

# Establishing an approach to mechanical ventilation

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**TE STEWART. Establishing an approach to mechanical ventilation. Can Respir J 1996;3(6):403-408.**

Technology in the intensive care environment has progressed at an exponential rate. This progression has particularly been noticeable in relation to mechanical ventilation where advancements have arguably surpassed improvements in patient morbidity and mortality. Ventilator-induced lung injury (VILI), which occurs secondary to lung overdistension and underinflation, may largely be responsible for this discrepancy. No matter which of the vast number of modes of mechanical ventilation are employed, simple principles can be followed that will prevent the development of VILI. A lung protective ventilatory approach incorporates the prevention of oxygen toxicity and the avoidance of lung over- and underinflation, while frequently using permissive hypercapnia. By establishing a lung protective approach early in the management of ventilated patients, the morbidity and mortality associated with respiratory failure may finally be reduced.

**Key Words:** *Ventilator-induced lung injury*

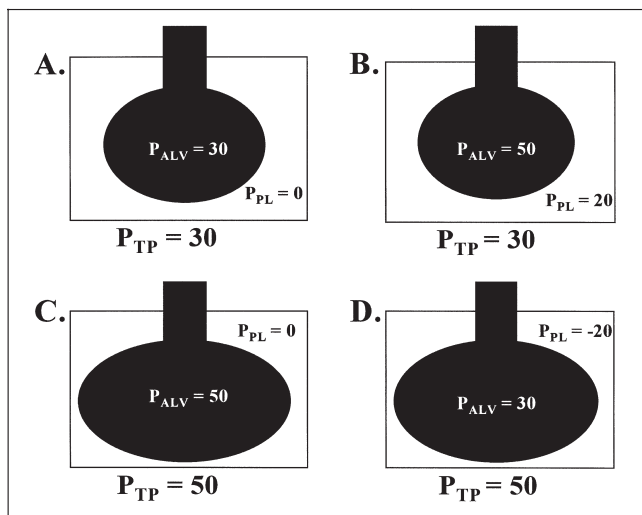
## Définir une approche pour la ventilation mécanique

**RÉSUMÉ :** La technologie dans le domaine des soins intensifs a crû de manière exponentielle, en particulier celle en matière de ventilation mécanique où l'on peut dire que les progrès dépassent ceux obtenus en terme de mortalité et de morbidité des patients. Les traumatismes pulmonaires induits par le ventilateur, souvent secondaires à une surdistension ou à une inflation insuffisante, pourraient en grande partie expliquer cette discordance. Quel que soit le mode de ventilation mécanique utilisé, on peut appliquer des règles simples pour prévenir les traumatismes pulmonaires induits par le ventilateur. Une approche de la ventilation qui privilégie la protection du poumon exige de prévenir la toxicité de l'oxygène et d'éviter une surdistension ou une inflation insuffisante des poumons, tout en faisant fréquemment usage de l'hypercapnie contrôlée. En définissant une approche de protection du poumon dès le début de la prise en charge des patients ventilés mécaniquement, la morbidité et la mortalité associées à l'insuffisance respiratoire pourraient enfin régresser.

The majority of patients requiring mechanical ventilation do so for very brief periods of time such as during the operative and perioperative period. For the most part these patients have good lung function and generally tolerate mechanical ventilation with conventional tidal volumes (VT) of 10 to 15 mL/kg without developing any adverse effects. On the other hand, patients in the intensive care environment frequently have or are at high risk for lung inflammation and injury, and may be prone to ventilator-induced lung injury

(VILI). VILI encompasses the spectrum of lung injury caused by mechanical ventilation. Classically, VILI was most commonly recognized clinically as pneumomediastinum, pneumoperitoneum, subcutaneous emphysema, pulmonary interstitial emphysema, systemic gas embolism and pneumothorax. These forms of VILI, which result from rupture of alveoli and subsequent tracking of air along the perivascular sheaths, are generally not thought to occur until airway pressures exceed 50 cm H<sub>2</sub>O (1,2). More recently it has been

