OBSERVATION

Smoking and Skin Aging in Identical Twins

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Background: A twin pair can provide a rare opportunity to control for genetic susceptibility and exposure variables, which often serve as major confounders in population-based studies on the relationship between smoking and skin aging.

Observations: We describe a unique twin pair who spent not only their first 2 decades of life together but also in their later decades had the same type of job at the same latitude, resulting in well-matched levels of significant sun exposure. However, the twins differed markedly in regard to smoking history; the twin with an approximately 52.5–pack-year smoking history showed more severe skin aging than did the nonsmoking twin.

Conclusion: The difference in skin aging illustrated by this twin pair may serve as a motivator for smoking cessation.

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THE UNDERLYING MECHANISM of skin aging remains to be elucidated, but the magnitude of the problem is of increasing concern. More than $160 billion was spent in 2005 on products and procedures aimed at reversing the signs of skin aging.

REPORT OF CASES

We describe a pair of identical female twins (twin 1 and twin 2) with a marked disparity in the degree of facial aging. Twin 1's facial skin exhibited extensive deep wrinkling, widespread lentigines, scattered hypopigmentation, and moderate skin laxity (**Figure 1**). Although twin 2's facial skin exhibited signs of mild to moderate photoaging (mild fine wrinkling, scattered lentigines, mild-density hypopigmentation, and mild skin laxity), her degree of facial aging was significantly less than that of her sister (**Figure 2**). We scored each twin's skin aging according to the 6-point photographic scale for photodamage created by Larnier et al.[1] According to that scale, grade 1 indicates mild; grade 2, mild to moderate; grade 3, moderate; grade 4, moderate to severe; grade 5, severe; and grade 6, very severe photodamage.[1] Twin 1 was assigned a grade of 5, whereas twin 2 was given a grade of 2.

At the time of the examination, the twins were 52 years old. In their early decades of life, they lived in multiple regions of the country because their father was an active-duty military officer with rotating assignments. Both twins' third through fifth decades of life were spent in the same town in Tennessee; in the year before the examination, twin 1 relocated to a town 60 miles south of twin 2. Twin 1 reported a medical history significant for tonsillectomy, hysterectomy, vertebral disk herniation, and recently diagnosed hypertension; twin 2 also reported a hysterectomy, as well as a cholecystectomy and degenerative joint disease. Neither twin had a documented history of any skin disease, including skin cancer. Both twins recounted having "frequent sunburns that were red and tender but not blistered" during their childhood. Both twins reported "somewhat regular" sun exposure during adulthood (on a scale of 0 [never] to 4 [very regularly]) because they both had worked as drivers for a delivery service for approximately 10 years. In addition, they never spent time in the sun trying to get a tan (on a scale of 0 [never] to 4 [very regularly]) and never used a tanning bed during adulthood (on a scale of 0 [never] to 4 [very regularly]). When they were in the sun without sunscreen, twin 1 reported that her skin burns moderately and tans gradually and twin 2 reported that her skin always burns easily and tans a little (on a scale of 0 [always burns easily, never tans] to 5 [never burns]). Within the preceding year, twin 2 had started using a daily

