higher risk of stroke, the next logical step in research would be to use preoperative noninvasive vascular studies to attempt to predict the risk of postoperative stroke in these patients. The goal of this research would be to identify patients whose risk is sufficiently high to justify a trial of prophylactic therapy, including carotid endarterectomy.

Implicit in the foregoing discussion is the assumption that carotid stenoses are involved in the pathogenesis of postoperative stroke, perhaps because of their hemodynamic or prothrombotic effects. Like Taylor et al.,[4] we also found that postoperative atrial fibrillation increases the risk of postoperative stroke. Similarly, a history of congestive heart failure and the presence of mitral regurgitation (on ventriculography) increase the odds of these events, suggesting that cardiogenic emboli may cause a number of these strokes or transient ischemic attacks. Also important are a history of myocardial infarction, stroke, or transient ischemic attack and a bypass pump time of more than two hours. Thus, these findings suggest that postoperative stroke is multifactorial and may be caused by a variety of pathogenetic mechanisms.

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OUTPATIENT VERSUS INPATIENT CARDIAC CATHETERIZATION

To the Editor: The article by Block et al. (Nov. 10 issue)[1] comparing outpatient and inpatient cardiac catheterization reported a high frequency of myocardial infarctions in the outpatient group. Myocardial infarction developed in 1.6 percent of the patients in the outpatient group (3 of 192) as compared with 0.5 percent of the inpatient group (1 of 189). There was no statistical significance in this threefold difference in myocardial infarction rate, although as the authors have suggested, this may be the result of a Type II statistical error.

The frequency with which myocardial infarction occurs as a possible complication of cardiac catheterization is quite low in modern studies. The Collaborative Study of Coronary Artery Surgery (CASS), which in contrast to Dr. Block's study, included patients with unstable angina, had a 0.45 percent combined incidence of myocardial infarction and fatal events within 48 hours of the procedure.[2] Unstable angina in the CASS study was the only variable statistically associated with the occurrence of nonfatal infarction, and it was present in the majority of the fatal infarctions as well. Other large, modern studies have reported myocardial infarction as a complication in 0.09 percent[3] and 0.07 percent[4] of patients undergoing cardiac catheterization.

Additional information on the four patients in the study of Block et al. in whom myocardial infarction occurred would be useful. How many hours after the cardiac catheterization did the myocardial infarction occur? Were there factors in each case that suggested that the development of the myocardial infarction was related to the outpatient protocol? What type of coronary disease did these four patients have, and in what functional class were they?

An analysis of this type may indicate whether this outpatient protocol played a part in the myocardial infarctions. For example, if early mobilization led to a large hematoma associated with hypotension followed by a myocardial infarction, this would be suggestive evidence that the infarction was related to the outpatient catheterization procedure. Alternatively, if the myocardial infarction occurred before mobilization, it would indicate that the patient's outpatient status was unrelated to the outcome.

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To the Editor: Block et al. concluded that outpatient cardiac catheterization offers substantial financial savings over inpatient catheterization, and they calculated an annual savings of $51 million if 15 percent were performed on an outpatient basis. However, they did not consider whether widespread use of the outpatient setting would increase the demand for the procedure, as appears to be true for cataract removal and other procedures. Demand may increase because patients and physicians perceive a procedure to be simpler and to have fewer risks when it can be performed in an outpatient setting. Yet if more procedures are done, the overall cost associated with a procedure may increase, even if the cost per procedure decreases. Thus, we must consider the effects of altered demand when estimating the costs associated with changes in medical practice.

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The above letters were referred to Dr. Block, who offers the following reply:

To the Editor: We reviewed our data concerning patients who had myocardial infarction. The onset of prolonged chest pain occurred at the time of cardiac catheterization in all instances. Patients were then listed as having a presumed myocardial infarction. No patients had prolonged chest pain or myocardial infarction while being monitored after their return to the surgical day care unit or after ambulation was begun in the outpatient group. Thus, we conclude that outpatient status had no bearing on the development of myocardial infarction.

In reviewing the specific patients who had myocardial infarction, it turned out that the patients who had prolonged chest pain in the cardiac catheterization laboratory were first listed as having presumed myocardial infarction and were then later also listed as having myocardial infarction; hence, each patient was tallied twice. Therefore, our total incidence of myocardial infarction was 0.5 percent (2 of 381 patients).

One patient who had a myocardial infarction had diffuse, severe three-vessel disease with stable angina pectoris. Neither embolism nor acute thrombosis occurred at cardiac catheterization to account for the myocardial infarction. The second patient was found to have less than total occlusion of the left anterior descending coronary artery. Percutaneous transluminal coronary angioplasty was performed. Prolonged chest pain developed, and myocardial infarction was confirmed by enzyme levels later in the hospi-

talization. Thus, only one patient had a myocardial infarction associated with the diagnostic catheterization — an incidence of 0.25 percent.

Our conclusion remains that outpatient catheterization seems to be a safe alternative for selected patients in stable condition.

