Effect of Smoking and Sun on the Aging Skin

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Smoking and ultraviolet radiation are known to have a detrimental effect on human skin. Important characteristics of the aging skin are elastosis and telangiectasia. The purpose of the study was to assess the relative importance of age per se, and the detrimental effects caused by sun exposure and smoking on the development of cutaneous elastosis and telangiectasia in a well-defined group of individuals. We made use of 966 individuals who participated in a case-control study to investigate environmental and genetic risk factors for skin cancer. Exposure measurements for sunlight and smoking were collected and the amount of elastosis and telangiectasia in the face and neck was recorded according to a four-graded score varying from none to severe. Relative risks were estimated using exposure odds ratios from cross-tabulation and logistic regression. Multivariate logistic regression was used to adjust for potential confounders. Among both sexes a strong association was observed between increasing age, sun exposure, and amount of elastosis. The association between increasing age, sun exposure, and amount of telangiectasia was strong among men, but less apparent among women. Smoking was also associated with elastosis among both sexes, and with telangiectasia predominantly among men. Intrinsic differences between men and women (e.g., hormones) or behavior differences (e.g., more frequent use of creams and cosmetics among women) could account for this apparent difference in the occurrence of telangiectasia. In contrast to elastosis, telangiectasia may not be a good marker of the aging skin, specifically not in women. ***Key words: aging/elastosis/skin cancer/smoking/telangiectasia/ultraviolet light. J Invest Dermatol 120:548–554, 2003***

Smoking is an important risk factor for the development of cutaneous squamous cell carcinoma (Aubry and MacGibbon, 1985; Karagas *et al*, 1992; Grodstein *et al*, 1995; De Hertog *et al*, 2001). Smoking (Kadunce *et al*, 1991; Davis and Koh, 1992; Ernster *et al*, 1995; Smith and Fenske, 1996; Demierre *et al*, 1999) and solar ultraviolet radiation (Fisher *et al*, 1997) are known to have a detrimental effect on human skin, which causes the skin to appear older. Important characteristics of skin aging are elastosis and telangiectasia (Calderone and Fenske, 1995). Other manifestations of skin aging are wrinkling, coarseness, laxity, atrophy, irregular pigmentation, and dryness (Calderone and Fenske, 1995). Skin aging is strongly associated with squamous cell carcinoma (Green *et al*, 1988; Green and Battistutta, 1990; Kricker *et al*, 1991).

Tobacco smoking has varying effects on the skin (Smith and Fenske, 1996). Smokers have enhanced facial aging and skin wrinkling compared with nonsmokers (Daniell, 1971; Kadunce *et al*, 1991; Davis and Koh, 1992; Grady and Ernster, 1992; Ernster *et al*, 1995; Smith and Fenske, 1996; Frances, 1998; Demierre *et al*, 1999). Smoking was found to be an independent risk factor for premature facial wrinkling even after controlling for sun exposure, age, sex, and skin pigmentation (Kadunce *et al*, 1991). There was a clear dose-response relationship, with facial wrinkling increasing in individuals who were smoking during longer periods and also with increasing number of cigarettes per day (Kadunce *et al*, 1991). Long-term exposure to solar radiation can lead to profound and structural changes in the skin (Calderone and Fenske, 1995), but smoking was shown to have an even greater effect on facial wrinkling than did sun exposure (Daniell, 1971). Some studies reported that women were more susceptible to the wrinkling effects of smoking (Ernster *et al*, 1995).

The purpose of this study was to assess the relative importance of age *per se*, and the detrimental effects caused by smoking and sun exposure on the development of cutaneous elastosis and telangiectasia in a well-defined group of individuals. To this purpose we made use of 966 individuals who participated in a case-control study to investigate environmental and genetic risk factors for malignant melanoma and nonmelanoma skin cancer (De Hertog *et al*, 2001).

PATIENTS AND METHODS

Study population The Leiden Skin Cancer Study was initiated in 1997 as a case-control study of the causes of skin cancer in the Dutch population and has been described before (Bastiaens *et al*, 2001; De Hertog *et al*, 2001; Kennedy *et al*, 2001). The medical ethical committee approved the protocol and all participants gave informed consent.

