Authors’ Response to “Invited Commentary: More Evidence of Increased Risks of Cancer among Alcohol Drinkers” by Dr. Blot

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In his invited commentary about our article (1) in this issue of the Journal, Dr. Blot (2) emphasized the indisputable carcinogenicity of alcohol based on epidemiologic and laboratory evidence, regardless of the lack of classic genotoxicity data (1). He concluded that the data presented in our article (2) added to a large body of epidemiologic evidence which incriminates heavy alcohol use as a risk factor for upper aero-digestive tract cancers with or without concomitant exposure to tobacco smoking. Although we wholeheartedly share Dr. Blot’s views on this issue, our argument was not nearly as cogent as his. We welcome the opportunity to comment on a couple of points he mentioned concerning our study and to discuss the potential effects of selection bias on the magnitude of the relative risk estimates for alcohol consumption in our case-control study (2).

We agree with Dr. Blot that we have interpreted the interaction between smoking and alcohol somewhat liberally. We believe that both the direction and intensity of interaction may be a function not only of the anatomic subsite but also of the type of alcoholic beverage. The different levels of the cumulative alcohol consumption variable used in our study were qualitatively heterogeneous with respect to the relative contribution of the different types of beverage consumed by our subjects. In Brazil, the group with high cumulative consumption is more likely to be composed of drinkers of cachaça, a sugar cane distillate, and spirits, whereas low or intermediate cumulative consumption levels may have included more beer or wine drinkers. Assuming that the net carcinogenic effect of alcohol drinking may include both the exposure to alcohol per se and a component due to exposure to other substances present in the beverages, it is conceivable that the overall joint effect given concomitant smoking may vary by type of beverage; hence, our expectation of a complex relation when both smoking and alcohol exposure are analyzed cumulatively. Dr. Blot remarked that we had not reported results by type of alcoholic beverage consumed. Given the many different model combinations needed to fully analyze the joint effects of tobacco and alcohol by type and anatomic site, we chose to restrict the report to an in-depth assessment of overall cumulative consumption. However, we are currently conducting summary analyses of independent and joint effects for each type of alcoholic beverage, which should provide clues with respect to the magnitude of the carcinogenic risk and shape of the dose-risk relationship for each beverage.

Finally, we can never overemphasize the fact that the high relative risks that we observed for heavy alcohol consumption in the absence of smoking may have been biased toward the null hypothesis because of the hospital sampling base for our control group. The latter included 26 percent of individuals with digestive system ailments, a sizable proportion of which may have been caused by excessive alcohol consumption (2). It is plausible to assume that, had our control group been selected randomly from the populations where we conducted the study, the risk elevations would have been more pronounced than they were, perhaps even for intermediate levels of alcohol consumption. We are currently assessing the extent of this selection bias by assigning separate smoking and alcohol relation scores for each diagnostic condition among the control patients and repeating the analyses by including only subsets of controls whose diseases had little or no putative relation with these two exposures.

REFERENCES