and an increased inspiratory time as compared to the conventional group. There was, however, no difference in the incidence of barotrauma or outcome in those patients. Both of these studies involved heterogeneous patient populations, in which the etiology of respiratory failure was diverse, usually a consequence of a systemic insult that resulted in diffuse parenchymal disease and dysfunction. This type of insult is quite distinct from that seen after smoke inhalation in both humans and animal models, in which edema resolves rapidly after resuscitation and repair of the airway mucosa typically occurs within 14 to 21 days.

The exact mechanism by which HFPV achieved the results reported in this study is not known. We hypothesize that the ability to maintain ventilation and oxygenation at lower peak airway pressures and inspired oxygen concentrations may decrease the iatrogenic injury that occurs with conventional mechanical ventilatory support. Extrapolation of the data reported by Tsuno[16] to humans would indicate that ventilation at lower peak airway pressures offers significant advantage, especially in lungs that have already been injured. In addition several studies now suggest that asymmetric high-frequency breaths improve clearance of secretions, results that have been obtained with high-frequency jet ventilators and high-frequency oscillators, both *in vitro* and *in vivo*.[13,20-22] Our clinical experience supports this finding. Patients with severe inhalation injury treated prophylactically with high-frequency percussive ventilation typically are found, by bronchoscopic examination, to have large deposits of secretions at the tip of the endotracheal tube. After removal of these secretions, the main stem bronchi and distal airways often are patent and free of pathologic secretions. The documented improvement in survival and the decrease in the incidence of pneumonia in patients treated with prophylactic HFPV, as compared to the recent historic cohort, indicate the importance of maintaining small airway patency in reducing the sequela of inhalation injury. The beneficial effects reported here and the paucity of ventilator complications support continued use and further evaluation of HFV in patients with inhalation injury.

References

1. Shirani KZ, Pruitt BA Jr, Mason AD Jr. The influence of inhalation injury and pneumonia on burn mortality. Ann Surg 1987; 205: 82–87.
2. Shimazu T, Yukioka T, Hubbard G, et al. Frequency of VA/Q rates following smoke inhalation. USAISR Annual Research Progress Report 1985.
3. Bland Rd, Kim MH, Light MJ, et al. High frequency mechanical ventilation in severe hyaline membrane disease. Crit Care Med 1980; 8:275–280.
4. Brichant JF, Rouby JJ, Viars P. Intermittent positive pressure ventilation with either positive end expiratory pressure or high frequency jet ventilation (HFJV), or HFJV alone in human acute respiratory failure. Anesth Analg 1986; 65:1135–1142.
5. Butler WJ, Bohn DJ, Bryan AC, et al. Ventilation by high frequency oscillation in humans. Anesth Analg 1980; 59:577–584.
6. El-Baz N, Faber LP, Doolas A. Combined high frequency ventilation for management of terminal respiratory failure: a new technique. Anesth Analg 1983; 62:39–49.
7. Hurst JM, Branson RD, DeHaven CB. The role of high frequency ventilation in post-traumatic respiratory insufficiency. J Trauma 1987; 27:236–242.
8. Hurst JM, DeHaven CB. Adult respiratory distress syndrome: improved oxygenation during high frequency jet ventilation/continuous positive airway pressure. Surgery 1984; 96:764–769.
9. Jibelian G, Lachmann B. Gas exchange during conventional and high frequency pulse ventilation in the surfactant deficient lung: influence of positive and expiratory pressure. Crit Care Med 1984; 12:769–773.
10. Kaiser KG, Davies NJ, Rodriguez R, et al. Efficacy of high frequency ventilation in presence of extensive ventilation perfusion mismatch. J Appl Physiol 1985; 58:996–1004.
11. Kolton MK, Cattran CB, Kent G, et al. Oxygenation during high frequency ventilation compared with conventional mechanical ventilation in two models of lung injury. Anesth Analg 1982; 61: 323–332.
12. Kumar BS, Beney K, Jastremski M, et al. High frequency jet ventilation versus conventional ventilation after surfactant displacement in dogs. Crit Care Med 1984; 12:738–741.
13. Freitag L, Long WM, Kim CS, Wanner A. Removal of excessive bronchial secretions by asymmetric high-frequency oscillations. J Appl Physiol 1989; 67(2):614–619.
14. Cioffi WG, Graves TA, McManus WF, Pruitt BA Jr. High-frequency percussive ventilation in patients with inhalation injury. J Trauma 1989; 29(3):350–354.
15. Mammel MC, Boros SJ. Airway damage and mechanical ventilation: a review and commentary. Pediatr Pulm 1987; 3:443–447.
16. Tsuno K, Prato P, Kolobow T. Acute lung injury from mechanical ventilation at moderately high airway pressures. J Appl Physiol 1990; 69(3):956–961.
17. Coalson JJ, King RJ, Winter VT, et al. O_2—and pneumonia-induced lung injury I. Pathological and morphometric studies. J Appl Physiol 1989; 67(1):346–356.
18. Carlon GC, Howland WS, Ray C, et al. High-frequency jet ventilation—a prospective randomized evaluation. Chest 1983; 84(5): 551–559.
19. Hurst JM, Branson RD, Davis K Jr, et al. Comparison of conventional mechanical ventilation and high-frequency ventilation. Ann Surg 1990; 211(4):486–491.
20. Hachenberg T, Wendt M, Deitmer T, Lawin P. Viscoelasticity of tracheobronchial secretions in high-frequency ventilation. Crit Care Med 1987; 15(2):95–98.
21. Freitag L, Kim CS, Long WM, et al. Mobilization of mucus by airway oscillations. Acta Anaesthesiol Scand 1989; 33(Suppl 90): 93–101.
22. Thangathurai D, Holm AP, Mikhail M, et al. HFV in management of a patient with severe bronchorrhea. Resp Mgmt 1988; Jan/Feb:31–33.