In short, cases were men and women, aged between 30 and 80 y, with histologically proven squamous cell carcinoma, basal cell carcinoma, or nonfamilial cutaneous malignant melanoma of the skin (De Hertog *et al*, 2001). Squamous cell carcinoma and basal cell carcinoma cases were newly diagnosed between January 1985 and December 1997 at the Department of

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Abbreviations: MMP, matrix metalloproteinase; TIMP, tissue inhibitor of metalloproteinase.

Dermatology of the Leiden University Medical Center. Malignant melanoma cases were newly diagnosed between January 1991 and April 1998 (De Hertog *et al*, 2001). Controls in the same age range were recruited at the ophthalmology outpatient clinic of the Leiden University Medical Center (De Hertog *et al*, 2001). This group was chosen because it consists of patients of the same University Hospital and living in the same region. Controls were excluded when they had either intraocular melanoma or any skin cancer in their history. Both cases and controls were excluded when they were transplant recipients, or suffered from rare hereditary skin disorders such as xeroderma pigmentosum or basal cell nevus syndrome (Gorlin's syndrome), or were members of familial atypical mole melanoma families, as these persons are at an increased risk of developing skin cancer. Persons with a dark skin (Fitzpatrick classification V and higher) (Fitzpatrick, 1988), both case subjects and controls, were also excluded, as persons with these skin types rarely develop skin cancers (Fitzpatrick, 1988).

All participants who were eligible for the study were sent a letter with an invitation to make an appointment at the dermatology outpatient clinic. Along with the letter a so-called Residence Work Calendar was sent. In this form, every change in residence or working habit during lifetime had to be marked. All participants were asked to fill in the Residence Work Calendar at home and bring it at their visit to facilitate the assessment of pattern of sun exposure during the interview.

Collection of data on risk factors for cutaneous malignancies The visit at the dermatology outpatient clinic was identical for all cases and controls, lasted about 90 min, and consisted of a standardized interview and a physical examination (De Hertog *et al*, 2001).

A trained interviewer collected data on smoking history and many other potential risk factors of skin cancer. Smokers were asked which type of tobacco they used (cigarettes, cigars, pipe, or a combination of these products), at what age they started smoking, and, if applicable, at what age they quitted. The numbers of cigarettes, pipes, and cigars per day per age period were noted. The total amount of tobacco products smoked was calculated by multiplying the daily tobacco consumption by the time the participants smoked (De Hertog *et al*, 2001). We did not inform the participants about the research question of the possible association between smoking and skin aging.

Information on propensity to burn rather than tan (skin type) and sun exposure, using a standardized questionnaire (obtainable from Dr. Bouwes Bavinck), was also collected during the interview. Hours spent outdoors were recorded for working and nonworking days between 9 a.m. and 5 p.m. in the months May to September. We distinguished between working and nonworking days as exposure to sunlight may be different depending on the profession during the week and behavior during the weekends. Sun exposure between October and April was not considered because at that time of the year at a latitude of 52° north sun exposure is too weak. The whole year was taken into account when people had lived in the tropics. Sun exposure during winter holidays to sunny or skiing resorts was also recorded. The Residence Work Calendar was used for remembering sun exposure in the past better.

During physical examination a dermatologist recorded the amount of elastosis and telangiectasia, using a four-graded score varying from none (–) to severe (+ + +). Elastosis was diagnosed on the back, sides, or front of the neck if skin thickening and a well-defined furrowed network were present and was graded as light (+), moderate (+ +), or severe (+ + +) (Green *et al*, 1988). When telangiectasia was observed on facial skin, it was graded in three categories from light (+) with only occasional foci of dilated vessels, through moderate (+ +), to severe (+ + +) where large areas of the face appeared florid with visible vessels (Green *et al*, 1988). These clinical features of elastosis and telangiectasia were assessed blindly with respect to sun exposure and smoking.

Statistical analysis All calculations were performed with the statistical software package JMP version 2 of the SAS Institute, Cary, NC. The data were analyzed using Student's t test and the χ^2 test. Relative risks were estimated using exposure odds ratio from cross-tabulation and logistic regression. Multivariate logistic regression analysis was used to adjust for potential confounders.

As only 18 out of 646 persons were exposed to tobacco products other than cigarettes we did not give different weights to the use of the different forms of tobacco, and all current and former smokers were pooled regardless of the tobacco products they used. Excluding these 18 persons from the analyses did not change the results. The outcomes of elastosis and telangiectasia were dichotomized into "no or light" and "moderate or severe".

