To the Editor:

We appreciate Dr. Matthay's editorial comments regarding pressure controlled inverse ratio ventilation and would like to respond to some of the issues raised. We disagree that attempts to define potential new methods of ventilatory support are "misguided". While it is true that significant mortality in intensive care units occurs from uncontrollable infection and multiorgan system failure, these deaths usually occur relatively late and often are the result of ventilatory failure. Specific therapy directed at these underlying processes may prove to increase survival; however, it does little good if the patient succumbs from hypoxemia and hypercarbia prior to any potential benefit of definitive therapy being realized. The 32 patients that were reported in our previous study on pressure controlled inverse ratio ventilation (PC-IRV) all had unacceptable clinical response to "conventional ventilatory modes". Many were acutely unstable and most were rapidly dying. While the overall mortality in the study group was 77 percent, these patients met similar entry criteria as the prospective ECMO study that was calculated to have an expected mortality in excess of 95 percent. What can we conclude from this? It is precisely because the study was retrospective that conclusions regarding efficacy—favorable or unfavorable—cannot be drawn from the mortality data. We agree with Dr. Matthay as stated in our article that a need exists for a prospective controlled trial of PC-IRV vs conventional ventilation with PEEP to provide efficacy data. Such a trial is now in progress at our institution. We based the need for a prospective study on data that was collected from the retrospective review of our clinical experience. In any trial of a new drug, device or treatment modality, the usual progress is from animal studies to limited open-label trials in human subjects to randomized, prospective trials of efficacy. PC-IRV appears to be following this path. To deny patients who have no other therapeutic options potential benefits of PC-IRV therapy on an individual basis simply because of the lack of a well-defined prospective trial strikes us as being too restrictive when one considers that most ventilatory modalities have not been proven efficacious in randomized prospective trials. PC-IRV is a complex ventilatory modality that requires a highly sophisticated treatment team consisting of physicians, nurses, and respiratory care practitioners. The decision to employ PC-IRV cannot be made lightly. Close bedside monitoring of the patient by the team is essential, as is a thorough understanding of the technique of inverse ratio ventilation, an appreciation of the risks involved, and the ability to deal with complications. We do not consider PC-IRV to be experimental but rather unreproved therapy.

It seems premature to state that retrospective studies are no longer warranted with regard to a mode of ventilation that has been reported in fewer than 200 patients. We view PC-IRV as a potential adjunct to conventional ratio ventilation in severe ARDS, and are actively collecting additional data that will allow better definition of the role, if any, for PC-IRV in patients with severe respiratory failure.

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To the Editor:

The above letters represent important responses to my editorial regarding how new modes of ventilation for ARDS should be evaluated.

In response to Dr. Gluck, I do agree that the authors of the manuscript regarding pressure-controlled inverse ratio ventilation in severe ARDS (Chest 1988; 94:755) provided an overly optimistic view of the results of their study in their discussion. Perhaps Dr. Gluck is right in indicating that the editorial staff of Chest should have been more critical of the manuscript and the authors conclusions regarding the data before it was approved for publication. However, I would argue that even under the best of circumstances, articles such as this will be published in which overly optimistic conclusions are drawn inappropriately from the data. The result is that other physicians then see this type of ventilatory support as a potentially lifesaving therapy. I agree with Dr. Gluck that feasibility studies should not be abandoned entirely. However, I believe that the weight of evidence at the present time argues strongly against the likelihood that this new mode of mechanical ventilation is going to result in a significant decrease in mortality for patients with ARDS. As I pointed out, the experience with high frequency ventilation, extracorporeal membrane oxygenation (ECMO) and high levels of positive end-expiratory pressure have all indicated that these new modes of ventilation do not improve survival. Therefore, my editorial was designed to caution physicians regarding accepting new modes of ventilation without a prospective, randomized trial demonstrating that the new mode is safe and more effective than conventional ventilatory modes.

