Monitoring the Mechanically Ventilated Patient

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The general purpose of monitoring is simple and clear—to follow in real time specific physiological values that can change rapidly and alter the patient’s clinical status. Especially in the intensive care setting, in which the vast majority of patients are admitted because of a primary respiratory problem or of respiratory complications during their illness, monitoring of the cardiorespiratory system alerts the clinician to sudden untoward events, aids in diagnosis, helps manage diagnosis, facilitates prognosis, and enables assessment of therapeutic response. Monitoring techniques can be classified into those pertaining to the output of the ventilatory process and those that characterize the load and capacity of the respiratory system \cite{1,2}.

Monitoring gas exchange

Arterial blood gas analysis

Analysis of the arterial blood gases provides data that are fundamental to the diagnosis of respiratory and metabolic disturbances and to assessing the effect of therapeutic interventions.

Arterial $O_2$ tension and saturation

The physiologic significance of hypoxemia depends on chronicity, compensatory mechanisms, hypoxic ventilatory response, and the tolerance of the vital organs most at risk, such as the heart and the brain. So, while some patients must be kept as fully saturated as feasible, maintaining less than full saturation may be appropriate for patients who are exposed chronically to moderate hypoxemia or in whom full $O_2$ saturation can be achieved.
only at the expense of high airway pressures or elevated fractions of inspired oxygen. In the absence of carbon monoxide, methemoglobin, or abnormal hemoglobin, arterial O$_2$ saturation can be estimated with acceptable accuracy from the PaO$_2$ and pH alone. If the arterial O$_2$ content is required, or if carboxyhemoglobin or methemoglobin concentrations are high, direct analysis by co-oxymetry must be requested. When obtaining blood samples for arterial blood oxygen tension (PaO$_2$), 15 minutes should elapse to allow equilibration after an increment in inspired oxygen fraction content. In contrast, because of the body’s acid-base buffering systems, arterial CO$_2$ concentrations respond exponentially after step changes in ventilation, with a half-time of more than 3 minutes during hyperventilation and a slower 16-minute half-time during CO$_2$ accumulation.

**Acid-base status, pH, and PaCO$_2$**

Normally, acids are generated by the hydration of CO$_2$ (respiratory acid) and by other processes of metabolism (metabolic acids). In disease states, hydrogen ion concentration can rise secondary to the production of excess lactate, generation of ketoacids, ingestion of certain types of alcohol or drugs, or failure of the body to excrete or metabolize the generated load of hydrogen ion. The body defends against radical changes in pH primarily by regulating its two pathways for eliminating acid: respiratory and renal. The Henderson-Hasselbach equation for the bicarbonate buffer system relates pH to the concentrations of bicarbonate and PaCO$_2$:

$$\text{pH} = 6.1 + \log \left\{ \frac{\text{HCO}_3^-}{(0.03 \text{ PaCO}_2)} \right\}$$

In this expression, knowledge of PaCO$_2$ (lung excreted) and pH (measured) enables the calculation of the HCO$_3^-$ (kidney excreted). Hydrogen ions are neutralized partially by combining with bicarbonate ion (producing CO$_2$) and by reversible oxidation of protein. The bicarbonate buffer system:

$$\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$$

generates CO$_2$ when H$^+$ is added to the extra cellular fluid. Rising CO$_2$ and H$^+$ concentrations stimulate the respiratory center, effectively eliminating H$^+$ by driving the preceding equation leftward as CO$_2$ is eliminated. Several days later, the healthy kidney will adapt to hypercapnia or hypocapnia by adjusting the bicarbonate level to help restore the normal ratio between bicarbonate concentration and PaCO$_2$. Respiratory compensation for metabolic disturbances is generally incomplete and occurs more reliably and vigorously in response to metabolic acidosis than alkalosis. The bicarbonate buffer system is not the only one available, as skeletal calcium and certain proteins, chiefly hemoglobin, play a significant role.

The normal ranges are, for arterial pH: 7.38 to 7.44 and for arterial PaCO$_2$: 35 to 45 mm Hg. Acidosis and alkalosis may be pathogenic or
compensatory. A pH less than 7.35 indicates acidemia, caused by metabolic or renal depletion of bicarbonate, hypoventilation relative to metabolic need, or both. Mixed venous gases, representing an admixture from tissues throughout the body, generally have a PaCO₂ that is 4 to 8 mm Hg higher and a pH that is 0.05 to 0.10 units lower than the arterial value.

The information available from ABG analysis allows the clinicians to determine pH and the relative contributions of respiratory and metabolic mechanisms. Because compensation is virtually never complete, the dominant underlying mechanism—acidosis or alkalosis—is suggested by the pH. Intensive care unit (ICU) clinicians must be alert for “triple” acid-base disorders in which two metabolic derangements with opposing influences on pH are in play. The anion gap calculation usually aids in the appropriate interpretation.

The anion gap, the difference between the serum sodium concentration and the sum of chloride and the bicarbonate ions, is normally is 13 mEq or less. Because the serum proteins are anions, the calculated gap should be increased by approximately 2.0 to 2.5 mEq/L for each g/dL of hypoalbuminemia. Another useful bedside computation is the “Δ/Δ,” the ratio of the anion gap to bicarbonate gap. As lactic acidosis develops, the anion gap increases relatively more than the HCO₃⁻ falls because the HCO₃⁻ has a wider volume of distribution. The ratio varies, but averages approximately 1.5 in moderate lactic acidosis—less if the acuity is extreme and more as the severity worsens.

Monitoring oxygenation

The human eye is not very good at detecting or quantifying arterial hypoxemia. Perhaps the most popular recent innovation in gas exchange monitoring has been the application of oximetry to the online assessment of arterial (SaO₂) and mixed venous O₂ saturations (SvO₂). PaO₂ reflects the maximal tension driving O₂ to the tissues, whereas saturation reflects O₂ content per gram of hemoglobin. Reflectance oximetry is used when a fiber-optic catheter continuously samples oxygen saturation in the pulmonary or systemic arterial bloodstream.

Arterial pulse oximetry

For patients supported by mechanical ventilation, transcutaneous pulse oximetry continuously measures SaO₂, enabling rapid adjustment of FiO₂, mean airway pressure and positive end-expiratory pressure (PEEP) and warning of arterial desaturation during weaning, sleeping, or changes of body position. Trends in oximetry values hold greater significance than the absolute value of O₂ saturation.

Pulse oximetry probes consist of a photo detector and two light-emitting diodes [3–5]. Probes are most frequently placed on fingers, ear lobes, nasal bridge, or forehead. The relative absorption of these spectrophotometric beams as they pass through the tissue (which differs for O₂ saturated and
desaturated blood) is converted into the appropriate saturation value by computer-stored algorithms. Phasic variations in tissue volume separate the incoming arterial component from venous and background absorption. Most units display pulse rate, and many display a simulated arterial waveform or other visual indicator of pulse intensity. A tracing with a waveform that varies dramatically with ventilation strongly suggests variation of stroke output synchronous with respiratory cycle—a condition typical for gas trapping and auto-PEEP. The pulse rate should be correlated to the ECG measured rate to assess signal quality. With a good pulse signal, pulse oximeters are quite accurate in their upper range (saturations >80%) but become less reliable as the patient desaturates or perfusion deteriorates [6,7]. Chaotic pulse rhythms (eg, atrial fibrillation) have unpredictable effects on the display values [8,9]. A direct determination of arterial blood saturation (preferably by co-oximetry) is the most definitive check of accuracy. Interpretation of pulse oximetry readings must account for a variety of factors that may artifactually influence the results. Common sources of artifact include inappropriate probe placement, motion artifact, ambient light, and electromagnetic radiation. Even if the device is functioning properly and is free from external interference, the results should be interpreted with particular caution in the presence of abnormal hemoglobin, nail polish, deeply pigmented skin, hypo perfusion, anemia, venous congestion, or tricuspid regurgitation or when certain vital dyes are used. It is important to fully understand the oxyhemoglobin dissociation relationship curve that is highly nonlinear (Fig. 1). A drop of a few percentage points in SaO₂ over the 95% to 100% interval reflects a much larger change in PaO₂ than does a similar decrement over the 80% to 85% interval. Other gas-measuring techniques (transcutaneous and transconjunctival measurements of O₂ and CO₂) have been used in recent years, but require frequent calibration, excellent skin and electrode preparation to ensure gas transfer to the skin surface, and regular site changes [10,11]. The validity of tissue oxygen saturation monitoring has yet to be verified in critically ill patients.