Analyses were performed in the total study population and subsequently in the groups with and without a history of nonmelanoma skin cancer, separately. The latter analyses were not substantially different from the total study, and therefore only the analyses performed in the total study population are presented.

RESULTS

A total of 966 individuals from The Netherlands participated in a case-control study to investigate environmental and genetic risk factors for malignant melanoma and nonmelanoma skin cancer. For this study we used the same data set as in our previous publication (De Hertog *et al*, 2001). Information about elastosis and/or telangiectasia was missing for 10 individuals. Therefore, we restricted the current analyses to 956 individuals.

Baseline characteristics of the population Characteristics of the study population according to severity of elastosis and telangiectasia are presented in **Table I**. In the study group overall, most people were women and had skin type I or II. About 25% had 40,000 or more hours of sun exposure in their lifetime, and about 35% had never smoked cigarettes. Among people with moderate or severe elastosis, there were significantly fewer women and people with skin type I or II than in the overall group (**Table I**). There were also significantly fewer women among the people with severe or moderate telangiectasia. People with (moderate or severe) elastosis or telangiectasia had significantly more sun exposure during their lifetimes than did people in the overall group (**Table I**). There were also significantly fewer nonsmokers in the groups with elastosis and telangiectasia (**Table I**). Moderate or severe elastosis and telangiectasia were more frequently present among individuals with a history of nonmelanoma skin cancer. Moderate or severe elastosis was present in 171 (44.3%) out of 386 individuals without any skin cancer and in 125 (78.6%) out of 159, 201 (67.5%) out of 298, and 99 (65.6%) out of 151 individuals with squamous cell carcinoma, nodular basal cell carcinoma, and

Table I. Baseline characteristics of the study population according to severity of elastosis and telangiectasia

	All No. (%)	Elastosis, moderate or severe No. (%)	Telangiectasia, moderate or severe No. (%)
Gender			
women	495 (51.8)	228 (44.6)[b]	147 (45.9)[a]
men	461 (48.2)	283 (55.4)	173 (54.1)
Age (y)			
24–49	226 (23.6)	33 (6.5)[b]	44 (13.8)[b]
50–59	231 (24.2)	111 (21.7)	65 (22.3)
60–69	283 (29.6)	195 (38.2)	115 (35.9)
70–79	216 (22.6)	172 (33.6)	96 (30.0)
Skin type			
III or IV	430 (45.0)	249 (48.7)[a]	135 (42.2), ns
I or II	526 (55.0)	262 (51.3)	185 (57.8)
Lifetime sun exposure (h × 1000)			
8–20	123 (12.9)	23 (4.5)[b]	22 (6.9)[b]
20–30	343 (35.9)	150 (29.4)	94 (29.4)
30–40	252 (26.3)	165 (32.3)	89 (27.8)
40 +	238 (24.9)	173 (33.8)	115 (35.9)
Lifetime exposure to cigarettes (no. × 1000)			
0	338 (35.4)	155 (30.3)[b]	101 (31.6)[b]
1–100	237 (24.8)	114 (22.3)	66 (20.6)
100–200	179 (18.7)	100 (19.6)	57 (17.8)
200 +	202 (21.1)	142 (27.8)	96 (30.0)

[a] $p < 0.05$.
[b] $p < 0.0001$.
ns, not significant.

superficial multifocal basal cell carcinoma, respectively. Moderate or severe telangiectasia was present in 99 (25.7%) of the controls and in 81 (50.9%), 131 (44.0%), and 60 (39.7%) of the individuals with the three different types of nonmelanoma skin cancer, respectively. Some patients had more than one type of skin cancer, which fact is reflected here by overlapping of the numbers of patients in the three different nonmelanoma skin cancer categories.

Calendar age is strongly associated with elastosis and telangiectasia As expected, age *per se* was strongly associated with the development of elastosis (**Fig 1**, *top left panel*). The odds ratios with 95% confidence intervals for individuals in the age groups 50–59, 60–69, and 70–79 y, respectively, compared with the age group 24–49 y are given in **Table II**, *part (a).* Adjustment for sex, skin type, hours of sun exposure per year, and number of cigarettes smoked per year did not change these odds ratios substantially.

Similarly, age *per se* was associated with the development of telangiectasia (**Fig 1**, *top right panel*), but the association was significantly stronger among men than among women (**Table II**, *part (a)*). Adjustment for skin type, hours of sun exposure per year, and number of cigarettes smoked per year did not change these odds ratios substantially.

