Consensus conference

Intensive Care Medicine

Intensive Care Med (1994) 20:64–79

Consensus conference on mechanical ventilation – January 28–30, 1993 at Northbrook, Illinois, USA

Part I

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Section I: Objectives of the consensus committee

"But that life may... be restored to the animal, an opening must be attempted in the trunk of the trachea, in which a tube of reed or cane should be put; you will then blow into this, so that the lung may rise again and the animal take in air. ... And as I do this, and take care that the lung is inflated in intervals, the motion of the heart and arteries does not stop..."

Andreas Wesele Vesalius, 1543

Although the concept of artificial respiration was recognized in the 16th century by Vesalius [1], it was not until the 20th century that mechanical ventilation became a widely used therapeutic modality. Over the past 30 years, and especially over the past decade, there has been an explosion of new ventilatory techniques which present a bewildering array of alternatives for the treatment of patients with respiratory failure. Unfortunately, although the number of options available to the clinician has appeared to increase exponentially, well controlled clinical trials defining the specific role for each of these modes of ventilation and comparing them to other modes of ventilation have not been forthcoming. In addition, over the past few years our understanding of the detrimental, as well as beneficial effects of mechanical ventilation has increased, along with novel strategies for limiting these negative effects.

These issues formed the impetus for the Consensus conference described in this document, which was held just outside Chicago, Illinois on January 28–30, 1993. The consensus committee was international in scope (Europe, North America, New Zealand) and consisted of individuals from a broad range of backgrounds (anaesthesia, critical care, pulmonary, respiratory therapy). The purpose of the conference was to summarize key concepts related to mechanical ventilation and to present recommendations based on these concepts for clinicians applying mechanical ventilation in the adult ICU setting. Due to the lack of randomized clinical studies on most aspects of ventilatory care, the underlying theme of this document is a physiological one; the basic tenet being that if the clinician understands the physiological principles, he/she can apply mechanical ventilation at the bedside in

This conference was sponsored by the ESCIM, the ACCP and the SCCM

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Abbreviations and definitions: A/C = Assist control ventilation; APRV = Airway pressure release ventilation; ARDS = Acute (adult) respiratory distress syndrome; Auto-PEEP = Increase (above set PEEP level) in end-exhalation alveolar pressure (also termed dynamic hyperinflation, intrinsic PEEP, also quantified as V_{EE}); CaO_2 = Content of oxygen in arterial blood; CMV = Conventional mechanical ventilation; COPD = Chronic obstructive pulmonary disease; CPAP = Continuous positive airway pressure; DH = Dynamic hyperinflation (see auto-PEEP); DO_2 = Oxygen delivery; ECMO = Extracorporeal membrane oxygenation; $ECCO_2R$ = Extracorporeal CO_2 removal; f = Respiratory frequency; FIO_2 = Fractional concentration of inspired oxygen; FRC = Functional residual capacity; HFJV = High frequency jet ventilation; ICP = Intracranial pressure; I : E = Inspiratory/expiratory ratio; Intrinsic PEEP: see auto-PEEP; IRV = Inverse ratio ventilation; IVOX = Intravascular blood gas exchanger; MalvP = Mean alveolar pressure; MAP = Mean airway pressure; MMV = Mandatory minute ventilation; MVV = Maximum voluntary ventilation; OAD = Obstructive airways disease; $P_{0,1}$ = Pressure measured 0.1 s after occlusion of the airway; $PaCO_2$ = Partial pressure of CO_2 in arterial blood; PaO_2 = Partial pressure of oxygen in arterial blood. PAP = Peak airway pressure; PCIRV = Pressure controlled inverse ratio ventilation; PCO_2 = Partial pressure of carbon dioxide; PEEP = Positive end-expiratory pressure; P_{Imax} = Maximum inspiratory pressure; P_{mus} = Pressure generated by muscle contraction; PPV = Positive pressure ventilation; PS = Pressure support; PSV = Pressure support ventilation; SaO_2 = Oxygen percent saturation (arterial); (S) IMV = (Synchronized) intermittent mandatory ventilation; TLC = Total lung capacity; VC = Vital capacity; VCO_2 = CO_2 production (elimination); V_D = Dead space; V_E = Minute ventilation; V_{EE} = End-expiratory lung volume; V_{EI} = End-inspiratory lung volume; V/Q = Ventilation/perfusion ratio; V_T = Tidal volume; VO_2 = Oxygen consumption (uptake)

a rational manner. We recognize that rational application of mechanical ventilation does not, in and of itself, guarantee the therapy will be beneficial to the patient. We await randomized clinical trial results for ultimate guidance.

The purpose of the consensus conference was not to deal with every possible aspect of mechanical ventilation. Rather, the focus was on treatment of patients with acute ventilatory failure and the principles of ventilation *after* the decision to initiate mechanical ventilation has been made. The technical needs and medical issues of ventilatory support in non-ICU settings were not dealt with specifically by this conference. These issues include ventilatory support during anesthesia and surgery; patient management during intra-hospital, land, or air transport; and long-term mechanical ventilation in the home. Also not covered were non-invasive (non-intubated) ventilatory support, negative pressure ventilation and methods and devices for respiratory support not primarily applied to the lungs, such as ECMO, $ECCO_2R$ or IVOX. This conference focused on the clinical application of mechanical ventilators, rather than on their design and operation. Thus, the participants consider these proceedings to be complementary to those of the 1992 AARC Consensus Conference on the Essentials of Mechanical Ventilators [2].

Despite the multidisciplinary and international composition of the conference, we were able to reach agreement on many difficult clinical issues. Yet even though we engaged in considerable discussion and debate, consensus was not possible on a number of aspects of ventilator care. This is hardly surprising, and merely reflects the variety of acceptable approaches that can be used to manage patients with respiratory failure. For example, it was not possible to agree that there was an optimum *mode* of ventilation for any disease state, or an optimum method of weaning patients from mechanical ventilation. However, in addition to the specific recommendations discussed in Section 2, there was general agreement on the following principles that should guide the use of mechanical ventilation:

- The underlying pathophysiology of various disease states varies with time, and thus the mode, settings and intensity of ventilation should be repeatedly re-assessed.
- Mechanical ventilation is associated with a number of adverse consequences, and as such, measures to minimize such complications should be implemented wherever possible.
- To minimize side effects, the physiologic targets do not have to be in the normal range. For example, at times it may be beneficial to allow the $PaCO_2$ to increase (controlled hypoventilation, permissive hypercapnia) rather than risk the dangers of lung hyperinflation.
- Alveolar over-distention can cause alveolar damage or air leaks (barotrauma). Hence, maneuvers to prevent the development of excess alveolar (or transpulmonary) pressure should be instituted if necessary. While recognizing that the causes of ventilator-induced lung injury are multi-factorial, the consensus committee generally believed that end-inspiratory occlusion pressure (i.e. plateau pressure) was the best, clinically applicable estimate of average peak alveolar pressure, and thus, was the most important target pressure when trying to avoid alveolar over-distention. Many individuals on the consensus committee felt that high plateau pressures ($>35\ cmH_2O$) may be more harmful in most patients than high values of FIO_2.
- Dynamic hyperinflation (gas trapping, Auto-PEEP, intrinsic PEEP) often goes unnoticed and should be measured or estimated, especially in patients with airway obstruction. Management should be directed towards limiting the development of dynamic hyperinflation and its adverse consequences in these patients.

This consensus document is divided into 2 major sections: Sections II–III summarize the objectives and specific recommendations of the consensus committee; Sections IV–VII review key principles regarding physiology, complications and modes of ventilation that form the basis for the recommendations.

Section II: Objectives of mechanical ventilation

Mechanical ventilation and continuous positive airway pressure (CPAP) are methods of supporting intubated patients during illness, and are not, in and of themselves, curative or therapeutic. Indeed, in certain clinical settings, there may be effective alternative therapies that do not require intubation and mechanical ventilation. The fundamental objectives for ventilatory support in acutely ill patients may be viewed physiologically and clinically, as detailed below. The following objectives should be kept in mind, not only when mechanical ventilation is initiated, but also at frequent intervals during the period of support; mechanical ventilation should be withdrawn whenever the underlying pathophysiologic rationale for initiating mechanical ventilation is no longer present.

A. Physiologic objectives

1. To support or otherwise manipulate pulmonary gas exchange

i) Alveolar ventilation (e.g. arterial PCO_2 and pH). In most applications of ventilatory support, the objective is to normalize alveolar ventilation. In certain specific clinical circumstances, the objective may be to achieve an alveolar ventilation greater than normal (as in deliberate hyperventilation to reduce intracranial pressure), or adequate but less than normal (as in permissive hypercapnia or acute-on-chronic ventilatory failure).

ii) Arterial oxygenation (e.g. PaO_2, SaO_2 and CaO_2). A critical objective of mechanical ventilation is to achieve and maintain a level of arterial blood oxygenation that is acceptable for the clinical setting, using an inspired oxygen concentration that is also acceptable. In most applications of ventilatory support, this means a $SaO_2 > 90\%$ (roughly equivalent to a $PaO_2 > 60\ mmHg$ assuming a normal position of the oxyhemoglobin dissociation curve), although other endpoints are appropriate in certain settings. There is no clinical evidence that a PaO_2 greater than normal is advantageous. Given other tech-

niques for improving oxygenation, this objective would seldom be the only reason for initiating mechanical ventilation. Because arterial oxygen content is determined by hemoglobin as well as PaO_2, and because systemic oxygen delivery is directly related to cardiac output (Q_t), as well as CaO_2, these factors must also be considered in therapy aimed at improving tissue oxygenation.