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**Figure 1** Four diagrammatic representations of an alveolus (black solid object) inside a chest wall (box) separated by the pleural space. Transpulmonary pressure ( $P_{TP}$ ) is the alveolar pressure ( $P_{ALV}$ ) minus the pleural pressure ( $P_{PL}$ ). **A** The recorded alveolar pressure is 30 while the pleural pressure is 0; thus, the transpulmonary pressure is 30 and the alveolus is maximally distended. **B** Although the alveolar pressure is very high (50), overdistension is avoided by an increase in pleural pressure, and thus the transpulmonary pressure remains 30. Example of this clinical situation are pleural effusions, abdominal distention and chest wall bandages. **C** The alveolar pressure is high and it is not opposed by high pleural pressures; thus, the alveolus becomes overdistended and exposed to ventilator-induced lung injury. **D** Although alveolar pressure remains relatively low, the alveolus is overdistended ( $P_{TP} = 50$ ) due to a very negative pleural pressure; a clinical scenario that this might be associated with is large patient effort or negative pressure ventilation

recognized (primarily from animal work) that VILI not only encompasses these air leaks but also may be manifested as high permeability pulmonary edema, hyaline membrane formation, decreased lung compliance, atelectasis, hypoxemia, etc, all of which are difficult to separate from the clinical and pathological features of acute respiratory distress syndrome (ARDS). This type of injury appears to occur at relatively low airway pressures and volumes that are commonly used clinically today. The implication (which is supported by the literature) is that traditional forms of ventilation may be imposing further damage on some patients, and that if clinicians employ ventilation strategies aimed at reducing VILI the morbidity and mortality of patients with lung injury may be reduced.

### VENTILATOR-INDUCED LUNG INJURY

**Role of pressure:** One of the earlier studies addressing the role of pressure was by Webb and Tierney (3) in 1974. They demonstrated that when normal rats are ventilated with peak inspiratory pressures (PIPs) in excess of 30 cm H<sub>2</sub>O ( $V_T$  29 mL/kg) for 1 h, pulmonary edema develops. This edema was only perivascular at a PIP of 30 cm H<sub>2</sub>O, but became alveolar edema associated with increased hypoxemia and reduced lung compliance at 45 cm H<sub>2</sub>O ( $V_T$  45 mL/kg). In a subsequent study, Dreyfuss et al (4) demonstrated that very

brief exposure (as brief as 5 mins) of rats to high PIP (45 cm H<sub>2</sub>O) resulted in endothelial disruption and an increase in microvascular permeability leading to peribronchovascular edema. These lesions were accompanied by high permeability alveolar edema, epithelial disruption and hyaline membranes when the exposure to the high pressure exceeded 20 mins. Similar findings have been confirmed in other animals such as sheep and dogs (5-7). The histological lesions of VILI progress in sequence from perivascular edema and endothelial injury to interstitial edema, on to epithelial injury and finally alveolar edema. Since high PIPs were commonly associated with these lesions, this form of VILI was originally referred to as barotrauma, although absolute pressure is not the only important factor.

**Role of lung stretching:** In the above studies the animals that developed VILI were exposed not only to high PIP but also to very high  $V_T$  (20 to 70 mL/kg). Dreyfuss et al (8) attempted to determine which of these (PIP or  $V_T$ ) was the major cause of VILI. In their study, normal rats were randomly assigned to ventilation for 20 mins in one of the following groups: (1) control: PIP = 7 cm H<sub>2</sub>O, positive end-expiratory pressure (PEEP) = 0 cm H<sub>2</sub>O,  $V_T$  = 13 mL/kg; (2) high pressure high volume: PIP = 45 cm H<sub>2</sub>O, PEEP = 0 cm H<sub>2</sub>O,  $V_T$  = 40 mL/kg; (3) high pressure low volume (achieved by strapping the rat's chest wall with elastic bands): PIP = 45 cm H<sub>2</sub>O, PEEP = 0 cm H<sub>2</sub>O,  $V_T$  = 19 mL/kg; and (4) low pressure high volume (achieved using a negative pressure ventilator): PIP = negative, PEEP = 0 cm H<sub>2</sub>O,  $V_T$  = 44 mL/kg. The end-points were macro- and microscopic changes, lung edema and protein leak. They found that more lung injury occurred in the two groups that were exposed to high volume (groups 2 and 4) than in those exposed to high pressure but low volume. They concluded that the key factor in the development of VILI is the total volume that the lung is exposed to and not the pressure per se. Thus VILI has been recognized as volutrauma rather than barotrauma because distending volume rather than pressure appeared to most important.

