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Cutaneous Effects of Smoking

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Abstract

Background: Cigarette smoking is the single biggest preventable cause of death and disability in developed countries and is a significant public health concern. While known to be strongly associated with a number of cardiovascular and pulmonary diseases and cancers, smoking also leads to a variety of cutaneous manifestations.

Objective: This article reviews the effects of cigarette smoking on the skin and its appendages.

Methods: A literature review was based on a MEDLINE search (1966–2004) for English-language articles using the MeSH terms cutaneous, dermatology, tobacco, skin, and smoking. An additional search was subsequently undertaken for articles related to smoking and associated mucocutanous diseases, with the focus on pathogenesis and epidemiologic data. Articles presenting the highest level of evidence and latest reports were preferentially selected.

Results: Smoking is strongly associated with numerous dermatologic conditions including poor wound healing, wrinkling and premature skin aging, squamous cell carcinoma, psoriasis, hidradenitis suppurativa, hair loss, oral cancers, and other oral conditions. In addition, it has an impact on the skin lesions observed in diabetes, lupus, and AIDS. The evidence linking smoking and melanoma, eczema, and acne is inconclusive. Anecdotal data exist on the possible protective effects of smoking in oral/genital aphthosis of Behçet's disease, herpes labialis, pyoderma gangrenosum, acral melanoma, and Kaposi's sarcoma in AIDS patients.

Conclusions: An appreciation of the adverse cutaneous consequences of smoking is important. Dermatologists can play an integral role in promoting smoking cessation by providing expert opinion and educating the public on the deleterious effects of smoking on the skin.

Sommaire

Antécédents: L'habitude de fumer est la plus importante cause évitable de décès et d'invalidité dans les pays développés et représente une préoccupation de santé publique non négligeable. En plus d'être associée de près à un nombre de maladies cardiovasculaires et pulmonaires, l'habitude de fumer cause également diverses manifestations cutanées.

Objectif: Le présent article passe en revue les effets de la cigarette sur la peau et ses phanères.

Méthodes: Recherche dans la base de données MEDLINE (de 1966 à 2004) des articles rédigés en anglais, en utilisant les termes clés: cutaneous, dermatology, tobacco, skin, et smoking (cutané, dermatologie, tabac, peau et fumer). Une recherche additionnelle a été entreprise sur les articles visant l'habitude de fumer et sur les maladies mucocutanées connexes, en portant une attention particulière à la pathogenèse et aux données épidémiologiques. Les articles comportant le plus haut niveau de preuves et les rapports les plus récents ont été retenus.

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Résultats: L'habitude de fumer est associée de très près à un nombre de conditions dermatologiques, y compris la cicatrisation lente des plaies, les rides et le vieillissement prématuré de la peau, les carcinomes cellulaires squameux, le psoriasis, l'hidrosadénite, la perte de cheveux, le cancer buccal et d'autres conditions de la bouche. De plus, l'habitude de fumer a des effets sur les lésions cutanées observées chez les diabétiques et les patients souffrant de lupus et de SEDA. Les preuves qui établissent un lien entre l'habitude de fumer et le mélanome, l'eczema et l'acné ne sont pas concluantes. Des données non scientifiques existent sur les potentiels effets protecteurs de la cigarette contre l'aphtose orale/génitale de la maladie de Behçet, l'herpès de la lèvre, pyoderma gangrenosum, le mélanome acral et le sarcome de Kaposi chez les sidatiques.

Conclusions: Une évaluation des conséquences néfastes de l'habitude de fumer est importante. Les dermatologues peuvent jouer un rôle important dans la promotion de la désaccoutumance au tabac en fournissant des opinions professionnelles à ce sujet et en éduquant le public sur les effets nocifs de l'habitude de fumer pour la peau.

