method for preventing inhalation exposures in most work places. Yet in the case of uncontrolled emergencies such as this one, there will always be a need for an effective means to protect the individual's lungs. Perhaps this disaster can spur engineers and materials scientists to find new ways to protect the lungs of those who risk their lives to save others.

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The Incremental Application of Lung-Protective High-Frequency Oscillatory Ventilation

This issue of *AJRCCM* (pp. 801–808) contains a report of the first prospective randomized trial of high-frequency oscillatory ventilation (HFOV) in 148 adult patients with acute respiratory distress syndrome (1). This study expands on the study by Fort and coworkers of 17 patients reported in 1997 (2) and the study of Mehta and coworkers of 24 patients reported in 2001 (3). It represents the next necessary step in the reintroduction of HFOV as a possible lung-protective approach to the atelectasis-prone lung of adult patients. Although the study was not powered to compare outcome following the two ventilator techniques, it does provide convincing evidence that HFOV is as safe and as effective as the moderate tidal volume conventional ventilation (CV) of their control arm that was the accepted "best CV" in October 1997 when this study was initiated.

Our concepts of "best CV," however, are in continuous flux. Considerable discussion defends their control arm mortality as compared with mortality in the Acute Respiratory Distress Syndrome Network Trial of 6 ml/kg ideal body weight tidal volumes (4). This discussion is useful to place their data in the context of a current "best practice" that continues to change even as we read their results.

The question of how best to use HFOV to protect the atelectasis-prone lung receives much scantier treatment. Current adult HFOV practice is dictated by the equipment available. The SensorMedics 3100B is currently the only adult oscillator. It is limited in the stroke volume that it can deliver at high rates against the impedance of the stiff lungs of a large patient, and like the SensorMedics 3100A, stroke volume is strongly and inversely related to frequency such that one has to decrease frequency if one is at maximal power and still needs a larger stroke volume. Hence this trial could not address the question of what constitutes optimal HFOV settings for the adult with acute respiratory distress syndrome. Since the study of Fort and coworkers in 1997, adult HFOV has tended to start at 5 Hz with a 33% inspiratory time and to decrease to 3 Hz if necessary to achieve CO_2 elimination (2). There is no experimental basis for limiting the frequency to 5 Hz. Neonatal HFOV is routinely done at 10 to 15 Hz, frequencies that have some theoretical basis in calculations of how to optimize the pressure cost of eliminating CO_2 while minimizing the risk of alveolar overdistention of the most normal parts of the lung (5). No such estimates exist for adult lungs. Optimal frequencies are likely lower than in neonates but are probably higher than 3 to 5 Hz. Until we have more powerful oscillators, these theories cannot be experimentally tested *in vivo*. Even within current constraints, a cleaner approach would set power at maximum and adjust frequency downward until one attained adequate chest-wall vibration. This would achieve ventilatory support at the smallest tidal volume possible with the existing device and would achieve a pattern most closely approaching the goals set out in the introduction (1). The HFOV reported here may not be the "best" that HFOV is capable were it possible to attain higher frequencies in adults.

A second design deficiency in this study is the absence of systematic volume-recruitment maneuvers. It has been known for 20 years that recruitment maneuvers are needed during HFOV to reverse atelectasis (6). HFOV is most lung protective in animal models when alveolar re-expansion is achieved using a volume-recruitment maneuver and then maintained with appropriate mean airway pressure (7). In neonatology, these maneuvers are used cautiously because of the preterm infant's vulnerability to intraventricular hemorrhages. Such constraints need not limit recruitment maneuvers in adults without intracranial pathology. Although recent studies have demonstrated the safety and efficacy of such maneuvers in adult acute respiratory distress syndrome (8), this experience was not available at the time of designing this trial. Because volume-recruitment maneuvers produce more even aeration at a lower maintenance mean airway pressure for the same Pa_{O_2} and FIO_2 than HFOV without

recruitment maneuvers, the potential for shear stresses and therefore lung injury should be reduced further by protocols that incorporate systematic effective recruitment maneuvers.

The criteria for weaning from HFOV to CV also need to be re-evaluated. In the initial trial of Fort and coworkers, levels of mean airway pressure were maintained until the $F_{I_{O_2}}$ decreased to less than 0.4 (2). Only then was the mean airway pressure weaned and the patient was transferred to CV when the mean airway pressure was 20 to 22 cm H_2O. In this trial, mean airway pressure was increased until the $F_{I_{O_2}}$ decreased to 0.6. Then both $F_{I_{O_2}}$ and mean airway pressure were weaned alternately between $F_{I_{O_2}}$'s of 0.6 to 0.5. CV was reinstituted at an $F_{I_{O_2}}$ of 0.5 and mean airway pressure of less than or equal to 24 cm H_2O. Patients therefore exited this trial of HFOV with gas-exchange criteria that serve as the entry criteria of many other ventilator trials. No justification is given for this design. Neonatal trials demonstrate clearly that a lung-protective effect with HFOV requires you to start early before the lung is damaged and continue until it is no longer vulnerable to ventilator-induced lung injury (9). This study initiated HFOV earlier than prior trials but also discontinued it sooner. This is the most puzzling design feature. A patient with a saturation of 88% on 50% oxygen still has a 40 to 50% venous admixture fraction, presumably from ongoing atelectasis or consolidation. The mean airway pressure of 24 cm H_2O also reflects a lung that is still requiring a rather high mean pressure to maintain this aeration. Patients being ventilated postoperatively following cardiopulmonary bypass, long surgeries, or massive transfusion, without primary lung pathology, generally have levels of mean airway pressure of 8 to 12 cm H_2O on an $F_{I_{O_2}}$ of 0.4 to 0.5. Such patients can be ventilated indefinitely without detectable lung injury. There must be some definable level of mean airway pressure and venous admixture at which the lung becomes vulnerable to ventilator-induced lung injury. It is more likely to be a range than a threshold value, but I doubt it is 24 cm H_2O. In neonatal ventilation, entire comparative trials of HFOV versus CV have been executed below the mean airway pressure at which HFOV was discontinued in this trial (10).

This trial definitely takes us one step further in the incremental reintroduction of lung-protective HFOV. It represents a tremendous amount of careful work within the limitations of both our knowledge of ventilator-induced lung injury and the technology available at the time of study design. As the authors stated, the next step in this saga will be to match a better HFOV protocol (i.e., with volume-recruitment maneuvers and higher frequencies) against whatever is the best lower frequency alternative at the time. At least such studies can now be designed with much more extensive evidence for the safety and possible benefit of such approaches.

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Muscle Mass, Not Body Weight, Predicts Outcome in Patients with Chronic Obstructive Pulmonary Disease

It has been known for many years that weight loss and low body weight are common in patients with advanced chronic obstructive pulmonary disease (COPD). Moreover, it has been shown that low body weight is associated with increased mortality independent of lung function in patients with COPD (1, 2). However, unlike starvation in which the predominant body compartment affected is fat, the weight loss of COPD is similar to that of other chronic diseases and preferentially involves the loss of muscle mass. It is this loss of muscle mass, rather than body weight per se, that is likely to be primarily responsible for the observed negative consequences. To the extent that body weight reflects lean body mass, body weight will be a good surrogate marker. But under conditions, such as obesity, in which body weight does not accurately reflect lean body mass, its discriminatory power will diminish markedly. Obesity is extremely common in the western world and is increasing in incidence. Thus, body weight may not be the ideal measure to reflect nutritional status in patients with COPD.

For example, body weight and body composition have been measured in 255 patients with COPD (3). Low body weight implying nutritional depletion was defined as a weight