2. To increase lung volume

i) End inspiratory lung inflation. To achieve sufficient lung expansion, with every breath (or intermittently), to prevent or treat atelectasis and its attendant effects on oxygenation, compliance, and lung defense mechanisms.

ii) Functional residual capacity (FRC). To achieve and maintain an increased FRC using PEEP in settings in which a reduction in FRC may be detrimental (e.g. decreased PaO_2, increased lung injury), as in ARDS and postoperative pain.

3. To reduce or otherwise manipulate
the work of breathing

i) To unload the ventilatory muscles. To reduce the patient's work of breathing when it is increased by elevated airway resistance or reduced compliance and the patient's spontaneous efforts are ineffective or incapable of being sustained. In these situations ventilatory support will be used until specific therapies (or other mechanisms) reverse the condition leading to the increased work load.

B. Clinical objectives

Because, at best, mechanical ventilation serves only to support the failing respiratory system until improvement in its function can occur (either spontaneously or as a result of other interventions), a primary objective should be to avoid iatrogenic lung injury and other complications. The other primary clinical objectives of mechanical ventilation are:

1. To reverse hypoxemia: To increase PaO_2 (generally such that $SaO_2 \geq 90\%$), whether through increasing alveolar ventilation, increasing lung volume, decreasing O_2 consumption, or other measures, to relieve potentially life- or tissue-threatening hypoxia.

2. To reverse acute respiratory acidosis: To correct an immediately "life-threatening" acidemia, rather than necessarily to achieve a normal arterial PCO_2.

3. To relieve respiratory distress: To relieve intolerable patient discomfort while the primary disease process reverses or improves.
There are well defined circumstances in which attempts to improve PaO_2 or pH to their normal ranges would present greater overall risks to the patient, and lower values of these parameters may be appropriate in such circumstances. In addition to the main clinical objectives listed above, other specific goals for mechanical ventilation, in appropriate settings, include the following:

4. To prevent or reverse atelectasis: To avoid or correct the adverse clinical effects of incomplete lung inflation, as for example in postoperative splinting or neuromuscular disease.

5. To reverse ventilatory muscle fatigue: In most instances this means unloading the ventilatory muscles in circumstances of acutely increased and intolerable loads.

6. To permit sedation and/or neuromuscular blockade: To allow the patient to be rendered incapable of spontaneous ventilation, as for operative anesthesia and certain ICU procedures and in certain disease states.

7. To decrease systemic or myocardial oxygen consumption: To lower systemic and/or myocardial VO_2 when the work of breathing or other muscular activity impairs systemic O_2 delivery, or produces an overload of the compromised heart. Examples include cardiogenic shock or severe ARDS.

8. To reduce intracranial pressure: In certain circumstances (e.g. acute closed head injury), to lower elevated ICP through controlled hyperventilation.

9. To stabilize the chest wall: In the unusual circumstance of loss of thoracic integrity sufficient to prevent adequate bellows function (e.g. chest wall resection, massive flail chest), to provide adequate ventilation and lung expansion.

Section III: Clinical recommendations

A. Mechanical ventilation for specific entities

Adult respiratory distress syndrome (ARDS). Although it has been argued that patients with ARDS are now more severely ill than those encountered in the past, the failure of ARDS mortality to decrease during the past 15–20 years is disappointing, particularly in light of the many technical advances in ICU care. Criteria that selected a severely hypoxemic subset of ARDS patients were established in the 1974–77 extracorporeal membrane oxygenation clinical trial. Recent work indicates that the survival of such severe ARDS patients treated with conventional mechanical ventilation only ranges from 0% to 15% (mean = 12.8±5.2%) [3]. This is not statistically significantly different from the ECMO clinical trial survival of 9% ($p = 0.15$). Recent changes in ventilatory management may have led to increased patient survival, but this has not been evaluated with controlled clinical trials [4–6].

There are no convincing data indicating that any ventilatory support mode is superior to others for ARDS patients. Nevertheless, reported increases in ARDS patient survival have been ascribed to new techniques such as Pressure Controlled Inverse Ratio Ventilation (PCIRV) and Low Frequency Positive Pressure Ventilation-Extracorporeal CO_2 Removal (LFPPV-ECCO$_2$R). If they are harbingers of new and effective therapy, their putative benefit may be linked to current concern about iatrogenic

lung damage induced by mechanical ventilation. Animal studies have clearly established the damaging effects of overdistention produced by the application of high peak transthoracic pressures to normal and injured lungs. In humans, the nonuniformly injured severe ARDS lung retains only a small fraction of compliant lung still capable of gas exchange. It has been argued that the application of commonly used tidal volumes (0.7 l, 10 ml/kg) to this small fraction of lung may produce similar damage [3]. The best correlate of this injury in animals is the plateau pressure. Conventional mechanical ventilator therapy might thus superimpose iatrogenic lung injury. The "lung rest" strategy used in neonatal ECMO therapy [7], intentional hypoventilation used in patients with ARDS [4], and reduction of peak pressures permitted by PCIRV or by LFPPV-ECCO$_2$R [8] are consistent with this argument. There is, however, no proof that any of these techniques alter the outcome of ARDS patients. A recent randomized controlled clinical trial of PCIRV plus LFPPV-ECCOO$_2$R failed to produce evidence of improved survival [9]. Of interest is the four-fold increase in survival of control patients treated with mechanical ventilation only, according to a computerized protocol [9].

Guidelines

1. The clinician should choose a ventilator mode that has been shown to be capable of supporting oxygenation and ventilation in patients with ARDS and that the clinician has experience in using.
2. An acceptable SaO_2 (usually $\geq 90\%$) should be targeted.
3. Based primarily on animal data, a plateau pressure ≥ 35 cmH_2O is of concern. We, therefore, recommend that when plateau pressure equals or exceeds this pressure, that tidal volume can be decreased (to as low as 5 ml/kg, or lower, if necessary). With clinical conditions that are associated with decreased chest wall compliance, plateau pressures somewhat greater than 35 cmH_2O may be acceptable.
4. To accomplish the goal of limiting plateau pressure, $PaCO_2$ should be permitted to rise (permissive hypercapnia) unless the presence or risk of raised intracranial pressure or other contraindications exist which demand a more normal $PaCO_2$ or pH. Rapid rises in $PaCO_2$ should be avoided. In the presence of normal renal function, slow reduction of tidal volume may also allow renal-induced compensatory metabolic alkalosis and the potential for a higher pH at given tidal volume.
5. Positive end-expiratory pressure (PEEP) is useful in supporting oxygenation. An appropriate level of PEEP may be helpful in preventing lung damage. The level of PEEP should however be minimized as PEEP may also be associated with deleterious effects. The level of PEEP required should be established by empirical trial and re-evaluated on a regular basis.
6. The current opinion is that FiO_2 should be minimized. The tradeoff however may be a higher plateau pressure and the relative risks of these two factors are not known. In some clinical situations when significant concerns over both elevated plateau pressure and high FiO_2 exist, consideration for accepting an SaO_2 slightly less than 90% is reasonable.
7. When oxygenation is inadequate, sedation, paralysis, and position change are possible therapeutic measures. Other factors in oxygen delivery (i.e. Q_t and hemoglobin) should also be considered.

Bronchopleural fistula. Bronchopleural air leak (bronchopleural fistula, BPF) occurs during mechanical ventilation in two general circumstances: as a localized lung or airway lesion (e.g. following trauma or surgery; complicating central line placement) and as a complication of diffuse lung disease (e.g. ARDS, *Pneumocystis carinii* pneumonia). Although most leaks are physiologically insignificant, BPF can predispose to atelectasis or inadequate inflation of ipsilateral or contralateral lung, interfere with gas exchange, and predispose to pleural spread of infection. It can also prolong mechanical ventilation thus predisposing to additional morbidity. Some BPFs are amenable to direct surgical repair (e.g. suture of bronchial tear; lobectomy for necrotizing pneumonia), but in most instances resolution of the BPF depends on resolution of the primary disease process.

Ventilatory support should provide adequate inflation for the uninvolved areas of lung and assure adequate gas exchange [10]. No single ventilatory mode or approach has been shown to be more effective than any other in managing patients with BPF. In the presence of a large air leak and difficulty in maintaining adequate ventilation, a ventilator capable of delivering high inspiratory flow rates and large delivered tidal volumes may be required. Use of independent lung ventilation (ILV) should be considered in the uncommon circumstance of inability to maintain contralateral lung inflation using adjustments of volumes and/or flows. Fortunately, ventilation of patients with BPF is usually adequate. The major problem is usually to facilitate closure of the leak, so that mechanical ventilator support may be withdrawn. In this circumstance, minimizing inflation pressures and tidal volume is the goal. Chest tube suction is necessary to evacuate continued gas leak, but the degree of suction exerts a variable effect on flow through the fistula [11].

