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Air pollution and the skin

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The increase of air pollution over the years has major effects on the human skin. The skin is exposed to ultraviolet radiation (UVR) and environmental air pollutants such as polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), oxides, particulate matter (PM), ozone (O_3), and cigarette smoke. Although human skin acts as a biological shield against pro-oxidative chemical and physical air pollutants, the prolonged or repetitive exposure to high levels of these pollutants may have profound negative effects on the skin. Exposure of the skin to air pollutants has been associated with skin aging and inflammatory or allergic skin conditions such as atopic dermatitis, eczema, psoriasis or acne, while skin cancer is among the most serious effects. On the other hand, some air pollutants (i.e., O_3, nitrogen dioxide, and sulfur dioxide) and scattering particulates (clouds and soot) in the troposphere reduce the effects of shorter wavelength UVR and significant reductions in UV irradiance have been observed in polluted urban areas.

Keywords: air pollution, ultraviolet radiation, particulate matter, polycyclic aromatic hydrocarbons, volatile organic compounds, ozone, skin, aging

INTRODUCTION

The human skin, and mainly the upper layer of the epidermis, plays the role of a barrier, but is also one of the first and major targets of air pollutants. Air pollutants include those of environmental origin, as well as those of anthropic origin (Valacchi et al., 2012). Major air pollutants with effects on the skin include the solar ultraviolet radiation (UVR), polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), nitrogen oxides (NOx), particulate matter (PM), and cigarette smoke. The actions of various air pollutants may be amplified in the presence of other air pollutants and with the interaction of UVR, and form major active components of the pro-oxidant smog (Baudouin et al., 2002; Katsouyanni, 2003; Kampa and Castanas, 2008).

Depending on the nature of these pollutants and the integrity of the skin, the modes of the penetration of pollutants differ. Alterations that disturb the skin barrier function, in either stratum corneum lipid metabolism or protein components of the corneocytes, are involved in the development of various skin diseases. The protective ability of the skin is not unlimited, and problems arise when an abnormal exposure to environmental stressors exceeds the skin's normal defensive potential (Valacchi et al., 2012).

Air pollutants may induce severe interference of normal functions of lipids, DNA and/or proteins of the human skin via oxidative damage (Adelman et al., 1988; Karten et al., 1988; Halliwell and Gutteridge, 1989; Stadtman, 1992; Gaboran et al., 1993; Menzel, 1994; Ames et al., 1995; Valko et al., 2006; Kampa and Castanas, 2008), leading to skin aging, inflammatory or allergic conditions such as atopic dermatitis, psoriasis and acne, and skin cancer (Kohen, 1999; Baudouin et al., 2002).

AIR POLLUTANTS AND EFFECTS ON THE SKIN

ULTRAVIOLET RADIATION

The solar UVR consists of three spectral areas: UVA (320–400 nm), UVB (280–320 nm), and UVC (180–280 nm). More than 95% of the solar UVR that reaches the earth's surface is UVA, 1–5% is UVB, whereas most UVC is absorbed by the O_3 layer and oxygen in the atmosphere and is thus a very small source of adverse human health effects (Dessinioti et al., 2010). Small changes in stratospheric O_3 increase the penetration of shorter ultraviolet wavelengths (UVA, UVB) at the ground level. The depletion of stratospheric O_3 by chlorofluocarbons (CFCs) and other industrially produced O_3 destructive substances presents a major problem in the environment and the human health (Schroeder et al., 2006). Despite the United Nations regulations, the stratospheric O_3 layer is still thinner than that one century ago, while there is one O_3 hole over the Antarctica and other openings over northern USA.

