

## UP WITH (OR IS THAT DOWN WITH) PEEP?

by John Marini MD



Preventing iatrogenic injury is among the highest priorities of clinical practice. With a view toward avoiding ventilator-associated lung injury (VILI) and speeding healing, debate has continued for more than two decades regarding the relative places of PEEP and tidal volume in managing the acute respiratory distress syndrome (ARDS). How best to combine those in the ventilatory recipe is a worthwhile goal poorly served by simple rules and numerical guidelines. Despite clear laboratory evidence that adequate PEEP reduces the potential for VILI, randomized clinical trials (RCT) have repeatedly failed to demonstrate survival advantages for its prophylactic (1) or therapeutic use (2). As is often the case, however, the source of discord appears to stem from imprecise disease definitions, oversimplification of inherent complexity, and uncoupling of mechanistic understanding from clinical trial design. Taking the time honored 'reductionist' approach of isolating the individual elements of the ventilatory prescription (e.g., tidal volume, PEEP) without fully understanding the interplay among them is risky when dealing with a phenomenon as complex as VILI.

Certain principles regarding the pathogenesis of VILI must be kept in mind. High transpulmonary pressure (reflected exactly by the end-inspiratory plateau pressure in an excised lung but only indirectly when the chest wall is intact) increases the stress experienced by all structural elements of expanding units. Repeated application of excessive tissue stresses—as by forcing high tidal volumes into noncompliant lungs—clearly inflicts injury. (This concept was

confirmed by the well executed ARMA randomized controlled trial of tidal volume conducted by the NIH-sponsored ARDS network (ARDSnet)). Furthermore, it is now understood that juxtaposition of open and closed lung units amplifies strain at the interfaces between them. Shearing trauma to the epithelium of terminal airway units occurs during repetitive closure and forceful re-opening at high pressure, and when tissue stresses are severe, the lungs may be torn by physical forces. The resulting "micro-wounds" to the delicate alveolar capillary membranes result in plasma leakage, hemorrhage and inflammatory edema. A quite different mechanism operates when forces are excessive but less extreme. A lung already predisposed to inflammation may experience VILI when the "second hit" of repeatedly high tidal ventilating pressures initiates an inflammatory cascade. Both types of VILI are most likely to occur in the earliest days of acute lung injury when collapse and edema are especially prevalent.

When PEEP succeeds in keeping open otherwise unstable lung units, it helps to diminish "stress focusing" that otherwise occurs at sites of mechanical heterogeneity. Conversely, to the extent that PEEP forces plateau pressures higher, it serves to amplify those same forces. Although considerable emphasis has been placed on avoiding the epithelial shearing effects of repeated opening and closure of terminal airway units, 'high risk' junctional interfaces may be generated whenever high transpulmonary pressures are applied, whether or not the tidal recruitment and collapse cycle is prevented.

Whatever the explanation for its effectiveness, PEEP confers an important and consistent benefit in reducing damaging stresses resulting from high airway pressures in the experimental laboratory. It also prevents the dissemination of bacteria and inflammatory debris to the periphery. Yet, until recently, clinical data supporting PEEP's utility in improving outcomes have been much less convincing. For example, an influential recent trial conducted by the ARDSnet group failed to show any advantage of a high PEEP strategy when plateau pressures were held within "lung protective" limits. This result helped to fuel an already heated controversy regarding the relative importance at the bedside of 'stretch' (tension within open units) and 'atelectrauma' (tension at the aforementioned high risk junctions). Actually, however, these data are quite consistent with theory. Any lung protective benefit of PEEP is expected to be unimpressive when plateau pressure—the lever arm of the stress fulcrum—is modest.

In contrast, a recently published Spanish RCT (ARIES) documented a striking mortality benefit from high-level PEEP titrated to a mechanical endpoint and applied very early in the clinical course to well-selected patients with severe ARDS. These results from the ARIES investigators corroborate the prior experience of Amato and coworkers, who also adjusted PEEP by mechanical measures in a very sick patient cohort, emphasized adequate recruitment, and avoided tidal over-distention. Both stand in apparent contrast to the considerably larger ARDS Network (ARDSnet) trial (ALVEOLI), which reported no routine benefit from aggressive PEEP of similar magnitude. Interpreted within the context of VILI pathogenesis, however, each clinical study conforms to an injury model underpinned by extensive laboratory data.

### WINTERIZE your pulmonary lab with the



## Turboaire Challenger

Portable arctic air for bronchial provocation and  
Exercise Induced Asthma studies all year 'round

- Economical operation
- Adult and pediatric adapters
- Uses standard PFT equipment
- Exercise or isocapnic hyperventilation
- Instant generation of cold dry air at -20°C
- No electricity, chemicals or liquids required



**Equilibrated  
Bio Systems, Inc.**

22 Lawrence Avenue - Suite LL2 • Smithtown • NY • 11787  
Phone 631-863-3500 • Fax 501-421-6575

CIRCLE READER ACTION CARD # 49

*Its Treatment Compliance... Continued from page 46*

treatment of sleep disordered breathing. National standards have now defined compliance as therapy that is used 5 hours per night for 5 days a week. Most insurances will not continue reimbursement or purchase the unit for the patient unless compliance meets this standard. While home care providers may have their own specific policies, most compliance is generally monitored during the first 2 weeks and then at one month and three month intervals. This monitoring is done by questionnaires, telephone calls, patient visits and most commonly by "smart card" technology. The small card that comes with the CPAP unit is mailed back to the company or sleep lab and the information is downloaded for interpretation. Some units use a modem or a computerized number the device provides.

