Basics of Mechanical Ventilation
B. Goals of Ventilation

1. ***What are the general goals of ventilation?*** Traditionally, clinicians have adjusted the tidal volume (TV) and the respiratory rate (RR) in mechanically ventilated patients with the primary goal of achieving normal PCO_2 and pH. However, ventilator strategies that solely target normal arterial blood gas (ABG) results may cause ventilator associated lung injury (VALI) or hemodynamic compromise. Thus, the goals of ventilation in the modern era should be to achieve acceptable, but not necessarily normal, PCO_2 and pH while avoiding patient harm. Specifically, in order to minimize the risks of macro- and microbarotrauma, the TV should be adjusted so that the plateau pressure (Ppl) is less than 30 cm H_2O. In order to avoid patient discomfort, hemodynamic compromise, and the risks of macro- and microbarotrauma, the respiratory rate should be adjusted so that there is minimal autopeep. These goals are summarized below and discussed further in ensuing sections.

General Goals of Ventilation
1. Acceptable PCO_2 & pH
2. Ppl <30 cm H_2O
3. Avoid Autopeep

   a. Goal #1 - Acceptable PCO_2 & pH
      1) ***What are the ways to manipulate the PCO_2?*** Recall that $PCO_2 = \{(K)(VCO_2)\} / \{(RR)(TV-V_d)\}$, where K = constant; $VCO_2 = CO_2$ production; RR = respiratory rate; TV = tidal volume; and V_d = dead space. Therefore, PCO_2 may be manipulated by adjusting the VCO_2, TV, RR, or V_d. For a mechanically ventilated patient, it is clinically easier to manipulate the TV or the RR than the V_d or the VCO_2. Increasing the TV will increase the minute ventilation and thereby decrease the PCO_2. However, this strategy is limited by the risks of macro- and microbarotrauma. Increasing the respiratory rate will also increase the minute ventilation and thereby decrease the PCO_2. However, this strategy is limited by the risk of autopeep. (See below for further discussion.) Decreasing CO_2 production and dead space are additional ways to manipulate the PCO_2. CO_2 production can be minimized by sedating and paralyzing the patient and treating fever. Since fat has a lower respiratory quotient compared to protein or carbohydrates, a lipid-rich diet will minimize CO_2 production for a given metabolic rate. Dehydration or excessive PEEP will decrease perfusion (Q) relative to ventilation (V). Therefore, avoiding dehydration and excessive PEEP will minimize dead space ventilation. Similarly, eliminating excessive ventilator tubing will reduce dead space. However, these methods generally have relatively small effects on the PCO_2. Extracorporeal CO_2 removal is effective in clearance of CO_2 but the method is not universally available and survival advantage has yet to be demonstrated. (Weber-Carsten. ICM 2009; 35:1100-5.) The options for lowering the PCO_2 are summarized in the table below.

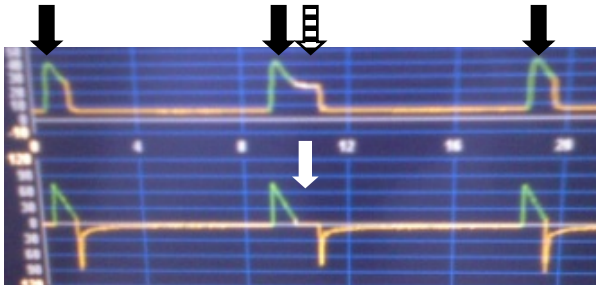
Major Methods	Other Methods
Treat Underlying Disease	Sedate & Paralyze Patient
Increase Tidal Volume	Treat Fever
Increase Respiratory Rate	High Fat Diet
	Avoid Dehydration
	Avoid Excessive PEEP
	Eliminate Excess Ventilator Tubing
	Extracorporeal CO_2 Removal