DISCUSSIONS

DR. HARVEY SUGERMAN (Richmond, Virginia): In this study, high-frequency percussive ventilation from 1987 through 1990 was associated with a significant decrease in, one, the incidence of pneumonia and, two, the mortality rate when compared, as mentioned, to historical controls for inhalational injury from 1980 through 1984 and mortality rate from 1980 through 1986.

As discussed in their paper, this is one of the only studies in which high-frequency ventilation has shown a significant decrease in mortality rate. It has been my experience and that of the literature that you can significantly, but only temporarily, improve blood gas parameters in ARDS patients with high-frequency ventilation. It prolongs death rather than improving survival.

The hypothesis proposed by Dr. Cioffi and his colleagues and supported by sheep inhalational injury studies in their laboratory is that high-frequency percussive ventilation improves bronchiopulmonary toilet of the small airways, which are plugged with soot and debris, with an increased alveolar recruitment and ventilation at lower peak airway pressures when high-frequency ventilation is provided early or prophylactically before the development of severe ARDS.

This has not been the case in nonburn septic patients in randomized prospective trials. Dr. Cioffi's study suffers from all of the potential weaknesses of a nonrandomized trial. In comparing inhalational injury and the risk of pneumonia, why did the authors compare data from 1980 to 1984 with 1987 to 1990?

What happened to the missing 3 years? Were other treatment modalities that could influence the development of pneumonia during these two time intervals changed, such as the use of H2 blockers *versus* carafate for the prevention of stress ulcers or TPN *versus* enteral feedings vis-a-vis the issue of bacterial translocation, and so on?

Were the methods of providing pulmonary toilet in the two groups, such as the nursing staff and inhalational therapists, unchanged during these two time periods?

Could prejudice have been inadvertently present in roentgenographic interpretation or were so-called blinded radiologists used to describe the presence or absence of pulmonary infiltrates?

Finally, using historical controls, were there any differences in the duration of mechanical ventilation *versus* duration of ventilation with high-frequency ventilation present?

We heard the duration of ventilation for high-frequency ventilation but not for the mechanical ventilatory group.

In 1988 this group reported their first positive experience with high-frequency percussive ventilation in 14 patients before the American Association for the Surgery of Trauma. Today we have heard more suggestive data in an additional 40 patients.

High-frequency ventilation has been a technique in search of documented therapeutic efficacy. Now is the time for a truly randomized prospective, perhaps multi-center trial for the study of high-frequency ventilation in burn inhalational injury patients.

DR. DAVID HERNDON (Galveston, Texas): Dr. Cioffi and Dr. Pruitt and their group must be commended on their impressive mortality statistics. A mortality rate as low as 18.5% in a group of patients with significant inhalation and burn injury requiring prolonged ventilatory support has never been reported in the United States before.

The usual mortality rates quoted are from 40% to 50%. This in respect to nationally reported mortality rates is clearly a great advance and allows Brooke still to be called the world's most famous burn unit.

However demonstration of a treatment effect in a patient population with this high rate of mortality is extremely difficult. Comparison to an historic cohort from 1980 to 1984 or 1986 is somewhat misleading. The investigators have admitted that.

I would like to know if more aggressive early surgical removal of the burn wound in a later period may have contributed to a decrease in the incidence of pneumonia by decreasing burn wound bacteremia as a source of hematogenous pneumonia. Has there been any effect of the more recently developed antibiotics?

The H2 blockers have been mentioned.

