logic and clinical evidence. The following approach is based on the fact that pharmacologic agents, or mediators, may exert opposite effects on different types of smooth muscle. Illustrative of this are the pharmacologic effects of acetylcholine and noradrenaline. Acetylcholine exerts a relaxant activity on vascular muscle, and a contractile activity on bronchopulmonary smooth muscle. Noradrenaline works the opposite way. An analogous situation appears to exist for adenosine, a metabolite that plays a key role in the pharmacologic effect of dipyridamole. Adenosine is a metabolic breakdown product from degradation of adenosinetriphosphate (ATP) that is released from cells into interstitial fluid and the circulation. Adenosine can be subjected to further catabolic breakdown or taken up again by cells. Dipyridamole blocks cellular uptake of adenosine, thus increasing its concentration in the blood stream and interstitial fluid. Indeed it has been demonstrated that dipyridamole increases endogenous adenosine plasma concentration, as well as the cardiovascular effect of exogenous adenosine. Increased concentration of adenosine will lead to enhanced stimulation of adenosine A2-receptors of coronary smooth muscle. This ultimately leads to coronary vasodilation, the effect aimed for in thallium-dipyridamole imaging. But how does this explain the pulmonary effect? It has been demonstrated in the guinea-pig that adenosine causes dose-dependent relaxation of tracheal smooth muscle, an effect potentiated by dipyridamole. On the contrary, in asthmatic patients inhalation of adenosine causes bronchoconstriction, as an effect that does not occur in healthy subjects. The bronchoconstrictory effect of adenosine can selectively be antagonised by theophylline. Antagonism occurs with theophylline concentrations that hardly influence basal airway caliber. Theophylline concentrations employed effectively blocked the adenosine-induced bronchoconstriction and not the effect of histamine, thus also pointing toward an adenosine receptor-mediated process. Studies have also demonstrated that adenosine-induced bronchoconstriction is independent from parasympathetic and/or β2-adrenoceptor-mediated mechanisms. Dipyridamole enhances adenosine-induced bronchoconstricition in asthmatic subjects. In patients suffering from chronic obstructive pulmonary disease (COPD), no untoward effects from dipyridamole or increased pulmonary sensitivity for adenosine has been demonstrated. So there seems to exist a fundamental difference between asthma and COPD pathophysiology regarding adenosine sensitivity of the airways. However, there is no information with respect to asthmatic bronchitis. COPD patients whose obstruction is partial reversible with β2 sympathomimetic drugs. Therefore, referring to the case reported by Lette et al and taking into consideration the patient being treated with salbutamol, one might wonder if asthma is not part of this patient's pathology. From this critical event it will be clear that selecting COPD patients for thallium-dipyridamole imaging any doubt about a possible asthmatic pathology has to be excluded. By taking this precaution, the high degree of safety can be maintained for this important diagnostic procedure.

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To the Editor:

In his interesting and well-referenced letter, Dr. Houben raises several points. Was our patient a "closet" asthmatic? Dr. Houben suggests that the patient may have been an asthmatic without our knowing it. As stated in our article, clinical history, physical examination and pulmonary function test results did not show any evidence of reversible small airways disease. We would not have performed histamine or metacholine provocative tests in the presence of advanced disease. He did not fit Burrows's definition of "chronic asthmatic bronchitis": What else could we have done to "exclude any doubt about a possible asthmatic pathology" in our patient?

Further, Dr. Houben states that "there seems to exist a fundamental difference between asthma and COPD pathophysiology regarding adenosine sensitivity of the airways", thus implying that asthma and COPD are distinct entities. COPD encompasses a large heterogeneous population of patients with variable degrees of bronchial inflammation, mucous hypersecretion, destruction of airspaces distal to the terminal bronchiole, and both irreversible and reversible chronic airway obstruction with a variable degree of small airway hyperresponsiveness. The relation between the small
airway hyperresponsiveness of asthmatics and that of COPD patients is a complex and controversial topic which is discussed in an excellent recent review article. If Dr. Houben wishes to make a clear distinction between the two entities, he must propose an investigative algorithm that clinicians could use to "exclude" the possibility of asthma in COPD patients with reversible obstruction. Otherwise, the discussion is purely academic and can only confuse clinicians facing the problem of having to select patients for the dipyridamole-thallium test.