The key factor probably is the transpulmonary pressure ( $P_{TP}$ ) that the alveoli are exposed to.  $P_{TP}$  is the difference in pressure between the alveolus ( $P_{ALV}$ ) and the pleural space ( $P_{PL}$ ):

$$P_{TP} = P_{ALV} - P_{PL}$$

Lung distention is directly related to  $P_{TP}$ . Normal lung tissue reaches its maximum distention when  $P_{TP}$  reaches 30 to 35 cm H<sub>2</sub>O (9). In the study of Dreyfuss et al (8) the animals in the high pressure low volume group probably did not demonstrate as much VILI because their  $P_{TP}$  was limited by chest wall strapping, which caused a rise in  $P_{PL}$ . This would explain why the animals in the negative pressure ventilation arm developed VILI: their  $P_{PL}$  would be very negative, resulting in high  $P_{TP}$  despite a low  $P_{ALV}$ . The importance of  $P_{TP}$  as the cause of VILI explains why, when extremely high airway pressures are generated that are offset by high  $P_{PL}$  (such as during coughing, sneezing, weight lifting, straining, etc), VILI does not occur (Figure 1). The importance of lung

overdistension (or  $P_{TP}$ ) as opposed to the absolute airway pressure has been confirmed in other studies (10,11).

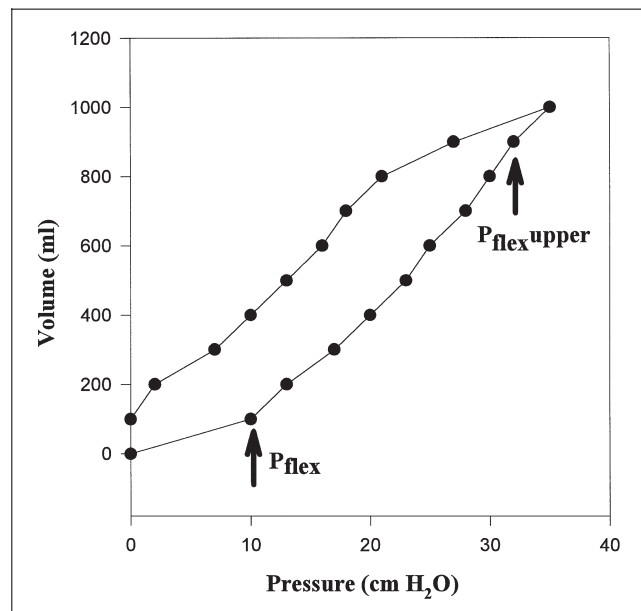
**Role of inadequate end-expiratory volumes:** It is important to note that the lung injury caused by overdistension was reduced (particularly alveolar flooding) by the use of PEEP in two of the above studies (3,8). This has led to debate over the role of maintaining some end-expiratory lung volume in order to prevent VILI. Sandhar et al (12), using a rabbit lung injury model, demonstrated that rabbits ventilated with PEEP above the inflection point ( $P_{flex}$ ) on the pressure volume curve (the point at which the slope of the inflation limb turns most upright, see Figure 2) as opposed to PEEP well below  $P_{flex}$  (approximately 3 cm H<sub>2</sub>O) developed less progressive lung injury. In a canine acid aspiration model, dogs ventilated for 5 h with  $V_T$  30 mL/kg and PEEP 3 cm H<sub>2</sub>O developed more pulmonary edema, hypoxemia and venous admixture than a group ventilated with  $V_T$  15 mL/kg and PEEP 12 cm H<sub>2</sub>O, despite having the same peak airway pressures, peak inspiratory lung volumes and pulmonary capillary wedge pressures (13). Some have argued, however, that this apparent protective effect of PEEP may be due largely to its effect on lowering cardiac output and, thus, preventing lung edema. This was speculated after rats protected from VILI with PEEP had a resurgence of lung injury following the addition of dopamine to maintain cardiac output (11). In order to separate the direct effects from the hemodynamic consequences of PEEP, Muscedere et al (14) studied isolated lavaged rat lungs and demonstrated that PEEP below the  $P_{flex}$  exacerbated lung injury, independently of hemodynamic effects. They suggested that VILI occurs with inadequate PEEP when opposing surfaces are repeatedly allowed to close followed by reopening, in effect causing shear injury.

