REVIEW ARTICLE

The impact of airborne pollution on skin

E. Araviiskaia,[1] E. Berardesca,[2] T. Bieber,[3] G. Gontijo,[4] M. Sanchez Viera,[5] L. Marrot,[6] B. Chuberre,[7] B. Dreno[8,*]

[1]Department of Dermatology and Venereal Diseases, First Pavlov State Medical University of St. Petersburg, St. Petersburg, Russia
[2]San Gallicano Dermatological Institute, Rome, Italy
[3]Department of Dermatology and Allergy, University of Bonn, Bonn, Germany
[4]Department of Dermatology, UFMG Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil
[5]Instituto De Dermatologia Integral, Madrid, Spain
[6]L'Oréal Advanced Research, Aulnay-sous-Bois, France
[7]L'Oréal Cosmétique Active International, Levallois-Perret, France
[8]Onco-Dermatology Department, CHU Nantes, CRCINA, University Nantes, Nantes, France
*Correspondence: B. Dreno. E-mail: brigitte.dreno@atlanmed.fr

Abstract

Indoor and outdoor airborne pollutants modify our environment and represent a growing threat to human health worldwide. Airborne pollution effects on respiratory and cardiac health and diseases have been well established, but its impact on skin remains poorly described. Nonetheless, the skin is one of the main targets of pollutants, which reach the superficial and deeper skin layers by transcutaneous and systemic routes. In this review, we report the outcomes of basic and clinical research studies monitoring pollutant levels in human tissues including the skin and hair. We present a current understanding of the biochemical and biophysical effects of pollutants on skin metabolism, inflammatory processes and oxidative stress, with a focus on polyaromatic hydrocarbons and ground-level ozone that are widespread outdoor pollutants whose effects are mostly studied. We reviewed the literature to report the clinical effects of pollutants on skin health and skin ageing and their impact on some chronic inflammatory skin diseases. We also discuss the potential interactions of airborne pollutants with either ultraviolet radiation or human skin microbiota and their specific impact on skin health.
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Conflicts of interest

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Introduction

Outdoor pollution is associated with about 3.3 million premature deaths per year worldwide, with the Asian continent bearing most of the burden.[1] In addition, household pollution, resulting mainly from solid fuel cooking, is a serious threat for human health[2] and is deemed responsible for nearly 4 million premature death per year worldwide.[3]

Airborne pollution is defined as contamination of outdoor and indoor environments by any chemical, physical or biological agent that modifies the natural characteristics of the atmosphere.[4]

The authors would like to mention that during the reviewing process of their work, Der Hautartz published an article written by Fuks *et al.* that focuses on the impact of ozone on skin: Fuks KB, Woodby B, Valacchi G. Skin damage by tropospheric ozone. Der Hautartz. Published online 18 January 2019. https://doi.org/10.1007/s00105-018-4319-y.

The main outdoor air pollutants, as defined by the United States Environmental Protection Agency (US EPA), derive from gaseous compounds (nitrogen dioxide [NO_2], sulphur dioxide [SO_2], carbon monoxide [CO]), particulate matter (PM) and heavy metals (Table 1) (for reviews[5,6]). In addition, nitrogen oxide compounds interact with volatile organic compounds (VOCs) upon ultraviolet (UV) photoactivation to generate ground-level ozone (O_3) (Table 1). Other classes of air pollutants are persistent organic compounds (POPs), semi-volatile compounds (SVOCs) and polyaromatic hydrocarbons (PAHs; Table 1). Moreover, some pollutants (e.g. ground-level O_3, PM) and specific PAHs like benzo[a]pyrene (B[a]P) and indeno [1,2,3-cd]pyrene (I[cd]P) may become more toxic in the presence of UV radiation.[7,8] Airborne PAHs are widespread (Table 1) and several of them are present in cigarette smoke (e.g. B[a]P), which is often used as a surrogate for air pollution in experimental settings.[9,10]

The household environment is a wide source of indoor air pollutants, although their contribution is often neglected.[3] The concentration of VOCs and SVOCs – emanating from household products (Table 1) and combustion of fuel used for cooking, heating and lighting – has been found to be higher indoors than outdoors.[11]

At the interface with the air, skin is the target of several environmental stressors.[5,10,12–14] Here, we provide an overview of how pollutants penetrate the skin via direct transcutaneous uptake or via indirect systemic distribution of inhaled or ingested pollution through the blood. We report on recent basic research studies investigating the biochemical and molecular changes induced by pollutants in skin and on clinical studies investigating the impact of pollutants on skin ageing and inflammatory skin diseases. Overall, the authors aimed to overview the main topics of the current knowledge on the impact of pollution on skin health and diseases to inform dermatologists so that they could adapt their daily clinical practice and specifically answer to the concerns of their patients.