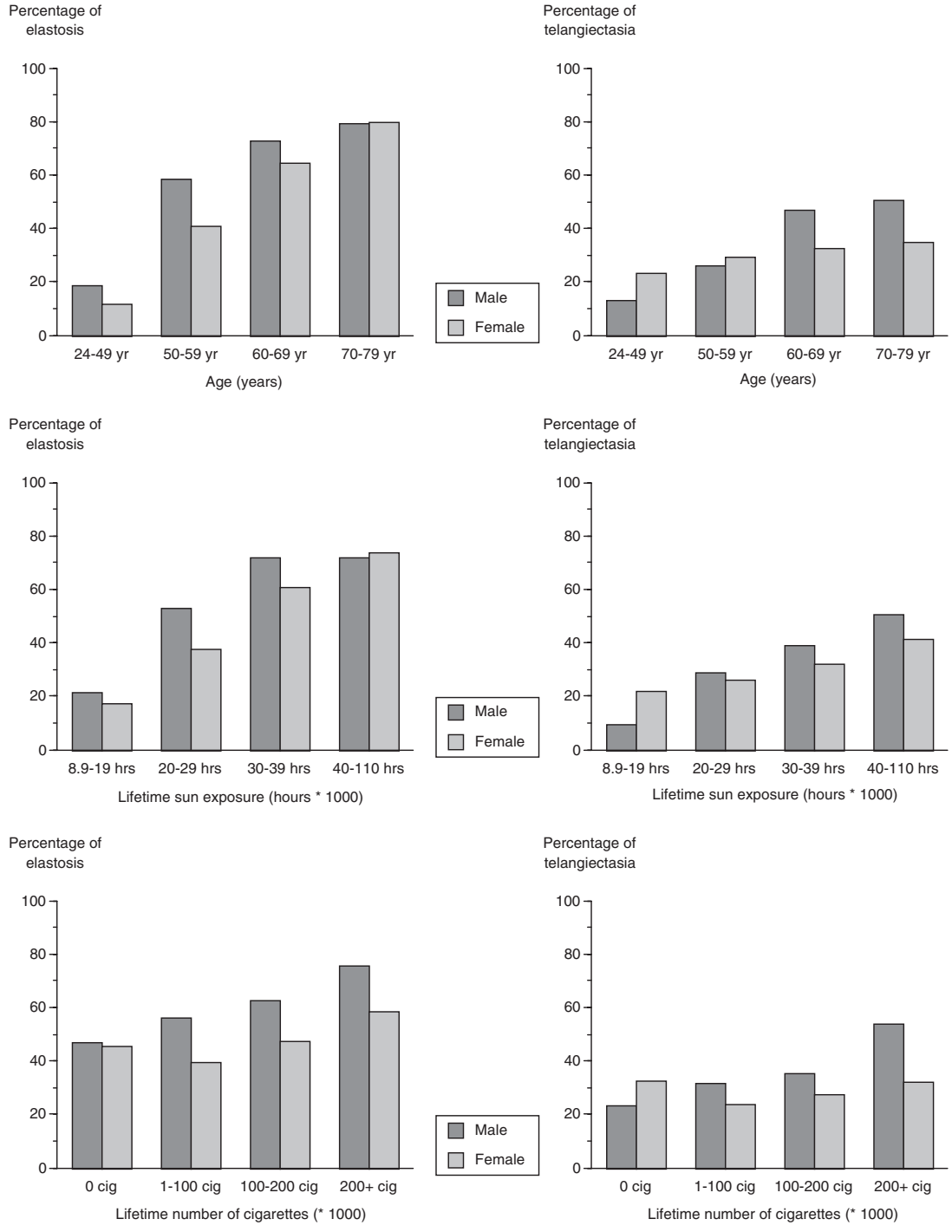

Figure 1. Age *per se* and detrimental effects caused by sun exposure are associated with the development of elastosis and telangiectasia among men and women. Smoking is associated with elastosis and telangiectasia among men. Smoking is not associated with telangiectasia among women.