The effects of UVR on human skin differ depending on the wavelength. While UVA has been implicated in skin aging (photoaging), it has been linked, along with UVB, in the development of cutaneous immunosuppression and skin cancers such as malignant melanoma, basal cell carcinoma (BCC), and squamous cell carcinoma (SCC) (photocarcinogenesis). However, UVA and UVB damage DNA through different mechanisms. As the depth of penetration into the skin is dependent on the wavelength, UVB is largely absorbed by epidermal cellular components (proteins, DNA), while UVA radiation penetrates deeply into the basal layer of the epidermis and dermal fibroblasts. (Fisher et al., 1997; Dessinioti et al., 2010, 2011; Valacchi et al., 2012). Increasing evidence demonstrates that UVA in combination with common environmental pollutants, like PAHs significantly increases visible photodamage in skin (Burke and Wei, 2009).

UVR can induce gene alterations or immunosuppresion (Baudouin et al., 2002; Aubin, 2003; Amerio et al., 2009; Huang et al., 2009; Valacchi et al., 2012). Reports of the effects of O_3 depletion noticed an increase in skin cancer in many countries associated with movements of the Antarctic "ozone hole" (Abarca et al., 2002; English et al., 2003), and a decrease of the age of skin cancer development (Al-Bareeq, 1995). For every 1% decrease

in O_3 there is a 2% increase in UVB irradiance, and therefore a 2% increase in skin cancer is predicted (Goldsmith, 1996). The amount of average annual UV radiation has been traditionally correlated with the incidence of skin cancer (Armstrong and Kricker, 2001). Data from 28117 cutaneous melanoma cases reported during 1978–1993 to the EUROCARE group of registries reported a significant seasonal variation (with a summer peak) in melanoma incidence in most of the Western European registries, which was higher for Southern countries than for Northern countries (Boniol et al., 2005).

POLYCYCLIC AROMATIC HYDROCARBONS (PAHS)

PAHs are among the most widespread organic pollutants (Epstein et al., 1999; English et al., 2003). The main source of atmospheric PAH benzo[a]pyrene is residual wood burning (Burke and Wei, 2009). It is also found in automobile exhaust fumes (especially from diesel engines), and in all smoke resulting from the combustion of organic material (including cigarette smoke).

Skin pigmentation may also occur in the absence of UV radiation (Tschachler and Morizot, 2006) and PAHs induce melanocyte proliferation and thereby skin pigmentation (tanning) in mice (Vierkotter et al., 2010). PAHs are frequently bound to the surface of combustion-derived PM and absorbed on the surface of suspended PM in the air in urban areas (Menichini, 1992). PAHs are converted into quinines, redox-cycling chemicals that produce reactive oxygen species (Penning et al., 1999). Those pollutants can be adsorbed on the surface of PM, making it toxic. Long term-exposed skin to PM-bound PAHs either through hair follicle or transepidermal absorption (Lademann et al., 2004) may lead to oxidative stress and skin aging. Ambient particles (like soot) may be able to reach melanocytes, release surface-bound PAHs and/or directly affect the function of cutaneous cells (Vierkotter et al., 2010).

PAHs have been implicated in the development of skin cancer. Activated PAHs produce epoxides and diols, respectively, which bind to DNA and initiate cutaneous carcinogenesis (Kelfkens et al., 1991; Fernandez and Banerji, 1995; Hecht et al., 2001; Baudouin et al., 2002). The carcinogenic action of benzo[*a*]pyrene was enhanced with the interaction of UVA (Kelfkens et al., 1991; Wei et al., 2003).

PAHs can lead to acneiform eruptions (Baudouin et al., 2002). 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is the most potent member of the group of polyhalogenated aromatic hydrocarbons. This lipophilic compound has a long elimination half-life (5–10 years depending on exposure levels) and exerts pleiotropic biological effects by binding to the intracellular aromatic hydrocarbon receptor. It is formed in any burning, waste incineration, metal production, and fossil-fuel and wood combustion. Chloracne was described in the case of Victor Yushchenko's poisoning with TCDD in 2005 by Sorg et al. (2009). Chloracne is a systemic toxic disease caused by the exposure to chloracnegens (halogenated aromatic hydrocarbons) and is characterized by acneiform skin lesions such as comedones and cysts mainly on the face (outer sides of the eye and behind the ears) and neck. Other manifestations of chloracne include fatigue, liver dysfunction, neuropathy, arthritis (Tindall, 1985).