Methods

A board of 6 dermatologists, E Araviiskaia, E Berardesca, T Bieber, B Dréno, G Gontijo, M Sanchez-Viera, and 2 scientists from L'Oréal L Marrot and B Chuberre was constituted. Literature review was performed by searching PubMed with the following key words: air pollution, outdoor pollution, indoor pollution, volatile organic compounds, particulate matter, $PM_{2.5}$, PM_{10}, photosensitizer, oxidative stress, environmental stressors, dermal uptake, skin pigmentation, acne, skin health, skin microbiome, skin ageing, photoaging. The most recent (September 2012 to June 2018) reviews and original articles on basic and clinical research were selected. Were excluded the studies presenting

Table 1 Various types of pollutants

Air pollutant class	Name†,‡	Potential sources of pollutants
Gaseous	Carbon monoxide†	Fossil-fuel combustion, vehicle emission
	Nitrogen dioxide†	Fuel combustion, wood burning, vehicle emissions, waste incineration
	Ozone†	Formed by interaction of VOCs and NOx compounds upon UV-photoactivation
	Sulphur dioxide†	Fuel combustion, vehicle emissions, maritime transport, electric utilities, industrial facilities, volcanoes
Heavy metals	Lead†	Metal refineries, battery manufacturing, waste incineration, industrial facilities, leaded fuel, lead-based paint, plumbing material
	Cadmium	Battery manufacturing, aircraft industry, television manufacturing
	Nickel	Casting, welding, battery manufacture
	Arsenic	Battery manufacture, minerals
Particulate matter (PM)§†	Coarse PM_{10} (2.5–10 μm)	Road dust, unpaved roads, forest fires, waste degradation including electronic waste, cooking processes
	Fine $PM_{2.5}$ (<2.5 μm)	Fossil-fuel combustion, industrial facilities, maritime transport, biomass burning, waste incineration, cooking
	Ultrafine $PM_{0.1}$ (<0.1 μm)	Vehicle emission, industrial facilities
Persistent organic compounds	Dioxins, dioxin-like polychlorinated biphenyls	Herbicides, pesticides, industrial processes, forest fires, volcanic eruptions
Polyaromatic hydrocarbons (PAHs)¶	Examples: acenaphthene, acenaphthylene, anthracene, benz[a]anthracene, benzo[a]pyrene (B[a]P)**, benzo[b] fluoranthene, benzo[k]fluoranthene, benzo[g,h,i] perylene, chrysene, dibenz[a,h]anthracene, fluoranthene, fluorene, indenol [1,2,3-c,d]pyrene (I[cd]P), naphthalene, phenanthrene, pyrene	Incomplete combustion of organic material such as biomass and garbage, vehicle emissions, fumes from asphalt roads, cigarette smoke, forest fires, volcanic eruptions and grilled or charred meats
Semivolatile organic compounds (SVOCs)	Examples: Butylated hydroxytoluene, diethyl phthalate, geranyl acetone, nicotine (in free-base form), parabens	Solvents, fragrances, bactericides, antimicrobial agents, flooring, furniture
Volatile organic compounds (VOCs)	Examples: Acetaldehyde, dimethylformamide, formaldehyde, hexane, styrene, toluene, xylene	Fuel combustion, aircraft emission, household products, chemical solvents, paints, varnishes, cigarette smoke

†"6-criteria" air pollutants as defined by US EPA United States Environmental Pollution Agency https://www.epa.gov/criteria-air-pollutants/naaqs-table
‡See http://ec.europa.eu/environment/air/quality/standards.htm for the European air quality standards
§Mixture between solid particles and liquid droplets found in the air
¶PAHs may be part of PM: 16 "priority" PAH pollutants defined by US EPA are listed as examples
**In Europe, the levels of PAHs in the air are estimated through benzo[a]pyrene monitoring (standard: 1 ng/m^3 per year)
NOx, nitrogen oxide compounds; UV, ultraviolet.

limited confidence in the estimated effect (e.g. low number of subjects enrolled, absence of statistics). Older articles were also included if relevant to the discussion. Furthermore, the design and relevant data of clinical studies have been provided as Table S1 (supporting information).