Lifetime sun exposure is associated with elastosis and telangiectasia Lifetime sun exposure was significantly associated with the development of elastosis (**Fig 1**, *middle left panel*). The odds ratios with 95% confidence intervals for individuals with 20,000–29,999, 30,000–39,999, and 40,000 and more hours of lifetime sun exposure, respectively, compared with the group with 8,932–19,999 h of lifetime sun exposure are given in **Table II**, *part (b)*. Adjustment for age, sex, and skin type decreased these odds ratios substantially, which was mainly attributed to the addition of age to the model. Considering the total group, the odds ratios with 95% confidence intervals adjusted for these factors were 1.3 (0.70; 2.4), 2.3 (1.2; 4.4), and 2.8 (1.3; 6.1) for individuals with 20,000–29,999, 30,000–39,999, and 40,000 and more hours of lifetime sun exposure, respectively, compared with the group with 8,932–19,999 h of lifetime sun exposure.

Lifetime sun exposure was also significantly associated with the development of telangiectasia although the strength of the association appeared to be less strong among women (**Fig 1**, *middle right panel*; **Table II**, *part (b)*). Considering men, the odds ratios with 95% confidence intervals adjusted for age and skin type were 2.0 (0.60; 6.7), 1.4 (0.37; 5.7), and 4.8 (1.2; 18.7), respectively, and considering women, the odds ratios adjusted for age and skin type were 1.4 (0.70; 2.8), 1.9 (0.81; 4.7), and 1.9 (0.64; 5.9), respectively.

Smoking is associated with elastosis among both sexes and with telangiectasia among men Smoking was significantly associated with elastosis, although the association appeared to be more pronounced among men than women (**Fig 1**, *lower left panel*; **Table II**, *part (c)*). Considering men, adjustment for age, skin type, and hours of sun exposure per year did not change the odds ratios substantially. The odds ratios adjusted for these factors were 1.2 (0.63; 2.2), 1.6 (0.85; 3.0), and 2.2 (1.1; 4.1), respectively. Among women, the odds ratios adjusted for age, skin type, and hours of sun exposure per year were 1.2 (0.71; 2.1), 1.6 (0.84; 2.9), and 1.8 (0.95; 3.4), respectively. A dose-response relationship was observed between the number of cigarettes smoked and the amount of elastosis among both sexes.

Smoking was also associated with telangiectasia among men, but this association was not present among women (**Fig 1**, *lower right panel*; **Table II**, *part (c)*). Considering men, the odds ratios adjusted for age, skin type, and hours of sun exposure per year were 1.3 (0.67; 2.4), 1.6 (0.81; 3.1), and 2.5 (1.3; 4.6), respectively. Among women, the odds ratios adjusted for age, skin type, and hours of sun exposure per year were 0.69 (0.41; 1.2), 0.91 (0.51; 1.6), and 0.99 (0.55; 1.8), respectively.

The relative contribution of age *per se*, sun exposure, and smoking is different for the development of elastosis and telangiectasia **Table III** presents the relative contribution of age *per se* and lifetime sun exposure to the development of elastosis and telangiectasia. Age *per se* contributes importantly to the development of elastosis in all the different sun exposure strata, except for the stratum with the highest amount of sun exposure. It is conceivable that the majority of individuals with extremely high sun exposure developed moderate or severe elastosis already before the age of 50 and our scoring system was not designed to score extremely severe elastosis, which may have developed in these patients after the age of 50 y. The effect of age *per se* on the development of telangiectasia is less pronounced and is only statistically significant in the strata with moderate sun exposure (**Table III**).

Sun exposure is strongly associated with the development of elastosis in the younger age groups (below the age of 60 y), whereas the association between sun exposure and elastosis disappears above the age of 60 y (**Table III**). Apparently, after the age of 60 y the baseline percentage of moderate and severe elastosis is too high to make it possible to discriminate between low and high sun exposure. By contrast, sun exposure is associated with the development of telangiectasia in the older age groups and is not apparent below the age of 50 y (**Table III**), which may indicate a different mechanism, e.g., increased atrophy of aging skin, which could make telangiectasia more visible.

Table IV presents the relative contribution of age *per se* and lifetime exposure to cigarettes to the development of elastosis and telangiectasia. Age *per se* contributes importantly to the development of both elastosis and telangiectasia in the nonsmokers and the three different smoking exposure strata (**Table IV**). The interaction between smoking and age *per se* in relation to the development of elastosis and telangiectasia appears to be less than the interaction between sun exposure and age *per se*, as the relation between age *per se* and elastosis and telangiectasia appears to be stronger in the nonsmokers and the three smoking strata compared with the four sun exposure strata.