Cigarette smoking is the single biggest preventable cause of death and disability in developed countries.[1] It shortens lifespan by an average of eight years, leading to 4.8 million deaths worldwide annually.[2] In North America, tobacco accounts for more deaths than alcohol, illicit drugs, HIV, hepatitis C, suicide, homicide, and motor vehicle accidents combined.[3]

The adverse effects of cigarette smoking on the health of the public are astounding and have been extensively documented.[4] The diversity of chemical components found in tobacco (4000 chemicals, of which 300 are known carcinogens)[5] is matched by the diversity of tobacco-related health problems. The strongest cause-specific associations are with cerebrovascular and other vascular diseases, pulmonary diseases, cancers, and oral diseases. While smoking directly or indirectly affects every organ system, an important consideration should be given to the cutaneous manifestations of smoking. The evidence regarding the effects of cigarette smoking on the skin and its appendages and the characteristic cutaneous signs of smoking (Table I) are reviewed herein. A literature review was based on a MEDLINE search (1966–2004) for English-language articles using the MeSH terms tobacco, skin, and smoking. An additional search was subsequently undertaken for articles related to smoking and identified associated mucocutanous diseases, with the focus on pathogenesis and epidemiologic data. Articles presenting the highest level of evidence and the latest reports were preferentially selected.

Cutaneous Effects of Smoking

Wound Healing

There is extensive literature on the adverse effects of cigarette smoking on wound healing.[6,7] In 1966, Roppo et al.[8] demonstrated that smoking decreases cutaneous blood flow by measuring the heat conductivity coefficient. Subsequently, Mosley and Finseth[9] established that digital blood flow and wound healing of the hand were impaired with nicotine administration. In 1984, intravital microscopy showed that arteriolar vasoconstriction and decreased blood flow occurred in the ear microcirculation of nude mice exposed to cigarette smoke.[10] In 1991, Goldminz and Bennet[11] reviewed a series of 916 flaps and full-thickness grafts, reporting a significant dose-dependent relationship between smoking and necrosis. Using a laser Doppler flowmeter to measure cutaneous microcirculation, smoking a single cigarette was shown to decrease the cutaneous blood flow in habitual smokers as well as in nonsmoking subjects; the recovery phase in smokers was shown to be slower, suggesting chronic damage to microcirculation.

The effects of smoking on cutaneous vasculature and tissue oxygen tension have been reviewed by Leow and Maibach.[13] Newer molecular biology techniques helped gain further insight into the pathophysiology of wound healing. Arredondo et al.[14] used polymerase chain reaction (PCR) and Western blotting to demonstrate that dermal fibroblasts exposed to nicotine undergo a significant decrease in their activity, leading to lower rates of migration, proliferation, and remodeling. Contraction of wound edges mediated by myofibroblasts is also disrupted by tobacco smoke.[15] Fibroblast stunting by nicotine is considered to play a major role in poor wound outcomes.[16] More recently, examining the effects of cigarette smoke on cell culture, Wong et al.[17] also demonstrated that exposure to smoke delays wound repair because of the inability of the fibroblasts to migrate into the wounded area, leading to an accumulation of these cells at the edge of the wound, and that the increase in cell survival coupled with the decrease in cell migration can lead to a buildup of connective tissue, thereby causing fibrosis and excess scarring.[17]

Smoking has been shown to significantly decrease the immune response, leading to poor wound healing. In particular, smoking decreases interleukin-1 production,[18] inhibits the early signals for B-cell transduction pathways,[19] decreases cytotoxicity of natural killer cells, and causes T-cell anergy.[20] By decreasing blood flow to damaged skin, smoking increases postsurgical infections, the result of effects on the normal pathways of repair and the response to foreign contamination.[21] For instance, in

TABLE 1

Characteristic cutaneous signs of smoking		
Clinical sign and reference	*Synonyms*	*Description*
Harlequin nail[125]	*Quitter's nail*	A demarcation line between the distal pigmented yellow nail and a newly developed proximal pink nail that is present after sudden cessation of smoking
Smoker's comedones[126]		Large, open comedones with furrows and nodules; characteristic of Favre–Racouchot syndrome
Smoker's face[26] (Fig. 1)		(a) Lines or wrinkles on the face typically radiating at right angles from the upper and lower lips or corners of the eyes, deep lines on the cheeks or numerous shallow lines on the cheeks and lower jaw (b) A subtle gauntness of the facial features with prominence of the underlying bony contours (c) An atrophic, gray appearance of the skin (d) A plethoric, slightly orange, purple, and red complexion
Smoker's melanosis[92]		Melanin pigmentation of the gingiva
Smoker's moustache[127]		Yellow-brownish discoloration of gray or white hairs of the moustache in heavy smokers
Smoker's nail[125] (Fig. 2)	Nicotine sign	Yellow pigmentation of the nail plate in chronic smokers
Smoker's palate[90]	Nicotine stomatitis, Leukokeratosis nicotina palati	Grayish-white coloration of the palatal mucosa that can be combined with red punctuate papules
Smoker's tongue[91]	Leukokeratosis nicotina glossi	Leukoplakia with pink-colored pin-point hemispherical depressions
Snuff dipper's lesion[84]	Smokeless tobacco keratosis, tobacco pouch keratosis	A white lesion in the oral cavity that is present at the site where smokeless tobacco is held

