significant role in the treatment of acute exacerbations of COPD if aminophylline, isoproterenol and ampicillin treatments are used concomitantly.

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To the Editor:

Dr. Glenny's letter refers almost entirely to a paper by Albert and co-authors, so we are not quite qualified to respond without access to the raw data of that study. However, after reviewing the paper by Albert and his colleagues on the effect of corticosteroid therapy in acute exacerbations of COPD, we believe that Dr. Glenny has a point and that there is probably no statistically significant difference in FEV1 between the placebo and steroid groups at the end of the trial. The significant differences reported by Albert and his colleagues may well be an artifact, as pointed out by Dr. Glenny, due to the lower initial FEV1 in the steroid group in spite of randomization, and the inappropriate method of calculating response as percent of the initial value which exaggerates the response in those with the lowest initial FEV1. Theophylline levels, sputum cultures and radiographic findings probably do not affect the results, as these variables ought to be equal in both groups due to randomization. This said, we take exception to being called staunch opponents of the use of corticosteroid therapy in COPD. Taking the attitude of therapeutic nihilism may prove more dangerous than overzealous use of corticosteroids in this disease. While Dr. Glenny has pointed out that the study by Albert and his colleagues probably does not have the statistical power to establish that corticosteroid therapy is beneficial in acute exacerbations of COPD, this should not be equated with lack of effect. Most of the studies on corticosteroid treatment of stable COPD have shown a small effect, although not always a statistically significant one as in our own study. We showed clearly that the probability of steroid response is inversely related to baseline FEV1. Thus a patient with a FEV1 of 700 ml has approximately 30 percent chance of being a responder to high-dose steroid therapy; if the FEV1 is 1,200 ml, the probability of response decreases to 5 percent. How response is defined is obviously of major importance, and while the inverse relationship between response and pulmonary function is a good example of regression to the mean, one cannot write off the positive response as only a statistical artifact. In fact, when viewed together the results of studies of corticosteroid therapy in COPD have been highly consistent. The differences in opinion have resulted because each study has only dealt with a part of the whole, thus reminding us of the five blind men examining an elephant. All in all, our investigation revealed this consistency but at the same time showed that corticosteroid therapy has less of a role in stable COPD than previously thought. We never said that there was no role at all. That would be premature at this date.

As we pointed out in our paper, spirometric measurements in small patient groups may be an inadequate assessment of the therapeutic effect of a drug on the airways. Using events such as morbidity and mortality as outcome measures, and using life-table analysis may be more appropriate but would obviously require a large population to determine a potential treatment effect. This approach would result in clinically significant information, ie, whether corticosteroid therapy could prevent acute exacerbations of COPD, reduce need for emergency room visits and hospitalization, reduce mortality and morbidity related to acute respiratory failure, etc. Increased rate of recovery resulting in shortening of hospital stay might also be a potential benefit that would be highly cost-effective. Life-table analysis and the study of events as an outcome has been used in cardiovascular disease (ie, the use of beta-blocker therapy to reduce mortality after myocardial infarction), but its application to pulmonary disease has been limited. It is perhaps time to look past the spirometer (and its inherent problems related to repeated measures which are difficult to deal with statistically) and begin measuring the outcome of our therapeutic interventions in events of clinical significance. Corticosteroids may well be a prime candidate for such an evaluation.

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Diagnosing Pneumocystis carinii

To the Editor:

We feel that the recent communication by Mones et al quantitating the total number of biopsy fragments required to diagnose or confidently exclude Pneumocystis carinii pneumonia in AIDS patients by fiberoptic bronchoscopy is a helpful contribution to those performing this procedure. We do not agree with their conclusions regarding the poor diagnostic efficacy of transbronchial brushings and lavage, which we and others have found to correlate well with biopsy results. We wish to re-state the importance of adequate sampling for these procedures as well.