**O₂ consumption**

Oxygen consumption may be helpful when determining nutritional requirements as well as the severity of shock. Assuming a stable tissue need for oxygen, measurements of VO₂ may help to gauge the hemodynamic response to therapeutic measurements. The total body oxygen consumption (VO₂) is often difficult to measure accurately at the bedside. Two primary methods are in general use: direct analysis of inspired and expired gases and the Fick method (computation of VO₂ from the product of cardiac output [CO] and the difference in O₂ content between samples of arterial and mixed venous blood). Neither method reflects average oxygen consumption when the patient’s metabolic rate fluctuates during data collection. Unfortunately, VO₂ measurements are not highly reproducible, so their differences are unreliable in assessing breathing effort associated with an imposed or
relieved ventilatory stress, particularly when the patient inspired a high fraction of oxygen.

Efficiency of oxygen exchange

The ideal $P_{A}O_2$ is obtained from the modified alveolar gas equation:

$$P_{A}O_2 = P_tO_2 - (PaCO_2/R) + [(PaCO_2 \times FiO_2 \times (1 - R)/R)]$$

Here $R$ is the respiratory exchange ratio (which normally varies from about 0.7 to 1.0) and the $P_tO_2$ is the inspired oxygen tension.

At sea level with a normally ventilated patient breathing room air, the alveolar gas equation can be simplified to:

$$P_{A}O_2 = 0.21 \times (760 - 47) - 1.25 \times (PaCO_2) \sim 100 \text{ mm Hg}$$

The difference between alveolar and arterial oxygen tensions, $P(A-a)O_2$, takes account of alveolar CO$_2$ tension and therefore eliminates hypercapnia.

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Fig. 1. Relationship of blood oxygen saturation (SaO$_2$) to blood oxygen tension (PaO$_2$) with the normal curve having a sigmoidal shape. The upper plateau of the relationship (90% saturation) reached at a PaO$_2$ of approximately 55 to 60 mm Hg.
from consideration as the sole cause of hypoxemia. The $P(A-a)O_2$ ranges from $\sim 10$ mm Hg (on room air) to $\sim 100$ mm Hg (on $FiO_2$ of 1.0), and changes nonlinearly with respect to $FiO_2$ as the extent of $V/Q$ mismatch increases. Finally, the $P(A-a)O_2$ may be influenced by fluctuations in venous oxygen content. The $O_2$ content of mixed venous blood ($SvO_2$) exerts an increasingly important effect on $SaO_2$, as ventilation/perfusion inequality or shunting develop [12–14]. Online measurements of $SvO_2$ with a fiber-optic Swan-Ganz catheter enable venous admixture ($Qs/Qt$) to be computed with relative ease. In the steady state:

$$Qs/Qt = (C_{A}O_2 - CaO_2)/(C_{A}O_2 - CvO_2)$$

where the oxygen content of alveolar capillary blood ($C_{A}O_2$), arterial blood ($CaO_2$), or mixed venous blood ($CvO_2$), are expressed in mL of $O_2$ per 100 mL of blood. Like $P(A-a)O_2$, the $Qs/Qt$ is also influenced by variations in $V/Q$ mismatching and by fluctuations in $SvO_2$ and $FiO_2$. If $Qs/Qt$ is abnormally high but all alveoli are patent, calculated admixture will diminish toward the normal physiologic value ($\sim 5\%$) as $FiO_2$ increases. Conversely, if the $Qs/Qt$ abnormality results from blood bypassing patent alveoli through intrapulmonary communications or through an intracardiac defect, there will be no change in $Qs/Qt$, as $FiO_2$ increases (true shunt).

Several pragmatic approaches have been taken to simplify bedside assessment of $O_2$ exchange efficiency. The first is to quantify $P(A-a)O_2$ during the administration of pure $O_2$. So, after a suitable wash-in time (5 to 10 minutes), pure shunt accounts for the entire $P(A-a)O_2$. Furthermore, if the hemoglobin is fully saturated with $O_2$, dividing the $P(A-a)O_2$ by 20 approximates shunt percentage (at $FiO_2 = 1.0$). The $PaO_2/FiO_2$ ratio is a convenient and widely used bedside index of oxygen exchange that attempts to adjust for fluctuating $FiO_2$. However, this simple ratio is affected by changes in $SvO_2$ and does not remain equally sensitive across the entire range of $FiO_2$, especially when shunt is the cause of admixture. The $PaO_2/P_{A}O_2$ ratio is another easily calculated index, which does not require blood sampling from the central circulation, but in the same way loses reliability in proportion to the degree of shunting. All of these indices fail to account for changes in the functional status of the lung that result from alterations in PEEP, auto-PEEP, or changes in patient’s position and ventilator settings. When measured under conditions of controlled ventilation, the oxygenation index:

$$PaO_2/(FiO_2 \times \text{mean Paw})$$

reflects the influence of average lung volume as well as oxygen supplementation and has gained widespread popularity in neonatal and pediatric practice. Despite this rationale, this indicator is not (as yet) widely used in adult critical care.
Monitoring ventilation and carbon dioxide

Carbon dioxide production and exchange

Carbon dioxide stores (~120 L of CO₂) are held in several forms (dissolved, bound to protein, fixed as bicarbonate) and distributed in compartments that differ in their volumetric capacity and ability to exchange CO₂ rapidly with the blood. Well-perfused organs constitute a small reservoir for CO₂ that is capable of quick turnover. The existence of large CO₂ reservoirs with different capacities and time constants of filling and emptying means that equilibration to a new steady-state PaCO₂ after a step-change in ventilation takes longer than generally appreciated—especially for step reductions in alveolar ventilation. With such a large capacity and only a modest rate of metabolic CO₂ production, the CO₂ reservoir fills rather slowly, so that PaCO₂ raises only 6 to 9 mm Hg during the first minute of apnea and 3 to 6 mm Hg each minute thereafter [15,16]. Measurements of CO₂ excretion are valuable for metabolic assessment, computations of deadspace ventilation, and evaluation of hyperpnea. The rate of CO₂ elimination is a product of minute ventilation (VE) and the expired fraction of CO₂ in the expelled gas. This value represents metabolic CO₂ production only if the patient remains metabolically stable during the period of gas collection. The quantity of CO₂ generated per minute depends on acid-base fluctuations, perfusion adequacy, and ventilation status with respect to metabolic needs. The rate of CO₂ production falls to negligible values during circulatory arrest. Based on the linkage between lung perfusion and CO₂ discharge, partial rebreathing techniques have been developed to monitor cardiac output noninvasively.

The volume of CO₂ produced by the body tissues varies with metabolic rate (fever, pain, agitation, sepsis, and so forth). The PaCO₂ must be interpreted in conjunction with the VE, especially in mechanically ventilated patients. Many vagaries of CO₂ flux can be eliminated by controlling ventilation and muscular activity.

Deadspace and deadspace fraction

The physiologic deadspace (Vₐ) refers to the “wasted” portion of the tidal breath that fails to participate in CO₂ exchange. A breath can fail to accomplish CO₂ elimination either because fresh (CO₂-free) gas is not brought to the alveoli or because fresh gas fails to contact systemic venous blood. A portion of tidal ventilation is wasted when CO₂-laden gas is recycled to the alveoli with the next tidal breath, as when tidal breaths are very small. Deadspace also rises when fresh gas distributes to inadequately perfused alveoli, so that CO₂-poor gas is exhausted during exhalation. Wasted ventilation is characterized as the sum of the “anatomic” deadspace and the “alveolar” deadspace. Because the airways fill with CO₂-containing alveolar gas at the end of the tidal breath, the physical volume of the airways corresponds rather closely to their contribution to wasted ventilation. When
the parenchyma is well aerated and well perfused, the anatomic deadspace of a breath of normal size is relatively fixed at approximately 1 mL per pound of body weight and predominates over the alveolar component. Quite the opposite happens in patients with most lung diseases, in whom alveolar deadspace predominates. Here, the lung is composed of well and poorly perfused units, so that the mixed alveolar gas within the airways at end exhalation has a CO₂ concentration lower than that of pulmonary arterial blood. Deadspace increases with advancing age and body size and is reduced modestly by recumbency, extended breath holding, and decelerating inspiratory flow patterns. Supine position reduces deadspace by decreasing the average size of the lungs, thereby increasing the number of well-perfused lung units. An external apparatus attached to the airway may add to the series deadspace, whereas tracheostomy reduces it. Diseases that increase V_D include low output circulatory failure, pulmonary embolism, pulmonary vasoconstriction, vascular compression, mechanical ventilation with high tidal volume or PEEP, and diseases that destroy either the number or function of alveoli.