Pollutant levels in the skin

Skin may be affected by environmental pollutants concentrating at its surface. Levels of uptake of airborne pollutants by the transcutaneous route have been reported to be similar to those measured after the inhalation of some indoor pollutants such as SVOCs and other VOCs[15–17] (Table 1). Dermal exposure and uptake have also been analysed in specific populations, such as in coke oven workers,[18] in asphalt-paving workers,[19,20] asphalt-roofing workers[21] and chimney sweeps[22] (Table 2). These studies all indicate that dermal uptake is a direct route of pollutant contamination (Fig. 1).

Radioactive-labelling studies established that inhaled ultrafine carbon particles could then be recovered in the blood.[23] Advances in bioanalytical methods have now revealed that PAHs and their metabolites can be found in the blood of adults,[24–27] children[28,29] and neonates,[26,30] as well as in urine[18,31–33] and maternal milk.[26] Thus, subjects of all ages and all types of organs can be exposed to pollutants. Once inhaled or ingested (e.g. in grilled meat[33,34]), pollutants may be distributed by the systemic circulation to the whole body and reach the dermis and the proliferative epidermal layer. Indeed, integrated PAHs have been detected in hair collected near the root and washed to eliminate externally accumulated pollutants[35] (Table 2). PAH concentrations have been found to be higher in hair from smokers than from non-smokers[35] (Table 2). Appenzeller *et al.*[36] found that levels of hair-incorporated nicotine correlated positively with cigarette consumption and proposed that PAH concentrations of over 1 nmol/g or the detection of more than two PAHs in one hair sample may indicate specific exposure of the subject to PAHs (Table 2).

Overall, these studies show that skin is targeted by pollutants, either by direct accumulation on the skin surface or by indirect distribution by the systemic route after pollutant inhalation or ingestion (Fig. 1). Hence, PAHs (Table 1) can be detected not only in the air, but also in all human bodily fluids and hair (Table 2), making them a good study tool to analyse the effects of airborne pollution on human skin health and diseases.

Biochemical changes and molecular mechanisms induced by pollutants

Metabolism and inflammatory processes

Pollutants may activate cell metabolism and inflammatory processes. In normal human epidermal keratinocytes (NHEKs) exposed to O_3, activation of the aryl hydrocarbon receptor (AHR) induced the expression of several cytochrome P450 genes, including CYP1A1.[37] AHR activation and increased CYP1A1 expression have also been reported after exposure to B[a]P,[38] $PM_{2.5}$[39] and water-soluble tobacco smoke extracts.[40]

Activation of the AHR pathway has also been implicated in the pathology of atopic dermatitis in humans. The neurotrophic factor Artemin (ARTN) has been identified as the missing link between pollution and AHR-CYP1A1 in an atopic dermatitis mouse model.[41] This prospective study also showed that epidermal CYP1A1 and ARTN messenger ribonucleic acid (RNA) levels were significantly higher in human skin samples from patients with atopic dermatitis ($N = 20$) than in those from patients with contact dermatitis ($N = 5$) or from healthy subjects ($N = 20$). AHR-dependent elevated expression of *CYP1A1* and *ARTN* was also detected in NHEKs and HaCaT cells exposed to diesel exhaust particles. Pollutants may therefore exacerbate atopic dermatitis symptoms via direct activation of AHR and subsequent ARTN overexpression.

Activation of the AHR pathway in NHEKs by PM or B[a]P has been linked to the induction of proinflammatory molecules, such as interleukin-8[38] and cyclooxygenase-2[42] via the production of reactive oxygen species (ROS) involved in oxidative stress processes.

Oxidative stress and potential interactions of airborne pollutants with UV light

A reduction in vitamin C and E levels after exposure to O_3 was first identified in the upper epidermis of mouse skin[43] (Table 3). Similar findings were reported in humans ($N = 20$) when forearm stratum corneum was experimentally exposed to environmental O_3 levels[44] (Table 3). A 10-fold increase in lipid peroxidation was also observed in the mouse epidermis after exposure to O_3.[43] In humans ($N = 9$), higher levels of oxidization of squalene, a human sebum-specific unsaturated fatty acid, have been reported in sebum experimentally exposed to cigarette smoke[45] (Table 3).

