In two recent studies, Wu et al. showed that fasting plasma levels of fluorescent oxidation products are markers of oxidative stress (1) and independently predict coronary heart disease in men (2). The authors concluded that this fluorescent assay may become a useful global marker for epidemiologic studies. As mentioned by Wu et al., “this method has not been widely used [as it may be] a nonspecific measurement of oxidation because it reflects a mixture of oxidation products” (1, p. 552). Indeed, fluorescent products in plasma and tissue reflect the accumulation of protein oxidation products, advanced glycation end products (AGE), and advanced lipoxidation end products (ALE) (3). Regarding the clinical value, this is not a limitation because all are related to the development and progression of cardiovascular disease. The increased accumulation of AGE and ALE is the consequence of a series of complex and sequential protein reactions, collectively called the Maillard reaction. AGE/ALE accumulation results from a combination of hyperglycemia, hyperlipidemia, oxidative/carbonyl stress, and decreased renal clearance of AGE precursors (3). Assessment of the accumulation of these end products serves as a measure of cumulative metabolic and oxidative stress.

In the Discussion section of their article, the authors state that “until now, a stable and easily measured oxidation marker that reflects systemic oxidative stress, predictive of chronic diseases and applicable in large-scale human studies, has not been available” (1, p. 556). Over the past several years, however, we have developed, validated, and clinically evaluated a new tool: the AGE-reader. The AGE-reader measures, noninvasively and rapidly, skin autofluorescence and has been validated as a measure of tissue AGE/ALE accumulation in healthy subjects, diabetic patients, and patients receiving hemodialysis treatment (4, 5). It is positively associated with markers of systemic inflammation and oxidative stress, such as C-reactive protein and neopterine under various conditions (6, 7) Furthermore, skin autofluorescence is independently and strongly related to long-term complications in diabetes and renal dysfunction (8, 9). Finally, skin autofluorescence is a strong and independent predictor of cardiovascular events and mortality (5, 10).

Wu et al. (1) observed an association between smoking and plasma levels of fluorescent oxidation products. Indeed, smoking is related to oxidative stress, and Dickerson and Janda (11) have shown that nornicotine, a constituent of tobacco and a metabolite of nicotine, causes protein glycation. To illustrate the value of fluorescent techniques as a diagnostic tool in measuring tissue damage in smokers, we investigated the relation between skin autofluorescence and smoking habits in otherwise healthy subjects.

We noninvasively measured skin autofluorescence in 31 cigarette smokers and 41 nonsmokers. Nonsmoking was defined as having never smoked cigarettes or other tobacco products or having stopped smoking more than 15 years ago. Smoking was defined as still smoking cigarettes or having stopped cigarette smoking less than 1 year ago. Skin autofluorescence was measured as described in detail previously (4).

Autofluorescence was significantly increased in smokers compared with nonsmokers (respectively, 0.015 (standard deviation, 0.004) vs. 0.011 (standard deviation, 0.002); *p* < 0.01). Multivariate analysis showed that approximately 50 percent of the variance in autofluorescence could be explained by the independent effects of age and smoking (*r* = 0.7, *p* < 0.01). The age-related increase in autofluorescence was 1.9 times higher in smokers compared with nonsmokers. Autofluorescence correlated with pack-years of smoking (*r* = 0.63, *p* < 0.01). After we controlled for possible...
confounding factors such as glycosylated hemoglobin, lipid profile, and renal function, the associations described above remained.

These results show that not only plasma but also tissue fluorescence is increased in cigarette smokers and may serve as a measure of cumulative tissue damage as a consequence of smoking. Fluorescent techniques are easy tools to use in assessing the risk of cardiovascular disease and long-term complications in chronic diseases such as diabetes.

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REFERENCES


Robbert Meerwaldt1, Thera Links2, Clark Zeebregts3, and Andries Smit2 (e-mail: r.meerwaldt@isala.nl)

1 Department of Surgery, Isala Clinics, Zwolle 8023AN, The Netherlands
2 Department of Internal Medicine, University Medical Center Groningen, 9700 RB Groningen, The Netherlands
3 Department of Surgery, University Medical Center Groningen, 9700 RB Groningen, The Netherlands

Editor’s note: In accordance with Journal policy, Wu et al. were asked whether they wanted to respond to this letter, but they chose not to do so at this time.