In summary, animal evidence has consistently demonstrated that VILI also incorporates a spectrum of injury that may be less commonly recognized clinically than the classical forms of barotrauma. The damage appears to be independently created by high  $P_{TP}$  (greater than 30 to 35 cm H<sub>2</sub>O) and the inadequate use of PEEP (less than  $P_{flex}$ ). The injury, which incorporates high permeability interstitial and alveolar edema as well as endothelial disruption, epithelial disruption and hyaline membrane formation (lesions similar to those found in ARDS), can be induced after a short period of ventilation in healthy lungs and can exacerbate the damage in previously injured lungs.

### LUNG PROTECTIVE VENTILATION STRATEGIES

Many now believe that animal findings are relevant to the care of mechanically ventilated humans. It is speculated that lung injury can be caused or exacerbated by conventional ventilatory techniques. If clinicians are attempting to limit the impact mechanical ventilation has on morbidity and mortality, current recommendations for a lung protective ventilation strategy (LPVS) suggest that, apart from limiting fraction of inspired oxygen ( $FiO_2$ ) to prevent oxygen toxicity ( $FiO_2$  less than 0.5 to 0.6),  $P_{TP}$  greater than 30 to 35 cm H<sub>2</sub>O as well as PEEP less than  $P_{flex}$  should be avoided (15).

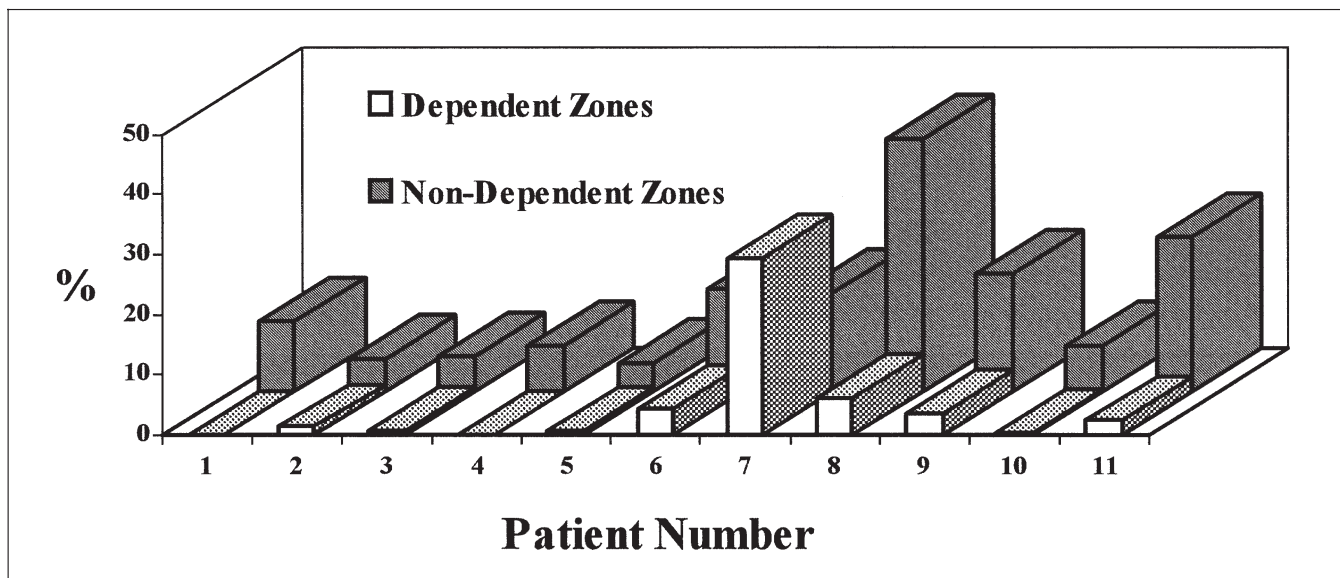
**PEEP:** Historically, PEEP has been used by clinicians in an



