Reply

Huber and Brockie say that one should ignore epidemiological associations with relative risks below 3.0. This is a philosophical, not a scientific point. The simple fact is that the 1.3 relative risk we obtained by pooling across studies was statistically significantly elevated above 1.0 ($p<0.001$). This 30% change in relative risk is about the same magnitude obtained when one pools all studies on the benefits of treating myocardial infarction with β-blockers, which led to the use of β-blockade after myocardial infarction as standard clinical practice.

The statement that there are “at least 300 or more reported risk factors for cardiovascular disease” is misleading. Hopkins and Williams (their reference 5) list 246 risk factors that have been identified in at least one paper as risk factors for cardiovascular disease. These risk factors, however, are not mutually exclusive or equally important. In particular, they list cigarette smoking, blood carboxyhemoglobin, blood nicotine, 16 different aspects of platelet factors for cardiovascular disease. These risk factors, either by authors, title, or journal. The library or any other University of California library.

Their statement that “the epidemiological studies of ETS and heart disease cited by Glantz and Parmley all report negative (less than 1.0 relative risk) or only weak associations” is misleading at best. Only one of the studies (the one funded by the tobacco industry) had a relative risk below 1.0.

Their statement that we “incorporated the same data twice” is incorrect. The footnote to Table 1 in our paper clearly states that we reported both the Gillis and Hole papers for completeness but we reported both the Gillis and Hole papers for completeness but.

Their statement that benzo[a]pyrene (BAP) has never been reported in measurable quantities in air polluted with environmental tobacco smoke is incorrect. Concentrations in the range of 3.3–23.4 ng/m³ have been measured in restaurants and public places (1989 Surgeon General’s Report, page 91).

Huber and Brockie are correct that 7,12-dimethylbenz[a,h]anthracene (DMBA) has not been reported in ETS. The question of whether DMBA is in ETS is, to some extent, a side issue. The essence of the monoclonal hypothesis of atherogenesis is that carcinogens such as polycyclic aromatic hydrocarbons (PAH) can initiate or accelerate the development of lesions. The distinction is between carcinogenic and noncarcinogenic PAHs in general. While DMBA has not been measured in ETS yet, many other carcinogenic PAHs have been identified, including the related PAH benzo[a]anthracene.

The letter closes with the innuendo that our findings are somehow dictated by a desire to affect public policy rather than to discover the truth. Even if this were true, it hardly applies to the editors or reviewers of Circulation who decided the manuscript warranted publication.

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The Dipyridamole-Thallium Test

We appreciate Dr. Pohost’s comments1 about our article, “Dipyridamole Thallium-201 Scintigraphy as a Preoperative Screening Test: A Re-examination of its Predictive Potential,”2 but take issue with his response. Our findings differ from those of previous studies by demonstrating that dipyridamole 201Tl scintigraphy has limited sensitivity for the detection of perioperative ischemia or adverse cardiac outcome and a lower negative predictive value than previously appreciated. Consequently, we have suggested that routine use of dipyridamole scintigraphy for preoperative screening of patients undergoing vascular surgery may not be warranted.

Dr. Pohost believes that we are discarding “a useful approach for preoperative risk assessment in this surgical population,” and notes that dipyridamole thallium testing is “a widely documented technique” with a “substantial body of literature” that demonstrates that it has “considerable value for predicting postoperative events.” However, most of the favorable studies that are quoted come from a small number of hospitals with some overlap of subjects.3-6 Additionally, intravenous dipyridamole has become available only very recently to most practicing physicians, resulting in relatively circumscribed clinical experience. We believe that such experience is too limited to allow a conclusive comment regarding this test’s merits and certainly too limited to declare this test a “standard” preoperative procedure. Such uncritical acceptance also would have enormous cost implications.

Why did dipyridamole 201Tl scintigraphy fail to consistently predict adverse perioperative cardiac outcomes in our patients? Dr. Pohost suggests that a patient selection bias may account for our finding; that is, we excluded the high-risk patients who would most likely benefit from the test. However, we excluded only those patients in whom we could not perform continuous perioperative electrocardiographic and transesophageal echocardiographic monitoring, such as those with paced rhythms, left bundle branch block, or esophageal disease; otherwise, we prospectively studied an unselected consecutive series of patients. Most previous studies, in contrast, have been retrospective, with no defined entry criteria other than referral for a scintigraphic study.

In our study, unlike previous studies, the results of the dipyridamole 201Tl scintigrams were blinded and unavailable to the clinicians providing care and to the investigators making the diagnosis of perioperative complications. We did not intend to suggest that such blindness was responsible for the “poor performance” of dipyridamole 201Tl scintigraphy in our study. Our blinding strategy was designed to optimize unbiased data acquisition and interpretation. Although blinding may be difficult to institute in clinical studies, we believe that it is only by blinding clinicians and investigators from test results that a number of sources of bias can be avoided and the independent value of a test be determined accurately.

Dr. Pohost correctly notes that the number of serious outcomes (death, myocardial infarction) in our patient series was small. However, the number of serious outcomes was similar to that obtained in several other series. Additionally, our outcome results were substantiated by our finding that more than one half of our patients who developed perioperative electrocardiographic and echocardiographic evidence of ischemia did not have a reversible defect on preoperative scintigraphy. This result is particularly noteworthy given the strong association of postoperative ischemia to adverse outcome.7 We are not surprised that patients without potentially jeopardized myocardium, as detected by dipyridamole scintigraphy, develop major postoperative complications. For example, myocardial infarctions usually are due to thrombosis, which may occur at the site of both noncritical and critical lesions during the postoperative hypercoagulable state. Heart failure and arrhythmias are more likely to be due to prior infarction and left ventricular dysfunction than de novo ischemia.8 Additionally, substantial increases in myocardial oxygen demand occur perioperatively that.
The dipyridamole-thallium test.
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