VOLATILE ORGANIC COMPOUNDS (VOCS)

Emission of VOCs originates from the use of organic solvents in paints, varnishes (e.g., aliphatic hydrocarbons, ethyl acetate, glycol ethers, methylene chloride, and acetone), vehicle refinishing products in repairing car paint, environmental tobacco smoke, stored fuels, exhaust from cars (e.g., benzene) and from emissions from industrial facilities (e.g., tetrachloroethene) (Dales et al., 2008; Kampa and Castanas, 2008; Okada et al., 2012). VOCs, with the presence of sunlight and NOx, cuase the formation of photochemical oxidant products - mainly O_3- at ground level, also called summer photochemical smog (Schroeder et al., 2006). VOCs (ingestion of hexachlorobenzene) may induce precancerous skin lesions in rats (Michielsen et al., 1999).

Research in cultured keratinocytes showed that exposure to VOCs increases cytokines, which could then favor the development of inflammatory and/or allergic reaction as atopic dermatitis or eczema (Ushio et al., 1999).

OXIDES

Nitrogen oxides are emitted mainly from mobile and stationary combustion sources. They react with O_3 or radicals in the atmosphere, forming NO_2. Among NOx, NO_2 is known to cause oxidative damage resulting in the generation of free radicals that may oxidize amino acids in tissue proteins and initiate lipid peroxidation of polyunsaturated fatty acids (Eberlein-König et al., 1998).

Atmospheric sulfur dioxide (SO_2) can be formed from both anthropogenic (fuel combustion from power generation and industrial processes) and natural sources (volcanic activity, forest fires). CO is another pollutant, a product of incomplete combustion from mobile sources (Kampa and Castanas, 2008). Carbon monoxide acts on cell metabolism through hypoxic and non-hypoxic modes of action, resulting from its ability to bind to heme and alter its function and metabolism.

The prevalence of atopic dermatitis has been steadily increasing over the past few decades in Europe (Schultz-Larsen, 1993) and some studies point to a higher prevalence of atopic dermatitis in children who live in areas with high air pollution (Dotterud et al., 1994; Hayashi et al., 1995; Werfel and Kapp, 1998). Most air pollutants act as unspecific irritants as well as immunomodulators, leading to elevated levels of total serum IgE (Suzuki et al., 1989; Eberlein-König et al., 1998; Kim and Bernstein, 2009). An East–West German comparative study showed that the prevalence of atopic eczema was higher in East Germany (sulfurous type pollution), but also exhibited stronger association with atopic eczema with NOx exposure (indoor) and with inhabitance in close proximity to heavy traffic (Schäfer and Ring, 1997; Tombácz et al., 2009). The effects of traffic-related air pollutants and climatic factors on eczema prevalence in middle-school students was assessed in Taiwan and showed that flexural eczema was associated with traffic-related air pollutants, including NOx and carbon monoxide, with the auxiliary presence of the lowest monthly mean relative humidity (Lee et al., 2008). Also, an increased risk for flexural dermatitis in children exposed to high levels of traffic-related air pollution has been reported (Annesi-Maesano et al., 2007).

PARTICULATE MATTER (PM)

Air pollutants, consisting of complex and varying mixtures of different size and composition particles suspended in the air was called PM. Factories, power plants, refuse incinerators, automobile, construction activities, fires and natural windblown dust are some of the main sources of PM (Poschl, 2005; Lazaridis et al., 2008; Dagouassat et al., 2012). Their major components are metals, organic compounds, material of biologic origin, ions, reactive gases, and the particle carbon core (Kampa and Castanas, 2008).