The direct detection of ROS in NHEKs exposed to B[a]P also illustrated the pollution-driven induction of oxidative stress processes in human skin cells.[38] Cellular ROS production has been shown to mediate PM-induced cytokine production in cultured primary keratinocytes.[46] Oxidative stress responses were also observed in HaCaT cells exposed to concentrated air particles[47] and in primary human keratinocytes exposed to cigarette smoke condensate[48] or diesel particulate extract.[49] Clinical evidence for an oxidative stress response occurring in humans after exposure to pollutants comes from two prospective clinical studies comparing the impact of pollution on subjects living in Mexico City ($N = 96$) and Cuernavaca ($N = 93$)[50] or in urban ($N = 79$) and rural ($N = 80$) areas of Shanghai.[51] Among several biochemical changes in sebum and the stratum corneum, vitamin E, squalene and ATP levels decreased. In contrast, oxidized protein levels were augmented (Table 3), indicating that skin antioxidant

Table 2 Detection of PAH levels in human skin and hair

Human tissue targeted	Number of samples (origin, period)	Pollutant type	Geometric mean, median (range) or mean ± SD concentration	Bioanalytical method	Author, date (country, period)
Skin surface	12 (coke oven workers: 5 consecutive 8-h shifts)†‡	Pyrene	21–166 μg/8 h leading to an estimated exposure of 4–34 μg/day and 119–893 nmol/week§	Sonicated extraction in dichloromethane + HPLC-fluo	Van Rooij *et al.*, 1993 (the Netherlands, September 1990)
	24 (nonsmoker asphalt workers: single 10-h shifts)†‡ 144 pads in total	$\sum_{16}$ PAHs Anthracene Fluoranthene Fluorene Phenanthrene Pyrene	85.79 μg (30.14–623.66)¶ 10.86 μg (3.86–142.19) 5.01 μg (1.33–55.12) 5.84 μg (0.48-9.09) 25.21 μg (5.82-213.88) 7.42 μg (1.32-55.12)	Sonicated extraction in dichloromethane + PTV/GC/MS	Fustinoni *et al.*, 2009 (Milan, Lodi, Italy, spring and summer 2003)
	26 (asphalt-roofing workers: 2–5 consecutive days)†‡	Benzo[a]pyrene Pyrene	3.3 ng/cm^2 11.0 ng/cm^2	DMSO extraction + HPLC	McClean *et al.*, 2007 (Ohio and Kentucky, USA, from April to September 1998)
	12 (asphalt paving workers: 6 smokers, three consecutive working-days monitored over 4 weeks)	$\sum_{6}$ PAHs including Phenanthrene Pyrene	 0.69 ng/cm^2 (0.034–15.76) (POD) 1.37 ng/cm^2 (–) (HW) 0.30 ng/cm^2 (0.087–7.67) (POD) 0.29 ng/cm^2 (0.03–6.1) (HW)	POD sampler and sunflower oil hand wash technique post shift	Cavallari *et al.*, 2008 (Wisconsin and Indiana, USA, August to October 2008)
	5 chimney sweeps (monitored at the end of a working day)	Benzo[a]pyrene Pyrene	Range: 12.3–40.4 ng (back of the hand)¶¶ Range: 30.9–70.3 ng (back of the hand)¶¶	Ultrasonic bath + filtration and HPLC-fluo	Kammer *et al.*, 2011 (Sweden)
Hair	50–100 mg of hair†† (6 smokers, 14 nonsmokers)	$\sum_{14}$ PAHs including: Benzo[a]pyrene Benzo[k]fluoranthene Chrysene Anthracene Fluoranthene Naphthalene	 1.1 ± 0.7 and 0.7 ± 0.3‡‡ pg/mg hair 1.2 ± 1.4 and 0.2 ± 0.1‡‡ pg/mg hair 2.7 ± 2.0 and 1.5 ± 0.5‡‡ pg/mg hair 8.2 ± 7.4 and 3.5 ± 2.4‡‡ pg/mg hair 24.1 ± 13.5 and 19.4 ± 11.1‡‡ pg/mg hair 511 ± 118 and 628 ± 348‡‡ pg/mg hair	n-hexane washing, alkaline digestion liquid extraction + HPLC-fluo	Toriba *et al.*, 2003 (Japan)
	105 hair samples (61 smokers, 44 nonsmokers)	$\sum_{12}$§§ OH-PAHs 2-OH-naphthalene 1-OH-naphthalene 9-OH-fluorene 9-OH-phenanthrene 2-OH-fluorene	24–67 190 pmol/g (median: 118 pmol/g) 213 ± 419 and 102 ± 77‡‡ pmol/g 5181 ± 17 029 and 1579 ± 1972‡‡ pmol/g 88 ± 5 and 140 ± 161‡‡ pmol/g 1570 ± 2182 and 4183 ± 8867‡‡ pmol/g 92 ± 104 and 28 ± 28‡‡ pmol/g	Water washing, liquid–liquid extraction with dichloromethane and then cyclohexane + GC-NCI-MS	Appenzeller *et al.*, 2012 (Luxembourg, 2007–2008)

†Airborne exposure and urinary metabolites (only the latter in McClean[21]) were also investigated and were correlated with dermal exposure.