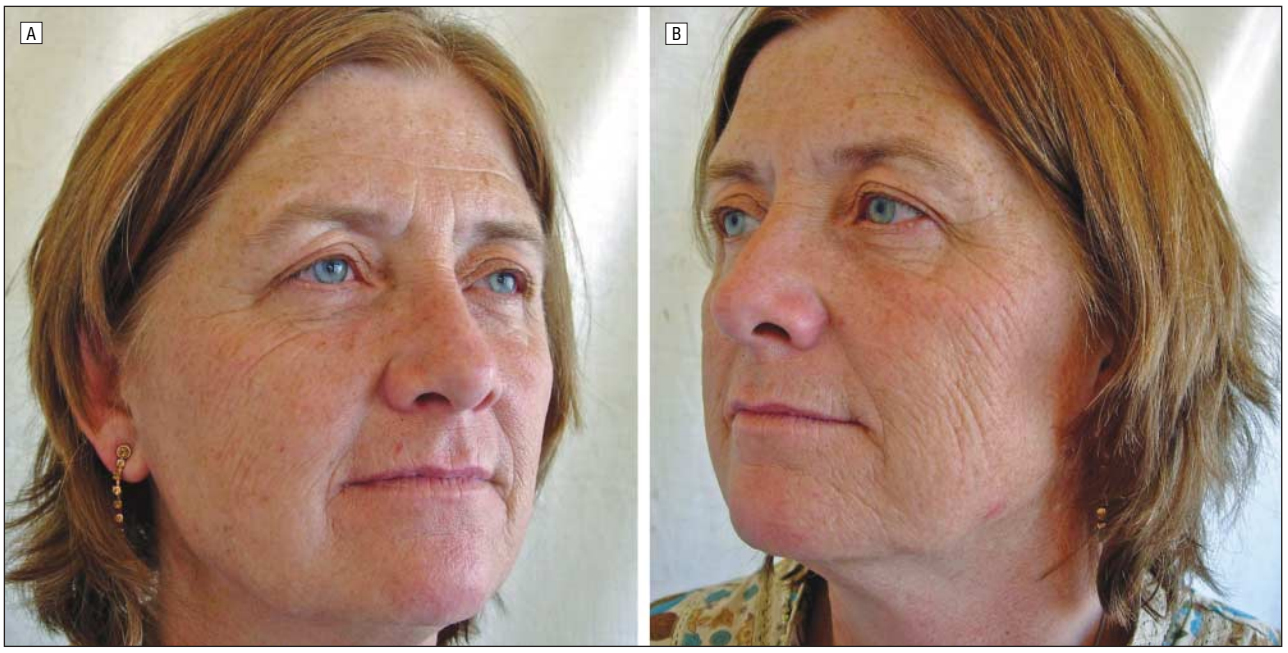

Figure 1. Twin 1, right (A) and left (B) profiles.

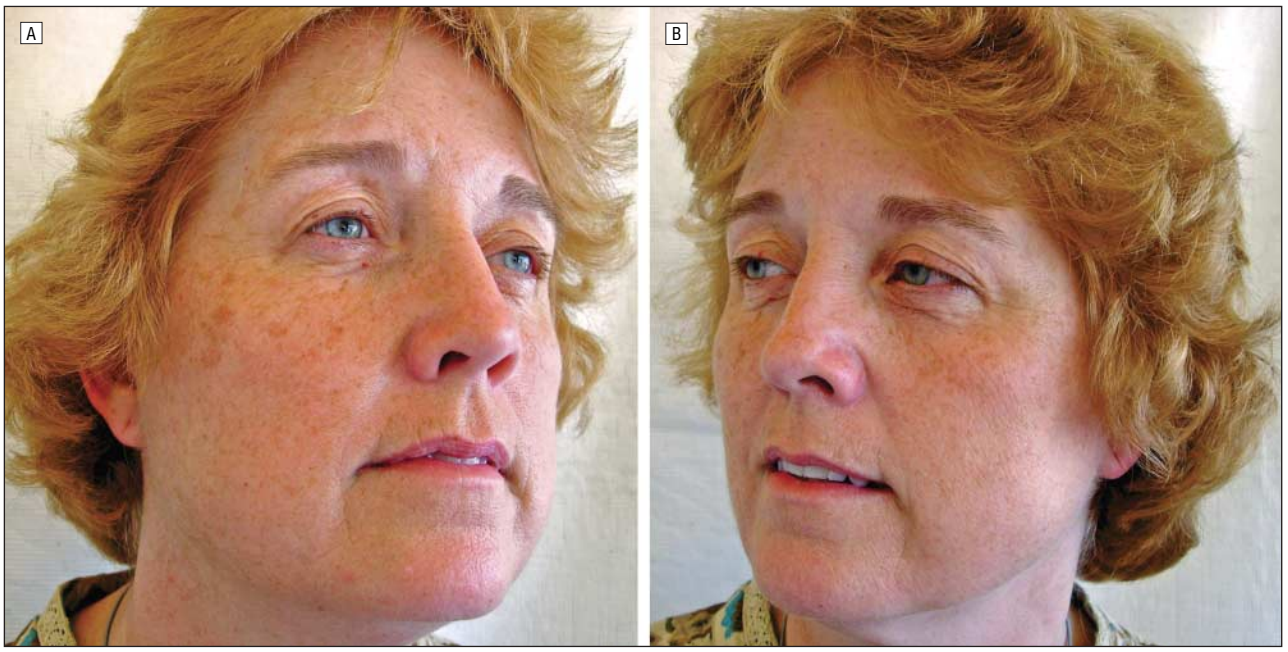

Figure 2. Twin 2, right (A) and left (B) profiles.

moisturizer with a sun protection factor of 15, whereas twin 1 used no skin care products. Neither reported use of a topical retinoid. Both twins reported minimal to no alcohol consumption, no routine exercise (on a scale of 1 [yes] to 2 [no]), and described themselves as very overweight (on a scale of 1 [very underweight] to 5 [very overweight]). Twin 1 was a cigarette smoker with an approximately 52.5–pack-year history, whereas twin 2 was a nonsmoker and had never smoked.