      2) ***What is an acceptable PCO_2 for mechanically ventilated patients?*** In general, PCO_2 of 40 and pH of 7.40 are typical targets since these are normal physiologic values. Frequently however, the minute ventilation needed to achieve these targets may be associated with unacceptably high airway pressures or autopeep, which can cause VALI or hemodynamic compromise. If PCO_2 of 40 is not possible because of high airway pressures or autopeep, then a higher PCO_2 level (sometimes > 100 mm Hg) may need to be tolerated. Under these circumstances, PCO_2 is allowed to rise in a controlled fashion, a strategy known as permissive hypercapnia. Other times, patients may have an elevated PCO_2 at baseline (i.e. chronic COPD). For these patients, their baseline PCO_2 level should be the target, rather than 40. Therefore, an acceptable PCO_2 level is one that is as close as possible to the baseline value and well-tolerated by the patient, but not associated with excessive airway pressures or autopeep.
      3) ***What effect does permissive hypercapnia have on the patient?*** The potential benefit or harm of permissive hypercapnia is still being investigated. What is known at present is that respiratory acidosis can cause vasodilatation and myocardial depression. Despite myocardial depression, the cardiac output can increase due to vasodilatation but the blood pressure tends to fall. (Weber. AJRCCM 2000; 162:1361-5). Because of these concerns, some advocate using $NaHCO_3$ or tromethamine as needed to keep the pH above 7.20-7.30.

b. Goal #2 - Ppl <30 cm H_2O

1) ***What is a peak inspiratory pressure?*** There are generally two airway pressures that are commonly followed in mechanically ventilated patients: the peak inspiratory pressure (PIP) and the plateau pressure (Ppl). As the name suggests, PIP is the maximal pressure in the ventilator circuit during inspiration.

2) ***What is a plateau pressure (Ppl)?*** Ppl is the alveolar pressure at end-inspiration. The figure shows a pressure-time curve on top and a flow-time curve on the bottom for 3 breaths. The black arrows point to the PIP (42 cm H_2O in this example). For the second breath, a brief end-inspiratory pause is introduced, causing cessation of air flow (white arrow). Since there is no air flow during this period, by definition, the pressure measured by the ventilator is equal to the alveolar pressure or the Ppl (striped arrow; 24 cm H_2O in this example).



3) ***What factors influence the PIP and the Ppl?*** PIP varies positively with the set PEEP, TV, inspiratory flow rate, and airway resistance but negatively with the compliance of the respiratory system. The Ppl also varies positively with the set PEEP and TV but negatively with the compliance of the respiratory system. Unlike PIP, the inspiratory flow rate and the airway resistance do not affect the Ppl. These relationships are summarized in the table below. Ppl is always less than or equal to the PIP.

	Increase in PEEP	Increase in Flow Rate	Increase in Resistance	Increase in TV	Increase in Compliance
PIP	Increase	Increase	Increase	Increase	Decrease
Ppl	Increase	No Effect	No Effect	Increase	Decrease

4) ***Consider a patient who is on mechanical ventilation for pneumonia. She has copious secretions and requires frequent suctioning. On the first day of mechanical ventilation, PIP is 35 and Ppl is 20. Next day on the same ventilator settings, PIP is now 60 but Ppl remains at 20. What could explain this situation?*** Notice that the PIP increased but the Ppl did not change while on the same ventilator settings. As summarized in the table above, this pattern is observed when either the inspiratory flow rate or the airway resistance is increased. Since the ventilator settings were not changed, a change in the inspiratory flow rate is not the explanation. Therefore, what likely happened in this patient is a buildup of secretions in the endotracheal tube, which decreased the effective diameter, and in turn increased the airway resistance. Aggressive suctioning of the tube or insertion of a new endotracheal tube would be indicated in this situation.

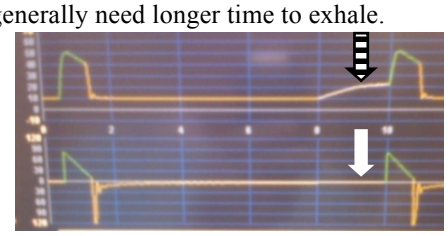
5) ***Which airway pressure is most relevant in terms of VALI?*** Both the PIP and the Ppl are important, but the pressure that is most relevant for microbarotrauma is the Ppl. Since Ppl is the pressure in the alveoli at end-inspiration, it is by definition the pressure to which the alveoli are exposed, as opposed to the PIP, which is the pressure to which the airways are exposed. The alveoli are more prone to overdistention injury than the airways since the alveoli have the thickness of only two cells: the endothelium and the epithelium. Therefore, Ppl is clinically the most relevant pressure to follow in terms of VALI.