Indeed, by requiring that "any doubt about a possible asthmaic pathology be excluded", Dr. Houben unwittingly places far greater restrictions on the test than the simple caution we propose in our article. We believe that if there is any clinical suspicion of coronary artery disease, the benefit from the test in most COPD patients far outweighs the risks, but that aminophylline and an intubation tray must be on hand for the rare occurrence of acute respiratory distress. A prospective trial on the incidence of bronchospasm in COPD patients undergoing dipyridamole-thallium imaging is presently under way at our institution. Preliminary results suggest that mild bronchospasm occasionally occurs (and is rapidly reversed by administration of aminophylline), but we have not encountered any new episode of severe bronchospasm in about 50 COPD patients (out of about 500 total patients) studied to date. Furthermore, Dr. Houben appears to suggest that dipyridamole-thallium imaging is absolutely contraindicated in asthmatic patients. There are a few published reports of severe dipyridamole-induced bronchospasm in asthma patients, but does this warrant depriving all asthmatic patients of the test, irrespective of the severity of small airway hyperresponsiveness or only those who are theophylline-dependent? Further clinical studies are necessary to address these questions.

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Survival After CPR

To the Editor:

In the September issue of Chest, Drs. Tortolani and co-workers report on the efficacy of norepinephrine and lidocaine infusions during cardiopulmonary resuscitation (CPR) after asystolic cardiac arrest ("In-hospital cardiopulmonary resuscitation during asystole: therapeutic factors associated with 24-hour survival."

Chest 1989; 96:622-26). In their retrospective analysis, survival was significantly greater in patients receiving therapy with norepinephrine, lidocaine, or both infusions together, compared to patients treated according to a standard regimen that included atropine and epi-nephrine. The authors do not report the circumstances during CPR that may have led to the initiation of lidocaine or norepinephrine infusions. It is quite possible that these infusions were begun after restoration of ventricular electrical activity (ie, as therapy for a new rhythm following asystole). Lidocaine and norepinephrine infusions simply might have identified those patients who recovered ventricu-lar electrical activity after asystolic arrest and thus be expected to have an increased likelihood of survival. It is therefore difficult to evaluate the findings of such a retrospective study, and emphasizes the need for a prospective and controlled evaluation of this problem.

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To the Editor:

Dr. Smith's observations are correct in that it is quite possible in some cases that these infusions were started after restoration of ventricular electrical activity. Unfortunately, the way the data were collected precludes us from determining with certainty when this was the case. This is an inherent limitation of the study, and as Dr. Smith points out, reflects the need for prospective, experimental studies. It would also seem to point to the need for improved documentation of CPR procedures for purposes of clinical research.

We feel that our study was valuable in that it examined statistical associations between outcome and the simple use or non-use of specific therapeutic measures in a large series of patients with a well-defined initial rhythm. This approach has generally not been applied in large scale clinical studies of CPR outcome. Earlier studies generally treated CPR as a single variable when, in fact, current guidelines and practices have resulted in a situation in which CPR can mean very different things in different instances. Our research was an attempt to examine the correlates of this variability, to explore the data for significant correlates of survival, and to utilize the clinical results for the generation of hypotheses which can be tested under more controlled conditions.

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Hemorrhage After Bypass Surgery

To the Editor:

It was with great interest that we read the recent study by Del Rossi et al entitled, "Prophylactic treatment of postperfusion bleeding using EACA." We agree with their assessment that postoperative hemorrhage after cardiopulmonary bypass is a major cause of morbidity and some mortality. We also congratulate the authors on accomplishing a significant study with a large group of patients. However, there are several points that we wish to discuss.

The changes in coagulation function that occur during cardiopulmonary bypass are undoubtedly complex and probably affect all aspects of the dynamic equilibrium of clot formation and breakdown. Platelet dysfunction and protein pro-coagulant precursor breakdown have been studied previously. It seems certain that platelet dilution, destruction, and dysfunction is the most common defect demonstrable. Del Rossi et al point out that plasminogen activation and