In this pair of twins with an identical genetic background, minor medical histories, and similar significant sun exposure histories, the clear difference between twin 1 and 2 was the extensive history of tobacco use in twin 1 that was absent in twin 2 (**Table**). This variable likely served as the major contributor to advanced skin aging in twin 1.

COMMENT

The first proposed correlation between smoking and premature skin aging was made by Solly[2] in 1856, when he reported a sallow complexion, wrinkled skin, and gaunt facial appearance in smokers. In 1971, Daniell[3] emphasized a link between prominent periorbital wrinkling and smoking habits. In 1985, Model[4] associated the term *smoker's face* with a list of telltale signs physicians can watch

Table. Demographic and Clinical Characteristics of Identical Female Twins

Characteristic	Twin 1	Twin 2
Age, y	52	52
Geographic location	Southeastern US	Southeastern US
Education	BS, elementary education	BS, elementary education
Ethnicity	White	White
Fitzpatrick skin type	II	II
Medical history	Tonsillectomy, hysterectomy, vertebral disk herniation, recently diagnosed hypertension	Cholecystectomy, hysterectomy, degenerative joint disease
BMI	30.1	33.0
Alcohol use, drinks/mo	<5	0
Smoking history, pack-years[a]	Approximately 52.5	0
Skin care regimen	None	Recent use of moisturizer with SPF 15
Use of retinoids	None	None
Sun exposure history, h[b]	>50 000	>50 000

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BS, bachelor of science; SPF, sun protection factor; US, United States.
[a] Number of packs of cigarettes smoked per day multiplied by the total number of years smoked.
[b] Cumulative lifetime sun exposure.

for to determine which of their patients had been smoking for at least 10 years.

Despite these clinical impressions, O'Hare et al[5] asserted that cigarette smoking played a minor role in causing wrinkling, noting that previous studies[2,3] linking smoking and increased wrinkling failed to consider confounding variables such as sun exposure history and were unblinded and therefore subject to bias. O'Hare et al evaluated 82 smokers and 118 nonsmokers who were 35 to 75 years of age and white. After controlling for confounding variables, the overall wrinkle score was greater for the smokers than for the nonsmokers, but the difference was not statistically significant ($P<.17$). O'Hare et al found that a positive smoking history accounted for only 6% of the explained variance in wrinkle scores between smokers and nonsmokers. Age was found to be the strongest independent predictor of facial wrinkling.

On the other hand, several studies[6-9] support a relationship between cigarette smoking and wrinkling. Kadunce et al[6] were the first to evaluate a possible relationship between cigarette smoking and wrinkling while controlling for age, sex, sun exposure, and skin pigmentation. Their study used a convenience sample of 109 smokers and 23 nonsmokers who were 35 to 59 years of age and of white western European ancestry. A self-administered questionnaire assessed age, sex, skin pigmentation, sun exposure history, and smoking history. Two clinicians who were blinded to the information provided in the questionnaire evaluated the degree of wrinkling by examining photographs of each subject. A smoking history of more than 0.9 pack-year was associated with a 3-fold (95% confidence interval [CI], 0.4-158.0) increase in wrinkling (when controlled for age, sex, sun exposure, and skin pigmentation). A sun exposure history of more than 50 000 hours was associated with an 8-fold (95% CI, 0.3-500.0) increase in wrinkling (when controlled for age, sex, smoking history, and skin pigmentation).