Guidelines

1. To facilitate closure
   a. Use the lowest tidal volume that allows adequate ventilation.
   b. Use a ventilatory mode and settings that minimized peak and plateau pressures necessary to maintain adequate ventilation.
   c. Consider permissive hypercapnia (discussed under recommendations 3 and 4 under ARDS) to minimize inspiratory pressures and volumes.
   d. Minimize PEEP
2. Consider independent lung ventilation (ILV) or high frequency jet ventilation (HFJV) in cases where a large air leak produces inability to inflate lung or failure to adequately oxygenate/ventilate.

Head trauma. Mechanical hyperventilation to arterial carbon dioxide levels of 25–30 mmHg acutely lowers intracranial pressure (ICP). Controlled data on the impact of hyperventilation in patients with head trauma is not available. Decreases in ICP do not necessarily reflect increases in cerebral perfusion pressure. Nevertheless, hyperventilation remains a mainstay of emergency therapy for acutely elevated ICP. There is no evidence to support the application of prophylactic hyperventilation in patients with head injury, who do not have raised ICP [12, 13]. In fact, there is a strong rationale for maintenance of normocarbia in most head injured patients without elevated ICP because a patient who has prophylactically been hyperventilated to a $PaCO_2$ in the high 20's and who suffers an acute increase in ICP, may not be expected to have an effective reduction in ICP following a moderate increase in minute ventilation. Since the

patient is already hyperventilated, a marked increase in minute ventilation may be required to effect a significant lowering of $PaCO_2$. The increase in mean airway pressure associated with a dramatic increase in minute ventilation may cause a paradoxical increase in ICP. Therefore, it is likely that stable head injured patients should receive mechanical ventilatory support at a level sufficient to produce normal arterial blood gases. Effective monitoring should be instituted to allow a rapid increase in ventilation and oxygenation, should signs of increased ICP or hypoxemia occur.

Recommendations

1. In the presence of increased ICP maintain $PaCO_2$ 25–30 mmHg or titrate to ICP if monitoring of ICP is available. Monitoring of ICP is desirable.
2. Maintain normocarbia in head injured patients with normal ICP.
3. When hyperventilation is used to decrease ICP, return to normocarbia should be gradual (over 24–48 h).

Myocardial ischemia and congestive heart failure. In patients with myocardial ischemia, modes of mechanical ventilation that increase work of breathing will increase oxygen demand and may detrimentally affect the myocardial oxygen supply/demand relationship [14, 15]. Resultant myocardial ischemia may decrease compliance of the left ventricle. The increasing pulmonary capillary pressure and decreasing lung compliance create a vicious cycle, as resistance and work of breathing increase further. Therefore, in patients with myocardial ischemia and some combination of high lung resistance and/or poor respiratory muscle function, spontaneous ventilation associated with an increase in the work of breathing is likely detrimental.

In severe congestive heart failure, positive pressure ventilation (PPV) would be expected to decrease venous return. PPV is likely to increase PaO_2 by increasing lung volume and reducing right to left shunting (Q_s/Q_t). Although the effect of PPV on the normal ventricle would be to decrease cardiac output by decreasing left ventricular (LV) filling (preload), the effect of positive pressure ventilation on a dilated failing LV operating on the flat (depressed) portion of the cardiac function curve will be different [16, 17]. In this circumstance, a reduction in transmural aortic pressure and associated decrease in wall stress and afterload might increase stroke volume.

Guidelines

1. In the presence of acute myocardial ischemia, choose modes of mechanical ventilation that minimize work of breathing.
2. When life-threatening hypoxemia accompanies severe congestive heart failure consider the potentially beneficial effect of PPV on decreasing venous return and improving oxygenation.
3. Consideration should be given to the assessment of the effect of PPV on hemodynamics should be given.

Neuromuscular disease. Patients with ventilatory failure due to neuromuscular disease (e.g. Guillain-Barre syndrome; cervical spinal cord injury) typically have normal ventilatory drive and normal or nearly-normal lung function [18]. Because the primary physiologic defect is ventilatory muscle weakness, they are predisposed to develop of atelectasis (from inadequate lung inflation) and pneumonia (from impaired cough and mucociliary clearance) [19, 20]. Their main needs during ventilatory management are provision of adequate lung inflation and aggressive airway management [21]. There is no evidence that either positive-pressure or negative-pressure ventilation is superior in this situation.

These individuals are at less risk for barotrauma than patients with intrinsic restrictive or obstructive lung disease, and they frequently prefer large tidal volumes (e.g. 12–15 ml/kg). Typically they are also more comfortable with high inspiratory flow rates. Whether full or partial ventilatory support should be provided depends on the patient's capabilities and the disease process: high quadriplegia (e.g. C1–2) lesion needs full ventilatory support whichever mode is used, whereas partial ventilatory support may be appropriate for individuals with some ventilatory capability, particularly during recovery, as long as patient comfort is maintained.

Guidelines

1. Large tidal volumes (12–15 ml/kg) with or without PEEP (5–10 cmH_2O) may be needed to relieve dyspnea. Adjust peak flow rate as needed to satisfy patient inspiration needs ($\geq$60 l/min peak inspiratory flow will typically be required).
2. Use total or partial ventilatory support based on the patient's inherent ventilatory muscle strength.

Obstructive airways disease (OAD). Acute respiratory failure in asthma and chronic OAD is associated with significant expiratory obstruction and hyperinflation. Resistance to inspiration is likely to be greater in the asthma patient because of airway edema and mucus. Both patient groups benefit from mechanical ventilation settings that maximize expiratory time, thus decreasing end-expiratory lung volume (V_{EE}), intrinsic (auto) PEEP and the risk for hemodynamic compromise [22]. With the same tidal volume, a higher (V_{EE}) would produce a higher end inspiratory lung volume (V_{EI}) and a greater risk for barotrauma [23].

The use of high inspiratory flow rates will maximize expiratory time and minimize V_{EE} and intrinsic PEEP (auto-PEEP, dynamic hyperinflation). This is accomplished, however, at the expense of higher peak airway pressure (PAP) in the central airways. Although PAP generated by increasing flow rate does not correlate closely with barotrauma as well as plateau pressure, the amount of central airway pressure that is actually transmitted to the alveolus (the actual risk factor for barotrauma) is difficult to judge. End inspiratory plateau pressure with volume cycled breaths rises as dynamic hyperinflation increases and may be reflective of increasing risk of barotrauma.

Guidelines

1. No evidence exists that one ventilator mode is better than another for initial management of OAD. The clinician should choose a ventilator mode he or she is familiar with and has used successfully in this setting.
2. Adjust the peak inspiratory flow rate to meet patient demands [24].
3. Monitor for and minimize dynamic hyperinflation (auto-PEEP) see Section IV, A-6.

a. It is desirable to utilize the least minute ventilation that produces acceptable gas exchange and leads to the greatest expiratory time. Maneuvers likely to accomplish this goal are:
   i. decrease in minute ventilation
   ii. increase in expiratory time
   iii. acceptance of hypercapnia
b. When dynamic hyperinflation exists in the presence of patient initiated mechanical ventilation, application of small amounts of ventilator applied PEEP may be helpful in reducing the work of breathing (see Section IV, A-6). However, application of ventilator PEEP above the level of initital auto-PEEP may lead to further hyperinflation and complications.

4. Based primarily on animal data and as discussed in the ARDS section, end inspiratory plateau pressure is also a concern in OAD, as it reflects hyperinflation. We believe that attempts to maintain plateau pressure less than 35 cmH_2O are worthwhile even though the impact on patient outcome is unknown. In the acutely ill patient with OAD, measurement of plateau pressure usually requires sedation and paralysis.
5. Use of volume-cycled assist control ventilation in the initial management of the awake OAD patient may be associated with significant risk of increasing hyperinflation and should be avoided [25].

Asthma. (1) We believe that a high plateau pressure is predictive of hyperinflation of lung units in the patient with asthma. A high peak airway pressure (PAP) may also predict hyperinflation. We recommend that plateau and peak pressures be minimized in patients with asthma. Unfortunately PAP is significantly influenced by ET tube size and inspiratory flows.

(2) Accept an elevated $PaCO_2$, as long as pH can be maintained at an acceptable level [26, 27].

(3) Paralysis and/or sedation may be necessary in some patients if the ventilation mode cannot be matched to the patient's needs (i.e. patient "fighting" the ventilator). Following paralysis and/or sedation a decrease in active expiratory effort may be associated with less airway collapse. The associated decrease in CO_2 production (especially of respiratory muscles) may also be advantageous in some circumstances. Paralysis is associated with acute and long-term complications.

COPD. (1) Mechanical ventilation of COPD patients with acute respiratory failure is unlikely to require high PAP or to present problems with CO_2 removal. In the presence of high PAP or difficulty in CO_2 removal in COPD, coexisting pathology should be considered (pneumothorax, pulmonary edema, mucus plugging, high degree of bronchospasm).

(2) Patients with chronic respiratory acidosis should have alveolar ventilation titrated to pH, not $PaCO_2$.