Except at very small tidal volumes, the fraction of wasted ventilation (V_D/V_T) tends to remain relatively constant as the depth of the breath varies [17,18]. The deadspace fraction can be estimated from analyzed specimens of arterial blood and mixed expired (P_ECO₂) gas:

\[
\frac{V_D}{V_T} = \frac{(PaCO_2 - P_ECO_2)}{PaCO_2}
\]

where P_ECO₂ is the CO₂ concentration in mixed expired gas, which can be determined on a breath-by-breath basis if exhaled volume is measured simultaneously. In healthy persons, the normal V_D/V_T during spontaneous breathing varies from ~0.35 to 0.15 depending on factors noted earlier (position, exercise, age, and so forth) [19,20]. In the settings of critical illness, it is not uncommon for V_D/V_T to rise to values that exceed 0.7 [21,22]. Deadspace accounts for most of the increase in the VE requirement and CO₂ retention that occur in the terminal phase of acute hypoxemic respiratory failure. In addition, changes in V_D/V_T occur during periods of hypovolemia or overdistention by high airway pressures, especially when progressive levels of PEEP are applied to support oxygenation [23–25]. Examination of the airway pressure tracing under conditions of controlled, constant inspiratory flow ventilation may demonstrate concavity or a clear point of upward inflection, indicating overdistention, accelerated deadspace formation, and escalating risk of barotrauma. Small reductions in PEEP or tidal volume may then dramatically reduce peak cycling pressure and V_D/V_T.

Monitoring of exhaled gas

Capnography analyzes the CO₂ concentration of the expiratory air stream, plotting CO₂ concentration against time or against exhaled volume, a display that provides more clinical information. After anatomic deadspace
has been cleared, the CO₂ rises progressively to its maximal value at end-exhalation, a number that reflects the CO₂ tension of mixed alveolar gas. When ventilation and perfusion are evenly distributed, as they are in healthy subjects, end-tidal PCO₂ (P_{ET}CO₂) closely approximates PaCO₂. Normally P_{ET}CO₂ underestimates PaCO₂ by 1 to 3 mm Hg, a gap that widens when ventilation and perfusion are matched suboptimally, as when alveolar deadspace admixes with CO₂-rich gas from well-perfused alveoli. Plotting CO₂ concentration against exhaled volume can yield estimates for the anatomic deadspace, as well as for the end tidal and mixed expired CO₂ concentrations (Fig. 2). The latter can be used to determine CO₂ production when mixed expired PCO₂, expressed as a percentage of barometric pressure, is multiplied by the minute volume.

While the normal capnogram is composed of an ascending portion, a plateau, a descending portion, and a baseline, in disease these sharp distinctions are blurred by differences of ventilation and perfusion (Fig. 3). Failure of the airway gas to equilibrate with gas from well-perfused alveoli invalidates P_{ET}CO₂ as a reflection of PaCO₂. Abrupt changes in P_{ET}CO₂ may reflect such acute processes as aspiration or pulmonary embolism, especially when VE and breathing pattern remain unchanged.

The capnogram also provides an excellent monitor of breathing rhythm. Close examination of the tracing contour and comparison with earlier waveforms may give helpful indications of circuit leaks, patient ventilator

![Expiratory Capnogram](image)

Fig. 2. Information available from an expiratory capnogram plotting PCO₂ concentration against exhaled volume. The slope of the alveolar plateau is a measure of ventilation heterogeneity. End-tidal PCO₂ (P_{ET}CO₂) reflects the concentration of CO₂ within the alveolar units that are last to empty. Although this value may parallel PaCO₂ in normal individuals, it is less reliable in disease. The Fowler deadspace (DS) is a close correlate of anatomic deadspace.
dyssynchrony, equipment malfunctions, secretion retention, and changes in underlying pathophysiology. In evaluating the P\textsubscript{ET}CO\textsubscript{2} it is essential to record and examine the entire capnographic tracing (not only the digital output). Breathing pattern can vary when gas flow is inhomogeneously distributed, as in airflow obstruction. Failure of the tracing to achieve a true plateau can occur because the sampling technique is inappropriate, exhalation is too brief, or ventilation is inhomogeneously distributed. The arterial to end-tidal CO\textsubscript{2} difference is minimized when perfused alveoli are recruited maximally [26]. On this basis, the (PaCO\textsubscript{2} – P\textsubscript{ET}CO\textsubscript{2}) difference has been suggested as helpful in identifying “best PEEP” [27–29].

Monitoring lung and chest wall mechanics

Mechanics of breathing

During mechanical ventilation the clinician must become familiar with all those properties of the lung and chest wall that determine the ease of chest expansion [30]. Certain of these properties can be assessed only under passive conditions (eg, compliance), others require active breathing effort (eg, maximal inspiratory pressure), while others can be determined with or without active breathing effort (eg, lung’s impedance properties). Finally, to separate static from dynamic variables, points of zero flow within the tidal cycle must be determined.

Pressure-volume relationships

Because the lung is a flexible and passive structure, gas flows to and from the alveoli driven by differences between airway and alveolar pressures. The
total pressure gradient expanding the respiratory system is accounted for in two ways: (1) in driving gas between the airway opening and the alveolus and (2) in expanding the alveoli against the recoil forces of the lung and chest wall. The pressure required for inspiratory flow dissipates against friction, while the elastic pressure that expands the respiratory system is stored temporarily in elastic tissues and is dissipated in driving expiratory flow [31].

The nonelastic impedance to airflow offered by friction and movement of the lung and the chest wall is termed “Resistance.” The elastic pressure these structures offer in opposing inflation is termed “Elastance,” and its inverse is termed “Compliance.” The normal airway resistance of a healthy adult is less than 4.0 cm H2O per liter per second when breathing spontaneously and rises approximately twofold when orally intubated with an endotracheal tube of standard size and length. The elastance of the lungs (EL) and the chest wall (ECW) add in series to comprise that of the respiratory system: 

\[ E_{RS} = E_L + E_{CW} \]

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Compliances add in parallel. At end-expiration, compliance values for the lung, chest wall, and integrated respiratory system of a spontaneously breathing, healthy adult patient of normal size and weight in the supine position are approximately 200, 150, and 85 mL/cm H2O, respectively.

Increasing the pressure applied across the normal lungs and chest wall increases lung volume, but the incremental relationship between pressure and volume varies markedly over the vital capacity range. Over a small segment, this relationship can be considered approximately linear over most regions of the pressure-volume curve. Therefore, assuming linearity, the elastic properties of the lung, chest wall, and integrated respiratory system can be described by single values for chord elastance (\( \Delta P/\Delta V \)) or its inverse, the chord compliance (\( \Delta V/\Delta P \)).

The same \( \Delta P \) will result in a different \( \Delta V \) for two lungs of identical tissue properties but different sizes. Examination of the pressure-volume relationship indicates that chord compliance differs according to the segment over which it is computed. That difference could result from a position shift along the pressure-volume relationship, an alteration of tissue elastic properties, or a variation in the ventilated capacity of the lung.

**Respiratory system compliance and elastance**

The pressure difference (\( \Delta P \)) required to expand the lung by a certain volume (\( \Delta V \)) is the corresponding change in transpulmonary pressure

\[ P_L = (P_{alv} - P_{pl}) \]

where \( P_{alv} \) = alveolar pressure and \( P_{pl} \) = pleural pressure. The lung elastance (\( E_L = \Delta P_L/\Delta V \)) is the pressure per unit of inflation volume required to keep the lung expanded under no flow (static) conditions, and the inverse of elastance is referred to as lung compliance (\( C_L = 1/E_L = \Delta V/\Delta P_L \)). The slope of the static pressure-volume relationship for the total respiratory system is

\[ C_{RS} = \Delta V/\Delta P_{alv} \]

In ventilator-derived calculations of compliance, \( \Delta V \) must be measured at the endotracheal tube or expired volume must be adjusted for the volume stored during
pressurized inflation in compressible circuit elements (with disposable external tubing and a low deadspace humidifier, approximately 3 mL of volume are stored per cm H$_2$O of peak cycling pressure). However, this figure may vary markedly, depending on the peak cycling pressure.