FIGURE 1 Prominent periorbital wrinkling associated with smoking.

a study of postoperative arthroplasty patients, smoking was found to be the single largest risk factor for complications related to wound healing.[22] Breast cancer surgery studies revealed similar results, with smoking associated with infections, necrosis, and epidermolysis.[21] As a result of poor wound outcomes, plastic surgeons often refuse to perform cosmetic breast surgeries and facelifts on patients who refuse to quit smoking.[23]

Wrinkling and Premature Skin Aging

Smoking and wrinkling have been anecdotally correlated for nearly 150 years, since Solly[24] reported a sallow complexion and wrinkled skin in smokers. In 1971, Daniell[25] described the characteristic prominent periorbital wrinkling with narrower, deeper, and more sharply contoured wrinkles in the crow's-feet area found in smokers. In 1985, Model[26] went on to define a "smoker's face" as a set of clinical signs to assist physicians in determining which patients had smoked for 10 years or longer. More recently, a silicone modeling technique with computer analysis of 350 participants revealed a 2.72 (95% CI 1.32–3.21) relative risk (RR) of moderate-to-severe wrinkling in smokers compared with nonsmokers.[27]

While a number of studies failed to consider the effects of sun exposure and other potential confounders in assessing the relationship between smoking and facial wrinkling,[28] a body of epidemiologic evidence serves to elaborate the link.[29] Kadunce et al.[30] demonstrated that heavy cigarette smokers (greater than 50 pack-years) were 4.7 times more likely to have facial wrinkles than non-

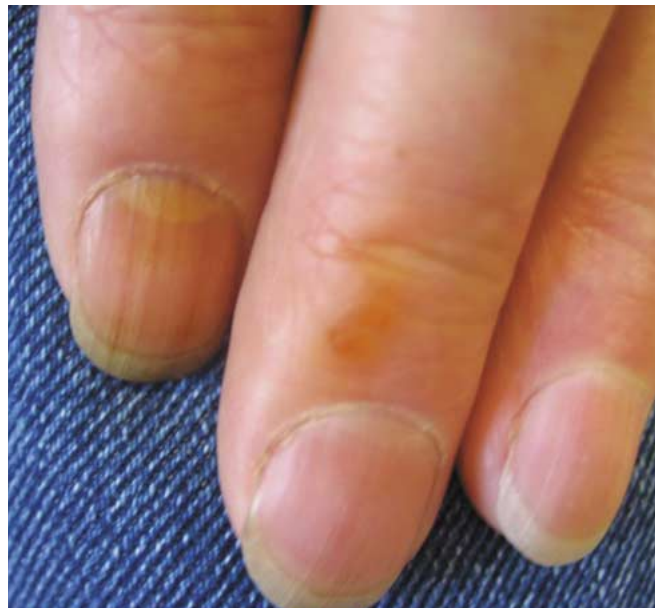
smokers (95% CI 1.0–22.6), independent of sun exposure. The combination of smoking and sun exposure had, in fact, a synergistic effect on skin aging. Chung et al.[31] also reported that smoking, sun exposure, and female sex were independent risk factors for wrinkles. In a large cross-sectional study of 1136 subjects, facial wrinkling was significantly more common in cigarette smokers and in current smokers, with the relative risk of moderate-to-severe wrinkling reported as 2.3 for men and 3.1 for women.[32]