In 1995, Ernster et al[7] conducted a cross-sectional study of 227 never smokers, 456 former smokers, and 228 current smokers who were 40 to 69 years of age and white. Each study subject was clinically examined and scored for facial wrinkling. Standardized photographs of the study subjects were also taken, and results of a blinded evaluation of the photographs were generally consistent with the clinical examination findings. A self-administered questionnaire combined with an interview assessed age, sex, smoking history, sun exposure history, body mass index, and alcohol consumption. With age, average sun exposure, and body mass index controlled for, the estimated relative risk of moderate to severe wrinkling for current smokers compared with never smokers was 2.3 (95% CI, 1.2-4.2) among men and 3.1 (95% CI, 1.6-5.9) among women. However, age was still the strongest independent predictor of facial wrinkling. Average daily sun exposure was positively associated with facial wrinkling in women but was not consistent in men, whereas body mass index was inversely associated with facial wrinkling in both sexes.

Chung et al[8] investigated the independent effect of cigarette smoking on wrinkling in an Asian population. Four hundred seven volunteers participated in the study, of which 194 participants had a smoking history of 0 to 0.9 pack-year and 213 participants had a smoking history of 1 to 120 pack-years. After controlling for age, sex, and sun exposure, an association was established between cigarette smoking and wrinkling that showed a significant trend with increasing pack-years. Compared with participants with a smoking history of 0 to 0.9 pack-year, participants with a smoking history of more than 30 pack-years showed a 2.8 (95% CI, 1.2-6.4) increase and those with a smoking history of more than 50 pack-years showed a 5.5 (95% CI, 2.0-15.6) increase in the prevalence odds ratio for wrinkling. Sun exposure longer than 5 h/d and female sex were also found to be strong independent factors in wrinkling.

While developing a photonumeric scale to assess photoprotected skin aging, Helfrich et al[9] were able to link the degree of aging in nonfacial, photoprotected skin to a history of smoking. Eighty-two patients participated in the study, of which 41 reported a history of cigarette smoking at some point in their lives (50%). Helfrich and col-

leagues found a correlation between the degree of aging in photoprotected skin and the number of years of smoking ($r=0.39$; $P<.001$), packs smoked per day ($r=0.41$; $P<.001$), and pack-years of smoking ($r=0.41$; $P<.001$). After controlling for the participant's age and other variables in a multiple regression model, they found that only the number of packs of cigarettes smoked per day was a major predictor of the degree of aging in photoprotected skin.[9]

Although these studies appear to implicate smoking as an independent risk factor for wrinkling, the pathophysiologic process of wrinkling in smokers is not exact; it is likely multifactorial[10] and may be convergent with other mechanisms of skin aging. For example, cigarette smoke appears to induce matrix metalloproteinases in the skin[11] and modulate type I transforming growth factor (TGF) β in cultured fibroblasts.[12] Similarly, UV irradiation has been shown to induce matrix metalloproteinases[13,14] in the skin and inhibit type I and type III procollagen synthesis through alteration of the nuclear transcription factor AP-1, type I TGF-β, and type II TGF-β receptor[15]; these changes have been linked to the degradation of dermal collagen,[15] a finding also central to chronologic aging. Collagen abnormalities may also impart elasticity to the skin, with studies reporting morphologic changes of elastic fibers found in the reticular dermis of smokers.[16] Just et al[17] established a correlation between deteriorating lung function and abnormal elastic fibers in the reticular dermis. In a histologic study by Boyd et al[18] comparing the facial skin of 17 smokers with that of 14 nonsmokers, a significantly higher amount of elastosis was noted in the smokers. However, because these studies did not control for sun exposure and age, the results must be interpreted with caution.

Smoking's effect on cutaneous microvasculature serves as yet another contributing factor. The nicotine found in cigarettes increases the level of vasopressin in the blood,[19,20] which in turn causes peripheral vasoconstriction and a proposed local dermal ischemia.[19-21] Postischemic reperfusion is a well-known source of reactive oxygen species (ROS); in addition, cigarette smoke compounds generate ROS.[22,23] Reactive oxygen species are thought to be a major component of UV injury and photoaging.[14] Reactive oxygen species are generated through photochemical interactions with biomolecules during irradiation itself and also in the post-UV period, when both keratinocytes and infiltrating leukocytes are thought to contribute ROS.[15] Many theories of chronologic aging implicate ROS, providing another area of convergent mechanisms between smoking, time, and photodamage.

Our observation of the striking effect of smoking on skin aging in this twin pair is compelling because it provides the closest possible control of several key confounding variables in skin aging. Such obvious visual demonstrations of the relationship between cigarette smoking and premature skin aging are valuable in public education. Wrinkles, rather than the deadly consequences of smoking, may prove to be the most powerful motivator for smokers to stop smoking.

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