Compliance measurements obtained under passive conditions may have therapeutic and prognostic value for patients with arterial desaturation. When PEEP is applied incrementally, $C_L$ and $C_{RS}$ tend to reach their highest values when lung units are recruited maximally without overstretching. This region also tends to be that associated with minimal ventilatory deadspace and shunt fraction and often coincides with maximal oxygen delivery [32,33]. Different tidal volumes may be associated with different “optimal PEEP” values. Although this guideline does not always apply, it is a good rule to avoid using values of end-expiratory pressure or tidal volume that depress thoracic compliance—unless objective evidence of significantly improved oxygen delivery is available and safe plateau pressure is not exceeded. Severe disease is implied when tidal compliance falls to less than 25 mL/cm H$_2$O. Maximal depression of $C_{RS}$ often requires 1 to 2 weeks to develop in the setting of acute lung injury [34,35]. Although $C_{RS}$ provides useful information regarding the difficulty of chest expansion, $C_{RS}$ does not necessarily reflect underlying tissue elastance. Ideally, compliance is referenced to a measure of absolute lung volume, such as functional residual capacity (FRC) or total lung capacity (TLC). $C_{RS}$ may differ greatly at the extremes of the vital capacity range, even in the same individual. Although lung and chest wall elastance values add in series ($E_{RS} = E_L + E_{CW}$), their corresponding compliances add in parallel, so that respiratory system compliance bears a complex relationship to the individual compliances of the lung and chest wall:

$$C_{RS} = \frac{(C_L \times C_W)}{(C_W + C_L)}.$$  

The fraction of expiratory airway pressure (PEEP) transmitted to the pleural space depends on the relative compliances of the lung and chest wall:

$$\Delta P_{pl} = PEEP \times \left[\frac{C_L}{(C_L + C_W)}\right].$$

**Chest wall compliance**

For critically ill patients, chest wall distensibility may be reduced by abdominal distention, pleural effusions, ascites, muscular tone, recent surgery, position, binders, and braces (Fig. 4). For a given lung volume, such reductions cause an increase in $P_{PL}$. In turn, $P_{PL}$ influences venous return, hemodynamic data, and calculations of chest mechanics based on airway pressure. An appropriate interpretation of tidal airway pressures depends on a valid assessment of intrapleural pressure. Specific values for peak airway pressure and $C_{RS}$ have different prognostic importance and therapeutic
significance as well, depending on whether the lung or chest wall accounts for the stiffness.

**Clinical utility of the pressure-volume curve**

In the setting of acute lung injury, perhaps only 20% to 30% of alveoli remain patent, while the others are atelectatic or occluded by lung edema, cellular infiltrate, or inflammatory debris [36]. Moreover, the mechanical properties of the lung differ in dependent and nondependent regions. For a supine patient, atelectasis predominates in dorsal sectors, where lung units tend to collapse under the influence of regionally increased pleural pressure and the weight of the overlying lung [37,38]. In this surfactant-deficient lung, there are tendencies for persisting collapse of dependent alveoli and/or tidal reopening and recollapse of lung units in the middle and dependent zones. The latter process subjects injured tissue to damaging shear forces when high inflation pressures are used [39]. According to current thinking, both persisting collapse of inflamed tissue and the tidal collapse cycle must be avoided. To aid in healing, the objective is to “open the lung and keep it open” without causing overdistention. Nondependent alveoli remain open and relatively compliant but are subject to overdistention by high peak tidal pressures (Fig. 5) [40]. Defining the pressure-volume relationship may help guide the ventilator settings needed to avoid the damaging effect of both tidal collapse and alveolar overdistention [41–43]. The PV curve is a composite of information from myriad lung units, and its contours are shaped by the relative proportion of units at various stages of distension. Many

![Fig. 4. The effect of PEEP (20 cm H2O, in this example) on lung volume is influenced by the compliance of the chest wall. Distending force across the lung is 25 cm H2O with a normal chest wall, but only 15 cm H2O with a stiff chest wall. A patient with stiff chest wall requires a higher PEEP to achieve the same distending force across the lung.](image-url)
investigators of barotrauma believe that sufficient end-expiratory alveolar pressure, PEEP$_{TOT}$, (ie, the sum of auto-PEEP and extrinsic PEEP) should be maintained to surpass the lower inflection point of the inspiratory PV curve when high end-inspiratory (plateau) pressures are in use [44–48]. The PEEP requirement varies with body size, stage and severity of lung injury, and chest wall compliance. At the same time, peak tidal alveolar pressure should not encroach on the upper deflection zone that signals widespread alveolar overdistention. A few sustained inflations to high static pressure may be necessary to open the lung in the initial stages of acute lung injury and periodic “recruiting breaths” may be needed when very small tidal volumes are used. The relevant pressure here, to achieve near-total recruitment, may be as low as 25 cm H$_2$O in some patients and as high as 60 cm H$_2$O in others, influenced heavily by the type and duration of lung injury and by chest wall characteristics.

Construction of the PV curve

There is no simple rule for choosing optimal PEEP that applies to all patients. Not only does the compliance of the lung and chest wall differ among patients, but so does the recruitability of the lung on which optimal PEEP depends [49]. Attempting to construct a PV curve by the traditional super syringe method involves disconnection of the patient from the ventilator, which may cause marked drops in mean and end-expiratory transalveolar pressures. This in turn may cause hypoxemia, bradycardia, arrhythmia,
and/or flooding of the airway with edema fluid. The process that has been followed in recent years is to apply a slow inflation at constant flow (≈2 L/min) delivered by the ventilator. Such curves may begin from relaxed FRC or PEEP. Construction of an expiratory PV curve has more theoretical appeal as a means of setting PEEP, as its contours are more directly influenced by the expiratory collapse that PEEP is intended to prevent (Fig. 6). Assuming that tidal volume has already been selected, tracking tidal compliance during decrements of PEEP from total lung capacity (proceeding from higher to lower values) has logical appeal for setting PEEP’s optimal value.

Calculation of $C_{RS}$ and $R_{AW}$ during mechanical ventilation

Inspiratory resistance

When a mechanical ventilator expands the chest of a passive subject, inspiratory $P_{AW}$ furnishes the entire force accomplishing ventilation. Because the pressure-volume relationships of the lung and chest wall are approximately linear over the tidal volume range and because the increment in the $P_{AW}$ necessary to drive gas flow is nearly unchanging under constant flow conditions, the corresponding $P_{AW}$ waveform resembles a trapezoid during inspiration, a shape composed of a triangle of elastic pressure and a parallelogram of resistive pressure (Fig. 7). The mechanically ventilated respiratory system can be described by inspiratory resistance and compliance, data that in daily clinical practice can be estimated from $P_{AW}$, during volume cycled, constant flow ventilation with an applied end-inspiratory pause. It should be emphasized, however, that the calculations of $C_{RS}$ and

![Fig. 6. Pressure-volume curve of the respiratory system. Cstart, starting compliance, computed as the ratio between the first 100 mL inflation and the corresponding pressure; LIP, lower inflection point; Cinf, inflation compliance, computed as the slope of the PV curve during inflation in its most linear portion; UIP, upper inflection point; Cfinal, final compliance. (Data from Rajkumar A, Karmarkar A, Knott J. Pulse oximetry: an overview. J Perioper Pract 2006;16(10):502–4; and Gattinoni L, Eleonora C, Caironi P. Monitoring of pulmonary mechanics in acute respiratory distress syndrome to titrate therapy. Curr Opin Crit Care 2005;11(3):252–8.)](image-url)
resistance from $P_{AW}$ can be made only when inflation is passive. When gas is prevented from exiting the lung at the end of tidal inspiration, $P_{AW}$ falls quickly to a plateau value. If this end-inspiratory “stop-flow,” “plateau,” or “peak static” ($P_s$) pressure is referenced to the end-expiratory alveolar pressure (total PEEP), the difference determines the component of end-inspiratory pressure necessary to overcome the elastic forces of inflating the chest with the delivered tidal volume. Total PEEP ($PEEP_{TOT}$) is the sum of applied PEEP and auto-PEEP. Effective compliance ($C_{eff}$) can be computed as follows:

$$C_{eff} = \frac{V_{Tc}}{(P_s - PEEP_{TOT})}$$

where the $V_{Tc}$ is the corrected $V_T$.