Particles in the nanosize range, especially those from traffic sources, are considered among the most harmful components of ambient PM, since their particular physical properties make them highly reactive toward biological surfaces and structures and induce oxidative stress in human skin (Vierkotter et al., 2010). The generation of oxidative stress by PM contributes to extrinsic skin aging (Donaldson et al., 2005; Vierkotter et al., 2010). Another study showed a significant correlation between PM pollution exposure (traffic particle and soot) and extrinsic skin aging signs, such as pigment spots on face, nasolabial folds, and wrinkles (Vierkotter et al., 2010).

OZONE

O_3 exists in the stratosphere and in troposphere (Baudouin et al., 2002; Madronich et al., 2011). Normally, O_3 is found in low concentrations at ground-level, originating from the stratospheric O_3 and hydrocarbons which are released by plants and soil. However, O_3 may be formed as a by-product of certain human activities, with the interaction of sunlight (UVR), hydrocarbons, VOCs and NOx, representing a major active component of the pro-oxidant smog (Baudouin et al., 2002; Schroeder et al., 2006; Madronich et al., 2011). The actions of O_3 could be amplified in the presence of other air pollutants, where concomitant exposure to UV irradiation and O_3 could reveal synergistic oxidative stress effects in skin (Baudouin et al., 2002; Burke and Wei, 2009).

Experimental evidence shows that O_3 can induce damage in the epidermis of murine skin, reduce the level of antioxidants such as a—topopherol (vitamin E) and ascorbic acid (vitamin C) and increase malondialdehyde (MDA) a lipid peroxidation product (Thiele et al., 1997a,b; Weber et al., 1999; Schroeder et al., 2006). These effects lead to barrier perturbations, the production of lipid ozonation products and inflammation (Podda and Fuchs, 2004; Schroeder et al., 2006; Valacchi et al., 2012). The first target of O_3 is the stratum corneum that contains a high level of unsaturated fatty acids and lipids (Packer and Valacchi, 2002; He et al., 2006), with the generation of ROS. O_3 stimulation results in disturbed activity of matrix metalloproteinases (MMPs), responsible for the degradation of extracellular matrix components such as collagen and elastin, implicated in extrinsic skin aging (Rittié and Fisher, 2002; Schroeder et al., 2006). Tropospheric O_3 exposure has been associated with urticaria, eczema, and contact dermatitis, in a study showing the cutaneous effects of O_3 by collecting data from almost 70,000 patients (Xu et al., 2011).

On the other hand, pollutants [i.e., O_3, nitrogen dioxide (NO_2), and SO_2] and scattering particulates (clouds and soot) in the troposphere reduce the effects of shorter wavelength UVR more than longer wavelength (Madronich et al., 2011). Large reductions in UV irradiance have been observed in polluted, urban areas when compared to pristine locations (Kazadzis et al., 2009; McKenzie et al., 2011). Significant reductions in UVB radiation can occur with naturally occurring pollutants, such as dust, volcanic ash, and wild fire aerosols (Jansen et al., 2013). In addition, a study in the co-existence of O_3 with other air pollutants, like PM with aerodynamic diameter of 10 lm or less (PM10), SO_2, and NO_2, didn't show any correlation with the increase in skin disorders (Xu et al., 2011).

CIGARETTE SMOKE

Cigarette smoke is a highly complex aerosol composed of thousands of chemical substances, including ROS, reactive nitrogen species and electrophilic aldehydes (Dube and Green, 1982; Church and Pryor, 1985; Valacchi et al., 2012). Environmental cigarette smoke contains carcinogens, such as benzo [a] pyrene and 4-(methylnitrosoamino)- 1-(3-pyridyl)-1-butanone (NNK), and also a large amount of oxygen radical forming substances, such as catechol, known to interact with the skin (Gottipati et al., 2008). Reactive oxidants and free radicals from cigarette smoke are associated with oxidative stress or secondary oxidative events, such as lipid peroxidation (Pryor et al., 1983, 1984; Church and Pryor, 1985; Chow, 1993; Boyd et al., 2002; Dietrich et al., 2003). Chemical substances from cigarette smoke activate transepidermal water loss, degeneration of connective tissue in the skin and increase of matrix metalloproteinases (MMP-1, MMP-3) (Jorgensen et al., 1998; Wolf et al., 1998; Yin et al., 2000; Just et al., 2007; Valacchi et al., 2012).