Post-operative patients. Few patients require mechanical ventilatory support past the immediate post anesthetic period. However, residual anesthetic effects, usually due to narcotics, or muscle relaxants, may require a variable period of mechanical ventilation. An anesthetic induced decrease in functional residual capacity coupled with thoracic or upper abdominal incision predisposes to atelectasis [28, 29]. These patients with little or no significant lung disease may be optimally managed with relatively little difficulty. The greatest concern for the clinician is to avoid iatrogenic complications of ventilatory support, including infection, decreased cardiac output, prolonged support requiring unnecessary sedation, hyperventilation, inspissated secretions, and unnecessary exposure to potentially toxic high inspired oxygen concentrations [30, 31]. Often, patients are unnecessarily ventilated in the post-operative period because of the mistaken belief that mechanical ventilation *per se* is beneficial in establishing a more physiologic cardiopulmonary status. Thus, patients who have undergone major operative procedures involving the head, thorax, or abdomen, may remain intubated and ventilated unnecessarily. Although prospective analysis has not determined whether such therapy has a significant rate of complication, no prospective analysis has provided evidence of beneficial effects of such therapy. Future studies should be designed to determine which, if any, patients and/or surgical procedures require ventilatory support past the immediate anesthetic emergence period.

Unilateral lung disease. Patients with unilateral lung disease who require mechanical ventilation are infrequently encountered. Therapeutic efforts have included placement of double lumen tracheal tubes to effect ventilation of each lung separately, positional changes of the patient, bronchial blockers, pneumonectomy, and alteration of inspiratory gas flows in order to improve overall lung function. Usually, such maneuvers ignore the effect of hypoxic pulmonary vasoconstriction on the affected lung and the physiologic principles underlying inflation of the lung during positive-pressure ventilation. Were it not for the restricting effect of the rib cage and diaphragm on lung inflation, the unaffected lung would receive the preponderance of the positive pressure breath and/or increase in lung volume secondary to application of CPAP. However, in the presence of an intact thorax, lung inflation depends upon increase in transpulmonary pressure, the difference between airway and pleural pressure. The individual with unilateral lung disease usually has a marked discrepancy in compliance between the two lungs. A lung with marked decrease in compliance will receive less volume for a given applied airway pressure. Therefore, the non-compliant lung will be ventilated less than will the normal, compliant lung. Should such patients experience significant arterial hypoxemia and/or hypercarbia, more aggressive means of ventilatory support must be considered, as with any type of advanced lung disease. These might include $ECCO_2R$, ECMO, high frequency ventilation, etc. The ability of these interventions to alter outcome is not known. To date, split-lung ventilation [32, 33], with a double lumen tracheal tube [34], and differential application of positive airway pressure has likewise not been shown to improve morbidity and mortality.

Guidelines

1. Initially utilize conventional ventilation techniques independent of presence of unilateral lung disease.
2. In the presence of difficulties in oxygenation a trial of ventilation with the least involved lung in the dependent position is appropriate.
3. If PEEP is applied, initially utilize a single lumen endotracheal tube.
4. In cases of inability to oxygenate with traditional PEEP application, independent lung ventilation with a double lumen ET tube may be tried (synchronization of ventilation is not necessary). This mode of ventilation has however not been proved to alter outcome.

B. Discontinuation of mechanical ventilation

The consensus committee agreed there were many correct ways to discontinue patients from mechanical ventilation. There are a number of basic principles that are important in discontinuing ventilatory support and these are covered in Section VII. Specific recommendations are given below:

1. Whichever technique is used for discontinuation of ventilatory support, the clinician should know the signs of increasing ventilatory insufficiency and patient distress, and discontinue or modify the process if they appear, persist, or worsen:
   a) Increasing tachypnea (e.g., beyond a total rate of 30–35 breaths/min) associated with patient distress;
   b) agitation, panic, diaphoresis, or tachycardia, unrelieved by reassurance and adjustment of the mechanical ventilation system.
   c) Acidemia: acute drop in pH to <7.25–7.30, associated with an increasing $PaCO_2$.
2. Excessive imposed work of breathing from demand valves or circuits, as indicated by substantial decreases in airway pressure during patient efforts, should be avoided during attempts at discontinuation of ventilatory support whether using a T-tube or the ventilator circuit.
3. If IMV is used, the rate and degree of withdrawal of ventilatory support should be guided by pH, PCO_2, total respiratory rate, heart rate, and signs of patient distress.
4. If PSV is used:
   a) The rate of reduction of the PSV level should be guided by total respiratory rate rather than by tidal volume. As a rule, respiratory rate should not exceed 30 breaths/minute.
   b) If a patient can maintain adequate gas exchange and comfort level on a low level of PSV (e.g., 5 cmH_2O) it is not necessary to reduce this to zero before extubation.
5. In patients in whom ventilatory support cannot be withdrawn successfully over a short period, a systemic approach should be taken to identify and treat contributing factors, such as:
   a) *imposed loads* in the apparatus that increase work of breathing (e.g., demand valves, small-diameter endotracheal tubes);
   b) *respiratory factors* (e.g., bronchospasm, excessive secretions, pharmacologic depression of ventilatory drive, persistence of underlying disease etc.);
   c) *nonrespiratory factors* (e.g., cardiovascular dysfunction, increased metabolic rate, acid-base problems, hypophosphatemia, manutrition, anxiety etc.).
6. In "difficult-to-wean" patients in whom discontinuation of ventilatory support occurs gradually over several days, it may be desirable to increase the level of support at night to enable the patient to rest effectively, as demonstrated by the ability to sleep.
7. Successful extubation requires the ability to protect the upper airway and clear secretions adequately in addition to successful discontinuation of ventilatory support. These factors should be considered and addressed both and both prior and subsequent to extubation.

Section IV: Physiological principles relevant to mechanical ventilation

A. Patient-related physiologic principles

The response to mechanical ventilation is governed by several physiologic relationships. Two cardinal rules apply:

1. Although the qualitative response of a given physiological variable to manipulation of ventilator settings may be predictable, the quantitative response is highly variable and patient specific. Thus, an increase in PEEP or level of ventilation usually improves PaO_2 at a given FIO_2. However, the extent of improvement in any given patient may be large or small, and the short term improvement may produce complications due to the higher pressures (barotrauma). Likewise, an increase in V_E may be expected to result in a lower $PaCO_2$ but the amount of reduction may be large or small and must be balanced against the potential complications relating to the increase in ventilatory pressures.

2. A ventilator manipulation designed to improve one relation or variable may have undesirable effects on other equally important relations or variables. For example, an increase in PEEP may improve PaO_2 but adversely affect cardiac output, thereby negating the improvement in PaO_2 at the tissue level. Likewise an increase in V_E to reduce PCO_2 may result in greater auto-PEEP or adverse effects on cardiac output. The extent of negative side effects of a given ventilator manipulation is, again, highly variable and patient specific. The physiologic relations that are most important to consider are:

1. Ventilation-perfusion (V/Q relations): The PaO_2 obtained at a given FIO_2 is a function of the uniformity (homogeneity) of distribution of ventilation and perfusion to different lung units. Units with relatively low ventilation and high perfusion are associated with incomplete oxgenation and, hence, a low PO_2 for a given FIO_2. Units with no ventilation at all but which continue to receive perfusion contribute to shunting, which is one extreme of V/Q inequality.

The distribution of ventilation among different units depends on:

a) Whether the unit is aerated or not at end expiration; units which are air free at end expiration (due to atelectasis or fluid filling) require very high inspiratory pressures if they are to receive any ventilation at all.

b) For aerated units, the distribution of ventilation is determined principally by regional compliance and resistance. Lung disease is invariably non-uniform, and this is the basic reason for the existence of serious V/Q mismatching and for difficulty in oxygenation. On theoretical grounds when the regional differences in mechanics are principally in resistance, distribution of ventilation should become more uniform with long inspiratory times and with decelerating flow patterns. Conversely, where the non-homogeneity involves regional compliances, shorter inspiratory times and square flow pattern should result in more uniformity. Whether equalizing regional ventilation is good or bad for PaO_2 is not entirely predictable since improving V_E of a poorly ventilated unit may or may not be beneficial, depending on the state of perfusion of that unit. It is also evident that by rendering the V_E distribution more uniform, some units (usually the healthy ones) will receive less ventilation as the poorly ventilated units receive more. If perfusion is preferentially distributed to the former, overall V/Q may worsen as distribution of V_E is improved.

The regional distribution of perfusion is determined principally by regional resistances in blood vessels supplying and draining different units. Regional resistances are related to gravity (dependent units have lower resistance), vasomotor tone and mechanical factors (e.g. lung volume or anatomic narrowing). Regional alveolar pressure (more appropriately, regional trans-pulmonary pressure) plays a critical role. When transmitted regional alveolar pressure is higher than pulmonary artery pressure (PAP) perfusion is arrested (West zone 1).

For a given degree of V/Q mismatching and FIO_2, PaO_2 is critically affected by mixed venous O_2 saturation (S_vO_2); lower venous O_2 sat is associated with lower

PaO_2. S_vO_2 is, in turn, dependent on cardiac output, metabolic rate and hemoglobin.

From the standpoint of oxygenation, the primary beneficial effect of increased distending pressure (PEEP or greater V_T) is the recruitment of non-functional or very poorly ventilated units. This benefit can be enhanced or mitigated through secondary and unpredictable effects on a) the distribution of ventilation to other units (by upward displacement of these units to more favorable or less favorable segments of pressure volume curve), b) on the distribution of perfusion (through effects on the relation between P_{alv} and PAP and on lung volume (and hence vascular dimensions)), and c) on mixed venous PO_2 (through effects on metabolic rate (less or more fighting, less or more work of breathing) or cardiac output).

