

# Effect of Differing Levels of Tobacco-Specific Nitrosamines in Cigarette Smoke on the Levels of Biomarkers in Smokers

David L. Ashley, Richard J. O'Connor, John T. Bernert, Clifford H. Watson, Gregory M. Polzin, Ram B. Jain, David Hammond, Dorothy K. Hatsukami, Gary A. Giovino, K. Michael Cummings, Ann McNeill, Lion Shahab, Bill King, Geoffrey T. Fong, Liqin Zhang, Yang Xia, Xizheng Yan, and Joan M. McCraw

## Abstract

**Background:** Smokers are exposed to significant doses of carcinogens, including tobacco-specific nitrosamines (TSNA). Previous studies have shown significant global differences in the levels of TSNA in cigarette smoke because of the variation in tobacco blending and curing practices around the world.

**Methods:** Mouth-level exposure to 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) measured in cigarette butts and urinary concentrations of its major metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) were examined among 126 daily smokers in four countries over a 24-hour study period.

**Results:** As mouth-level exposure of NNK increased, the urinary NNAL increased even after adjustment for other covariates ( $\beta = 0.46$ ,  $P = 0.004$ ). The relationship between mouth-level exposure to nicotine and its salivary metabolite, cotinine, was not statistically significant ( $\beta = 0.29$ ,  $P = 0.057$ ), likely because of the very limited range of differences in mouth-level nicotine exposure in this population.

**Conclusions:** We have shown a direct association between the 24-hour mouth-level exposure of NNK resulting from cigarette smoking and the concentration of its primary metabolite, NNAL, in the urine of smokers. Internal dose concentrations of urinary NNAL are significantly lower in smokers in countries that have lower TSNA levels in cigarettes such as Canada and Australia in contrast to countries that have high levels of these carcinogens in cigarettes, such as the United States.

**Impact:** Lowering the levels of NNK in the mainstream smoke of cigarettes through the use of specific tobacco types and known curing practices can significantly affect the exposure of smokers to this known carcinogen. *Cancer Epidemiol Biomarkers Prev*; 19(6); 1389–98. ©2010 AACR.

## Recommended Citation:

Ashley DL, O'Connor RJ, Bernert JT, Watson CH, Polzin GM, Jain RB, et al. Effect of differing levels of tobacco-specific nitrosamines in cigarette smoke on the levels of biomarkers in smokers. *Cancer epidemiology, biomarkers & prevention: A publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2010 Jun;19(6):1389-1398.

**Link to PDF:** <http://cebp.aacrjournals.org/content/19/6/1389.full.pdf+html>