‡Pollutant exposure and dermal uptake was evaluated by exposure pads (18-mm to 60-mm diameter) that were mounted at different body sites (jaw/neck, upper arm, shoulder, wrist, groin and ankle), or wrist only for McClean *et al.*[21]

§It was estimated that about 75% (28–95%) of the total dose of pyrene on average is absorbed through the skin.

¶Dermal and airborne exposure were estimated to contribute similarly to the total internal dose of PAHs.

††2–3 cm of hair cut near the hair root from the back of the head. Except for naphthalene, all values were higher in smokers than in nonsmokers, with a significant difference ($P < 0.05$) for benzo[k]fluoranthene, chrysene and anthracene.

‡‡Mean ± SD values in smokers and nonsmokers, respectively.

§§12 PAHs selected on the basis of being the most frequently analysed in urine. Details are provided for the most commonly detected PAHs in hair samples: 2-OH-naphthalene ($N = 64/105$), 1-OH-naphthalene ($N = 13/105$), 9-OH-fluorene ($N = 13/105$), 9-OH-phenanthrene ($N = 9/105$) and 2-OH-fluorene ($N = 8$).

¶¶Each number represents the sum of five consecutive tapes (3 × 5 cm^2).

BaP_{eq}, benzo[a]pyrene equivalent; DMSO, dimethyl sulfoxide; GC/MS, gas chromatography coupled with mass spectrometry; GC/NCI/MS, gas chromatography-negative chemical ionization-mass spectrometry; HPLC-fluo, high performance liquid chromatography and fluorescence detection; OH-PAHs, monohydroxy-PAHs; PAHs, polyaromatic hydrocarbons; POD, passive organic dermal; PTV, programmable temperature vaporisation; (–), missing value.