During inflation with a constant flow profile, the $P_D$ (peak dynamic pressure) is the maximal pressure achieved just before the end of gas delivery, which drives gas to the alveolar level at the selected flow rate and expands lungs and chest wall by a full $V_T$. The difference between $P_D$ and $P_s$ quantifies the gradient driving gas flow ($V$) at end-inspiration and varies with the resistance of the patient and endotracheal tube as well as with inspiratory gas flow setting. Under conditions of passive inspiration with constant inspiratory flow, the ratio of $(P_D - P_s)/V_{end - insp}$ is the airway resistance ($R_{AW}$). The ratio of the delivered tidal volume (corrected for the compression volume of the external circuit) to $(P_D - PEEP_{TOT})$ reflects the overall difficulty of chest expansion, if $V_T$ and inspiratory flow settings do not change, during passive inflation. This index had been termed “dynamic characteristic”:

$$DC = \frac{V_{Tcorr}}{(P_D - PEEP_{TOT})}.$$
Because $P_D$ is influenced both by the frictional and elastic properties of the thorax, in a patient receiving the same $V_T$ and inspiratory flow, it may be considered a simple indicator of bronchodilator response under passive conditions. During controlled inflation with constant square wave inspiratory flow and stable airway resistance ($R_{AW}$), the slope of inspiratory pressure ramp should reflect $C_{RS}$. However, an estimate of $C_{RS}$ made by this technique is inappropriately low, unless auto-PEEP is taken into account. When there is occult positive end-expiratory pressure (auto-PEEP) at the onset of inspiration, the relevant pressure for chest expansion is $(P_S - PEEP_{TOT})$, not $P_S - PEEP$.

**Expiratory resistance**

For the same average flow rate, expiratory resistance routinely exceeds inspiratory resistance, even in the normal airway. For the patient connected to a mechanical ventilator, expiratory resistance arises in the endotracheal tube and exhalation valve as well as in the native airway. While the resistance across the exhalation valve and external tubing can be monitored easily, the total expiratory resistance (the quotient of the difference between alveolar pressure and pressure at the airway opening and the expiratory flow) is difficult to measure directly. However, it can be estimated knowing expiratory flow just before an occlusion of the airway opening and the “stop-flow” pressure (as an estimation of alveolar pressure). Alternatively, the expiratory resistance is the quotient of the time constant (the time required to expel 63% of the tidal volume during unexponential deflation, also equal to the product of Resistance and Compliance) and respiratory system compliance. Modern equipment can provide the requisite display of exhaled volume against time.

Expiratory resistance has important consequences, giving rise to auto-PEEP, dyspnea, and differences between mean airway pressure and the mean alveolar pressure that actually determines average respiratory system distension under passive conditions. Average expiratory flow and expiratory resistance increase as VE rises and the I:E ratio extends, reducing the time available for expiration and boosting average expiratory flow. Except when very mild, the patient must contend with the effects of expiratory resistance by allowing dynamic hyperinflation or by increasing expiratory muscle pressure. New generation ventilators employ techniques to minimize the expiratory resistance of the circuitry.

Depending on its nature, length, diameter, patency, and angulations, the endotracheal tube contributes greatly to $R_{AW}$. The turbulent flow developing in a narrow or partially occluded tube is the reason for its flow-dependent resistance. If endogenous bronchial resistance is the variable of interest, $P_{AW}$ should be sensed at or beyond the carinal tip of the endotracheal tube. This can be accomplished with an intraluminal catheter or by using a tube specially designed for measuring pressures at this site.
Value of continuously monitoring $P_{AW}$ and flow

Flow tracing

Modern ventilators offer the option of displaying both airway pressure and airflow or montages of one variable against the other. When used in conjunction with a simultaneously recorded airway pressure, the flow tracing is an invaluable aid in determining a number of parameters of clinical interest. A glance at the flow tracing usually is sufficient to determine the inspiratory mode of the ventilator and may yield clues in detecting patient-ventilator asynchrony. Flow must be known to compute airway resistance and the work of breathing, as well to detect auto-PEEP. A linear, biphasic flow profile, rather than a unexponential one, may give a clear indication of expiration flow limitation. A rippling inspiratory flow tracing indicates secretion retention within the central airways. A proto-expiratory “stutter step” suggests central airway occlusion (Fig. 8) [50]. The “zero flow” points of the airway and esophageal pressure tracings define the dynamic mechanical limits of the respiratory cycle, which are required in computations of mouth occlusion pressure ($P_{0.1}$), minimum airway resistance, and auto-PEEP. The flow tracing is also helpful when

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**I. BEFORE BRONCHOSCOPY**

![Before bronchoscopy](image1)

**II. AFTER BRONCHOSCOPY**

![After bronchoscopy](image2)

Fig. 8. (I) Before bronchoscopy. Simultaneous airway pressure and flow tracings recorded during mandatory constant flow machine cycles. A single protoexpiratory flow “stutter step” (arrow A) is followed by a unexponential flow profile on each deflation, except for the one that follows the end-inspiratory pause (arrow B). Note the rising (inverted) plateau on the airway pressure tracing during the pause maneuver (arrow C) that could be accounted for the early decompression of the less-obstructed peripheral airways, followed by contribution of the more severely obstructed lung units. (II) After bronchoscopy. Airway pressure and flow tracings during triggered pressure control ventilation. Note (1) attenuated stutter step of the first exhalation (arrow A) that disappears after the application of the end-inspiratory pause on the next breath; (2) absence of the inverted plateau during the pause (arrow C, compare with panel A). (Adapted from Gattinoni L, Eleonora C, Caironi P. Monitoring of pulmonary mechanics in acute respiratory distress syndrome to titrate therapy. Curr Opin Crit Care 2005;11(3):252–8; with permission.)
adjusting the inspiratory period during pressure-controlled ventilation to maximize inspiratory tidal volume and avoiding unintended end-inspiratory pause and excessive auto-PEEP.

Airway pressure tracing

The continuous tracing of $P_{AW}$ provides equally useful information. Apart from enabling estimation of $R_{AW}$ and $C_{RS}$, the waveform of inspiratory airway pressure traced during a controlled machine cycle provides graphic evidence of the inflation work performed by the ventilator at the particular combination of tidal volume and flow settings in use. When inflation occurs passively during constant flow, the area under the pressure-time curve is proportionate to the work performed by the machine to inflate the chest, and the pressure measured half-way through inspiration ($P$) is the work per liter of ventilation under those conditions. When average flow and tidal volume are matched to spontaneous values, $P$ is a good estimate of the pressure needed to ventilate the patient during pressure-support ventilation [51,52].

Also, the shape of airway pressure tracing provides information of clinical interest. Using constant inspiratory flow, concavity of the airway pressure ramp reflects patient effort during triggered cycles. An upward inflection of the terminal portion of the inspiratory airway pressure tracing during passive inflation, suggests that the combination of end-expiratory pressure and the specific tidal volume generates pressures that risk overdistention and barotrauma. Conversely, convexity of the $P_{AW}$ tracing indicates that inflation is becoming easier as the breath proceeds. Such a profile can be seen when volume is alternately recruited and derecruited during the breathing cycle, when auto-PEEP is present, or when resistance is highly volume dependent. Last, variations in the peak dynamic pressure of the machine-aided breaths suggest asynchrony between the respiratory rhythms of the patient and ventilator.

Mean airway pressure

The mean airway pressure ($mP_{AW}$) recorded under passive conditions is the only measurable analog of the mean alveolar pressure and relates intimately to the forces that drive ventilation and hold the lung distended (Fig. 9). The mean airway pressure is the average pressure that distends the alveolus and passive chest wall and therefore correlates with alveolar size and recruitment, as well as with mean intrapleural pressure. It is also the average pressure available to drive expiratory flow. When mean airway pressure ($mP_{AW}$) is measured without patient effort, it correlates directly with arterial oxygenation in the setting of pulmonary edema and lung injury, with back pressure to venous return, as well as with minute ventilation. Mean airway pressure can be raised by increasing VE, PEEP, or by extending the inspiratory time fraction. It is therefore a crucial variable to monitor when the clinician changes ventilatory parameters.
The actual relationship between $mP_{AW}$ and $mPalv$ can be expressed as:

$$MPalv = mPAW + VE(R_{EX} - R_{IN})$$

where the $R_{EX} - R_{IN}$ is the calculated difference between expiratory and inspiratory resistances [53,54]. This mean pressure difference tends to be positive and may be impressively large in severe airway obstruction, high ventilation requirements, or inverse ratio ventilation.

**Auto-PEEP effect**

Considerable confusion has arisen regarding the terms “auto-PEEP” or “intrinsic PEEP.” The pressure applied to the airways by the clinician is termed PEEP or “extrinsic PEEP.” The pressure measured when all airflow is stopped is termed “Total PEEP.” “Auto-PEEP” is the difference between total PEEP and extrinsic PEEP (the prefix “auto” derives from the Greek term “self”).

