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Correlating exposure to environmental tobacco smoke exposure with increased incidence of lung cancer in non smokers : is cotinine a valid marker ?

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ABSTRACT

Environmental Tobacco Smoke (ETS) is a complex mixture of Exhaled Mainstream (EMS) and Sidestream Smoke (SS) composed of gases and Respirable Suspended Particles (RSP). It is both a highly diluted and an aged mixture the composition of which is difficult to assess. Based mainly on syllogisms it has been hypothesized that exposure to low levels of ETS increases the risk of lung cancer in nonsmokers. There is no question that nonsmokers living in the presence of smokers are exposed to tobacco smoke constituents. But, to conclude on the significance of such an exposure, in term of increased incidence of lung cancer in non smokers, can only rely on a quantitative biomonitoring of exposure to agents proven to play a causative role in lung carcinogenesis. Nether nicotine nor its metabolites are likely to be precise markers of exposure to such chemicals. Molecular epidemiology offers a promising, but still to be validated, tool to meet such a challenge by measuring proteins and/or DNA adducts in serum or urine samples.

Key words: tobacco smoke, cotinine, lung cancer, cancer risks.

INTRODUCTION

ENVIRONMENTAL TOBACCO SMOKE (ETS) is a complex mixture of exhaled mainstream smoke (EMS) and sidestream smoke (SS) composed of gases and respirable suspended particles (RSP) [see Table I (1-3) for definitions]. It has been hypothesized (4,5) that exposure to low levels of ETS increases the risk of lung cancer in non smokers. Two syllogisms support this hypothesis: [1] a). if ETS is chemically analogous to mainstream cigarette smoke (MS) ; and b). MS is known to cause lung cancer in active smokers; then c). ETS causes lung cancer in passive smokers; [2)] a). if ETS contains lung carcinogens; and b). it is generally assumed that no dose threshold exists for carcinogens; then c). ETS is a lung carcinogen. There is no question that non smokers living in the presence of smokers are exposed to tobacco smoke constituents. Self-reported exposure to ETS as well as the use of biomarker like nicotine or cotinine are certainly valid means to help epidemiologists register the extent of such exposure. However, its significance in terms of increased incidence of lung cancer in non smokers cannot simply be derived from syllogisms. For a molecular toxicologist, such a conclusion can only rely on a quantitative biomonitoring of exposure to agents proven to play a causative role in lung carcinogenesis.

Definitions
Environmental tobacco smoke or ETS: A mixture of diluted and aged gases and solid suspended particles resulting from a combination of sidestream smoke (SS) (80-90%) and exahled mainstream smoke (EMS) (10-20%).
Mainstream smoke or MS: The cigarette smoke drawn through the tobacco into smoker's mouth.
Exhaled mainstream smoke or EMS: The fraction of MS not retained by the smoker and exhaled in the air. (EMS is not identifical to MS because it has been substantially depleted in vapor phase constituents and because the particulate matter is likely to have increased its water content).
Sidestream smoke or SS: The smoke emitted by burning tobacco between puffs and/or the aerosol emitted in the surrounding air from a smoldering tobacco product between puff drawing and/or all of the tobacco smoke issued apart from the MS which is delivered to the smoker.
Respirable suspended particles or RSP: The solid phase of the aerosol.

Table I: Definitions (1, 2, 3)

Indeed, since the exposure level to ETS is likely to be low compared to active smoking (3,6), since many confounding factors (like radon exposure, misclassification of light smokers, former smoking habits, and dietary factors) are likely to exist, one has to recognize that the classic epidemiological methods alone may not be sufficiently sensitive for scientifically establishing that ETS exposure plays a significant role in the incidence of lung cancer in ETS-exposed non smokers (3). Such a conclusion needs to be supported by dosimetry which not only confirms personal records of ETS exposure in quantitative measures of a reliable parameter, but also demonstrates that such an exposure has indeed led to a significant intake of carcinogenic components. Various biomarkers of exposure to cigarette smoke [see Table 2 (3, 7-10)] have already been proposed with the aim of developing a quantitative approach to the epidemiology of diseases in non smokers, particularly lung cancer. These include measures of plasma, salivary and/or urinary concentrations of either (a) a major, specific tobacco smoke molecule and/or its main metabolites or (b) the end-products of the metabolic activation of carcinogenic components in tobacco smoke.

The aims of the present paper are :

1) to review the data on the quantitative biomonitoring of exposure to ETS based on nicotine and/or cotinine measurements in physiological fluids.