6) ***What is an acceptable Ppl goal?*** Although there is no conclusive data, in general, the Ppl should be kept <30 cm H_2O to minimize the risk of volutrauma in most patients. If the Ppl is >30, TV or PEEP may need to be reduced to achieve this goal. However, as will be discussed below, keeping the Ppl <30 may not be sufficient to avoid VALI in many ARDS patients.

c. Goal #3 - Avoid Autopeep

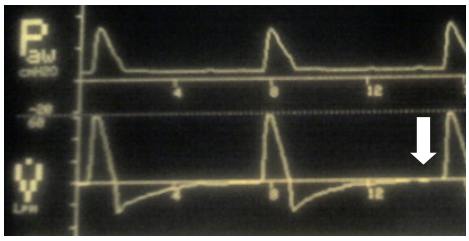
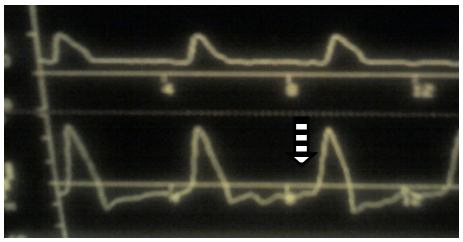
1) ***What is autopeep?*** Autopeep refers to the buildup of additional positive pressure in the lungs due to breath stacking. If the next breath starts before complete exhalation of the previous breath, some air will be trapped. This trapped air causes the alveolar pressure at end-expiration to be higher than the PEEP, which is termed autopeep. Normally at end-expiration, the alveolar pressure should be equal to the ventilator pressure which will be PEEP. Since the pressures in the alveoli and the ventilator are equal, there should be no air flow typically at end-expiration. However, in the presence of autopeep, since the alveolar pressure is higher than the ventilator pressure, there will be persistent expiratory air flow at end-expiration. Patients with obstructive airway disease are more vulnerable to breath stacking because they generally need longer time to exhale.

2) ***How can autopeep be measured?*** Autopeep can be estimated by introducing an end-expiratory pause in flow (white arrow) and measuring the corresponding airway pressure (striped arrow). During this pause in flow, the pressure measured by the ventilator is equal to the alveolar pressure. In this example, the set PEEP is

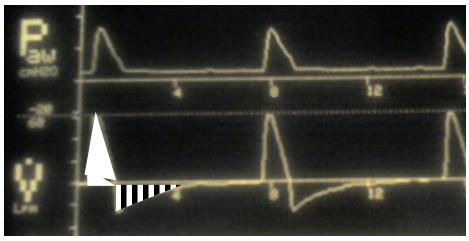
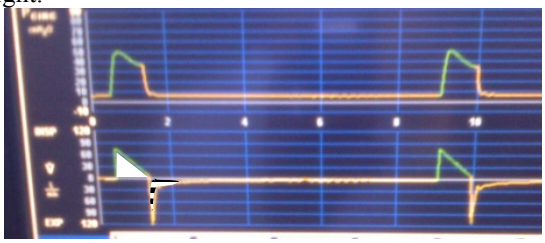


10 but the total PEEP is 22 due to autopeep of 12. Because the patient must cooperate with the expiratory pause, it is not always possible to measure the autopeep in a spontaneously breathing patient in this fashion.

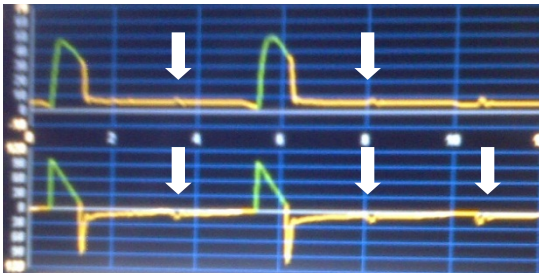
3) ***What is the problem with autopeep?*** Autopeep is associated with all of the potential hazards of set PEEP including macro- and microbarotrauma, hemodynamic compromise due to reduced cardiac output, and increase in dead space. In addition, autopeep is uncomfortable for the patient and causes increased work of breathing. Autopeep is also known as "occult PEEP" because it often goes unrecognized by the clinician. Clinically, if a mechanically ventilated patient is hypotensive, agitated, or requires heavy sedation, autopeep should be considered carefully, especially if the patient has wheezing or a history of obstructive lung disease.
4) ***If it cannot be measured, are there other clues that autopeep may be present?***
   a) ***How does the flow-time curve offer clues about the presence or absence of autopeep?*** As explained above, one way to look for autopeep is to examine the flow-time curve that is available on most ventilators. By convention, inspiratory flow is positive and expiratory flow is negative. The figures below show two different patients with pressure-time curves on top and flow-time curves on the bottom. As shown on the left, normally, a patient who exhales completely prior to the start of the next breath will have no flow at end-exhalation (white arrow). The absence of end-expiratory flow suggests that the alveolar pressure at end-expiration is equal to the ventilator pressure (i.e. no autopeep). However, when there is air flow at end exhalation as shown in the right figure (striped arrow), it implies that the patient was still exhaling and the alveolar pressure is higher than the set PEEP (i.e. autopeep). Notice that examination of the flow vs. time curve simply indicates whether or not autopeep is likely to be present. However, it does not quantify the amount of autopeep.