Hyperinflation may occur in the setting of high levels of ventilation when insufficient time elapses between inflation cycles to reestablish the equilibrium (resting) position of the respiratory system. That usually happens in the presence of increased airway resistance and a lengthy exhalation time constant. Auto-PEEP does not necessarily indicate dynamic hyperinflation, unless expiration occurs passively. Even under passive conditions, the extent of dynamic hyperinflation that results from auto-PEEP is a function of respiratory compliance. Auto-PEEP does not necessarily signify airflow obstruction, because it develops any time that VE is high enough and/or the combination of frequency and I/E ratio leaves insufficient expiratory time for decompression to relaxed FRC. Moreover, auto-PEEP varies markedly from one site to another within the obstructed lung (tending to be greatest in the dependent lung regions), and this distribution changes with variations of
body position. The dynamic hyperinflation associated with auto-PEEP may hold adverse consequences for hemodynamics, respiratory muscle function, and lung mechanics. Barotrauma is an obvious risk of serious hyperinflation [55]. Unlike restrictive lung disease, obstructive lung disease allows excellent transmission of the alveolar pressure to the pleural space. Thus, the hemodynamic consequences of the auto-PEEP effect may be more severe than those incurred by a similar level of PEEP intentionally applied to a patient with adult respiratory distress syndrome (ARDS). Immediately after intubation, cardiac output tends to drop as the auto-PEEP impedes venous return during passive inflation. This adverse effect of auto-PEEP is particularly important to keep in mind during cardiopulmonary resuscitation, when gas-trapping secondary to vigorous ventilation further compromises marginally adequate blood flow.

During active breathing efforts, auto-PEEP dramatically increases the work of breathing, presenting an increased threshold load to inspiration, impairs the strength of the inspiration muscles, and depresses the effective triggering sensitivity of the ventilator. For cases in which expiration is flow limited during tidal breathing, the addition of low levels of PEEP, less than the original auto-PEEP, replaces auto-PEEP effectively and therefore improves subject comfort and work of breathing, without substantially increasing lung volume or peak cycling pressure (in patients in whom expiration is not flow limited, PEEP raises both) [56]. At the bedside, total PEEP can be quantified by occluding the expiratory port of the ventilator at the end of the period allowed for exhalation between mechanical breaths. On modern machines this is an automated function. The auto-PEEP so measured, however, only characterizes the volume-weighted average value of those channels that remain patent at end-expiration.

**Variability of auto-PEEP**

Pleural pressure follows a gravitational gradient, so transpulmonary pressure and alveolar dimensions are least and the tendency for airway closure greatest in the most dependent regions [57]. Therefore, even if the time constants were otherwise perfectly uniform throughout the lung, there would be a tendency for those units in dependent areas to trap more gas than those located above them.

Minute ventilation is a powerful determinant of auto-PEEP [58]. In a perfectly uniform lung with a single time-constant, variations in f and VT that do not change minute ventilation have only a modest effect on the observed auto-PEEP. In the diseased lung, however, regional time constants vary widely. While auto-PEEP still remains highly dependent on total ventilation in the great majority of severely obstructed patients, end-expiratory flows from the slowest compartments are so small in some patients that changing the cycling frequency (and therefore the minute ventilation) may have only limited effects on gas trapping. For the same minute ventilation, variations in retained secretions, bronchospasm, apparatus resistance, tissue edema,
body position, and muscle tone alter the deflation time constant and the extent of gas trapping encountered at an unchanging VE.

**Methods for determining auto-PEEP**

The presence of auto-PEEP should be suspected whenever detectable flow persists to the very end of tidal expiration. Such flow often is audible with a stethoscope positioned over the trachea or if wheezing persists to the very end of the expiratory cycle. This flow can be transduced and displayed graphically on the bedside monitor; however, the magnitude of expiratory flow does not correlate with the magnitude of auto-PEEP. End-expiratory flow for example may result from widespread severe obstruction, or moderate obstructions confined to a smaller subpopulation of alveoli [59]. Finally, auto-PEEP may lurk behind airways that have been sealed completely by mucus plugs.

Because auto-PEEP varies on a breath-by-breath basis during spontaneous breathing, it cannot be quantified precisely under these conditions. If passive conditions are established, an estimate of auto-PEEP can be determined by a variety of methods [60]. Two methods are based on the principle of counter-balancing auto-PEEP, either by end-expiratory occlusion or by the dynamic airway pressure needed to initiate inspiratory flow (Fig. 10). Plateau pressure reflects the degree of dynamic hyperinflation of all open lung units more faithfully than does direct measurement of auto-PEEP itself, which gives an average of the auto-PEEP values from only those units that remain in communication with airway opening. With tidal volume and extrinsic PEEP unchanging, the discrepancy in plateau pressure encountered during an extended expiratory cycle (compared with the ordinary tidal cycles that preceded it) reflects “measurable” auto-PEEP. Two of the most important effects of

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**Fig. 10.** Simultaneous tracings of airway pressure (\(P_{aw}\)) and airflow during controlled volume-cycled ventilation with constant inspiration flow in a patient with airflow obstruction. \(P_D\) represents an end-inspiration airway pressure under a dynamic condition, \(P_Z\) at the point of flow cessation, and \(P_S\) after complete equilibration among all alveolar and airway pressures. Alveolar pressure can be estimated by the stop-flow technique in midexpiration or at end-exhalation (AP1). Auto-PEEP also can be estimated under dynamic conditions as the airway pressure above the set PEEP value that is needed to counterbalance elastic recoil and stop expiratory airflow (AP2).
auto-PEEP, those on hemodynamics and work of breathing, are mediated by pleural pressure, which can be measured directly as esophageal pressure (Pes).

**Esophageal pressure**

Knowledge of intrapleural pressure often facilitates clinical decision making. A thin esophageal catheter (≈2 mm diameter) inflated with 1 mL of air in the 10-cm-long balloon is inserted through the esophagus into the stomach and then carefully withdrawn to a point just above the position where negative pressure deflections are initially observed during spontaneous inspiration efforts. Because no significant change of transpulmonary pressure can occur without a change in lung volume, good balloon position is indicated by nearly identical deflections of esophageal and airway pressures during an occluded spontaneous breath.

In the upright position, Pes reflects the absolute value of global intrathoracic pressure with acceptable accuracy, but Pes overestimates average resting intrathoracic pressure in the supine position and underestimates it in the prone position. With the patient recumbent, Pes overestimates pleural pressure, but changes in pleural pressure are tracked well. Useful graphics of dynamic pressure-volume and flow-volume enable estimation of force generation during all patient-initiated breaths (spontaneous or assisted) and allow partitioning of transthoracic pressure into its lung and chest wall components during passive inflation. Furthermore, Pes aids in interpreting pulmonary artery and wedge pressures under conditions of vigorous hyperpnea or elevated alveolar pressure (PEEP, auto-PEEP). The Pes can be used to compute the work of breathing across the lung and external circuitry or to calculate the product of developed pressure and the duration of inspiratory effort (pressure-time product). It has been suggested that fluctuations in central venous pressure can serve a similar purpose, but the damped vascular pressure tracing yields a low-range estimate of effort. This underestimation occurs because venous return tends to rise as intrathoracic pressure falls and declines as intrathoracic pressure rises.

**Transdiaphragmatic pressure**

Transdiaphragmatic pressure (Pdi) is the difference between Pes and the gastric pressure (Pga) [61]. Theoretically generated by a single inspiratory muscle (the diaphragm) Pdi can be used to quantify its effective contractile force. Clinically, the Pdi is rarely used. Occasionally it is measured in conjunction with phrenic nerve stimulation or voluntary efforts to investigate diaphragmatic paralysis.

**Abdominal pressure**

An increased intra-abdominal pressure (IAP) increases chest wall stiffness. Abnormally high IAP values, as measured by bladder pressure, are
found in many ICU patients. Very high IAP values are associated with restrictive lung physiology and systemic acidosis.

**Monitoring breathing efforts**

*Oxygen consumption of respiratory system*

The oxygen consumed by the ventilator pump (VO$_2$R) estimates respiratory muscular effort at its most basic level: cellular metabolism. Although difficult to measure, the VO$_2$R theoretically accounts for all factors that tax the respiratory muscles, i.e., the external workload (W) and the efficiency (e) of the conversion between cellular energy and useful work (VO$_2$R = W/e). Two patients with different chest configurations, patterns of muscle activation, or degrees of coordination between the muscles of inspiration and expiration may perform identical external work (W) but consume vastly different amounts of O$_2$ in the process. Because VO$_2$R cannot be measured directly, total body oxygen consumption (VO$_2$) is tracked as ventilatory stresses are imposed or relieved, perturbing the respiratory system. Unfortunately, VO$_2$ is difficult to measure in unstable patients, so that other measures of respiratory muscle effort usually are sought.

