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Acute and Chronic Effects of Cigarette Smoking on sRAGE

To the Editor:

I read the article by Pouwels and colleagues with great interest (1). To the best of my knowledge, the authors for the first time have explored the acute effect of cigarette smoking on the serum levels of sRAGE (soluble receptor for advanced glycation end products). They elegantly showed a significant reduction of serum sRAGE levels in subjects who smoked three cigarettes within 1 hour. This effect was shown in patients with chronic obstructive pulmonary disease as well as in young and old healthy control subjects without airway obstruction. Based on a time-course study using three healthy subjects, the authors claimed that the maximum decline of serum sRAGE levels occurred after approximately 8 hours of cigarette smoking, which was not fully restored after 48 hours. In fact, the data presented in Figure 2B in Reference 1 demonstrate that the serum sRAGE values remained persistently low after 48 hours and were almost similar to the maximum decline values observed after 8 hours of cigarette smoking. The latter finding suggests that active smokers who regularly smoke several cigarettes per day should have lower serum levels of sRAGE than never smokers. However, Pouwels and colleagues did not observe any difference in sRAGE values between active smokers and never smokers (data not shown). To support this finding, the authors cited previous studies that also found no difference in sRAGE levels between smokers and nonsmokers, and stated that recent smoking within the smokers group may be the reason why some studies found decreased serum sRAGE levels in smokers (1). Unfortunately, Pouwels and colleagues did not cite our study in which we found elevated serum sRAGE levels in otherwise healthy, nondiabetic cigarette smokers (2).

Cigarette smoke is known to increase the formation of AGEs and the expression of RAGE (3, 4). However, the effect of cigarette smoking on sRAGE is inconsistent across the literature. Decreased, elevated, and unchanged levels of sRAGE were found in different studies, as reviewed by Prasad and colleagues (5). However, most of those studies, as I explained previously (6), were not specifically designed to explore the effect of smoking on sRAGE and thus were confounded by the presence of other diseases or conditions that affect sRAGE levels. Therefore, in our study, we specifically aimed to compare sRAGE levels between cigarette smokers and nonsmokers, controlling for the majority of confounding variables (2). In that study, we showed for the first time a significant elevation of sRAGE in cigarette smokers, a strong correlation between sRAGE and the number of cigarettes smoked per day, and an independent association of sRAGE with smoking habit (2). Although the exact mechanism of this apparently surprising finding is not yet known, we proposed a number of scientifically valid explanations (2, 6). Now, Pouwels and colleagues have identified the acute effect of cigarette smoking on sRAGE, which is the opposite of the chronic effect of smoking previously identified by our group (2). Therefore, further studies are required to explore the true effect of cigarette smoking on serum sRAGE levels and to explain the discrepancy among these studies. These issues need to be resolved before we can consider sRAGE as a biomarker for inflammatory conditions or as a protective factor against AGEs and other RAGE ligands. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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