   b) ***How does the area of the flow-time curve offer clues about the presence or absence of autopeep?*** Another way to look for autopeep is to compare the area under the inspiratory flow curve with the area above the expiratory flow curve. Recall that the area under the inspiratory flow curve is the inspired tidal volume and the area above the expiratory flow curve is the expired tidal volume. Under normal conditions when there is no air trapping, the two areas should be equal. This is the case for the flow-time curve below on the left, where the area for the inspiratory flow curve is shown in white and the area for the expiratory flow curve is shown in stripes. However, if the area of the expiratory curve is grossly smaller than the area of the inspiratory curve, it is suggestive of significant air trapping and autopeep. This is the case for the flow-time curve below on the right.

   c) ***How does ineffective triggering offer clues about the presence or absence of autopeep?*** For a patient to spontaneously trigger a ventilator breath, the patient's inspiratory effort has to decrease the alveolar pressure to a level below PEEP. Patient may fail to trigger the ventilator in the setting of severe neuromuscular weakness or insensitive trigger settings, but by far, the most common cause is autopeep. (Leung. AJRCCM 1997; 155: 1940-8.) Patient's inspiratory effort has to eliminate all of the autopeep before the alveolar pressure can fall below PEEP. In the figure to the right, ineffective triggering is demonstrated by white arrows.

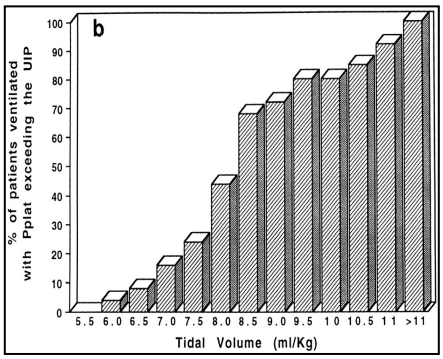


5) ***Who is likely to have autopeep?*** Patients who need a longer time to exhale, such as those with obstructive airway disease, are most susceptible to developing autopeep. These patients are particularly susceptible to autopeep in setting of a fast respiratory rate, large TV, and long inspiratory time. Among these factors, a fast respiratory rate is especially important. For illustration, consider a COPD patient whose ventilator settings are: FIO_2 30%, TV 0.6 L, rate 10, PEEP 5. Assume that the patient is not breathing over the ventilator (i.e. the patient's respiratory rate is also 10) and the TV is delivered over 1 second (i.e. inspiratory time = 1 second). Since the respiratory rate is 10, patient must be breathing every 6 seconds. If the IT is 1 second, the expiratory time must be 5 seconds. Thus, this COPD patient would have 5 seconds to exhale the 0.6 L of TV. As summarized in the table below, if the respiratory rate increases to 15, 20 or 30, the expiratory time decreases to 3, 2, or 1 second, respectively. Since it is unlikely that a patient with severe COPD will be able to exhale fully in 1 or 3 seconds, such a patient will likely have significant autopeep.

Respiratory Rate	Breath-to-Breath Time (sec)	Inspiratory Time (sec)	Expiratory Time (sec)
10	6	1	5
15	4	1	3
20	3	1	2
30	2	1	1

6) ***How can autopeep be minimized?***
   a) The ways to decrease autopeep include reducing the respiratory rate, sedating the patient (to minimize anxiety and tachypnea), and treating the underlying bronchospasm (β_2-agonists, steroids, etc.).
   b) Increasing the inspiratory flow rate or shortening the IT will also lengthen the time available for expiration and thereby reduce autopeep. However, unless the patient is sedated, these strategies may not affect the patient's respiratory rate and there may be little improvement in autopeep.
   c) Reducing the TV can also theoretically reduce autopeep since there will be less air to exhale. Unfortunately, the effects are generally modest. In some cases, patient may increase the spontaneous respiratory rate in order to preserve the minute ventilation. If so, the autopeep may fail to improve or may even paradoxically worsen. (Tobin. AJRCCM 2001; 163: 1059-63.)