The pathophysiology of wrinkling and premature skin aging in smokers is likely multifactorial. Elastic fibers in sun-protected skin of smokers have been shown to be morphologically similar to those in solar elastosis (photodamage), with broader and more fragmented mid- and reticular dermis elastic fibers.[33] In a histologic study comparing the forehead skin of 17 smokers with that of 14 nonsmokers (randomly selected), a significantly higher amount of elastosis was noted in smokers.[34] The phototoxic properties of tobacco smoke activated by radiation with UVA and UVB have also been reported.[35] One study noted that smoking decreases water content of the stratum corneum, which may account for the dry skin appearance of smokers.[36] Connective tissue fibers are adversely affected by smoking, the result of elastin catabolism[37] and reduced collagen crosslinking and synthesis.[38] The mRNA of the matrix metalloproteinases MMP-1 and MMP-3, directly involved in collagen breakdown, are upregulated by smoking.[39,40] More recently, tobacco smoke extracts were noted to modulate TGF-β1 in cultured fibroblasts.[41] Cigarette smoke represents one of the greatest exogenous sources of free radicals, including superoxide anion, which may also accelerate elastosis.[42]

Squamous Cell Carcinoma

The association between tobacco smoking and cutaneous squamous cell carcinoma (SCC) has been confirmed by several investigators.[43,44] In one of the largest studies, Grodstein et al.[45] prospectively examined the risk of developing cutaneous SCC in relation to skin type, sun exposure, cigarette smoking, and other factors. They showed during an 8-year observation of a cohort of 107,900 predominantly white young women that smokers had a 50% greater chance of developing cutaneous SCC than nonsmokers (RR 1.5; 95% CI 1.1–2.1).[45] More recently, De Hertog et al.[46] preformed a hospital-based case-control study that includeed 161 patients with SCC, 301 with nodular basal cell carcinoma, 153 with superficial multifocal basal cell carcinoma, 125 with malignant melanoma, and 386 controls. The authors found that tobacco smoking was an independent risk factor for SCC (RR 2.3; 95% CI 1.5–3.6) and that current smokers were in fact 3.3 times more likely (95% CI 1.9–5.5) to get SCC compared with a 1.9 relative risk for former smokers (95% CI 1.2–3.0).[46]

FIGURE 2 Discoloration of the nail in smokers.



Basal Cell Carcinoma

While there is clear evidence that smoking is a risk factor for the development of SCC, the link between smoking and basal cell carcinoma (BCC) remains controversial.[47] Most of the evidence connecting smoking and BCC has been obtained in females. Milan et al.[48] studied 290 pairs of same-sex Finnish twins, of which a single twin was diagnosed with BCC between 1976 and 1999. A significantly increased risk was associated with smoking status in females but not in males, and the risk was higher in dizygotic than in monozygotic twin females, possibly indicating the presence of a genetic predisposition.[48] In one retrospective analysis, young women with a BCC were more likely to have a past or current history of cigarette smoking; however, sun exposure may have been a significant confounder.[49] In a cross-sectional retrospective case-controlled study of 112 patients with biopsy-proven BCC of the eyelid and sex-matched controls with other eyelid disorders, Wojno et al.[50] noted that BCC of the eyelid is associated with cigarette smoking in women (OR 2.87) but not in men.[50] Furthermore, in a retrospective chart review of 220 patients undergoing Mohs sugery for BCC, cigarette smoking was shown to be associated with an increased prevalence of BCCs larger than 1.0 cm in diameter.[51]

In contrast to the above reports, large population-based studies by Van Dam et al.[52] as well as by Corona et al.[53] did not show an association between BCC and smoking. No significant link was found between smoking and nodular basal cell carcinoma or superficial multifocal basal cell carcinoma by De Hertog et al.[46]

It has been proposed that a decreased level of vitamin A in smokers may contribute to diminishing free-radical protection or to suppression of the inflammatory response to UVB after exposure to nicotine.[49] Also,

smoking may contribute to differentiation of BCC toward its sclerosing form, potentially related to an increase in peritumoral mast cell numbers.[54]

Melanoma

While a number of studies have examined the relationship between smoking and cutaneous melanoma, the evidence has not been conclusive; the majority of the studies has been limited by low power due to small sample sizes as well as by case-controlled designs with a number of inherent potential biases.[55–59] In a Danish case-control study including 474 cases of cutaneous malignant melanoma and 926 controls, Osterlind et al.[60] found no association between melanoma risk and tobacco smoking. A large case-control study by De Hertog et al.[46] also showed no significant association between smoking and melanoma. Interestingly, using a Cox multivariate analysis in a study of 196 patients with Stage I melanoma, heavy smokers were found to present with thicker lesions than their nonsmoking counterparts.[61] Overall, further studies with more statistical power and reduced potential biases are needed to establish the relationship between smoking and melanoma.