You have noted also that a wide variety of high-frequency ventilators are available, and varying reports of efficacy in the literature have been received. The incidence of barotrauma, specifically pneumothoraces due to gas trapped behind inspissated mucosal casts, has been discouraging in inhalation injury patients. However the ventilator you used is very specific and seems to overcome many of these adverse effects with a very low incidence of barotrauma.

My major question is, is this complicated ventilator commercially available or will it become commercially available? I'm not aware of it being so. If it is, then I think, as Dr. Sugerman did, concurrent multicenter studies based on your encouraging preliminary results might be warranted to determine mortality effects, whether specific for this machine or specific for this excellent treatment team.

I would also like the authors to speculate as to whether our general level of burn care has improved to such an extent that we might also recontemplate randomized studies that would treat barotrauma by use of extracorporeal membrane oxygenation.

Previous attempts in the 1970s, when burn wound sepsis was rampant, were unsuccessful, but mortality statistics are sufficiently decreased, and early excision of the wound would prevent many of the septic complications that were seen before. Or perhaps the new technique of intravenacava filamentous O_2–CO_2 exchange rods being tested in multiple centers for support of adult respiratory distress syndrome might make more sense than a jet ventilator.

DR. EDWIN DEITCH (Shreveport, Louisiana): I will limit my remarks to a few questions, some of which have been covered before but, nonetheless, I think they need to be stated again.

I wonder whether the authors are now ready to carry out a prospective randomized study to verify these results. There are several reasons to do so. The first is that this high-frequency ventilator technique that they are proposing is much more time consuming, technically demanding and more expensive than conventional mechanical ventilation.

And second, and perhaps more important, all too often in the past studies carried out using historical controls, even one as well defined as this one, fail to verify the encouraging results of the initial study.

There are many reasons why this phenomenon occurs, not the least of which is the special attention directed toward these patients by a highly motivated investigational team. Perhaps the fact that Dr. Cioffi and his coworkers were performing bronchoscopy on these patients to remove debris may have made this a study of repeated bronchoscopy as much as ventilatory support.

I have two other related questions. One is that it has become apparent in the last several years that the intubated patients receiving antacids or H2 blockers for stress ulcer have an increased incidence of gram-negative pneumonia and even death.

Therefore I wonder whether the authors are still using H2 blockers, what they're using, and whether they have changed their therapy to use sucralfate to prevent colonization of the stomach with potential pathogens.

Related to that, do you have any data on the bacteriology in these patients and if so was it different from the historical controls? I ask this question because pneumonia due to gram-negative enteric bacilli or pseudomonas is associated with a higher mortality rate than pneumonias caused by gram-positive organisms.

Therefore, if you are shifting your flora due to changes in therapy, you may also be shifting your results.

DR. ANTHONY MEYER (Chapel Hill, North Carolina): I would like to compliment the authors on their continued evaluation of this alternate method of ventilation for inhalation injury. I have a few questions.

You had a relatively low incidence of necrotizing tracheobronchitis and barotrauma. Is this consistent with the incidence in your conventionally ventilated patients?

Is there any evidence or data on pulmonary compliance in these patients? Obviously it is difficult to measure using this mode of ventilation, but if pulmonary fibrosis is one of the key hallmarks of ARDS and late pulmonary problems, and if this is indeed triggered by the barotrauma of conventional ventilation, this might be a significant physiologic alteration using this type of support.

There is a relatively high incidence of pneumonia in the historical series. And because of this and many of the other reasons, I would like to join the chorus in suggesting that a true prospective randomized study should be carried out to evaluation further the technique.

I think it is interesting that this sophisticated pulmonary management is being discussed before a surgical society rather than something that is only discussed before pulmonary medicine groups.

DR. WILLIAM CIOFFI (Closing discussion): First I would like to address the recurring question of why we did not perform a randomized trial.

When we started this study, we did a trial in which we enrolled 20 patients to see if we could see a decrease in the incidence of pneumonia or change in mortality rate, and indeed we did. We entertained the thought of a prospective randomized trial at that time. By doing the calculations, we discovered that it would require more than 230 patients to have satisfactory type one and type two errors. It took us almost 4 years to enroll 54 patients in this trial, so we were looking at more than a decade to complete the study with all the problems that would occur in treatment changes in 10 years or more.

Second we have used these predictors for at least one decade in our institute, if not longer, and in other studies have found them to be entirely reliable in predicting results from other types of studies, not just including the ventilator study discussed here today.

Third because doing this randomized trial will be difficult in a period of time that is reasonable, we have begun a study in primates looking at high-frequency ventilation in two forms, high-frequency percussive ventilation discussed here today and high-frequency oscillation as compared to conventional ventilation in a long-term support model in which we ought to be able to discern whether the differences we see in patients will hold out in the primate model. That trial is now underway.