2. ***Should the goals of ventilation be different for ARDS patients?*** ARDS is characterized by diffuse lung inflammation, increased permeability of endothelial-epithelial barrier, noncardiogenic pulmonary edema, atelectasis, and fibrosis. Physiologically, high shunt fraction, increased dead space, and reduced lung compliance are common. Consequently, hypoxia and hypercarbia can be quite severe. Most of these patients will die unless they receive mechanical ventilation. On the other hand, attempts to normalize the ABG results may require the use of high FIO_2, PEEP, and TV, which in turn may lead to oxygen toxicity, macro- and microbarotrauma, RACE injury, and hemodynamic compromise. Therefore, the general goals of ventilation summarized in the table above (and the goals of oxygenation to be discussed in the next chapter) are particularly important for ARDS patients. In addition, since high TV is more likely to cause microbarotrauma in ARDS patients, TV restriction is important as discussed below.
   a. ***What is the appropriate TV for ARDS patients?***
      1) The inherent difficulties in obtaining PV curves make it difficult to design a large multicenter trial that relies on PV curves to set the appropriate TV for individual patients. Therefore, it was helpful when a PV-curve-based study of 25 ARDS patients offered helpful empirical data on the relationship between the TV and the likelihood of violating the UIP. (Roupie. AJRCCM 1995; 152: 121-8.) As can be seen from the graph to the right, TV of 6 and 12 ml/kg violated the UIP in <5% and in 100% of the patients, respectively. Notice that even a modest TV of 8 ml/kg violated the UIP in about half of the patients.



      2) ARMA Trial. NEJM 2000; 342: 1301-8. This multicenter PRCT compared high (12 cc/kg) vs. low (6 cc/kg) TV among 861 patients with ARDS/ALI. It should be noted that based on Roupie's study described above, it could be inferred that <5% of the low-TV patients vs. 100% of the high-TV patients would have violated the UIP. Furthermore, in order to adjust for obese patients whose actual weight may significantly differ from their ideal weight, this study used ideal body weight (IBW) to set the TV, using an equation based on height and sex of the patient as follows: Male [IBW = 50.0 + 2.3 (Height Inches – 60)]; Female [IBW = 45.5 + 2.3 (Height Inches – 60)]. For both groups, the PEEP and the FIO_2 were set in an identical predetermined fashion as follows:

FIO_2	30	40	50	60	70	80	90	100
PEEP	5	5-8	8-10	10	10-14	14	14-18	20-24

a) As shown in the table below, the in-hospital mortality was significantly lower with the low-TV strategy.
b) The low-TV strategy also reduced the duration on the ventilator, the risk of organ failure, and the serum levels of an inflammatory cytokine, IL-6. The risk of pneumothorax was not different.

	High TV, 12 ml/kg	Low TV, 6 ml/kg	P
Mortality	39.8%	31.0	=0.007
Off Ventilator at Day 28	55.0%	65.7%	<0.001
Organ Failure Free Days	12	15	=0.006
IL-6 (log transformed)	2.5 to 2.3	2.5 to 2.0	<0.001

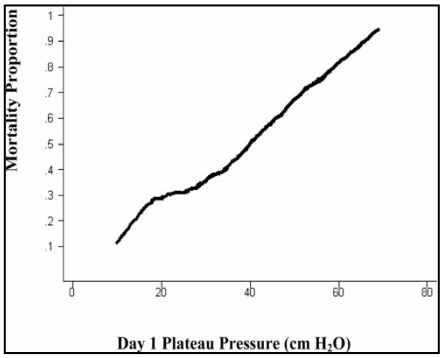
3) Other studies have also evaluated the role of low TV in ARDS patients but have failed to show significant mortality reduction (Brochard. AJRCCM 1998: 158: 1831-8. Stewart. NEJM 1998; 338: 355-61). One major difference between the ARMA study and these negative studies is the size of the study. It is likely that the negative studies lacked statistical power. Furthermore, a much larger difference in TV was tested in the ARMA study compared to the negative studies. The ARMA study also used ideal body weight, rather than actual body weight to set the TV, which is potentially very important for obese patients. Finally, a meta-analysis of these RCTs suggests an overall survival benefit of low TV strategy (pooled OR 0.75 [95% CI 0.58-0.96], P = 0.02) in ARDS patients. (Putensen. Annals of Internal Medicine 2009; 151: 566-76.)

