thirds of the cardiac cycle. During the imaging, subjects (heart rates: 55 to 100 beats per min) were requested to hold their breath, typically for 30 to 50 s. In each subject, three to seven imaging series were performed, from which mean velocity profiles were determined.

Mean (±SE) peak pulmonary arterial blood velocity (Fig 1) ranged from 16.2 to 48.5 cm/s and occurred at times ranging between 8.2 and 22.4% of the cardiac cycle after the R-wave. Within experimental uncertainty, no significant retrograde blood motion was observed during later cardiac phase. Because of significant vessel movement from image to image throughout the cardiac cycle, the cross-sectional area of the pulmonary artery could not be determined reliably.

It is clear that if a new procedure such as the present method is merely added to existing diagnostic techniques, it will surely increase utilization of resources, regardless of how much it may reduce risk of mortality or improve diagnostic accuracy.

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Why Be Limited To Nocturnal Noninvasive IPPV?

To the Editor:

The article by Claman and colleagues (December 1996),¹ was well written, but there were at least three important problems with it. For one, it lumped together the assessment and treatment of neuromuscular, sleep-disordered breathing, and lung disease patients. Why should a goal be "to reduce the PaCO₂ by no more than 10 to 15 mm Hg" for neuromuscular patients? This brings about the second problem. Because the article limits itself to nocturnal-only use of intermittent positive pressure ventilation (IPPV), neuromuscular patients managed in this way cannot avoid developing respiratory failure. Although mouthpiece/lipseal IPPV was mentioned for nocturnal ventilatory support, simple mouthpiece IPPV is the most important and preferred method of daytime ventilatory support for neuromuscular patients and the main reason that, unlike what this paper suggests, the great majority of neuromuscular disease patients should never require tracheostomy. Most nocturnal-only IPPV users require continuous ventilatory support during intercurrent respiratory tract infections.

The third important oversight is the neglect of the role of expiratory muscles in the elimination of airway secretions.² One should not discuss nocturnal ventilatory (muscle) assistance while ignoring weakness of expiratory muscles, the main cause of respiratory failure in these patients. The statement, "patients with severe neuromuscular weakness, prominent pulmonary secretions, or significant bulbar dysfunction may respond poorly to noninvasive techniques, and tracheostomy is frequently necessary for effective treatment" adds nothing to the understanding of the problem. The reasons that neuromuscular patients "respond poorly to noninvasive techniques" is because they eventually weaken to the point that they require daytime ventilatory support and manually and mechanically assisted coughing to clear airway secretions. Tracheostomy only eventually becomes necessary when bulbar musculature is so weak that peak-assisted cough flows cannot exceed 160 L/m² and mechanical insufflation-exsufflation is ineffective.³ Although the majority of amyotrophic lateral sclerosis patients eventually will require tracheostomy, virtually no patients with Duchenne muscular dystrophy, other non-Duchenne myopathies, or spinal muscular atrophy types 1, 2, 3, or 4 should ever require tracheostomy.

For most neuromuscular patients, continuous noninvasive IPPV initially becomes necessary only during intercurrent respiratory tract infections, which can almost always be managed without intubation. Our goals are to maintain normal alveolar ventilation around the clock and to create the cough flows required to eliminate airway secretions. It is just because we do not limit ourselves to nocturnal-only, noninvasive IPPV that we have numerous neuromuscular patients who have required 24-h ventilatory support for many years, but who have never undergone polysomnography, translaryngeal intubation, tracheostomy, or even hospitalization. It does a great disservice to patients with ventilatory failure on the basis of neuromuscular weakness to permit chronic hypercapnia and speak about oxygen supplementation, which in itself may render nocturnal noninvasive IPPV less

Figure 1. Mean (±SE) pulmonary arterial blood velocity in cm/s as fraction of cardiac cycle in five normal human subjects. Abbreviations LA, MA, PE, LE, and HO refer to separate subjects.
effective and hasten respiratory failure.4 I recommend that all who are interested read further on the subject.5

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To the Editor:

We appreciate Dr. Bach’s comments regarding our recent review entitled “Nocturnal Noninvasive Positive Pressure Ventilatory Assistance.” As noted in the title, our primary intent was to review issues specifically associated with nocturnal ventilatory assistance. We did not intend to minimize the importance of many of the therapeutic efforts described by Dr. Bach in caring for patients during wakefulness. We agree that ventilatory assistance may need to occur for 24 h per day, and not be limited to nocturnal hours. This aspect of care, albeit important, was not the topic under review. We have written a general review article of this field, and appreciate Dr. Bach’s perspective regarding neuromuscular patients.