**Figure 2)** Typical static pressure-volume curve of a patient with acute respiratory distress syndrome, which demonstrates pertinent points to the prevention of ventilator-induced lung injury. The inflection point ( $P_{flex}$ ) or the critical opening pressure of the lungs in this example is at approximately 10 cm H<sub>2</sub>O. The upper inflection point ( $P_{flex\ upper}$ ) where maximum distension of normal lung tissue occurs is slightly greater than 30 cm H<sub>2</sub>O. Based on current concepts of lung protective ventilation strategies, the end-expiratory pressure should be above  $P_{flex}$  and the transpulmonary pressure below  $P_{flex\ upper}$

attempt to recruit collapsed, consolidated and atelectatic lung; to prevent collapse and atelectasis; and to reduce  $FiO_2$  in order to avoid oxygen toxicity. Today, PEEP greater than  $P_{flex}$  should also be used as a means to prevent VILI. In most patients a  $P_{flex}$  is not present, but in those with acute lung injury (particularly the early stages of ARDS),  $P_{flex}$  does exist when measured on a static pressure-volume curve (16) (Figure 2). At times, measurements of static pressure-volume curves may not be feasible; thus, in patients with acute lung injury, high risk for ARDS and established ARDS, we generally assume  $P_{flex}$  in the range of 10 to 15 cm H<sub>2</sub>O. Unless contraindicated, as a component of a LPVS, we use total PEEP (sum of delivered PEEP and intrinsic PEEP) in this range until the lung injury has resolved (defined as dissipation of bilateral pulmonary infiltrates and/or  $FiO_2$  less than 0.4).

**Overdistension:** Lung overdistension is thought to occur when  $P_{TP}$  is greater than 30 to 35 cm H<sub>2</sub>O. When esophageal balloons are not available to measure  $P_{PL}$ , peak  $P_{ALV}$  (plateau pressure) is generally used as a surrogate for  $P_{TP}$  (this assumes a  $P_{PL}$  close to 0, a situation that is not always true, especially in patients with massive ascites, pleural effusions, etc). The point of lung overdistension can also be measured with the aid of the static pressure-volume curve. On the ascending (inspiratory) limb there is a point where compliance suddenly worsens (upper inflection point;  $P_{flex\ upper}$ ) (Figure 2). For most patients ventilated with conventional  $V_T$  of 10 to 15 mL/kg,  $P_{flex\ upper}$  is not exceeded and the lung is



**Figure 3** Percentage of lung area occupied by parenchymal air cysts (evidence of ventilator-induced lung injury) as assessed by computed tomographic (CT) scan of the thorax in 11 patients with severe acute respiratory distress syndrome. CT scans were performed on a mean of day  $38.8 \pm 4.3$ . In dependent zones the average area occupied by parenchymal air cysts was  $4.5 \pm 8.5\%$ , while in nondependent zones it was  $14.9 \pm 11.3\%$