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ANTIBIOTICS FOR THE TREATMENT OF FEBRILE CHILDREN WITH NEUTROPENIA AND CANCER

To the Editor: The question of whether vancomycin should be included routinely in the initial empirical antibiotic regimen for febrile, neutropenic patients with cancer is important and relevant. Gram-positive organisms are increasing in incidence, and many are resistant to or poorly covered by most regimens that do not contain vancomycin. Thus, some authorities have recommended that vancomycin be part of the initial therapy. On the other hand, vancomycin should not be overused, because it is expensive, it is potentially toxic, and it can be associated with the emergence of resistant organisms. In addition, certain of the beta-lactam–resistant gram-positive organisms, such as coagulase-negative staphylococci, are relatively indolent pathogens. Consequently, another approach is to reserve vancomycin for patients with documented gram-positive infections or with clinical infections in which a resistant gram-positive organism is likely to have a role.

Two recently published studies have addressed this issue.[1,2] Although certain regimens that did not contain vancomycin were associated with an increased incidence of secondary gram-positive infections, neither study demonstrated any increase in morbidity specifically attributable to the lack of vancomycin in the initial regimen. Shenep et al. (Oct. 20 issue) reported the results of their randomized trial comparing regimens with and without vancomycin, and they concluded that vancomycin should indeed be included as part of the initial empirical therapy.[3] However, this conclusion is not fully substantiated by the data they present.

In their study, more gram-positive secondary infections were seen in the group without vancomycin, but in eight of nine of these, no excess morbidity was reported to be due to delaying vancomycin treatment until after the organism was recovered. The weight of their conclusions and recommendations appears to rest entirely on a single case of fatal gram-positive sepsis that occurred in a patient not receiving vancomycin, and it was due to an organism that was susceptible to the antibiotic regimen the patient was receiving at the time. Also, clearing of this organism occurred only after treatment with another beta-lactam (cefotaxime) in combination with the vancomycin. To make generalized recommendations about the utility of empirical vancomycin based on this case is somewhat misleading, and it defeats the purpose of a randomized trial. The authors also contend that the increased cost of routine empirical vancomycin might be offset by less frequent need for cultures or other antibiotics such as amphotericin B, but their own trial substantiates neither of these possibilities.

Clearly, no empirical regimen can cover realistically every potential pathogen or completely eliminate the risk of breakthrough infections in patients with persistent neutropenia. This trial underscores the fact that serious and even fatal infections can occur in such patients, despite "appropriate" antibiotics. It fails, however, to demonstrate any important or clear-cut liability attributable to an empirical regimen containing no vancomycin.

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The above letter was referred to the authors of the article in question, who offer the following reply:

To the Editor: We have routinely included vancomycin in the initial empirical antibiotic regimen for febrile children with neutropenia since 1983. Concern over the expense and toxicity of this agent and the possible emergence of resistant organisms prompted us to conduct a double-blind, randomized study comparing the standard regimen (A) — vancomycin, ticarcillin, and amikacin — with a less costly one that we believed would be as effective but would produce fewer complications. We anticipated that routine use of the latter regimen (B) — ticarcillin–clavulanate and amikacin — could save as much as $100,000 annually at our institution.

We were surprised to find that incidences of nephrotoxicity and rashes, including the red-man syndrome, did not differ appreciably between the two treatment groups. However, 9 of 48 patients (19 percent) receiving regimen B had breakthrough gram-positive bacteremias (7 symptomatic, 1 fatal) as compared with only a single asymptomatic episode among 53 subjects (2 percent) given regimen A ($P = 0.006$). With only 1 fatality among 101 patients, we recognized that an inordinately large study population would be needed to establish on a sound statistical basis a significant difference in mortality rates between the two regimens. When informed that regimen A was the more expensive regimen containing vancomycin, the entire study team agreed that the difficulty of rescuing patients from gram-positive bacteremia outweighed vancomycin's added cost. This judgment was influenced by the experience of Kramer and colleagues,[1] who encountered four episodes of fatal gram-positive bacteremia among 21 patients initially treated with ceftazidime alone, as compared with none among 37 who received ceftazidime plus vancomycin.

Drs. Rubin and Pizzo properly emphasize that the results of our study must be interpreted cautiously with regard to their relevance to other institutions and other antibiotic regimens. In settings where gram-positive bacterial infections are not a major problem, the use of vancomycin may not be warranted. Otherwise, we maintain that adding vancomycin to an aminoglycoside plus a carboxypenicillin[2] or a third-generation cephalosporin[1] can prevent, without excessive toxicity, potentially fatal bacteremias due to gram-positive organisms.

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RECOMBINANT HUMAN GM-CSF IN MYELOSUPPRESSION OF CHEMOTHERAPY (CONTINUED)

To the Editor: Although the report by Antman et al. (Sept. 8 issue)[1] presents encouraging data about the use of recombinant human granulocyte–macrophage colony-stimulating factor (rhGM-CSF) to promote hematopoietic recovery after cytotoxic chemotherapy, it also raises concerns about the ability of rhGM-CSF to decrease the morbidity and mortality of infections associated with myelosuppressive chemotherapy. Despite a decrease in the duration of neutropenia in patients receiving rhGM-CSF, 2 of 14 patients in the treatment group died of sepsis, as compared with none of the 12