2. Relation between ventilation and $PaCO_2$: The relation between minute ventilation (V_E) and $PaCO_2$ is:

$$PaCO_2 = 0.863\ V_{CO_2}/[V_E(1-V_D/V_T)]$$

where V_{CO_2} is CO_2 production in ml/min STPD, a reflection of the metabolic activity of tissues, and V_D/V_T is equal to the tidal volume to dead space ratio.

This equation emphasizes the fact that $PaCO_2$ is determined by the relationship between metabolic rate and ventilation, and not solely by the absolute level of minute ventilation. The bracketed term reflects the fact that not all breathed gas (V_E) is useful for CO_2 exchange; only the fraction $(1-V_D/V_T)$ is effective.

In normal subjects much of the dead space is due to the volume of the conducting airways (anatomic dead space). Since this volume changes little with tidal volume, V_D/V_T tends to decrease as V_T increases and V_D/V_T rarely exceeds 0.3 (i.e. 30% of V_T). In ventilated patients, particularly those with intrinsic lung disease, V_D/V_T can reach extremely high values (e.g. $0.7-0.8$) and deadspace is principally related to ventilated but poorly perfused lung regions (alveolar deadspace). In such cases V_D/V_T need not decrease with an increase in V_T since the higher alveolar pressure required to generate the larger V_T may increase alveolar deadspace (increasing the amount of zone I, see above). Thus, quantitatively, the change in $PaCO_2$ as V_T is increased may not be predictable. The response of PCO_2 to changes in V_E is further confounded by possible effects of changes in ventilator settings on metabolic rate (see above equation). Thus, a patient may become more relaxed (and hence lower VCO_2) or more agitated as ventilator settings are adjusted. Increases in V_D/V_T and VCO_2 should be considered whenever a change in V_E does not result in the expected change in $PaCO_2$ or whenever a large V_E is required to maintain a reasonable $PaCO_2$.

The above equation also emphasizes the effectiveness of accepting a higher $PaCO_2$ (permissive hypercapnia) or of lowering metabolic rate (e.g. by sedation, paralysis) in reducing the required level of ventilation. A lower ventilation is usually associated with lower distending pressures. To the extent that high distending pressures contribute to barotrauma and negative hemodynamic consequences, permissive hypercapnia and reductions in metabolic rate may help reduce the complications of ventilatory support.

3. Thoracic pressures and cardiovascular function. Blood returns to the thorax along a pressure gradient from peripheral vessels to the right atrium (RA). To the extent that intrathoracic pressure affects RA pressure, it may alter the gradient for venous return. Since cardiac output cannot be different from venous return, an increase in intrathoracic pressure will, all else being equal, tend to reduce cardiac output. This effect is enhanced in the presence of hypovolemia.

Right ventricular output can also be affected by changes in RV afterload. The latter is affected in a complex way by lung volume; an increase in lung volume tends to increase the resistance of alveolar vessels while decreasing the resistance of extra alveolar vessels. The net effect on total resistance is unpredictable. Changes in RV afterload can aggravate or minimize the effect of changes in intrathoracic pressure on RA pressure.

Changes in intrathoracic pressure also affect left ventricular function; a higher intrathoracic pressure acts to reduce LV afterload. Where poor LV function is limiting C.O., an increase in thoracic pressure may result in better LV emptying, with secondary consequences on RV afterload (decrease) and venous return (increase). Changes in lung volume may also reflexly affect peripheral vascular tone.

It is clear that effects of changes in ventilator settings on hemodynamics are complex. However, in general, cardiac output is adversely affected by increases in intrathoracic pressure, although the actual response varies.

4. Tissue oxygenation. One of the main objectives of ventilatory support is to insure that tissues are provided with their O_2 requirements. The rate at which O_2 is delivered to the tissues (O_2 delivery, DO_2) is a function of cardiac output (Q_t), Hemoglobin (Hgb) and O_2 Saturation (SaO_2). Thus:

$$DO_2 = 1.39\ Hgb \times SaO_2 \times Q_t + 0.003 \times PaO_2$$

DO_2 represents the theoretical maximum for O_2 consumption by the tissues. In practice, tissues cannot extract all the delivered oxygen. As oxygen delivery is reduced, the tissues are capable of increasing the fraction extracted such that their O_2 needs are met. A point is reached, however, where the fraction of O_2 that can be extracted reaches a maximum level. As O_2 delivery decreases below this critical level, the O_2 needs of the tissues cannot be met. This state (O_2 extracted < amount warranted by metabolic activity) may ultimately result in tissue damage and can, theoretically, account for multisystem failure in critically ill patients.

The critical level of O_2 delivery is related to the metabolic activity of tissues (the higher the activity, the higher the critical DO_2) and to the maximum fraction that tissues can extract from delivered O_2. In disease, metabolic rate (i.e. VO_2) is often high. There is also evidence that in some clinical states (notably sepsis) the maximum fraction that can be extracted is reduced. Both factors tend to raise critical DO_2.

Mechanical ventilation affects two of the main determinants of DO_2, namely SaO_2 and Q_t. Often, ventilator measures that are aimed at increasing one variable cause an opposite change in the other (e.g. PEEP may improve SaO_2, but concomitantly may reduce Q_t). Where maintaining a reasonable PaO_2 (e.g. >60 mmHg) requires PEEP in excess of 10 cmH_2O it is important to consider whether the net effect (after allowing for possible adverse effects on Q_t) is beneficial (i.e. increase in DO_2), whether the remaining benefit, if any, warrants the extra risk of high PEEP or FIO_2, and whether the same improvements in DO_2/VO_2 relation may not be accomplished less dangerously through reduction in metabolic rate or by increasing hemoglobin.

5. Respiratory mechanics. The pressure required to produce a given tidal volume (V_T) in a given time (T_i = inspiratory time) is a function of the elastic and resistive properties of the respiratory system. The elastic properties are defined by the static pressure-volume (P-V) relation. This relation is sigmoidal with the system being most compliant (lowest elastance) in the midvolume range and becoming substantially stiffer near the upper (TLC) and lower volume extremes. Normally, end expiratory volume is at about 40% of vital capacity, and tidal changes in volume occur in the middle, most compliant, range. In ventilated patients the tidal volume may be located near the upper or lower extremes of the P-V curve where the system is naturally stiff. The former situation – V_T encroaching on TLC – occurs under two conditions: 1) when vital capacity is extremely small as a result of severe intrinsic lung disease. Here, the flat portion of the P-V curve might lie within the target V_T. 2) In the presence of high PEEP (external or intrinsic) which increases FRC.

Tidal volume occurs in the stiff range near residual volume (RV) under two conditions: 1) with obesity and abdominal distension which forces end-expiratory volume (the starting position for the next breath) to be in the low range of vital capacity. In this case, the increased stiffness is partially related to chest wall stiffness and partially to alveolar collapse. A variable portion of the applied pressure is, therefore, dissipated across the chest wall and not the lung (i.e. less likelihood of barotrauma for the same distending pressure), 2) when airway or alveolar closure occurs at higher than normal volumes. In this situation, airway closure may occur within the V_T range, and this derecruitment causes the lung to appear stiffer.

When measured compliance [V_T/(plateau pressure minus end-expiratory pressure (total PEEP))] is too low, it is important to ascertain whether this is in part due to the V_T cycling near one of the volume extremes and, if so, whether cycling is occurring near TLC or RV. This has important implications both in terms of identifying the underlying pathophysiology (is the increased stiffness due to structural changes (true stiffness or not) and in defining the ventilator strategy to be used to minimize barotrauma. This distinction can be made with simple manipulations of ventilator output while monitoring airway pressure. One simple approach is to decrease V_T for 1–2 breaths and then assess compliance with the smaller V_T. An increase in compliance as V_T decreases suggests that lung volume is near the stiff upper part of the P-V curve. An unchanged compliance indicates that V_T is cycling in the linear midrange. Conversely, if compliance decreases as V_T is lowered, volume is likely cycling near the stiff lower range of the P-V curve. In this case, addition of PEEP should improve the operating compliance (by raising end expiratory volume towards the more compliant range). This should be helpful, particularly during weaning.

The conventionally measured compliance reflects the elastic properties of both chest wall and lung. A low measured compliance may be due to stiff lungs and/or a stiff chest wall or to a small fraction of the lung being ventilated (e.g. ARDS). Increased lung stiffness is the predominant mechanism with intrinsic lung disease, with auto-PEEP and where there is airway or alveolar closure in the V_T range (see above). Increased chest wall stiffness may be the predominant cause of decreased compliance with primary chest wall disease (e.g. kyphoscoliosis) or where obesity or abdominal distension cause V_T to cycle near RV where the chest wall is naturally stiff (see above). Determination of the contribution of lung and chest wall to decreased compliance is possible only by concurrently (with Paw) estimating pleural pressure using an esophageal catheter. Thus, if Paw during an inspiratory hold is 40 cmH_2O higher than end-expiratory pressure (PEEP) while the corresponding value from pleural pressures (i.e. Ppl during plateau minus Ppl at end expiration) is 30 cmH_2O, then the lung contributes a quarter of the stiffness while the chest wall contributes three quarters, and so on. Where increased lung stiffness is the major reason for decreased compliance, the lung receives the brunt of the distending pressure and, all else being the same, the risk of barotrauma will theoretically, be greater.