not overdistended. However, the majority of patients with acute lung injury demonstrate a  $P_{flexupper}$  when exposed to  $V_T$  of 10 mL/kg (17). Overdistension occurs in this setting because a much lesser amount of lung is available for ventilation. This evidence has come from computed tomography (CT) scans that have refuted the commonly held misconception that pulmonary infiltrates in ARDS are found throughout all lung fields (as one may be led to believe by plain chest roentgenograms). CT scans have consistently demonstrated that pulmonary infiltrates (less available for ventilation) are usually greatest in dependent lung zones, with preservation of normal, more compliant lung in nondependent zones (18,19). A small amount of the most healthy (nondependent) lung exposed to the  $V_T$  usually reserved for the entire lung would lead one to expect overdistension to occur in that lung. Human autopsy studies have confirmed that, among other factors, histological evidence of barotrauma is correlated with the higher  $V_T$  that the patients were exposed to (20). As well, there seems to be a predominance of intraparenchymal air cysts (evidence of VILI) as demonstrated on CT scan in nondependent lung zones in ventilated patients with ARDS (21) (Figure 3). Others have demonstrated that this evidence of VILI on CT scan is primarily in the dependent lung zones (22). This discrepancy in the location of the VILI may be best explained by the different mechanisms of VILI. If the lesion is due purely to overdistension, one would expect it to occur in nondependent lung zones where the most compliant lung is likely to be. However, if inadequate PEEP is the culprit, then one would expect this damage primarily in lung zones prone to collapse (dependent lung zones), as has been confirmed in animal studies (13). Wherever the injury is most predominant, the message remains the same: when caring for patients such as these, clinicians have a substantially reduced lung volume to work with. Thus, if conventional  $V_T$  (10 to

15 mL/kg) is used, the lung will be prone to overdistension and VILI.

**Permissive hypercapnia:** The problem of overdistension has led many to speculate that the cost of maintaining 'normal'  $PaCO_2$  (35 to 45 mmHg) in some patients is too great, and that perhaps  $V_T$  should be reduced to avoid overdistension, even at the expense of accepting lower ventilation and at times a higher than 'normal'  $PaCO_2$  (permissive hypercapnia). Permissive hypercapnia is not a ventilation strategy in itself, but it is a potential component of an LPVS. Roupie et al (17) demonstrated that, in order to avoid overdistension (plateau pressure less than  $P_{flexupper}$ ), permissive hypercapnia is required in the majority of patients with ARDS. Although permissive hypercapnia has been accepted as the standard of practice in ventilated patients with airflow obstruction, it has been recommended in patients with ARDS only in recent years (15). The first reported trial looking at a ventilation strategy for ARDS that incorporated permissive hypercapnia was very exciting because it achieved a marked reduction in mortality of 16%, compared with an expected mortality of 39.6% (23). However, this trial has been criticized because it was not randomized or controlled. Controlled trials have demonstrated that reductions in  $V_T$  to 6 mL/kg, compared with 12 mL/kg without hypercapnia, are well tolerated and potentially associated with lower morbidity in general surgical intensive care unit patients (24). More recently, a randomized controlled trial involving 28 patients with early ARDS (15 randomized to an LPVS accepting permissive hypercapnia and 13 to a conventional ventilation strategy maintaining a normal  $PaCO_2$ ) demonstrated a better evolution of lung function in patients in the LPVS arm (25). In this small group of patients mortality was not reduced, but the likelihood is that in a larger group of patients this significant reduction in morbidity will be translated into a reduction

in mortality. In fact, in a follow-up to this trial a decrease in mortality is occurring (personal communication).

**Effects of hypercapnia:** Much debate revolves around the potential adverse effects of permissive hypercapnia. Most of the literature recording the consequences of hypercapnia involves acute hypercapnia, which is likely to be very different from a more slowly induced chronic hypercapnia that occurs in this setting. Nonetheless the potential consequences of permissive hypercapnia and/or associated acidosis include impaired oxygenation (related to reduced ventilation pressures, effect on the alveolar gas equation, shift of the oxygen dissociation curve), catecholamine surge (resulting in increased cardiac output, heart rate, peripheral vascular resistance, systemic vascular resistance and blood pressure), direct vasodilation (raised intracranial pressure, coronary steal), increased need for sedation and paralysis (related to ventilatory drive), skeletal muscle weakness, myocardial depression, decreased seizure threshold, less response to defibrillation and inotropes, and increased blood letting (in order to follow blood gases more closely). Due to these potential concerns, permissive hypercapnia is generally avoided in patients with intracranial lesions, severe right- or left-sided heart failure, severe angina and predisposition to malignant arrhythmias. Otherwise, it is used with caution as a component of an LPVS while we anxiously await confirmation of the adverse effects.