Again, exposure to cigarettes is associated with the development of elastosis in the younger age groups (below the age of 70 y), whereas the association between exposure to cigarettes and elastosis disappears above the age of 70 y (**Table IV**). By contrast, exposure to cigarettes is associated with

Table II. Non-adjusted odds ratios to develop elastosis and telangiectasia with increasing age, amounts of sun exposure, and exposure to cigarettes

	Total group ($N = 966$)	Only men ($N = 461$)	Only women ($N = 495$)
(a) Odds ratios with increasing age			
Elastosis			
Age groups (y)			
20–49	1	1	1
50–59	5.4 (3.4; 8.5)	6.1 (3.1; 11.9)	5.2 (2.8; 9.7)
60–69	13.0 (8.3; 20.3)	11.7 (6.2; 22.2)	13.7 (7.3; 25.8)
70–79	22.9 (13.9; 37.5)	16.7 (8.4; 33.0)	29.6 (14.2; 61.7)
Telangiectasia			
Age groups (y)			
20–49	1	1	1
50–59	1.6 (1.1; 2.5)	2.1 (1.1; 4.9)	1.4 (0.79; 2.3)
60–69	2.8 (1.9; 4.2)	5.8 (2.9; 11.5)	1.6 (0.92; 2.7)
70–79	3.3 (2.2; 5.0)	6.7 (3.3; 13.5)	1.7 (0.96; 3.1)
(b) Odds ratios with increasing amounts of sun exposure			
Elastosis			
Lifetime sun exposure (h × 1000)			
8–20	1	1	1
20–30	3.4 (2.0; 5.6)	4.1 (1.8; 9.5)	2.9 (1.5; 5.5)
30–40	8.2 (4.9; 13.9)	9.5 (4.0; 22.2)	7.4 (3.8; 14.4)
40 +	11.6 (6.8; 19.8)	9.5 (4.2; 21.4)	13.6 (6.2; 29.8)
Telangiectasia			
Lifetime sun exposure (h × 1000)			
8–20	1	1	1
20–30	1.7 (1.0; 2.9)	3.8 (1.3; 11.4)	1.3 (0.68; 2.3)
30–40	2.5 (1.5; 4.2)	6.1 (2.0; 18.3)	1.7 (0.90; 3.1)
40 +	4.2 (2.5; 7.2)	9.7 (3.3; 28.4)	2.5 (1.2; 5.0)
(c) Odds ratios with increasing exposure to cigarettes			
Elastosis			
Lifetime exposure to cigarettes (no. × 1000)			
0	1	1	1
1–100	1.1 (0.77; 1.5)	1.4 (0.85; 2.4)	0.77 (0.49; 1.2)
100–200	1.5 (1.0; 2.1)	1.9 (1.1; 3.4)	1.1 (0.64; 1.8)
200 +	2.8 (1.9; 4.0)	3.5 (2.0; 6.2)	1.7 (0.96; 2.9)
Telangiectasia			
Lifetime exposure to cigarettes (no. × 1000)			
0	1	1	1
1–100	0.91 (0.63; 1.3)	1.5 (0.83; 2.7)	0.64 (0.39; 1.1)
100–200	1.1 (0.74; 1.6)	1.8 (0.96; 3.3)	30.79 (0.45; 1.4)
200 +	2.1 (1.5; 3.0)	33.8 (2.2; 6.5)	0.99 (0.55; 1.8)

Table III. Association of increasing age and lifetime sun exposure with moderate or severe elastosis and moderate or severe telangiectasia

Lifetime sun exposure (h × 1000)					
Age (y)	8–20 No. (%)[a]	20–30 No. (%)[a]	30–40 No. (%)[a]	40 + No. (%)[a]	Test for trend
Elastosis					
24–49	93 (9.7)	115 (12.2)	13 (53.8)	5 (60.0)	p = 0.00008
50–59	18 (44.4)	118 (44.9)	68 (47.1)	27 (66.7)	p = 0.05
60–69	8 (25.0)	74 (71.6)	94 (69.1)	107 (70.1)	p = 0.35
70–79	4 (100.0)	36 (83.3)	77 (79.2)	99 (77.8)	p = 0.53
Test for trend	p = 0.00001	p < 0.00001	p < 0.00001	p = 0.12	
Telangiectasia					
24–49	93 (17.2)	115 (22.6)	13 (7.7)	5 (20.0)	p = 0.88
50–59	18 (22.2)	118 (23.7)	68 (30.9)	27 (44.4)	p = 0.03
60–69	8 (12.5)	74 (37.8)	94 (39.4)	107 (45.8)	p = 0.09
70–79	4 (25.0)	36 (33.3)	77 (39.0)	99 (53.5)	p = 0.0002
Test for trend	p = 0.81	p = 0.03	p = 0.05	p = 0.11	