The other component to the distending pressure is that related to resistance. In ventilated patients total resistance is made up of two components, endotracheal (ET) tube resistance and resistance of the patient's airways. In many cases ET tube resistance is the major component of total resistance. The resistance of the ET tube is not constant, but increases with flow rate. With the exception of obstructive diseases, the patient's resistance normalized for lung volume (specific resistance) is normally very small. In obstructive diseases, resistance is high and is often volume dependent, being higher at low lung volume. It should be remembered that the measured resistance value is determined by the size of the aerated compartment; thus in ARDS (a condition in which the aerated capacity may be only 1/3 of normal), the measured resistance value may be high, while the specific resistance is normal or low.

Whereas total elastance and total resistance determine the total distending pressure required to attain a given V_T in a given T_i, regional differences in respiratory mechanics can importantly influence the distribution of inhaled volume within the lungs. This may result in some lung regions becoming relatively overdistended even though total V_T may be reasonable. The regional distribution of V_T is affected in a complex way by the under-

lying reason for nonhomogeneity (i.e. regional differences in resistance or compliance), inspiratory time and flow pattern.

The total distending pressure applied at any instant (P_{tot}) is the sum of pressure applied to overcome elastic recoil (P_{el}, a function of volume above passive FRC and the P-V curve), and the pressure applied to overcome resistive elements (P_{res}, a function of flow rate and resistance):

$$P_{tot} = P_{el} + P_{res}$$

In paralyzed or apneic patients P_{tot} is entirely supplied by the ventilator and $P_{aw} = P_{tot}$. When the elastic and resistive properties are known, P_{tot} can be estimated. Any difference between P_{aw} and P_{tot} is a reflection of the pressure generated by the patient. This approach can thus be utilized to assess the extent of patient effort and, hence, adequacy of ventilatory support.

6. Dynamic hyperinflation and auto-PEEP. Dynamic hyperinflation (DH) is defined as failure of lung volume to return to passive FRC (volume at which elastic recoil equals external PEEP) prior to the onset of the next inspiration. Whenever this happens, alveolar pressure remains higher than external PEEP throughout expiration, and unless airways completely collapse, expiratory flow continues until the onset of the next inspiration.

Auto-PEEP is the difference between alveolar pressure and external airway pressure at end expiration. A difference (i.e. auto-PEEP) will always exist whenever expiratory flow continues until the end of expiration (this is the gradient for flow). In the passive patient such a gradient can only result from dynamic hyperinflation since alveolar pressure in this case reflects only passive elastic recoil; a gradient thus means lung volume did not return to passive FRC. In the patient with active expiratory muscles, alveolar pressure is also affected by the pressure generated by expiratory muscles. A gradient (auto-PEEP) can therefore exist even though volume is at, or even below, passive FRC. Auto-PEEP in the active patient does not necessarily signify the presence of dynamic hyperinflation and its magnitude is not an index of the magnitude of dynamic hyperinflation. This is important to recognize, since the physiologic consequences and management of auto-PEEP due to dynamic hyperinflation and to expiratory activity differ (see below). Expiratory muscle activity frequently exists in the presence of high respiratory drive and/or high expiratory resistance.

Dynamic hyperinflation develops in the setting of high expiratory resistance or expiratory flow limitation and is influenced by the compliance of the respiratory system, the volume from which exhalation begins and the expiratory time. In ventilated patients the delay in emptying may be patient related (obstructive diseases) or, very commonly, may be due to "plumbing" problems (narrow ET tube, kinking or water clogging of exhalation tube, poor exhalation valve... etc.). Measurement of airway pressure (P_{aw}) during expiration helps to distinguish between problems intrinsic in the patient and ET tube, from problems within the external circuit (high P_{aw} during exhalation points to the latter causes).

Auto-PEEP (dynamic hyperinflation, air trapping, intrinsic PEEP) has been described in many conditions (e.g., COPD, Asthma, ARDS) and can occur whenever minute ventilation is relatively high. Dynamic hyperinflation most commonly occurs, however, in the setting of severe airflow obstruction. Here, the ventilation requirements may be modest, but expiratory resistance is often several fold greater than its inspiratory counterpart.

The consequence of dynamic hyperinflation are related to the associated changes in lung volume and pleural pressure. 1) It causes tidal volume to cycle closer to TLC where compliance is low (see above). More distending pressure is required to attain the same V_T. 2) It interferes with triggering in the AMV or pressure support modes; the patient has to generate enough pressure to offset auto-PEEP plus trigger sensitivity before triggering occurs. 3) Because of 1 and 2, it increases the work of breathing during weaning attempts. 4) It affects hemodynamics in a manner similar to external PEEP and 5) it can cause overestimation of the pressure difference required for tidal ventilation and subsequent underestimation of the true compliance of the respiratory system.

Auto-PEEP in the absence of dynamic hyperinflation (i.e. end expiratory lung volume at or below passive FRC) does not cause tidal volume to cycle near TLC (in fact it may have an opposite effect by reducing end-expiratory lung volume below passive FRC), has little effect on triggering, does not increase work of inspiratory muscles (in fact it may spare inspiratory muscle work through sharing of total work between inspiratory and expiratory muscles), and does not result in underestimation of true compliance. In fact, where volume begins below passive FRC due to of expiratory muscle activity the opposite (over estimation of compliance) may occur. Administration of external PEEP under these circumstances serves no purpose and may make it more difficult for expiratory muscles to reduce lung volume.

In the passive state, and for a given degree of expiratory obstruction the two variables that are most critical in determining extent of dynamic hyperinflation (DH) are total minute ventilation (V_E) and the I:E. A higher V_E will cause more DH whether the high V_E is the result of a large V_T or high expiratory frequency (f). In the former case (larger V_T) more time is required to return lung volume to the passive FRC, whereas in the latter case (high f), less time is available to empty the same V_T. It is for this reason that reduction in V_E (through permissive hypercapnia or reduction in ventilatory demand) is one of the most effective ways of reducing DH. At a given f, the I:E ratio determines the time for delivery of the V_T. Higher values tend to increase auto-PEEP.

Measurement: Auto-PEEP should be suspected in all patients with airways obstruction or whenever the flow tracing demonstrates persistent flow at end exhalation. During *passive* ventilation (patient is not making respiratory efforts) auto-PEEP can be measured by comparing the end-expiratory airway occlusion pressure (easily measured in only a few currently available ventilators) with the set level of PEEP or by observing the amount of positive airway pressure required to initiate inspiratory flow.

A helpful method for executing end-expiratory port occlusion in the passive patient uses the ventilator's inflation onset as the timing mechanism with a Braschi valve. Auto-PEEP can also be measured using plateau pressures. Operationally, plateau pressure is first recorded during a single cycle of volume controlled ventilation at the usual ventilating frequency. (To avoid further hyperinflation, the end-inspiratory pause should not be applied for more than a single cycle.) Inflation is then prevented for approximately 20 s by a marked reduction in frequency, after which a single end-inspiratory plateau pressure is remeasured. The difference in plateau pressures is auto-PEEP.

Another similar method is first to measure the additional (dynamically trapped) volume released when a single routine tidal inflation is delayed by 20–30 s, and then to divide the measured trapped volume by respiratory system compliance. Under passive conditions, compliance is perhaps best judged by dividing the difference in static end-inspiratory ("plateau") pressures observed at two distinctly different tidal volumes into that volume difference. This, however, is valid only if compliance is constant throughout V_T (i.e. V_T is fully within the linear segment of the P-V curve).

In a passively ventilated patient, the effect of PEEP on lung and chest volumes can be accurately assessed by observing the peak dynamic or static airway pressures. Failure of these pressures to rise in response to adding PEEP indicates dynamic airway compression, flow limitation and potential benefit to the addition of PEEP.

Finally, when auto-PEEP results from dynamic airway compression, the least PEEP increment required to evoke a detectable increase in lung volume or peak cycling pressure is sometimes considered to be the pressure required to counterbalance the original level of auto-PEEP. This technique is invalid, however, when expiration is not flow limited (i.e. when DH is due to a simple increase in resistance and not to flow limitation). Moreover, the applied pressure needed to counterbalance the "critical" pressure approximates only 75%–85% of the auto-PEEP determined by expiratory port occlusion.

In patients with active respiratory efforts (i.e. assist mode, PSV etc.) auto-PEEP can not easily be approximated by the end-expiratory occlusion, since expiratory muscle activity can influence the measured value. It can also be estimated as the esophageal pressure deflection required to initiate inspiration, or to terminate expiratory flow. Interestingly, auto-PEEP estimated by this method is usually less than that measured by end-expiratory port occlusion. Although the reason for this disparity remains unclear, it has been argued that gas begins to flow into the lung when auto-PEEP in the least affected units has been overcome.

As indicated above, the auto-PEEP measured in patients with active respiratory efforts need not reflect dynamic hyperinflation. There are currently no accepted methods of assessing the extent of dynamic hyperinflation in patients with active respiratory efforts. The use of external PEEP in these cases should be based more on clinical response to graded external PEEP (i.e. more or less distress) than on the measured value of auto-PEEP.