We feel our excellent correlation of bronchial brushing with biopsy (84 percent overall, 89 percent on initial biopsy) was due to use of a large sampling brush (7 mm) and preparation of at least four slides per brushing. Similarly, we feel our excellent (86 percent) correlation of bronchoalveolar lavage with biopsy occurred because the lavages were performed using two or three irrigations of 30 ml of saline solution through the bronchoscope wedged in a segmental

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bronchus, following which at least 40 ml of aspirate per lavage were obtained. A cell button was then prepared for examination.

We would like to also note that we now stain our brushing, biopsy, and bronchoalveolar lavage specimens with an improved rapid methamine silver stain. The silver stain step is completed in one minute, with sensitivity equal to classic methods.¹

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To the Editor:

We appreciate the positive comments of Hartman and Koss on the treatment of the biopsy fragments in our study.¹ Although the use of the word "correlation" in their report is not clear to us, we realize the high degree of sensitivity of bronchial brushings (BB) and bronchial washings (BW) in their hands. This is the result of their competence, but probably obeys to other factors such as the use of a large brush, large volumes of saline solution for washings, and the number of slices prepared—up to ten per case. Their use of a simple and reliable modification of the methenamine silver stain is also noteworthy.² Yet our study clearly shows that the actual diagnostic contribution of BB and BW to that of transbronchial biopsy with the touch preparation (TP) is only 2 percent. For such a small gain, it seems to us, it is too onerous to use so much technical time, expense, and professional effort in evaluating BB and BW specimens. Indeed, since the publication of our paper we have taken the additional step of eliminating altogether the TP which allows a diagnosis the same day of the biopsy but overall raises the diagnostic yield only 1 percent.

Because of the high degree of awareness among our clinicians, patients suspected of having Pneumocystis carinii pneumonia are often treated before the results of fiberoptic bronchoscopy. Repeat biopsy seems justifiable in patients with a high suspicion index and non-representative biopsy specimens. Adherence to the roentgenographic and pathologic criteria set forth in our paper probably eliminates the 3 percent false negative rate that can be expected with this approach.

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Coronary Artery Bypass Grafting in Young Adults

To the Editor:

In a recent article,¹ Cohen et al noted unfavorable long-term results in their patients who had undergone coronary bypass grafting at 35 years of age or less. Young adults with coronary artery disease do present special problems, but the discouraging experience documented for their small group of patients (40 patients less than 36 years old) is not representative of the palliation that can be achieved for patients in this age group.

In a study of 107 patients who had undergone coronary bypass grafting at age 35 years or less and who were followed for ten years after surgery (mean postoperative interval, 115 months), we documented survival of 94 percent at five and 85 percent at 10 postoperative years, and event-free survival of 77 percent at five and 53 percent at ten postoperative years.² Both survival and event-free survival were adversely influenced by elevated serum cholesterol (>300 mg/dl) and diabetes. An important observation was that the patency of saphenous vein grafts in young adults was inferior to vein graft patency in older patients. Our studies of bypass graft patency³ and those of others⁴ have shown that long-term vein graft patency is decreased by the presence of hyperlipidemia and diabetes, and it seems likely that the adverse influences these coronary risk factors exert on the clinical result after bypass surgery may be mediated by an increase in the development of vein graft atherosclerosis. Young adults with coronary artery disease tend to have important risk factors and appear particularly prone to the development of vein graft atherosclerosis.

Fortunately, the internal mammary artery is available as an alternative bypass graft. The long-term patency of internal mammary artery grafts is not decreased by the presence of hyperlipidemia, diabetes, or any other coronary risk factor. For our series of young adults, the patency rate of internal mammary artery grafts was 93 percent, compared with 56 percent for saphenous vein grafts. Although the ten-year clinical results in our young adults treated surgically were not equivalent to those in the age-matched normal population, they were not nearly as dismal as those noted by Cohen et al.¹ Young adults are subject to vein graft failure and should receive revascularization with mammary artery grafts, including bilateral mammary artery and sequential mammary artery grafts, whenever feasible. With these techniques, coronary artery surgery can offer many young adults effective palliation.

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