Psoriasis

A number of studies have elucidated an association between smoking and psoriasis, reviewed by Naldi.[62] The most striking link has been established between smoking and palmoplantar pustulosis (PPP), which is thought to be exacerbated, or possibly induced, by smoking. It is, however, important to recognize that a large proportion of these studies have been limited in size and potentially confounded by other variables, such as alcohol consumption and stress, which are often associated with smoking.[63]

In a case-control study of 108 patients with psoriasis and matched controls from the community, Mills et al.[64] reported a significant positive association between psoriasis, current smoking status (OR 2.7), and smoking habits prior to onset of the disease (OR 3.75), with a significant dose–response relationship between the number of cigarettes smoked per day and psoriasis.[64] Subanalysis of patients with the palmoplantar variant of psoriasis showed a significant association with smoking prior to onset of the disease (OR 3.6). In a more recent multicenter case-control study of 404 psoriasis patients and 616 controls, the risk for psoriasis was higher in smokers compared with nonsmokers, and the association with smoking was stronger and more consistent among women than men. A particularly strong association was also found between smoking more that 15 cigarettes per day and pustular psoriasis (OR 0.5).[65] Several observational and case-control studies have demonstrated up to 94% prevalence of tobacco use in patients with PPP.[66–68]

Eczema

The association between eczema and smoking has been a subject of controversy.[69] One study of 678 preschool children correlated a positive history of maternal smoking with atopic dermatitis.[70] Karvonen et al.[71] showed a link between infectious eczematoid dermatitis and smoking, while Edman[72] reported an association between vesicular palmar eczema and smoking. On the other hand, in a case-control study by Mills et al.[73] there was no significant difference between the prevalence of smoking in patients with atopic dermatitis and matched controls.

Acne

Acne is a common condition, but the epidemiologic evidence linking it to smoking is conflicting. In an observational study of 165 patients, Mills et al.[74] found a lower than expected prevalence of acne in smokers. This study further suggested that the anti-inflammatory effects of some of the components in the cigarette smoke could be responsible for reduced rates of acne.[74] However, in a recent cross-sectional study of 896 citizens of Hamburg, Germany, logistic regression analyses demonstrated a dose-related linear relationship between acne prevalence and severity and cigarette consumption, which was not affected by age, gender, or social class.[75]

Hidradenitis Suppurativa

An observational study by Konig et al.[76] of 63 German patients with hidradenitis suppurativa showed an overwhelming 88.9% prevalence of current smokers and 4.8% of former smokers. However, smoking cessation did not lead to disease improvement in the study.[76] Breitkopf et al.[77] demonstrated 85% prevalence of smoking in 149 patients with hidradenitis suppurativa. Potential mechanisms include alteration of apocrine activity by smoking, as well as alterations of neutrophilic granulocytes.[78]

Hair Loss

The pathogenesis of hair loss induced by smoking is multifactorial and was recently reviewed by Trueb.[79] Cigarette smoke affects the microvasculature of the dermal hair papilla, leads to DNA damage of the hair follicle, causes imbalance in the follicular protease/antiprotease systems affecting hair growth cycle, and increases release of proinflammatory cytokines resulting in follicular microinflammation and fibrosis.[79] Furthermore, it increases hydroxylation of estradiol and inhibition of the enzyme aromatase creating a relative hypoestrogenic state.[80] An observational study by Mosley and Gibbs[81] suggested that a relationship exists between smoking and premature gray hair in both men and women, as well as hair loss in men, although no conclusions about causal relationship could be drawn.