**Direct measures of external mechanical output**

*External work of breathing*

Work of breathing is a global measure of respiratory pump activity and reflects the imposed respiratory load. The mechanical work of breathing and breathing effort are not synonymous terms. If breathing is inefficient, great effort can be expended without developing forceful pressures or accomplishing measurable external work. Mechanical work is accomplished when a pressure gradient (P) moves the lung or relaxed chest wall through a volume change. At any volume (V) above relaxed FRC, pressure resulting from a flow (V) dissipates against frictional and elastic forces in the following way:

$$P = R_{AW}(V) + V/Crs$$

Average developed pressure (P) for the tidal inflation ($V_T$) during the inspiratory period (ti) can be approximated as follows:

$$P = R_{AW}(V_T/ti) + V_T/2CRS + \text{auto-PEEP}$$

and is numerically equivalent to the work per liter of ventilation, while work per tidal breath (Wb) can be quantified as the product of P and $V_T$. Thus, if $R_{AW}$, $CRS$, ti, and $V_T$ are known for the spontaneously breathing subject, the external work rate for inspiration can be computed easily. Exhalation normally proceeds passively, dissipating elastic energy stored during the inspiratory half cycle.
Bronchospasm, retained secretions, and mucosal edema are the primary reversible factors that increase $R_{AW}$. Lung edema and infiltration, high lung volumes, pleural effusions, abdominal distention, and supine posture reduce $C_{RS}$. In the clinical setting, such computations serve to estimate the pressure support level needed to achieve most ventilatory needs. When the ventilator performs the entire workload for a passive patient, total inflation pressure ($P$) is simply $P_{AW}$, that is approximated by the inflation pressure at midcycle (when inflation is achieved with a constant-flow waveform). With pressures and volumes expressed in their customary units, a convenient work unit is the joule or watt-second, $1\text{ J} = 10\text{ cm H}_2\text{O} \times 1\text{ L}$. Total inspiratory mechanical work per minute is the product of $P$ and minute ventilation or $W_b$ and $f$, the breathing frequency.

To accurately estimate the work rate of spontaneous breathing, flow delivery during passive inflation must approximate the mean inspiratory flow rate of spontaneous breathing, the tidal volume delivered must be similar, and no inflation effort must occur. Unfortunately, such preconditions often cannot be accomplished without deep sedation or paralysis.

**Influence of auto-PEEP on work of breathing**

Auto-PEEP imposes a threshold load on inspiration. The patient must supply a pressure sufficient to counterbalance auto-PEEP before central airway pressure falls sufficiently to trigger the ventilator or initiate a pressure-supported breath. The threshold load imposed by auto-PEEP effectively reduces the triggering sensitivity of the machine to a value equal to the sum of auto-PEEP and the set trigger sensitivity value. When expiration is flow limited during tidal breathing, low levels of continuous positive airway pressure (CPAP) or PEEP can help restore triggering sensitivity and reduce the work of breathing. Moreover, during pressure-support ventilation, PEEP that counterbalances auto-PEEP leaves a greater proportion of the inspiratory pressure available to power inflation, often resulting in an increased tidal volume for the same value of pressure-support. Although low-level PEEP also tends to improve the distribution of ventilation, PEEP should not be used if it causes the peak dynamic cycling pressure to rise significantly.

**Work measurements**

Although the work of breathing can be estimated using the equation of motion, an esophageal balloon is required to directly measure work during spontaneous, machine-assisted, or pressure-supported breathing. During spontaneous breathing cycles, the fluctuations in Pes reflect patient efforts to overcome the impedance of the lung and external circuit. Inspiratory inflections of the $P_{AW}$ waveform quantify the pressure needed to suck gas through the inspiratory circuit to the point of pressure measurement. While care must be taken to include any component attributable to auto-PEEP, it must be understood that surreptitious or overt expiratory efforts may contribute to the “inspiratory” work calculation. Inspiratory work can be
quantified by electronically integrating the product of Pes and the flow or by measuring the area within a plot of Pes against inspired volume. The work done in expanding the chest wall cannot be directly measured during active breathing. To exclude the resistance of the endotracheal tube, \( P_{AW} \) must be sampled between the tube tip and the carina, a site at which much deeper pressure fluctuations may be seen during inspiration. The resistance of standard endotracheal tube often exceeds 10 cm H\(_2\)O/L/sec and is commonly offset during inspiration by pressure support.

During patient-initiated but machine-assisted breathing cycles, it is often assumed that patient work becomes negligible. Indeed, the ventilator is fully capable of performing the entire work of breathing if the patient were to cease effort immediately after triggering inspiration. However, relaxation does not occur abruptly once the machine cycle begins. Instead, patient effort continues in direct proportion to the intensity of respiratory drive. When the ventilator requirement or sense of dyspnea is high (eg, when the ventilator is poorly adjusted with respect to sensitivity, peak inspiratory flow rate, inspiration duration, or tidal volume), exertion levels may approach those of unsupported breathing [62]. Interestingly, resistance and compliance do not influence the work of breathing during triggered cycles, provided that the machine fully satisfies the patient’s peak inspiratory flow demand (\( \approx 4 \times VE \)) [58]. However, if the patient’s flow demand exceeds the delivery rate, the patient works against the resistance of the endotracheal tube and the ventilatory circuitry, as well as against the innate impedance characteristics of the chest. Clues to patient exertion during triggered machine cycles are provided by the airway pressure tracing, as already described. Peak dynamic pressure itself may not be much different from expected, in as much as inspiratory effort slackens near the end of inflation. During Pressure-Support Cycles, inspiratory airway pressure is maintained nearly constant by the machine at the pre-set level. Therefore, patient effort can be gauged directly only from a Pes tracing.

**Pressure-time product**

Isometric components of muscle tension that consume oxygen without contributing to volume change fail to register as externally measured work, accounting in large part for the lack of agreement between force generation and Wb. A pressure-time product (PTP = \( P \times ti \)) parallels effort and VO\(_2\)R more closely than Wb because it includes the isometric component of muscle pressure and is less influenced by the afterload to contraction. When average inspiratory pressure (\( P \), as computed earlier) is referenced to the maximal isometric pressure that can be generated at FRC (Pmax) and inspiratory time (ti) is expressed as a fraction of total cycle length (ttot), a useful effort index is derived:

\[
\text{Pressure-time index (PTI)} = \frac{P}{P_{max}} \times \frac{ti}{ttot}
\]

Values of PTI that exceed 0.15 identify highly stressful breathing workloads that may not be sustainable [63,64].
Monitoring ventilatory drive and breathing pattern

Importance of assessing ventilatory drive

Considering that ventilatory drive is a primary correlate of dyspnea and the ability to ventilate, it is remarkable that so little clinical attention has been paid previously to drive measurement. Heightened ventilatory drive increases work expenditure during triggered machine cycles and often signals pain, sepsis, and important perturbations of the cardiopulmonary system. During machine-assisted breathing, ventilatory drive plays a more important role in determining the energy expenditure of the patient than any other indicator of ventilatory mechanics. Derangements in ventilatory drive also may furnish clues regarding the ability of the patient to wean from ventilatory support. Several recent clinical studies demonstrate that most patients who failed to wean from mechanical ventilation have elevated drives to breathe and limited ability of drive to respond to increases in ventilatory loads (eg, increased PaCO2) [65,66].

Ventilatory drive indices

Several methods can be used to index drive. When respiratory mechanics and strength reserves are normal, minute ventilation directly parallels the output of the ventilatory control center. Unfortunately, such preconditions are seldom met in the clinical setting. Minute ventilation can be viewed as the product of mean inspiratory flow rate (the quotient of tidal volume and inspiratory time, VT/\( t_i \)) and the inspiratory time fraction or duty cycle (\( t_i/t_{tot} \)):

\[
VE = \frac{VT}{t_i} \times \frac{t_i}{t_{tot}}
\]

Both components yield useful and largely ignored clinical information. Mean inspiratory flow (\( VT/t_i \)) provides a valid index of drive but its value also depends on the mechanical properties of the ventilatory system. The pressure generated against an airway surreptitiously occluded 100 msec after the onset of inspiratory effort (the \( P_{0.1} \)) is measured before the occlusion is recognized consciously, so that the corresponding outflow from the respiratory center is representative of the unimpeded cycles that preceded it. As an isometric measurement, the \( P_{0.1} \) is influenced by muscle strength and lung volume but does not depend on respiratory mechanics.