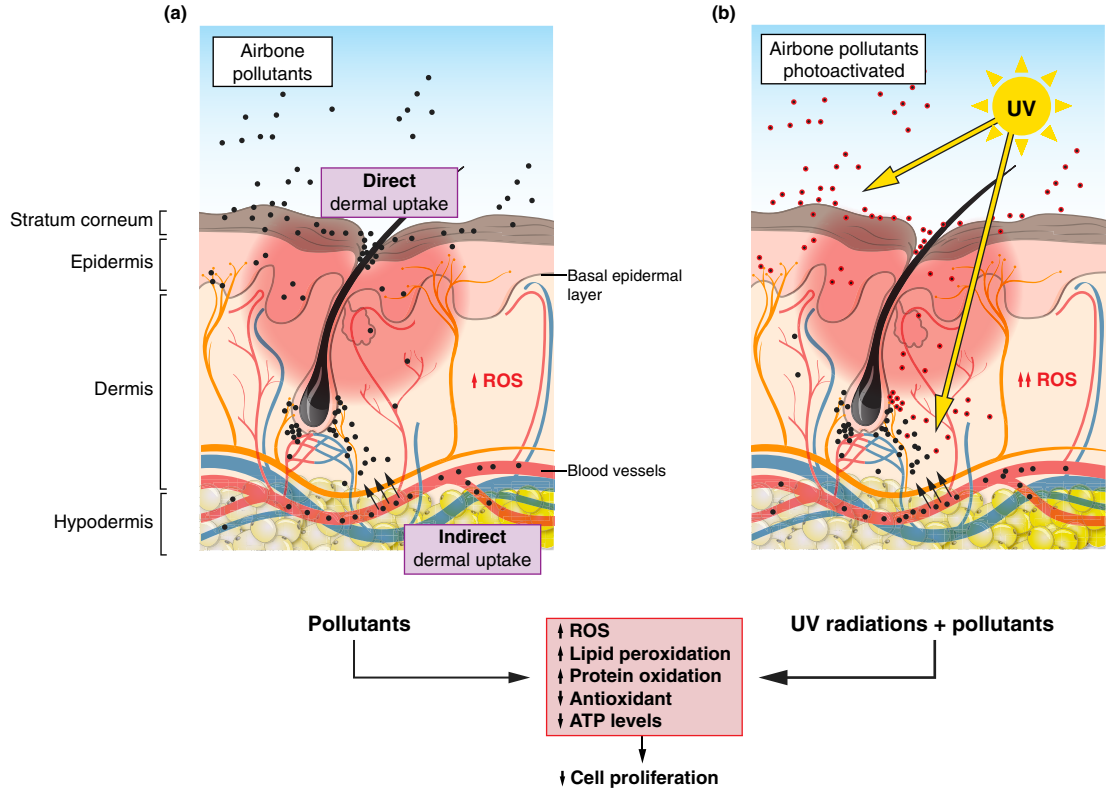

Figure 1 Direct and indirect pollution uptake – Biochemical and clinical effects of pollutants and potential interactions with UV light. Direct dermal uptake with the accumulation of airborne pollutants (PAHs, PM, O3; black dots) on the stratum corneum and subsequent penetration. Indirect dermal uptake in the dermis and basal epidermal layer with the systemic blood distribution of inhaled or ingested pollutants that may have been metabolized (black dots). Left panel: Airborne pollutants (black dots) penetrate the skin directly or indirectly (black arrows) and induce biochemical effects such as an increase in the production of ROS via the aryl hydrocarbon receptor, an elevation of lipid peroxidation, protein oxidation and cell death (apoptosis), and a reduction in cell proliferation and antioxidant and ATP levels. Clinically, the effects of pollutants correspond to the exacerbation of skin ageing processes, the symptoms of inflammatory diseases (e.g. atopic dermatitis) and the deregulation of skin moisture. Right panel: UV radiation penetrates the skin where it might induce the production of ROS. In addition, some pollutants located at the surface or within the skin might induce the production of ROS (red and black filled circles). The combination of UV radiation and pollutants might exacerbate the biochemical and clinical effects of airborne pollutants. ATP, adenosine triphosphate; O3, ground-level ozone; PAHs, polycyclic aromatic hydrocarbons; PM, particulate matter; ROS, reactive oxygen species; UV, ultraviolet.

molecules were depleted in subjects exposed to elevated pollution levels. These studies show that pollutants induce an oxidative stress response in human skin.

Moreover, in vitro experiments showed that the induction of cytotoxic[7,8] and oxidative[8,52] mechanisms by some PAHs was increased when human keratinocytes were exposed to both PAHs and UVA in particular (for a review[53]). In mouse skin, UVA exposure significantly increased the toxic impact of B[a]P[54] or cigarette smoke,[55] including the induction of squamous cell carcinoma (SCC).[55] In humans, more smokers exposed to sunlight present facial wrinkles ($N = 12$) than either smoking ($N = 9$) or sun-exposed subjects ($N = 34$) alone.[56] An increase in elastosis was found in the sun-exposed skin of the forehead and cheeks of smokers ($N = 17$) vs. non-smokers ($N = 14$).[57] Moreover, a meta-analysis[58] showed that smoking was associated with SCC, whose main risk factor is UV exposure.[59] In recent prospective studies on skin cancer, current smoking was associated with SCC,[60] but an inverse association was found for basal cell carcinoma (BCC)[60] or melanoma.[61] However, the authors suspected a bias resulting from the reduced skin cancer screening in current smokers.[60,61] Although pollutants and sunlight seem to interact,[62] further clinical investigations are required to understand their specific impact on skin health.

Table 3 In vitro and in vivo skin changes in oxidation status after exposure to pollutants

Antioxidant status	Effect of pollutant vs. control	Pollutant or area	Skin or sebum collected from	Author, date
Vitamin C (ascorbic acid)	26% loss $P < 0.05$ Student's *t* test	O_3 (10 ppm) 2 h	Mouse epidermis	Thiele *et al.*, 1997
Vitamin E (α-tocopherol)	55% loss $P < 0.01$ Student's *t* test	O_3 (10 ppm) 2 h	Mouse epidermis	Thiele *et al.*, 1997
Vitamin E (α-tocopherol)	70% loss	O_3 (0.8 ppm) 2 h	Human epidermis	He *et al.*, 2006
Lipid peroxidation	10-fold increase $P < 0.001$ Student's t test	O_3 (10 ppm) 2 h	Mouse epidermis	Thiele *et al.*, 1997
Lipid peroxidation	2.3-fold increase	O_3 (0.8 ppm) 2 h	Human epidermis	He *et al.*, 2006
Squalene peroxidation	270% increase	Cigarette smoke	Human sebum	Pham *et al.*, 2015
Squalene concentration	1.8-fold reduction $P < 0.001$ Mann–Whitney	Mexico City vs. Cuernavaca	Human sebum	Lefebvre *et al.*, 2015
% squalene in lipids	1.4-fold reduction $P < 0.05$ Student's *t* test	Urban vs. rural Shanghai	Human sebum	Lefebvre *et al.*, 2016
Ratio vitamin E/squalene	11-fold reduction $P < 0.001$ Mann–Whitney	Mexico City vs. Cuernavaca	Human sebum	Lefebvre *et al.*, 2015
Oxidized proteins	2.5-fold reduction $P < 0.05$ Mann–Whitney	Mexico City vs. Cuernavaca	Human stratum corneum	Lefebvre *et al.*, 2015
ATP	2.7-fold reduction $P < 0.001$ Mann–Whitney	Mexico City vs. Cuernavaca	Human stratum corneum	Lefebvre *et al.*, 2015