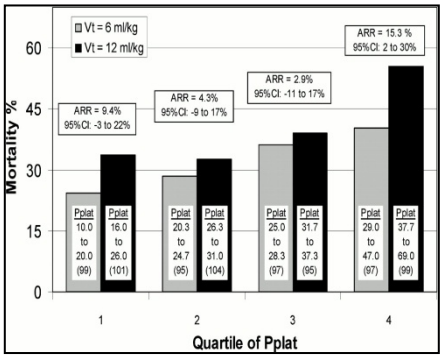
	ARDS Network, N=861	Brochard, N=116	Stewart, N=120
TV Compared	6.2 vs. 11.8 cc/kg	7.1 vs. 10.3 cc/kg	8.1 vs. 12.2 cc/kg
Weight Used	Ideal Body Weight	Actual Body Weight	Actual Body Weight

b. ***Which is more important, limiting the Ppl or the TV?*** Since TV and Ppl are positively correlated, in theory, an alternative to limiting the TV is to limit the Ppl instead. (Eichacker. AJRCCM 2002; 166:1510-4) If so, it may be safe to ventilate a patient at any TV as long as the the Ppl is not elevated. This is still a controversial issue and more studies would be helpful. However, as discussed below, the current evidence suggests that limiting the TV is a more prudent approach for ARDS patients.

1) ***Is volume or pressure more important for VALI?*** In animal models of VALI, the relevant mechanism of lung injury appears to be volutrauma from physical overstretching of the alveoli, rather than high pressure per se, hence the term, volutrauma. (Dreyfuss. ARRD 1988; 137: 1159-64. See chapter on VALI for further discussion.) Furthermore, a dyspneic patient often actively inspires while the TV is being delivered by the ventilator, which would lower the measured Ppl. If such a patient were to be pharmacologically paralyzed, the airway pressure would increase since the diaphragm no longer generates the negative pressure. In theory, such patients may be at risk for volutrauma even though the Ppl is low.

2) ***Is TV reduction to 6 ml/kg of IBW still necessary if the Ppl is already low? Is there a safe level of Ppl?*** Hager. AJRCCM 2005; 172: 1241-5. In a secondary analysis of the 787 ARDS patients in the ARMA study, a safe level of Ppl could not be demonstrated. Furthermore, even within each quartile of Ppl, there appears to have been a survival benefit when the TV was reduced to 6 ml/kg of IBW.





3) In summary, experimental animal study by Dreyfuss demonstrates that lowering the TV is more relevant than limiting the Ppl in terms of VALI. The study by Hager further demonstrates TV reduction to 6 ml/kg is still likely to be beneficial in terms of survival, even when the Ppl is low. Therefore, the current literature suggests that TV reduction is a more prudent strategy than Ppl limitation in ARDS patients.

c. ***Is TV of 6 ml/kg necessary for all ARDS patients?*** In theory, the ultimate goal of TV restriction in ARDS is not to achieve some arbitrary TV such as 6 ml/kg, but rather to stay below the UIP so as to avoid the risks of macro- and microbarotrauma. Since the UIP varies substantially from one ARDS patient to another, the TV needed to stay below the UIP also varies. For example, in the PV-curve-based study of 25 ARDS patients already described (Roupie. AJRCCM 1995; 152: 121-8.), the UIP varied from 18 to 40 cm H_2O (mean of 26). Correspondingly, TV that would violate the UIP also varied from 350 to 1240 ml (mean of 610 ml). Given these findings, uniformly

limiting the TV to 6 ml/kg for all ARDS patients (i.e. 420 ml for a 70 kg man) would be unnecessarily restrictive for many patients. Ideally, if the UIP could be determined for each patient, the TV could be appropriately individualized. Unfortunately, since PV curves are not routinely determined outside of research settings, the UIP for a specific patient is not typically known and such individualized approach to TV setting is not widely practiced at this time. Instead, the current recommendation is to follow a "one-size-fits-all" method of setting TV to 6 ml/kg in order to avoid the UIP for >95% of ARDS patients.

SUGGESTED READING

Key Original Articles

Roupie. Titration of tidal volume and induced hypercapnia in acute respiratory distress syndrome. American Journal of Respiratory and Critical Care Medicine 1995; 152: 121-8.

ARMA Study. The ARDS Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. New England Journal of Medicine 2000; 342: 1301-8.

Hager. Tidal volume reduction in patients with acute lung injury when plateau pressures are not high. American Journal of Respiratory and Critical Care Medicine 2005; 172: 1241-5.

Burton W. Lee, MD
Medstar Washington Hospital Center, Associate Professor of Medicine, Georgetown University, USA
burton.w.lee@medstar.net
Senior Consultant for Critical Care Education & Training, National Institute of Health, USA
burton.lee@nih.gov
Head of Internal Medicine, AIC Kijabe Hospital, Kenya
burton.w.lee@gmail.com