Smoking is correlated with deeper periorbital wrinkling (Solly, 1856; Daniell, 1971; Freiman et al., 2004). Premature facial skin aging in smokers, with a characteristic pattern of wrinkling and orange-purple skin discoloration, was defined as *smoker's face* (O'Hare et al., 1999). Heavy cigarette smokers were 4.7 times more likely to have facial wrinkles than non-smokers, independent of sun exposure (Kadunce et al., 1991; Freiman et al., 2004), although the combination of smoking and sun exposure may have a synergistic effect on skin aging.

Cigarette smoke is associated with psoriasis (Kavli et al., 1985; Mills et al., 1992; Gupta et al., 1996; Naldi et al., 1999; Armstrong et al., 2011). A recent meta-analysis of prevalence studies included a total of 146,934 psoriasis patients and reported an association between psoriasis and current or former smoking (pooled OR: 1.78, 95%|CI: 1.52–2.06, and pooled OR: 1.62, 95% CI: 1.33–1.99, respectively), concluding that smoking is an independent risk factor for the development of psoriasis (Armstrong et al., 2014). The effect of smoking could be mediated by the ROS and in particular by the disturbed balance of oxidants and antioxidants, indicated with low levels of vitamin C and glutathione, and high levels of superoxide dismutase and malonaldehyde in cutaneous tissues (Isik et al., 2007; Armstrong et al., 2011; Valacchi et al., 2012).

A higher prevalence of acne among smokers and a correlation between the severity of acne and the number of smoked cigarettes has been shown (Schäfer et al., 2001). A study of 226 post-adolescent women with acne reported smoking in 66.3% of patients and there was an association of smoking with comedonal post-adolescent acne compared to the papulopustular form ($p < 0.0001$). The authors reported that although the correlation between acne and smoking is still controversial, there is

a hyperkeratizing effect of cigarette-smoke compounds, and in particular of nicotine. Nicotine is an agonist of acetylcholine (ACh) and may induce comedogenesis (the formation of comedones) via the stimulation of ACh nicotinic receptor on epidermal keratinocytes (Capitanio et al., 2010).

Tobacco smoking has been associated with cutaneous SCC, (Leonardi-Bee et al., 2012) and keratoacanthoma, (El-Hakim and Uthman, 1999), while the link between smoking and BCC remains controversial (van Dam et al., 1999; Wojno, 1999; Corona et al., 2001; De Hertog et al., 2001; Boyd et al., 2002; Milan et al., 2003; Leonardi-Bee et al., 2012; Valacchi et al., 2012).

CONCLUSIONS

Major air pollutants with effects on the skin include the solar UVR, PAHs, VOCs, NOx, PM, O_3, and cigarette smoke. Considerable effects mediated by air pollutants on the human skin may contribute to skin aging, atopic dermatitis, skin cancer, psoriasis, and acne.

Oxides have been associated with increased prevalence of atopic dermatitis as well as exacerbations of the disease in children. VOCs, with the presence of sunlight and NOx, cause the formation of photochemical oxidant products -mainly O_3- at ground level, also called summer photochemical smog. Exposure to O_3 has been associated with urticaria, eczema, contact dermatitis, and other nonspecific eruptions. Exposure to PM contributes to extrinsic skin aging (wrinkles, pigmented macules or spots). Cigarette smoking has been associated with skin aging (wrinkles, skin dryness, skin dyschromias), and the combination of smoking and sun exposure may have a synergistic effect on skin aging. Furthermore, it has been associated with skin cancer (SCC, BCC), psoriasis and acne vulgaris.

On the other hand, pollutants (i.e., O_3, NO_2, and SO_2) and scattering particulates (clouds and soot) in the troposphere reduce the effects of shorter wavelength UVR and significant reductions in UV irradiance have been observed in polluted, urban areas.

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