To continue with Dr. Sugerman's questions, other treatment modalities have not changed significantly in our unit in the past 10 years.

Our mode of nutritional support is enteral and has remained enteral for 10 years, with TPN being used in less than 5% of patients.

Our diagnosis and treatment of pneumonia also has remained the same in the studied period of 10 years.

Respiratory therapy has not changed significantly. Frequent bronchoscopy for pulmonary toilet in patients with severe inhalation injury has been the standard in the unit for approximately 10 to 15 years.

Dr. Sugerman also asked whether the duration of ventilatory support was similar in the high-frequency patients as compared to the conventional patients. Unfortunately I do not have that data for the 1980–1984 patients. But I would say that 15 days of support in these patients indicates a rather severe insult. The patients are weaned as quickly as possible from this ventilator, and it has been my experience in patients who have not been placed in the trial for other reasons that it is easier to wean the patients from high-frequency ventilation than conventional support.

Dr. Herndon asked about our excision practices. In the past decade, our day of first excision has decreased by about 3 days in patients with burn size discussed in this paper. He also asked whether the incidence of hematogenous *versus* bronchopneumonia or airway pneumonia has changed. Hematogenous pneumonia has been relatively infrequent in the past decade, and bronchopneumonia is responsible for almost all our pneumonias. I don't think that later excision in the earlier group had much to do with the incidence of pneumonia.

Our antibiotic therapy has been relatively unchanged. The standard antibiotic therapy in our unit is Amicacin and Vancomycin and has been that way for almost the entire period of the 1980s.

Several discussants asked about stress ulcer prophylaxis and whether we use H2 blockers. Until 5 or 6 months ago the standard of care was H2 blockers and antacids titrated to keep the gastric pH above 4.5.

We just started a trial comparing sucralfate to standard therapy, but of the patients reported in this study, only two of the last five patients were enrolled in that study. So all patients were on H2 blockers, and the idea of nonacid neutralizing therapy to decrease pneumonia does not enter into play.

The barotrauma reported in our series is low. It is lower than it has been in the past. The incidence of significant barotrauma as far as pneumothoraces was one patient of 54. Most ICUs report incidence of barotrauma approximately 4%. Two patients did have significant subcutaneous emphysema but never developed a pneumothorax.

Dr. Herndon asked whether this device was commercially available. It was approved by the FDA approximately 1 year ago and is now commercially available through Percussion Air Corporation, which is a company owned by Dr. Bird, who developed this form of ventilation.

Dr. Herndon also asked us to speculate whether other forms of support, total rest of the lungs using either ECCOR or the new intravenacaval device, the IVOX, might be of more benefit. In those studies it is still a requirement that the patient be kept on high mean airway, low peak pressure ventilation to splint the lung. And it might be that some high-frequency ventilation in combination with extracorporeal support might be the answer. The studies that are using that form of therapy, however, are all on ARDS patients.

Dr. Deitch asked not only about why not a prospective study, which I've already covered, but also about the costs. The cost of this ventilator is approximately one fifth of a 7200 ventilator. So cost is not really an issue.

The first two forms of this ventilator were exceptionally hard to use, as we reported in our early review; however the VDR for the most current form of this ventilation is very easy to use. We have residents who rotate 1 month from multiple institutions. And by the end of 1 month, most residents are capable of using this ventilator and are able to support the patients at night on their own.

Dr. Deitch also asked about the etiology of our pneumonia, our gram negatives *versus* gram positives. We have had a predominance of gram-positive pneumonias at our institute for more than a decade, and that incidence has not changed.

He also asked about comparing it to a population from 1980 to 1984 and 1987 to 1990. We are just starting to look at the data in the intervening years. And the incidence of pneumonia before use of this ventilation from 1985 to 1987 had not changed in patients with inhalation injury compared to the 1980 to 1984 group.

Finally Dr. Meyers asked about necrotizing tracheobronchitis. It is our impression that it has been significantly decreased with the use of this ventilator, despite the fact that there are reports in the literature using this form of ventilation in neonates, in which that incidence approaches one third to one half of patients.

However we only had two patients, the very first patient and a latter patient entered in the trial, both of whom survived. And it appeared to be more an indication of the severity of their insult.

Finally, Dr. Meyers, we have not done compliance measurements to indicate the severity of the insult.

In closing I would like to add that many discussants compared this form of support in patients with inhalation injury to those studies in the literature that deal with ARDS patients. I would emphasize that the insult in our patients is distinctly different from ARDS. It is a self-limiting disease process, which, if it can be left to heal on its own, should do so in 10 to 14 days. We feel strongly that conventional mechanical ventilatory support impairs that healing process and that the use of low-pressure ventilation by the use of this device or other high-frequency devices may just allow the natural process of healing to occur.