ATP, adenosine triphosphate; O_3, ozone; ppm, parts per million.

Pollutants and skin ageing

Pollutants are known to be associated with skin ageing.[63] Vierkötter *et al.*[64] used data from the SALIA study cohort[65] to conduct the first epidemiological study comparing the clinical signs of skin ageing between women exposed to higher (Ruhr area, $N = 211$) and lower (rural area, $N = 189$) levels of airborne pollution. A one-unit increase in traffic-related particles was associated with increased numbers of lentigines (age-associated pigment spots) on the forehead and cheeks, as well as with increases in nasolabial fold wrinkles. The risk of lentigines was higher after increased exposure to $PM_{2.5}$ than after increased exposure to PM_{10}. A specific association between NO_2 exposure and the appearance of facial (cheek) lentigines in German Caucasian ($N = 806$) and Chinese Asian ($N = 1072$) cohorts has also been reported.[66]

This skin ageing analysis was then extended to indoor pollution in two cross-sectional studies assessing the impact of cooking with solid fuels on Chinese women living close to Beijing (Pingding, $N = 402$) or Shanghai (Taizhou, $N = 727$).[67] The pooled analysis indicated that solid fuel use increased the risk of facial coarse wrinkles and the risk of fine wrinkles on the back of the hands. Further signs of skin ageing included more pronounced laxity of the eyelids and cheeks. In a further study, Ding *et al.*[68] found a direct association between ageing (2 cohorts $N = 874$ and 1003) and indoor $PM_{2.5}$ exposure measured in 30 households close to Shanghai.

These studies emphasize the association of outdoor and indoor pollution with signs of ageing in exposed skin. Of note, in a Dutch clinical study ($N = 956$),[69] the risk to develop elastosis was associated with smoking in a cigarette-dependent way.

Pollutants and skin microbiota

The equilibrium of human skin microbiota plays a key role in skin health (see our previous review[70]). In a German study, 21 bacterial strains, isolated from the volar forearm and the neck of 11 subjects, could use B[a]P as their only carbon source.[71] Four isolates were found to completely degrade B[a]P, possibly preventing dermal B[a]P uptake, while partial B[a]P degradation might generate toxic metabolites. Moreover, He *et al.*[44] observed that the skin microflora of the forearm of 20 women was almost halved after exposure to atmospheric-equivalent O_3 levels for 2 h. These studies suggested interactions between skin microbiota and airborne pollutants. Whether traffic-related air pollutants can affect the equilibrium of human skin microbiota, as suggested for the gut microbiota of Californian adolescents,[72] remains to be investigated.

Pollutants and inflammatory skin diseases

Acne and hyperseborrhea

Krutmann *et al.*[73] recently reviewed three Asian studies that suggested a pollutant-specific relationship between elevated levels of airborne pollutants and an increased prevalence of acne. Elevated levels of $PM_{2.5}$, PM_{10} and NO_2 were associated with an increase in the number of acne-related outpatient visits to a

dermatology clinic in Beijing.[74] Pollutants were also listed as one of the acne exposome factors in a recent review by Dreno *et al.*[75]

The impact of pollution on sebum excretion rates was investigated in the two clinical studies comparing the skin parameters of subjects living in Mexico City and Cuernavaca[50] or in urban and rural Shanghai districts.[51] The mean sebum excretion rate on the forehead was higher in subjects from Mexico City than in those from Cuernavaca. This effect was not observed in the Shanghai study, either because of the lower level of pollution in Shanghai than in Mexico City or because of differences in sebum between Asian and Caucasian subjects.[51] However, a similar increase in facial skin dryness was observed in subjects exposed to pollution in both studies.