[a]No. refers to the total number of individuals in that category. The percentage refers to individuals with moderate or severe elastosis and telangiectasia within that category, respectively.

Table IV. Association of increasing age and lifetime exposure to cigarettes with moderate or severe elastosis and moderate or severe telangiectasia

Lifetime exposure to cigarettes (no. × 1000)					
Age (y)	0 No. (%)[a]	1–100 No. (%)[a]	100–200 No. (%)[a]	200 + No. (%)[a]	Test for trend
Elastosis					
24–49	88 (9.1)	73 (13.7)	46 (19.6)	19 (31.6)	p = 0.008
50–59	88 (40.9)	56 (37.5)	39 (61.5)	48 (62.5)	p = 0.004
60–69	93 (60.2)	56 (75.0)	52 (65.4)	82 (76.8)	p = 0.02
70–79	69 (79.7)	52 (78.8)	42 (78.6)	53 (81.1)	p = 0.87
Test for trend	p < 0.00001	p < 0.00001	p < 0.00001	p < 0.00006	
Telangiectasia					
24–49	88 (22.7)	73 (11.0)	46 (26.1)	19 (21.1)	p = 0.89
50–59	88 (25.0)	56 (26.8)	39 (20.5)	48 (41.7)	p = 0.11
60–69	93 (32.3)	56 (46.4)	52 (32.7)	82 (51.2)	p = 0.04
70–79	69 (42.0)	52 (32.7)	42 (47.6)	53 (56.6)	p = 0.06
Test for trend	p = 0.006	p = 0.0004	p = 0.02	p = 0.007	

[a]No. refers to the total number of individuals in that category. The percentage refers to individuals with moderate or severe elastosis and telangiectasia within that category, respectively.

the development of telangiectasia only in the older age groups and is not apparent below the age of 60 y (**Table IV**).

DISCUSSION

As expected, a strong association was observed between increasing age and the amount of elastosis among both men and women. There was also a strong association between increasing age and the amount of telangiectasia among men, but this effect was less pronounced among women.

Similarly, increased lifetime sun exposure was strongly associated with the amount of elastosis among both sexes and the amount of telangiectasia among men. The effect of increased lifetime sun exposure on the amount of telangiectasia was also less pronounced among women. The effect of sun exposure on the development of elastosis was only apparent in the younger age groups (below the age of 60), whereas the effect on the development of telangiectasia was more pronounced in the older age groups.

Smoking was identified as an independent risk factor for the development of elastosis among both men and women, although smoking was strongly associated with gender (De Hertog *et al*, 2001). Twenty-three percent of the men were current smokers and 58% were former smokers. Among the women these figures were 17% and 36%, respectively (De Hertog *et al*, 2001). The association between smoking and elastosis was also independent of sun exposure, despite the fact that there was a significant difference in hours of yearly sun exposure between smokers and nonsmokers (De Hertog *et al*, 2001). Current smokers spent 574 ± 198 h per y (mean ± standard deviation) in the sun, former smokers 562 ± 169, and nonsmokers 531 ± 162 (p = 0.01) (De Hertog *et al*, 2001).

Smoking was also identified as an independent risk factor for the development of telangiectasia among men, but, unexpectedly, no such association was observed among women. The effect of smoking on the development of elastosis was again only apparent in the younger age groups (below the age of 60), whereas the effect on the development of telangiectasia was again more pronounced in the older age groups.

The association between smoking and elastosis in our study is in agreement with earlier studies, which reported that cigarette smokers were more wrinkled than nonsmokers (Daniell, 1971; Kadunce *et al*, 1991; Grady and Ernster, 1992). Excessive sun exposure and smoking were independent risk factors for wrinkling; both lead to cumulative skin damage (Kadunce *et al*, 1991).

