and improves adult acne. *Benef Microbes* 2016; **7**: 625–630.
39 Leclerc-Mercier S, Buisson V, Dreno B. New regulations for oral contraceptive prescription in France in 2013: what is the impact on adult female acne? *Eur J Dermatol* 2016; **26**: 345–349.
40 Wierckx K, Van de Peer F, Verhaeghe E *et al.* Short- and long-term clinical skin effects of testosterone treatment in trans men. *J Sex Med* 2014; **11**: 222–229.
41 Walker J, Adams B. Cutaneous manifestations of anabolic-androgenic steroid use in athletes. *Int J Dermatol* 2009; **48**: 1044–1048, quiz 8.
42 Kraus SL, Emmert S, Schon MP, Haenssle HA. The dark side of beauty: acne fulminans induced by anabolic steroids in a male bodybuilder. *Arch Dermatol* 2012; **148**: 1210–1212.
43 Lee WJ, Park KH, Sohn MY, Lee WC, Lee SJ, Kim DW. Ultraviolet B irradiation increases the expression of inflammatory cytokines in cultured sebocytes. *J Dermatol* 2013; **40**: 993–997.
44 Plewig G, Kligman AM. Ultraviolet Radiation. ACNE and ROSACEA. Springer Berlin Heidelberg, Berlin, Heidelberg, 1993: 674–677.
45 Suh DH, Kwon TE, Youn JI. Changes of comedonal cytokines and sebum secretion after UV irradiation in acne patients. *Eur J Dermatol* 2002; **12**: 139–144.
46 Narang I, Sardana K, Bajpai R, Garg VK. Seasonal aggravation of acne in summers and the effect of temperature and humidity in a study in a tropical setting. *J Cosmet Dermatol* 2019; **18**: 1098–1104.
47 Sardana K, Sharma RC, Sarkar R. Seasonal variation in acne vulgaris–myth or reality. *J Dermatol* 2002; **29**: 484–488.
48 Pham DM, Boussouira B, Moyal D, Nguyen QL. Oxidization of squalene, a human skin lipid: a new and reliable marker of environmental pollution studies. *Int J Cosmet Sci* 2015; **37**: 357–365.
49 Capitanio B, Lora V, Ludovici M *et al.* Modulation of sebum oxidation and interleukin-1alpha levels associates with clinical improvement of mild comedonal acne. *J Eur Acad Dermatol Venereol* 2014; **28**: 1792–1797.
50 Krutmann J, Moyal D, Liu W *et al.* Pollution and acne: is there a link? *Clin Cosmet Investig Dermatol* 2017; **10**: 199–204.
51 Lefebvre MA, Pham DM, Boussouira B, Bernard D, Camus C, Nguyen QL. Evaluation of the impact of urban pollution on the quality of skin: a multicentre study in Mexico. *Int J Cosmet Sci* 2015; **37**: 329–338.
52 Lefebvre MA, Pham DM, Boussouira B *et al.* Consequences of urban pollution upon skin status. A controlled study in Shanghai area. *Int J Cosmet Sci* 2016; **38**: 217–223.
53 Das M, Misra MP. Acne and folliculitis due to diesel oil. *Contact Dermatitis* 1988; **18**: 120–121.
54 Fabbrocini G, Kaya G, Caseiro Silverio P *et al.* Aryl hydrocarbon receptor activation in acne vulgaris skin: a case series from the region of Naples, Italy. *Dermatology* 2015; **231**: 334–338.
55 Tarun J, Susan J, Suria J, Susan VJ, Criton S. Evaluation of pH of bathing soaps and shampoos for skin and hair care. *Indian J Dermatol* 2014; **59**: 442–444.
56 Nguyen SH, Dang TP, Maibach HI. Comedogenicity in rabbit: some cosmetic ingredients/vehicles. *Cutan Ocul Toxicol* 2007; **26**: 287–292.
57 Dreno B, Bettoli V, Perez M, Bouloc A, Ochsendorf F. Cutaneous lesions caused by mechanical injury. *Eur J Dermatol* 2015; **25**: 114–121.
58 Araviiskaia E, Berardesca E, Bieber T *et al.* The impact of airborne pollution on skin. *J Eur Acad Dermatol Venereol* 2019; **33**: 1496–1505.
59 Wolkenstein P, Machovcova A, Szepietowski JC, Tennstedt D, Veraldi S, Delarue A. Acne prevalence and associations with lifestyle: a cross-sectional online survey of adolescents/young adults in 7 European countries. *J Eur Acad Dermatol Venereol* 2018; **32**: 298–306.