Atopic dermatitis and eczema

The link between atopic dermatitis (AD) and pollution has always been very controversially discussed, because the scientific evidence remains scarce in contrast to asthma.[10,76–78] As for other complex diseases where gene–gene and gene–environment interactions play a role, it is important to distinguish between the potential impact of pollution (including prenatal exposure) on the development of AD[79–81] and the role of pollution as provocation factor for flares, which has been shown in several cross-sectional studies[82] and provocation studies.[83] Furthermore, some gaseous pollutants may also contribute to an increase of AD. As previously discussed (see above), the AhR expressed in the skin may link AD and pollution with a mechanism involving the neurotrophic factor Artemin.[41] Furthermore, it is assumed that airborne pollutants (e.g. PM_{10}, NO_2, SO_2 and O_3), as well as so-called xenobiotics, may have a mid- to long-term impact on relevant genes through epigenetic mechanisms (e.g. microRNAs, methylation or acetylation).

In a time-series analysis conducted from 2011 to 2015 (N = 72 305 outpatient visits for eczema) in a hospital in southwestern China, Li *et al.*[84] found a positive correlation between outpatient visits for eczema and air pollutants (NO_2, SO_2, PM_{10}), but not relative humidity, suggesting that air pollutants specifically increase the symptoms of eczema. This hypothesis has also been proposed after the multivariable analysis on the data of an Italian survey (N = 10 083 subjects aged 20–44 years)[85] that found that the prevalence of eczema was associated with living close to industrial plants and heavy traffic in particular, and in a Belarusian retrospective study conducted in infants aged 0–2 years with AD (N = 1965).[86] In their meta-analysis, Ngoc *et al.*[78] found an association between pollutants and eczema thus reinforcing the hypothesis that living in a polluted environment favours atopy and exacerbates specific inflammatory skin disease symptoms in both children and adults.

In a prospective study on AD patients aged 5 years at most (N = 177), Kim *et al.*[87] investigated the daily short-term effects of airborne pollutants in young children (aged 2 ± 1.6 years) with AD in the Seoul Metropolitan Area: a 10-unit increase in PM_{10}, NO_2 and O_3 was found to aggravate same-day symptoms. Girls appeared to be specifically affected by PM_{10}, whereas boys were impacted by NO_2 and O_3 increases. In a further study[88] conducted on 125 children aged 6 years at most, the risk of experiencing pollution-induced disease symptoms was shown to be higher in dry–moderate weather conditions. In contrast, 10-unit increases in $PM_{2.5}$ or O_3 and 2-unit increases in NO_2 or SO_2 did not correlate with worsening of AD symptoms in Japanese school children (N = 339).[89] This difference may have been associated with the $PM_{2.5}$ levels being two-fold lower in the Japanese study than in the Korean study. The results of their comparative study of skin parameters in adults in Mexico City and Cuernavaca also led Lefebvre *et al.*[50] to suggest that pollution augmented the prevalence of atopic skin diseases: subjects in Mexico City experienced more episodes of atopic eczema or urticaria than those from Cuernavaca.

Overall, the symptoms of chronic inflammatory skin diseases seem exacerbated when adult and paediatric subjects are exposed to high pollution levels.

Conclusion

Outdoor and indoor pollutants are widespread in both urban and rural environments. Inhaled or ingested pollutants can be distributed to the whole body via the systemic circulation, making both the air-exposed superficial and deep skin layers pollutant targets. Basic and clinical studies have provided growing evidence of the interactions of pollutants with skin. Pollutants may activate cutaneous metabolism and inflammatory pathways and induce oxidative stress by lowering the levels of antioxidants in particular. Skin is also the target of another known source of oxidative stress that is UV radiation. The interactions of pollutants with either UV light or human skin microbiota require further clinical investigations to evaluate their specific impact on skin health. Both outdoor and indoor pollution were found to intensify the signs of skin ageing such as facial lentigines and wrinkles. Living in a polluted environment may also reduce skin moisture, increase the rate of sebum excretion and likely exacerbates the symptoms of chronic inflammatory skin diseases both in children and adults. Home location, type of work and diet all lead to internal and external exposure to various pollutants, with clinical consequences that may accumulate or synergize.[90] Pollutants are just one component of the exposome[75,90,91] meaning that both internal and external factors are to be considered when establishing protecting measures from pollution, which require the development of standardized methods for their evaluation.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Summary of the design and of some relevant results of the clinical studies included in the review.