The exact mechanism by which smoking causes elastosis is still poorly understood (Ernster *et al*, 1995). The effects of tobacco smoke may be topical due to the drying or irritating effect of cigarette smoke on the skin or, alternatively, the effect could be systemic. Tobacco smoke is capable of damaging collagen and elastin in lung tissue (Smith and Fenske, 1996) and may cause similar changes in the skin of smokers. The sun-protected skin of smokers has an increased size and number of elastic fibers (Frances *et al*, 1991; Boyd *et al*, 1999). These elastic fiber changes resemble those of sun-damaged skin except that they are in the reticular dermis and not in the papillary dermis, as in solar elastosis (Smith and Fenske, 1996). Cigarette smoke has been shown to increase plasma neutrophil elastase activity (Weitz *et al*, 1987).

Matrix metalloproteinases (MMPs) are zinc-dependent proteases that degrade dermal collagen and other extracellular matrix molecules (Lahmann *et al*, 2001). The proteolytic activity of MMPs is inhibited by tissue inhibitors of metalloproteinases (TIMPs) (Lahmann *et al*, 2001). MMP-1 is elevated in the skin of smokers compared to nonsmokers but the TIMP-1 is not, suggesting that smoking-induced MMP-1 might be important in the skin aging effects of tobacco smoking (Yin *et al*, 2000; Lahmann *et al*, 2001). MMPs can also be induced by ultraviolet radiation by which way sunlight may induce photo aging (Fisher *et al*, 1997).

Smoking has also an effect on the cutaneous microvasculature, which is constricted by acute and long-term smoking (Tur *et al*, 1992). Nicotine increases blood levels of vasopressine, which is a vasoconstrictor causing an acute decrease of capillary and arteriolar blood flow in the skin leading to chronic ischemia of the dermis (Reus *et al*, 1984; Richardson, 1987; Frances *et al*, 1991). The chronic ischemia, in turn, could lead to proliferation of small blood vessels, which are visible as telangiectasia. Alternatively, atrophy of the overlaying epidermis may cause superficial blood vessels to appear more visible.

There are several possible explanations why telangiectasia caused by smoking is present among men but not among women. First, hormonal differences between men and women could provide an explanation why women who have been smoking for extended periods are protected from the effects of smoking on the development of telangiectasia. Second, other factors that may explain the differences between men and women in the amount of observed telangiectasia may be differences in utilization of cosmetic products by women or the use of products that are utilized to treat photodamage such as retinoic acid, azelaic acid, and α-hydroxy acids (Clark, 1996; Farmer and Naylor, 1996; Gilchrest, 1996; Bergfeld, 1997; Kang and Voorhees, 1998). Information about the utilization of cosmetic products or cosmetic procedures such as exfoliation, peeling, and the use of antioxidants was not routinely collected in our study, but it is likely that in our study women were more exposed to these substances than men were. Third, misclassification among women because of make-up use during the physical examination should also be considered. Make-up or residues of these cosmetic products on the face may have influenced the scoring patterns for telangiectasia among women.

The fact that not all smokers develop elastosis and telangiectasia indicates that genetic factors may also contribute (Frances, 1992; Smith and Fenske, 1996), either by an increased genetic sensitivity or from a greater susceptibility of the person's cutaneous vasculature to damage from chemicals within tobacco (Boyd *et al*, 1999). A genetic sensitivity to cigarette smoke is quite likely as some families are more wrinkling prone than others (Kadunce *et al*, 1991).

The effect that smoking has on the skin may be utilized as a public education message. As many antismoking campaigns have not addressed the cosmetic issues related to smoking the public's awareness of the association between smoking and elastosis is still low (Demierre *et al*, 1999). Wrinkles may be a more powerful motivator to help individuals stop smoking than the more deadly consequences of smoking such as lung cancer, emphysema, chronic bronchitis, cardiovascular disease, and various cancers (Kottke, 1991; Davis and Koh, 1992; Frances, 1992; Smith and Fenske, 1996; Demierre *et al*, 1999).

In conclusion, smokers among both sexes in our study seemed vulnerable to the development of elastosis. Women, however, seem less likely to develop tobacco-induced telangiectasia than men are and they also show a less pronounced effect of age *per se* and sun exposure on the development of telangiectasia. Therefore, in contrast to elastosis, telangiectasia may not be a good marker to characterize the aging skin, especially not in women.

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ADDENDUM

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