In response to Dr. Tharratt's letter, I am pleased that he has decided to do a prospective, randomized trial of pressure controlled-inverse ratio ventilation. One of my concerns with Dr. Tharratt's study was the way in which he interpreted the results. It seems that Dr. Gluck had the same concern. Dr. Tharratt interpreted the data more optimistically than is reasonable. Thus, physicians reading this article may have been left with the impression that this new mode of ventilation offers a substantial, potentially lifesaving option for patients with severe ARDS. I believe that is not the impression that should have been conveyed by the article. Of course, feasibility studies with new treatments will always be a reasonable first step for testing some new therapeutic modalities for a variety of clinical problems, including acute respiratory failure. However, in view of the dismal record of new modes of mechanical ventilation for decreasing modality in ARDS, I believe that investigators should be very cautious about applying new therapy without a prospective.
P Carinii Infection

To the Editor:

Pneumocystis carinii is usually considered an airborne alveolar pathogen. Yet granulomatous2 and necrotizing4 pneumoniae have been related to P carinii infection. We had the opportunity to examine a surgical lung biopsy specimen from a 40-year-old man with acquired immunodeficiency syndrome (AIDS) complicated by bilateral pneumothorax.

The patient was a drug addict with a two-year history of AIDS. He had presented in the previous year with two bouts of P carinii pneumonia (PCP) treated with sulfamethoxazole-trimethoprim, and pulmonary tuberculosis (Tuberculosis hominis) treated for six months with isoniazid, ethambutol, rifampicin, and pyrazinamide. He was on preventive therapy against PCP with aerosolized pentamidine. One month before surgery, he complained of fever, cough, and purulent sputum. Treatment with a combination of amoxycillin and clavulanic acid was prescribed. Chest x-ray examination showed bilateral interstitial pulmonary infiltrates. Two bronchoalveolar lavages did not yield any specific findings of diagnostic value. The occurrence of a bilateral pneumothorax brought the patient to our intensive care unit. Chest x-ray film and thoracic CT scan showed bilateral nodular infiltrates predominating on the upper left lobe. There was no obvious excavation of the lesions. Surgical abrasion of the pleural cavity with lung biopsy was decided.

On gross examination, the lung specimen was spotted with granulomas. On histologic examination, the lesions were centered on bronchi, septa and pleura (Fig 1). They consisted of necrosis surrounded by foamy alveolitis. In several nodules, giant cell granulomas (Fig 2) and calcified deposits were observed. Some lesions were exclusively necrotic, angio-invasive, and destructive to the septa and pleura. In all these foci methenamine silver stain showed numerous cysts of P carinii in the necrosis, vascular walls and lumen. The patient was treated with trimethoprim and recovered.

Granulomatous and cavitary PCP, as well as pneumothoraces, have been described in patients with AIDS. Few histologic descriptions of the lesions have been reported. In our case, the necrotic and invasive behavior of PCP is unusual as the ability of P carinii to penetrate into the lung parenchyma is not commonly recognized. It would even appear that P carinii can enter the blood vessels and "metastasize" to the pleura. The pleural necrotic lesions seem to be the cause of pneumothoraces. Preventive treatment using aerosolized pentamidine may play a pathogenic role either by damaging the normal lung tissues or enhancing the entry of P carinii into the parenchyma which, if such were the case, could be observed with increasing frequency.

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The Role of Dipyridamole in Bronchospasm

To the Editor:

In their article entitled, "Severe bronchospasm followed by respiratory arrest during thallium-dipyridamole imaging", Lette et al1 attempt to find an explanation for this dramatic reaction after dipyridamole. They hold the opinion that inhibition of pulmonary uptake of prostaglandin E2, a bronchodilatory lipid-derived mediator, might be the responsible mechanism. However, there exists a more plausible explanation that is supported by ample pharmacologic trial comparing the results to conventional ventilator therapy.

As I stated in my editorial, the initial enthusiasm with high frequency ventilation, high levels of positive end-expiratory, and extracorporeal membrane oxygenation ultimately proved to be unfounded once prospective randomized studies were done. Therefore, I support the plan to test pressure controlled inverse ratio ventilation in a prospective randomized trial.

I hope other institutions will not use pressure controlled inverse ratio ventilation until there is solid evidence that it improves outcome in patients with acute respiratory failure or ARDS.

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Figure 1. Lung biopsy: necrotic foci (arrow head) located along the septa and pleura (H and E, ×50).

Figure 2. Lung biopsy: granulomas with giant cells (H and E, ×50).

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