Reasons for non-compliance include: problems with interface comfort (mask or nasal prongs/pillows), humidification, pressure level, aesthetics or belief the treatment is not really necessary or that weight loss or change in lifestyle will correct one's apnea. These concerns can be addressed with proper mask fits, daily care of the interface, changing masks or prongs on a routine basis, using cool or heated humidity based on patient comfort and good patient education and explanation for need of therapy. Involvement in a sleep/awake group is very helpful with regard to a patient's perception of equipment use and need for treatment.

There is no panacea when it comes to patient compliance with prescribed care, whether in the hospital or the home. As clinicians, we know patients need to follow their therapeutic regimen and it is up to us, as professionals, to educate, explain the need for treatment and to follow-up on the prescribed therapy. Oftentimes, patients look to their respiratory therapist for direction and as a source of knowledge. RTs, especially in the home care setting, need to accept this role and meet the challenge of improving patient compliance with home care therapy.

*Osteomyelitis... Continued from page 52*

rates especially among elderly debilitated diabetic patients. Therapy for these infections is a combination of surgical debridement of dead tissue (or amputation), antibiotics, nutritional support and adjunctive hyperbaric oxygen when appropriate. The benefits of HBOT are improvement of tissue oxygen needed for healing, improvement of phagocyte function (to kill organism), reduce edema and improve circulation of affected areas. Treatment protocols vary slightly among these infections. For example, with one of the most common and serious of these infections, gas gangrene, also called clostridial myonecrosis the individual treatment is 2.5 to 2.8 ATA for 90 minutes. Three treatments are given the first day (usually after surgery), followed by two additional on the second and third days. The maximum number to treatment days is usually 10. Gas gangrene can be



**"You report to Anderson. Anderson reports to me... Who do I report to?"**

categorized as traumatic or spontaneous and is a rapidly spreading infection with mortality from 25% (traumatic) to 67-100% (when caused by C septicum).

For necrotizing fasciitis (referred to in the newspapers as the "flesh-eating bacteria") a rapid spreading inflammatory process located deep in the skin, the protocol is similar at 3 ATA for 90 minutes. Three treatments are given in the first 24 hours after surgery. After that, two are given daily until improvement seen and the schedule can be reduced to once daily. Typically the maximum number of treatments are 10-15 total. These types of cases, although seen infrequently, are considered urgent and time must be made available in a busy HBOT schedule to accommodate them. These patients are truly benefited by adjunct HBOT, but unfortunately it still is not always considered due to lack of awareness in the medical community. The marketing of HBOT benefits is a certainly a challenge but efforts must continue for improved outcomes.

*Ken Capek, RRT, CHT, MPA is Director of Respiratory Care and Hyperbaric Oxygen Therapy at Englewood Medical Center in Englewood, NJ. He appears regularly in Focus and can be reached at Ken.Capek@ehmc.com*

*Up With PEEP... Continued from page 54*

Using high PEEP when few unstable units exist or plateau pressure is kept below levels which fully "unfold" the lung and begin to overstretch it is not likely to help. If lung tissue is not inherently recruitable (or has not been opened by enough airway pressure), even high PEEP will not be effective; if plateau pressure is not in a threatening range (generally, above 25 cmH<sub>2</sub>O), high PEEP is not needed to avoid VILI—even if collapse persists and/or tidal re-opening recurs. In fact, using high PEEP in such settings alters blood flow, raises mean alveolar pressure, and may actually increase overall collagen strain. But when unstable and potentially recruitable units are prevalent and plateau pressures are high, applying sufficient PEEP is vitally important to minimize junctional stresses. It does so by reducing the number of units "at risk" (via sustained recruitment) and by preventing repeated cycles of tidal collapse/high pressure re-opening. Therefore, when considering the potential value of PEEP in preventing VILI, three vital elements are in play: 1) recruitability of injured tissue 2) magnitude of the end-inspiratory tidal plateau and 3) level of PEEP in relation to lung unit closing pressures. Just how much tissue can be recruited by using high airway pressure and sufficient PEEP is a topic currently under hot debate. Whatever their opinions on the prevalence of unstable units and inherent recruitability of the acutely injured lung, most knowledgeable investigators would agree that the lung should be exposed transiently to "high enough" pressure to open the collapsed units most at risk by some type of recruiting maneuver that involves high PEEP, and many would set PEEP decrementally as tidal pressures are ratcheted downward, depending on response. The process should be an empiric one and not governed by rigid numerical mandates.

Although the last word has not been written about PEEP's value and risk, we are coming progressively closer to reconciling VILI theory, laboratory science, and RCT confirmation. Considering what's clinically at stake and given the enormous expenditure of investigational effort and resources, it's about time.

*Dr. Marini, MD, Professor of Medicine at the University of Minnesota, is a clinician-scientist whose investigative work has concentrated in the cardiopulmonary physiology and management of acute respiratory failure. In the majority of his research, he has been positioned at the interface between basic physiology and clinical medicine so as to develop insights into advancing clinical practice.*