7. Respiratory muscle output and endurance: Laboratory studies have shown that inspiratory muscles fatigue when forced to generate pressures in excess of critical levels [35]. The critical pressure output above which fatigue occurs is a function of inspiratory muscle strength (e.g. maximum inspiratory pressure, MIP). It is not clear whether fatigue occurs outside the laboratory setting, where inspiratory muscle output is spontaneously selected by the patient and not imposed (as in the laboratory). Nonetheless, the laboratory results point out the limited capacity of inspiratory muscles to sustain relatively high pressure outputs.

It is very difficult to assess the potential for fatigue in the ventilated patient. Whereas actual muscle output can be estimated, through measurement of work of breathing the pressure generated by muscle contraction or P_{mus} (see above), the denominator (maximum possible output) is difficult to determine. Furthermore, the critical fractions developed in the laboratory (e.g. tension-time index >0.15) need not apply in the critically ill patient. So far, the best indication of whether the patient's muscles are overstressed remains the clinical impression of respiratory distress.

8. Control of breathing. There is tremendous interindividual variability in the level of ventilation desired by patients (i.e. ventilatory demand). The range extends from a few l/min (as in patients with chronic CO_2 retention) to >30 l/min (e.g. in sepsis). High levels of ventilatory demand are related to high metabolic rate (muscle activity, fever), excessive V_D/V_T, or to a lower CO_2 set point where the patient targets a subnormal PCO_2 (metabolic acidosis, neural reflexes, central problems). In the presence of high V_E demand, high V_E output by the ventilator is required in order for the patient to feel comfortable. In turn, high V_E output by the ventilator translates into greater distending pressure (more volume and flow) and greater tendency for auto-PEEP. In patients with high ventilatory demands, every effort should be made to identify the mechanism and, if possible, correct it. Should the distending pressures required to maintain comfort remain excessive, forced reduction in ventilatory drive through sedation and, if necessary, paralysis (to reduce metabolic rate) may be appropriate. At present, there are insufficient data to indicate the precise pressures (or volumes) that must be avoided (see complications, Section V-B).

B. Ventilator-related physiologic principles

During spontaneous unassisted breathing, contraction of the diaphragm and other accessory muscles of inspiration results in a decrease in intrathoracic pressure, followed by a corresponding decrease in alveolar and airway pressures. These decreased pressures cause an increase in thoracic volume and the movement of a tidal volume into the lungs. Relaxation of ventilatory muscles returns these pressures and volumes to their resting levels. That is, the elastic recoil of the thoracic cage and of the lung increases intrathoracic pressure, causing an increase in alveolar and airway pressure, allowing exhalation of the tidal volume. During mechanical ventilatory assistance the

magnitude and the direction of these pressures may be grossly altered with potential adverse effects as outlined elsewhere in this text. As a result, the appropriate selection of gas delivery settings and monitoring of system pressures is important.

1. Ventilator settings

(i) Volume. In volume-targeted (i.e. volume cycled) ventilation, a machine-delivered tidal volume is set to be consistent with adequate gas exchange and patient comfort. The tidal volume selected in adults normally varies from about 5 to 15 ml/kg of body weight [36, 37]. Numerous factors: lung/thorax compliance, system resistance, compressible volume loss, oxygenation, ventilation, and barotrauma are considered when volumes are selected [36]. Of critical importance is the avoidance of localized overdistension [38]. This can generally be accomplished by selecting tidal volumes that remain on the steep aspect of the pressure/volume curve of the patient/ventilator system and by ensuring that peak airway and alveolar pressures do not exceed a maximum target [37, 39]. Although controversy exists regarding specific target levels, many would agree that with a peak alveolar pressure greater than 35 cmH_2O raises concern regarding the development of barotrauma and ventilator-induced lung injury increases [37, 40]. With pressure-targeted (in pressure limited) ventilation, delivered tidal volume varies depending upon target pressure selected, system impedance and the patient's spontaneous ventilatory pattern.

(ii) Respiratory rate. Setting of mandatory ventilator gas delivery rate is dependent upon the mode of ventilation selected, the delivered tidal volume, dead space to tidal volume ratio, metabolic rate, target $PaCO_2$ level, and level of spontaneous ventilation [36]. With adults, set mandatory rate normally varies between 4 and 20/min, with most clinically stable patients requiring mandatory rates in the 8 to 12/min range [36] in patients with either acute or chronic restrictive lung disease, mandatory rates exceeding 20/min may be necessary, depending upon desired minute ventilation and the targeted $PaCO_2$. Along with $PaCO_2$, pH, and comfort, the primary variable controlling the selection of mandatory rate is the development of airtrapping and auto-PEEP [22]. As with the selection of most ventilator settings, development of airtrapping should be avoided because of its effect on V/Q matching, work of breathing, and barotrauma [22, 41].

(iii) Flow rate. The selection of peak inspiratory flow rate during volume-targeted ventilation is primarily determined by the level of spontaneous inspiratory effort. In patients triggering volume-targeted breaths, patient effort, work of breathing, and patient ventilator synchrony depends on the selection of peak inspiratory flow [42]. Peak inspiratory flows should ideally match patient peak inspiratory demands. This normally requires peak flows to be set at 40 to 100 l/min, depending on V_E and drive to breathe. During controlled ventilation, peak flows may be set lower than 40 lpm in order to establish a specific inspiratory time. With pressure-targeted ventilation the peak inspiratory flow is determined by the interaction of the set pressure, respiratory resistance and patient effort. The specifics of how *quickly* the pressure target is reached is defined by the manufacturer.

(iv) Inspiratory time/I:E. The selection of a specific inspiratory time and I:E is generally based on hemodynamic response to ventilation, oxygenation status and level of spontaneous breathing. In spontaneously breathing patients gas delivery should be coordinated with patient inspiratory effort to ensure synchrony. This normally requires an inspiratory time of about 0.8 to 1.2 s and an I:E of about 1:2 to 1:1.5 [43]. During controlled mechanical ventilation, inspiratory time or I:E may be lengthened in order to elevate mean airway pressure and enhance oxygenation [44]. When lengthening inspiratory time and I:E, the impact of these alterations on the cardiovascular system must be carefully monitored. The primary factors limiting increases in both inspiratory time and I:E are patient discomfort, the need for sedation, the development of auto-PEEP and hemodynamic comprise [44].

(v) Flow profile. Few data identifying differing physiologic responses to inspiratory flow profiles are available when adjusted for the same tidal volume and T_I/T_{TOT} [45, 46]. Essentially no differences exist between square, decelerating and sine wave delivery profiles in terms of gas exchange or work of breathing, and these approaches appear to be equally acceptable in the majority of patients requiring ventilatory support, provided that the mean flow rate is adequate. No data supporting the use of an accelerating flow pattern are currently available. Selection of flow profile is only available in volume-targeted approaches to ventilation. With all pressure-targeted modes, an exponentially decelerating pattern is normally established as the ventilator attempts to rapidly achieve the pressure target set and to maintain the target constant throughout the inspiratory phase.

(vi) Sensitivity. Since mechanicial ventilators and artifical airways impose a resistive load on the spontaneously breathing ventilator-assisted patient, ventilator-trigger sensitivity should be set at the most sensitive level that prevents self-cycling. Generally, this is -0.5 to -1.5 cmH_2O. Recently introduced flow cycling systems are generally more efficient than pressure cycling approaches but the clinical significance of this is unclear [2, 47]. These systems should also be set at maximum sensitivity (1 to 3 l/min).

(vii) FIO_2. The selection of the FIO_2 is dependent on the target PaO_2, PEEP level, mean airway pressure (MAP), and hemodynamic status. In general, as a result of concerns regarding the effect of high FIO_2's on lung injury, the lowest acceptable FIO_2 should be selected. However, the effect of FIO_2 on lung injury must be balanced by the effect of airway and alveolar pressures on lung injury. In those patients who are most difficult to oxygenate, FIO_2 can be minimized by optimizing PEEP and MAP, by deep sedation with or without pharmacological paral-

ysis, and by lowering the minimally acceptable SaO_2 to $<90\%$ while ensuring adequate cardiac output [48].

(viii) PEEP. Positive end-expiratory pressure (continuous positive airway pressure) is applied to recruit lung volume, elevate mean airway pressure, and improve oxygenation [49]. PEEP may decrease venous return and preload of the left ventricle [50], as well as decreasing the triggering work of breathing caused by auto-PEEP [41]. The optimal level of PEEP depends on the desired physiologic response. In ARDS, PEEP level is established in conjunction with FIO_2 and inspiratory time settings to establish a target PaO_2 (SaO_2) or O_2 delivery. Although it is difficult to identify an upper limit for PEEP in this setting, most would agree that the lower limit should be at or above the lower inflection point on the pressure/volume curve in the early phase of acute lung injury [51]. This is generally a PEEP level of about $8-12\ cmH_2O$. As with any pressure, avoidance of high PEEP levels is desirable.

2. Pressure measurements

During the delivery of a positive pressure breath, system pressure can be measured in a number of locations (internal to the ventilator, at the airway opening, and at the carina). The farther away the measurement is from the alveoli, the greater the possible difference from actual alveolar pressure. During patient triggering, alveolar pressure is more negative than carinal pressure, which is more negative than airway opening pressures, which are more negative then internal ventilator pressures [52]. Because of resistance to gas flow during a positive pressure breath, pressure measured internal to the ventilator is greater than airway opening pressure, which is greater than carinal pressure, which is greater than alveolar pressure [52]. Pressure measured at all of these locations is only equal during periods of zero flow.