Oral Lesions

Numerous dental and gingival conditions are associated with tobacco use and are the subjects of several comprehensive reviews.[82–84] The evidence that tobacco increases the risk of oral cancers is overwhelming,[85,86] and

these malignancies are associated with significant mortality.[87]

A Swedish study of 596 individuals with oral disease demonstrated a positive correlation between tobacco use and leukoplakia, frictional white lesion, coated tongue, hairy tongue, and excessive melanin pigmentation, but a negative correlation for geographic tongue and aphthous ulcers.[88] Tobacco-associated oral nonmalignant lesions also include leukoplakia,[89] leukokeratosis nicotina palati,[90] and leukokeratosis nicotina glossi.[91] Characteristic hyperpigmentation of the oral cavity found among tobacco smokers is termed smoker's melanosis.[92] Biopsy of such lesions is necessary to establish a diagnosis and exclude other etiologies. Chewing tobacco is known to be associated with a variety of oral lesions. For instance, a snuff dipper's lesion typically appears at the site of tobacco contact with the oral cavity and usually resolves within a week of cessation of tobacco use.[84]

Diabetes-Associated Skin Lesions

Because of its adverse effects on cutaneous blood flow and immune response,[93,94] smoking increases the risk of developing ulcers and their infectious rates in patients with diabetes.[95] Also, in a retrospective case-control study of 15 patients with necrobiosis lipoidica diabeticorum (NLD) matched with 5 control subjects with diabetes mellitus, a significant association was found between smoking and NLD (60% vs 20%, $p = 0.003$).[96]

Lupus Erythematosus

Tobacco smoking increases the cutaneous manifestations of systemic lupus erythematosus (SLE) and has also been demonstrated to interfere with the efficacy of antimalarial therapy.[97,98]A British case-control study of 150 patients with SLE and 300 age- and sex-matched controls demonstrated almost double the risk of SLE in smokers (OR 1.95; 95% CI 1.14–3.31).[99] Another case-control study of 125 patients with SLE and 125 controls showed that cigarette smoking before SLE diagnosis and ex-smoking before SLE diagnosis significantly increased the risk of development of SLE (OR 6.69 95% CI 2.59–17.28 and OR 3.62; 95% CI 1.22–10.70, respectively).[100] In a recent meta-analysis that included seven case-control and two cohort studies, Costenbader et al.[101] demonstrated a statistically significant link between SLE and smoking. This association was specifically present in current smokers (OR 1.50; CI 1.09–2.08), although past smoking was not found to be associated with the development of SLE.[101]

Discoid lupus erythematosus (DLE) has also been linked to smoking. Gallego et al.[102] examined smoking habits in two patient populations with DLE. One group was compared with matched dermatology patients while the second group was compared with the corresponding statewide population. For both groups, the current smoking prevalence was much higher than that of the comparison population.[102]

AIDS-Associated Skin Lesions

Smoking is associated with a number of HIV-related skin conditions.[103] For instance, oral thrush and hairy leukoplakia are known to be more prevalent in patients with HIV and AIDS who smoke.[104,105] Smoking can also significantly decrease the efficacy of antiretroviral therapy.[106]

Protective Effects of Smoking

In contrast to numerous adverse mucocutanoeus effects of smoking, several protective associations have been described.[107] A decreased incidence of aphthous ulcers[88,108] as well as of oral and genital aphthosis and other manifestations of Behçet's disease have been noted in smokers[109–111] Goedert et al.[112] reported a decreased prevalence of Kaposi's sarcoma in AIDS patients, while Green et al.[113] and Lear et al.[114] showed protective effects of smoking on acral melanoma. A decreased prevalence of recurrent herpes labialis in smokers has also been reported.[115] Presumably due to its anti-inflammatory properties,[116] smoking is known to be a protective factor against ulcerative colitis,[117] and a few reports described successful treatment of its associated cutaneous manifestation, pyoderma gangrenosum, with nicotine.[118–120] Recently, several studies demonstrated the beneficial effects of smoking on pemphigus vulgaris,[121–123] likely as a result of nicotine's effects on the keratinocyte cholinergic network affected in pemphigus.[124]

Conclusions

Encouraging smoking cessation is one of the most effective interventions that physicians can do to improve the health and prolong the lives of their patients.[1] Smoking is directly or indirectly associated with a significant number of adverse cutaneous effects, and while anecdotal evidence exists of some beneficial actions of smoking on skin diseases, it pales into insignificance compared to the overwhelming epidemiologic body of evidence of the harmful and hazardous outcomes.[107] Dermatologists can play an integral role in promoting smoking cessation by providing expert opinion and educating the public on the deleterious effects of smoking on the skin. Given the public's quest for an unblemished and youthful appearance, increasing awareness about the association of smoking with a variety of cutaneous conditions, such as facial wrinkling, should be incorporated into a powerful public health message to promote a smoke-free lifestyle.

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