Although no absolute guidelines can be given as to how high to allow  $PaCO_2$  to rise and how low to allow pH to drop when using ventilation strategies that incorporate permissive hypercapnia, clinicians need to be vigilant for the potential complications and to intervene when they become unacceptable. With the many tools available, intervention for the complications may be possible without exposing the patient to lung-damaging pressures and volumes. For example, if adverse effects of the high  $PaCO_2$  and associated acidosis are too great, clinicians have several options. These include reducing carbon dioxide production, such as by reducing temperature, inducing paralysis and avoiding overfeeding; reducing apparatus, anatomic and alveolar deadspace (by removing connectors or monitors attached to the endotracheal tube, high frequency ventilation, tracheal gas insufflation and inhaled nitric oxide augmenting lung perfusion); and treating metabolic acidosis (by dialysis, augmenting oxygen delivery and buffers). As well, when oxygenation is difficult to maintain ( $SaO_2$  88% to 90% or greater on  $FiO_2$  less than 0.6) using an LPVS, methods may be incorporated to improve oxygenation within the guidelines of the ventilation strategy by, for example, an increase in mean airway pressure (via higher PEEP, high frequency ventilation and inverse ratio ventilation); and improved ventilation-perfusion match-

**TABLE 1**  
**Ten commandments of a lung protective ventilation strategy (LPVS)**

1. An LPVS should be implemented immediately on intubation in all patients who do not have contraindications
2. Transpulmonary pressure should be maintained <30 to 35 cm  $H_2O$
3. Unless contraindicated  $FiO_2$  should be kept as low as possible (<0.6) to maintain minimally acceptable arterial saturation (88% to 90%)
4. PEEP should be kept above the inflection point on the static pressure-volume curve until resolution of lung injury
5. Although not desired, permissive hypercapnia is often an acceptable necessary component of an LPVS
6. Clinicians should be aware of and vigilant for the adverse effects of permissive hypercapnia
7. Faced with unacceptable adverse effects of a high  $PaCO_2$  or low pH, clinicians should employ strategies to reduce these before ventilating outside the guidelines of an LPVS
8. Faced with unacceptable oxygenation ( $FiO_2 >0.5 \pm SaO_2 <8\%$ ) clinicians should employ strategies to improve oxygenation before ventilating outside the guidelines of an LPVS
9. When all else fails and patient safety necessitates ventilation outside the guidelines of an LPVS, reimplementation should begin as soon as possible
10. Patients are individuals and do not behave predictably; thus, proper mechanical ventilation requires repeated bedside reassessment by the clinician

*FiO<sub>2</sub> Fraction of inspired oxygen; PEEP Positive end-expiratory pressure*

ing, by repositioning (including an attempt at prone position), inhaled nitric oxide and augmented cardiac output. With all this in mind, Table 1 outlines the 'ten commandments' for implementing lung protective ventilation strategies.

## CONCLUSION

Studies in animals have consistently demonstrated that VILI can occur in a very short time with the ventilator settings frequently used in intensive care units today. Human studies confirm that VILI is common and that (although not proven conclusively) when strategies are implemented to avoid VILI, morbidity and perhaps mortality can be reduced. Current recommendations for mechanical ventilation should include the early implementation of an LPVS (including the potential use of permissive hypercapnia) in all patients unless contraindicated. Clinicians should be aware of the potential complications of permissive hypercapnia and develop strategies to deal with these complications that, it is hoped, will avoid the need to venture beyond the recommendations of an LPVS. It is anticipated that broader use of current ventilation recommendations will yield improved patient care.

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