environmental tobacco smoke (ETS), which was updated in the June 8, 1994, issue of *JAMA*, is an impressive piece of work. The trend is clear: passive exposure to cigarette smoke is a risk. But I fear the authors dilute that point by incorporating too many tenuous variables in their statistical analyses. They acknowledge the problem of such factors as childhood recall of exposure and make attempts to control for it, but seem unwilling to admit that these and other data (eg, social exposure) are essentially not quantifiable by present methods. Inclusion of all these variables therefore led to a few implausible outcomes, which could give a window of solace to those who would defend ETS.

The most implausible conclusion was that "[t]he excess risk of lung cancer among women ever exposed to ETS during adult life in the household was 24%; in the workplace, 39%; and in social settings, 50%." Social exposure was defined as exposure of 2 or more hours per week from sources other than occupational and household. Even with this liberal definition, only 189 of 615 cases reported social exposure; on the other hand, 509 of 653 cases reported household exposure (spouse and other). The authors attempted to measure the relative influence of these two factors, but is it really feasible to do so?

Along that same line, household exposure was broken down by type of tobacco smoked by spouse. Of 433 cases exposed, 386 were to cigarettes, 85 to cigars, and 86 to pipes—ie, 557 types of exposure, so there is obvious overlap. And what was the type of tobacco during social exposure for those exposed to pipes at home? This is not a plea for even further subdivision of groups, simply to point out that there theoretically would be no end to it. Thankfully, no attempt was made to separate the effects of mainstream (exhaled) smoke vs sidestream smoke. The different effects of the two may be important, but that also is immeasurable.

Nonetheless, this study provides more evidence that passive exposure to cigarette smoke is a risk. Attempts to finetune the data into infinite subgroups should not be necessary to emphasize that main conclusion.

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1. Fontham ETH, Correa P, Reynolds P, et al. Environmental tobacco smoke and lung cancer in nonsmoking women. *JAMA*. 1994;271:1752-1759.

In Reply.—We concur with Dr Kirkland that subgroups of exposure are of less interest than total exposure to ETS and, as noted in our report, some exposures are more likely to be accurately recalled and reported than others. However, to estimate the risk of exposure to ETS, it is necessary to ask specific questions about exposures in a variety of settings during different time periods and then to summarize those data as we did in Table 5 for all childhood exposures combined and in Tables 7 and 8 for all adulthood exposures combined. The study was designed to collect data on a finite number of subgroups and to combine the subgroup data to categorize study subjects into levels of exposure ranging from little or none to lengthy. The unit of exposure was "years," which does not presume a level of precision that is unachievable (eg, hours per day per year).

To inquire only about a spouse's smoking habit or about exposure in the workplace would provide a glimpse of one part of the total picture in which individuals are actually exposed to greater and lesser degrees at home, in the workplace, in carpools, during bridge games, and so forth. Estimates of risk in those various settings were provided in the report, but were certainly not the main focus. As noted on page 1758, "[a] positive dose response between ETS exposure during adult life and lung cancer risk was found when individual sources of exposure, such as household, occupational, and social settings, were examined separately, and this pattern of risk was clearest when these exposure sources were considered jointly. The point estimates are somewhat higher for exposures in occupational and social settings than within households, but these differences are not statistically significant." While exposures in occupational and social settings may be equally or more important than household exposures because the concentration of ETS, a function of the number of active smokers, may be much higher and the opportunity to reduce the concentration by opening a window may not exist, our data suggest great consistency because the confidence intervals around these estimates are all virtually superimposable and all point estimates are consistent with a small to moderate effect.

We likewise concur with Dr Kirkland as to the main conclusion: long-term exposure to ETS increases the risk of lung cancer in women who have never used tobacco.

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Hypotension During Sham Apheresis in a Patient Taking ACE Inhibitors

To the Editor.—Dr Agishi[1] discusses the evidence that anaphylactoid reactions could occur during low-density lipoprotein (LDL) apheresis performed with the dextran sulfate–cellulose (DSC) adsorption columns[2] in patients taking angiotensin converting enzyme (ACE) inhibitors.[3] This adverse reaction is triggered by the entrapment of the Hageman factor, high-molecular-weight kininogen, and prekallikrein into the DSC column, leading to kallikrein activation and bradykinin generation. Bradykinin is usually inactivated rapidly by kinases I and II,[3] which are identical to ACE and are inhibited by ACE inhibitors. Therefore, increased generation and decreased catabolism of bradykinin may explain this adverse reaction during the LDL apheresis.

Recently, we observed a case of hypotension in a patient treated with an ACE inhibitor during an LDL-apheretic procedure without the DSC column (sham apheresis). After obtaining informed consent, we routinely perform sham apheresis in candidates for chronic LDL apheresis to check its feasibility (eg, adequate venous blood flow and the psychological impact on the patient). Schematically, the LDL apheresis is performed as follows: the plasma first is separated by a hollow polysulfone fiber filter (Sulflux FS-05, Kaneka Corp,