We are not as enthusiastic as Dr. Bach regarding simple mouthpiece intermittent positive pressure ventilation (IPPV) during sleep. Elimination of secretions remains a significant management issue, but there is no specific advantage of the mouthpiece interface over other interface modalities. More importantly, a mouthpiece interface may be associated with oral air leakage, risk of aspiration, and dental malocclusion. A nasal mask interface may allow oral clearance of secretions or emesis during assisted ventilation, or oral airflow in the event of equipment failure.

Dr. Bach takes issue with the suggestion that PaCO2 be reduced by 10 to 15 mm Hg during nocturnal ventilatory assistance. We trust Dr. Bach did not interpret the review to suggest that the normalization of diurnal PaCO2 is to be avoided, when in fact we were referring to PaCO2 during sleep. We have adopted a conservative approach in the degree of aggressiveness of ventilatory assistance during sleep due to concern regarding the potential for hyperventilation and development of respiratory alkalineosis during nocturnal ventilatory assistance in the sleeping patient, especially in thin patients in whom it is relatively easier to hyperventilate than obese patients. Alkalineosis may promote central apnea, possibly through increases in upper airway resistance,2,3 and may also decrease cerebral blood flow. In addition, to our knowledge, there have been no scientific studies documenting the need to normalize PaCO2 during sleep as a requisite for the clinical benefit from nocturnal noninvasive IPPV assistance.

Like Dr. Bach, we are enthusiastic regarding the benefits of nocturnal IPPV assistance, and hope that Dr. Bach’s remarks will help spark further interest and discussions in this evolving field.

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Steroid-Responsive Interstitial Pneumonitis After Fludarabine Therapy

To the Editor:

Fludarabine phosphate is a 2-fluoro-s’s monophosphat derivative of vidarabine that is resistant to deamination by adenosine deaminase and possesses improved solubility compared to vidarabine. Fludarabine monophosphate has substantial activity against chronic lymphocytic leukemia (CLL) and low-grade non-Hodgkin’s lymphomas.1 There have been several reports of interstitial pulmonary toxicity related to fludarabine administration. This pulmonary toxicity appears responsive to steroids.2,3 In some of these reported cases, pathologic confirmation was not available and other medications were administered concurrently or prior to fludarabine.4 In addition, infectious interstitial pneumonia is conclusively ruled out in only one report.4 We report a case of a patient who was followed at our institution over a 2-year period, and who developed pulmonary toxicity after fludarabine therapy for CLL. This condition was documented radiographically and responded to steroid therapy, recurred upon rechallenge with fludarabine, and was confirmed at postmortem examination.

A 71-year-old man presented with progressive splenomegaly, 15-lb weight loss over the preceding 4 months, early satiety, and low-grade fevers. The WBC was 20,800/mm3, RBC 3,710/mm3, and platelet count was 144,000/mm3. Lymphocytes measured 82% and morphologically appeared to be small mature lymphocytes with approximately 20% larger atypical lymphoid cells with nucleoli. Bone marrow aspiration and biopsy revealed a monotonous infiltrate of small mature lymphocytes. Flow cytometry was as follows: CD19 87%, CD20 90%, kappa 86.9%, lambda 0.1%, CD5 93%, CD2 6%, CD7 5%, CD11C 3%, and CD5+CD19 86%. CT scan revealed massive retroperitoneal lymphadenopathy and splenomegaly. Fludarabine (50 mg for 5 days every 28 days) was initiated and the patient received five courses, resulting in the disappearance of peripheral lymphadenopathy and nodular remission upon repeat bone marrow examination. After the