(i) Peak. Peak pressure is the maximum pressure obtainable during active gas delivery. In volume-targeted ventilation, peak pressure is dependent upon both compliance and airways resistance, as well as tidal volume, peak flow and flow pattern. For a given compliance and airway resistance, higher peak flow results in higher peak airway pressure. Generally, with all other variables equal, an accelerating flow profile results in a higher peak airway pressure than any other profile, since the highest flows are delivered with this pattern at end inspiration. With pressure-targeted ventilation, the peak inspiratory pressure is approximately equal to the target pressure. However, because of the high initial flow and the decelerating flow pattern in pressure-targeted ventilation, the initial system pressure may exceed the pressure target by about $1-3\ cmH_2O$.

(ii) Plateau. This is normally defined as the end-inspiratory pressure during a period of at least 0.5 s of zero gas flow [43]. It should be measured on the first breath after the setting of an inflation hold and requires passive ventilation. The plateau pressure is the pressure required to counterbalance end-inspiratory forces and roughly approximates the average peak alveolar pressure. With pressure-targeted ventilation, the pressure target approximates to the plateau (alveolar) pressure if a period (0.5 s) of zero delivered gas flow is observable.

(iii) Mean. The system pressure averaged over the entire ventilatory period is defined as the mean airway pressure. Because expiratory resistance usually exceeds inspiratory resistance [53], mean airway pressure as displayed on monitoring devices almost always underestimates mean alveolar pressure to some extent (MalvP) [44]. MalvP can be estimated from the mean airway pressure (MAP) by the following formula:

$$MalvP = (V_E/60)(R_E - R_I) + MAP$$

where R_I and R_E are inspiratory and expiratory resistances respectively. Provided sufficient PEEP is applied to seek out recruitable lung units, oxygenation and MAP demonstrate a predictable and quantifiable direct relationship [44].

(iv) End-expiratory. This is the airway pressure at the termination of the expiratory phase, normally equal to atmospheric or the applied PEEP level. However, in patients with prolonged inspiration or short expiratory times, end-expiratory alveolar pressure may be further elevated as a result of the development of auto-PEEP. Alveolar and airway pressures are not the same unless periods of no-flow are established. That is, end-inspiratory airway pressure normally exceeds alveolar pressure because of resistance to gas flow, whereas end-expiratory alveolar pressure may exceed airway pressure because of the development of auto-PEEP and MalvP always exceeds MPA.

3. Machine problems

(i) Demand valves. In all assisted modes of ventilation, the patient must activate gas delivery. This requires a pressure differential sufficient to trigger the ventilator. Once triggering occurs, sufficient gas flow must be provided to meet inspiratory demand. Both of these processes impose work on the patient. The amount of effort required to activate any given ventilator varies greatly and is generally greater with pressure-triggering than flow-triggering [54]. The addition of PEEP or CPAP may increase imposed work because of the adjustments the ventilator must make to maintain PEEP/CPAP during spontaneous breathing [55]. Although the work imposed by these systems is generally minimal, total imposed work of breathing can be significant when demand valves are considered in series with the work imposed by endotracheal tubes and humidifier systems.

(ii) Humidifiers. Three different types of humidifiers are used during mechanical ventilation: bubble-through, passover, and artificial noses. Of these, the passover humidifier is the only one that does not have the potential to impose added work of breathing. Bubble-through humidifiers have minimal effect on imposed work of

breathing if the machine sensing of patient effort is on the expiratory side of the circuit or at the circuit "Y". However, if patient effort is sensed on the inspiratory side, imposed work of breathing may be markedly increased because of the need to create a pressure gradient across the humidifier [55]. Artificial noses represent a resistance load placed in series with the endotracheal tube and demand valve [24]. Their effect on work of breathing is dependent on length of use, patient ventilatory drive and design of the valve [56]. In general, artificial noses should not be used in patients with marked ventilatory muscle dysfunction, particularly if small-sized endotracheal tubes are used and if the development of auto-PEEP is an ongoing issue. Regardless of humidifier used, it should be able to establish at the carina a temperature of 30–32 °C with an absolute humidity of 30 mg/ml [57].

(iii) Apnea ventilation. Many ventilators do not incorporate back-up apnea ventilation during pressure support or CPAP breathing. As a result, careful setting of low respiratory rate, low tidal volume, and low minute volume alarms are critical for the safe application of these modes of ventilation. In ventilators where apnea ventilation is available, apnea of definable time periods results in the provision of a backup control mode volume-targeted approach to ventilation. Resumption of spontaneous breathing or practitioner intervention restablishes the original ventilatory mode.

C. Patient-ventilator interactions

The use of a mechanical ventilator often superimposse a clinician-selected pattern of ventilation on the patient's natural breathing rhythm. Under these circumstances, certain interactions between patient and ventilator will occur. These fall into two categories: a) the response of the mechanical breath delivery system to patient efforts, and b) the response of patient efforts to ventilator settings.

1. Response of the breath delivery system to patient efforts

If the ventilatory demands of the patient do not coincide with the quantity (or quality) of ventilation provided by the ventilator, patient-ventilator dys-synchrony can impose an inspiratory muscle load. This, in turn, leads to increased oxygen consumption of the respiratory muscles and patient discomfort which is diagnosed as the patient "fighting" the ventilator. This detrimental patient-ventilator interaction may be due to the patient's "inappropriately" high ventilatory drive or to inappropriate ventilator settings or circuits. If the clinician determines that this problem is due to "inappropriate" patient demands, it may be appropriate to use sedation or paralysis to eliminate patient respiratory effort. Conversely, the problem may relate to the ventilatory mode or ventilator setup being used. These detrimental interactions between patient and ventilator can occur during any of the following phases of breath delivery.

(i) Triggering. Triggering is the initiation of gas delivery. Significant imposed ventilatory muscle loads can be imposed by insensitive or unresponsive triggering [54, 58] systems. In addition, the presence of auto-PEEP [41, 59], narrow endotracheal tubes [60], obstructed airways and stiff parenchyma [81] will serve to magnify the insensitivity or unresponsiveness of the triggering system. Attempts to maximize trigger sensitivity and responsiveness through demand valve adjustments or through the counter-balancing of auto-PEEP with applied PEEP are appropriate. Unfortunately, over-sensitive valves can result in spontaneous ventilator cycling independent of patient effort.

(ii) Gas delivery. Gas flow from the ventilator is governed (or limited) by a set flow (flow limited) or set pressure (pressure limited) on most ventilators [62]. Any patient effort during flow limited breaths will only result in a decrease in airway pressure since additional flow above what is set is not available [63, 64]. This can produce a significant imposed load on the ventilatory muscles. In contrast, any patient effort during a pressure limited breath will result in an increase in flow but no change in airway pressure [65, 66]. A patient's flow demands are thus theoretically more readily met by a pressure limited breath strategy [61, 65]. The capability of adjusting the rate of rise of airway pressure during pressure limited breaths further enhances control of this variable [67, 68].

(iii) Cycling. On current systems, gas delivery can be terminated by set volume, set time or set flow [62]. With volume or time cycling, continued patient effort is ignored by the machine and this can lead to the patient pulling against a closed inspiratory flow valve. Conversely, active expiratory efforts by the patient with volume or time cycling results in elevation in airway pressure which can result in automatic breath termination in association with a high pressure alarm limit. Flow cycling gives the patient more control than breath cycling [62, 65, 66]. Usually flow cycling is set to occur at 25% of peak flow. Increasing patient effort can thus delay cycling such that more gas is delivered. Conversely, decreasing efforts (or even initiation of expiratory efforts) cause these flow criteria to be met earlier and thus a smaller volume of gas is delivered over a shorter period. Synchrony between end of patient effort and end of pressure limiting is, however, not assured even with flow cycling [66]. Depending on the strength of patient efforts vs. set pressure, on respiratory mechanics, and on the flow level at which cycling occurs, pressure may continue beyond the patient's inspiratory effort (thereby interfering with expiration) or may terminate prematurely before the end of the patient effort.

2. Response of patient efforts to ventilator settings

Ventilator settings, such as V_T, flow rate, and pattern with flow-limited volume-cycled breaths; or the pressure level and rate of pressure rise with pressure limited breaths are capable of a) altering the activity of mechanoreceptors in the airways, lungs and chest wall, b) altering blood gas tensions and c) eliciting respiratory sensation in

conscious or semiconscious patients [65, 69]. In turn these can alter the rate, depth and timing (T_i, T_e) of respiratory efforts through neural reflexes, chemical control (chemoreceptors) and behavioral responses. These changes in patient effort may modify expected responses to changes in ventilator settings. These modifications may take several forms including a) failure of V_E or V_T to change in the expected direction or to the expected magnitude as ventilator settings are changed to increase or decrease these variables, b) periodic breathing, with periods of apnea, as PCO_2 cycles around the CO_2 set point, c) loss of synchrony between patient and ventilator, d) changes in ventilatory demand (increase or decrease) as a result of altered level of consciousness (following a change in ventilator settings), or of changes in mechanoreceptor output (acting via reflex or behavioral mechanisms). There are very few systematic studies on the effect of various changes in ventilator settings on pattern of patient effort. This information is needed particularly with the current shift in emphasis from controlled ventilation methods to patient-interactive methods (e.g. PSV).

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