Breathing pattern, frequency, and duty cycle

The breathing pattern also offers valuable information. When muscular strength is limited, patients tend to meet VE requirements by increasing frequency (\( f \)) without raising \( V_T \). Although smaller breaths require less effort, the cost of rapid, shallow breathing may be increased deadspace ventilation and the need for a higher VE to eliminate CO2. Thus, although work per breath (Wb) is controlled by limiting tidal volume, total work (the product
of \( f \) and \( W_b \) per minute tends to increase when \( f \) exceeds some optimal value. A very high and continuously rising frequency (to rates > 30 breaths/minute) is generally accepted as a sign of ventilatory muscle decompensation and impending fatigue. It should be noted, however, that some patients increase \( f \) to a stable value of more than 35 breaths/minute and remain compensated, especially when VE rises proportionally to the rise in breathing frequency, or the patient has inherent restrictive physiology.

In recent years, considerable attention has focused on the \( f/V_T \) ratio, or rapid shallow rebreathing, index, a simply computed bedside parameter that seems to indicate the ability or inability of mechanically ventilated patients to breathe without mechanical assistance [67–70]. Discontinuation of ventilator support is unlikely to prove successful if \( (f/V_T) \) exceeds approximately 105 breaths/minute liters within the first minute of a brief trial of fully spontaneous breathing. Although hardly infallible, this simple guide does seem to have clinical utility.

As the ventilatory muscles fatigue, the duty cycle (\( t_i/t_{tot} \)), the fraction of each breathing cycle spent in inspiration, also changes. When there is a breathing stress, the \( t_i/t_{tot} \) of spontaneous breathing normally increases from about 0.35 to a value of 0.40 to 0.50. At the limits of compensation, the \( t_i/t_{tot} \) fails to increase with further stress and may actually decline.

At times of maximal effort, noteworthy alterations may be observed in the pattern of activation and coordination of the ventilatory muscle groups. Although normally passive, expiratory muscles may be called into play whenever the inspiratory muscles face a burden that is stressful in relation to their capability (eg, during expiratory flow obstruction, when the patient is anxious, when machine-controlled inspiration duration is excessive, and at high level of VE). Visible use of the accessory muscles, especially the sternocleidomastoid group, may also signal the approach to the limits of the ventilatory compensation.

Asynchrony between the peak excursions of the chest and abdominal compartments and paradoxical inward movement of the abdomen on inspiration are two indicators of diaphragmatic dysfunction or fatigue [71]. These motions also reflect the normal response of a compensated system to stress. Asynchrony between the excursions of rib cage and abdomen may be a stage in the development of full-blown abdominal paradox.

Inductance (impedance) plethysmography provides a noninvasive means of monitoring \( f \), \( V_T \), \( t_i/t_{tot} \), and respiratory muscle coordination. With this technique, loose elastic bands encircle the chest and abdomen. Changes in compartmental volume create proportional changes in the cross-sectional areas of the electrical inductance loops. Fluctuations of compartmental motion can be summed to estimate overall tidal volume changes. The ratio of maximal compartmental amplitude to tidal volume (the MCA/\( V_T \) ratio) correlates with ventilatory distress and provides tangible evidence of mechanical inefficiency. Impedance plethysmography can also be used as an apnea detector in nonintubated patients and may prove helpful in
monitoring volume changes during pressure-cycled modes of ventilation (eg, pressure support, pressure control).

**Monitoring strength and muscle reserve**

*Strength measures*

The two most common measures of respiratory muscle strength are the vital capacity (VC) and the maximal inspiratory pressure (MIP) generated against an occluded airway. Without full patient cooperation, it is questionable that any measure of strength can reflect the full capability for pressure development.

*Vital capacity*

In cooperative patients, VC tends to be well preserved relative to MIP because small applied pressures achieve relatively large volume changes. Vital capacity generally should be measured upright rather than supine, because certain conditions, such as diaphragmatic paralysis, may demonstrate a positional reduction of more than 30%. A routine measurement of VC involves a single forceful effort from residual volume to total lung capacity. However, many weak patients fail to sustain inspiratory effort long enough to achieve their potential maximum. Others simply refuse or cannot fully cooperate with the testing. Thus, for critically ill patients, the VC has proven to be a disappointing and unreliable measure of strength. A one-way valve can be used to achieve a “stacked vital capacity” even when patients do not cooperate fully with testing. An involuntary deep breath may also be induced by stimulating cough and a crude estimate of inspiratory capacity obtained from the recorded exhaled volume.

*Maximal inspiratory pressure*

The maximal inspiratory pressure (MIP) is an isometric pressure optimally measured in a totally occluded airway after 20 seconds or 10 breathing efforts. A one-way valve directed toward expiration can ensure that inspiration efforts begin from a lung volume low enough to achieve maximal mechanical advantage. The $P_{AW}$ during the MIP maneuver should be measured continuously, either with a needle gauge or by a pressure transducer linked to recording apparatus. Ideally, the MIP effort is sustained for at least 1 second. It should be kept in mind that the validity of MIP in uncooperative patients depends on the strength of ventilatory drive. In a fully cooperative patient the intensity of a voluntary effort is likely to exceed that elicited by simple airway occlusion unless the stimulus is both sustained and strong [72,73].

*Measures of endurance*

Endurance is the ability of a muscle to sustain effort, determined by the balance between the supply and demand of muscular energy. Two simple indices
of ventilatory power reserve—the ratio of $V_E$ requirement to maximal voluntary ventilation (MVV) and the $V_T/V_C$ ratio—have long been used to predict the outcome of machine withdrawal. On empirical grounds, it has been suggested that ratios higher than 50% portend weaning failure. Interestingly, newer laboratory data confirm that only about 50% to 60% of the MVV can be sustained longer than 15 minutes without ventilatory fatigue [69].

**Pressure-time index**

Measured accurately, the MIP can be used in conjunction with P to judge endurance and the likelihood of weaning success. In the laboratory setting, a diaphragmatic $P/P_{\text{max}}$ ratio higher than 40% (with $t_i/t_{\text{tot}} = 0.40$) or a pressure-time index ($\text{PTI} = P/P_{\text{max}} \times t_i/t_{\text{tot}}$) greater than 0.15 predicts the inability to indefinitely sustain a target workload. No confirmatory data are available yet for the specific clinical setting of the weaning trial.

**Sequential measurements of drive**

A practical indication of declining power reserve may also be provided by a comparison of drive indices (such as the $P_{0.1}$) measured sequentially during the stress period. Patients who fail to increase ventilatory drive in response to increased $\text{PaCO}_2$ are prone to alveolar hypoventilation and weaning failure. In the future, monitoring the response of such indices as $P_{0.1}$ to an imposed stress or CO$_2$ loading may provide valuable clinical indications of breathing reserve.

**Patient-ventilator interaction**

**Specific problems: patient–endotracheal tube–ventilator circuit**

Smooth interaction between the patient and the ventilator may be interrupted by malfunctioning of the ventilator system, worsening of cardiopulmonary mechanics, or by factors completely unrelated to ventilation. Malfunctions of the ventilator system prevent adequate ventilation or oxygenation and usually present as altered states of consciousness, changes in vital signs, or unexplained deterioration in blood gases. When a crisis develops suddenly during mechanical ventilation, the patient should be ventilated manually to distinguish if the problem is related to the patient or to the ventilator. The difference between exhaled and set tidal volume is crucial data. Checking the airway pressure profile and comparing the peak dynamic ($P_D$) and static ($P_S$) pressure against previous values also provides essential information. A large disparity between $P_D$ and $P_S$ suggests a resistance problem in the tube or airways. Failure to generate or hold pressure during circuit occlusion indicates a system leak.

An important distinction must be made between massive atelectasis and tension pneumothorax. Note that a pneumothorax without tension may not elevate peak pressure or reduce tidal volume noticeably. Nonpulmonary causes of discomfort (distention of the bladder, pain, and so forth) should
not be overlooked. When agitation develops, hypoxemia frequently occurs, increasing both the drive to breathe and dyspnea. Increasing the FiO₂ often relieves hypoxemia and can undo the self-reinforcing process of agitation. In fact, increasing FiO₂ is a good first option whenever desaturation accompanies agitation.

Modern ventilators are equipped with audible alarms that sense excessive or inadequate system pressure, failure to exhale a set minimum of tidal volume, or disconnection of the patient from the machine. Endotracheal tubes often kink, block with secretions, or become constricted by the teeth of a biting patient [74–76]. Tubes that are poorly placed or secured may migrate into the larynx, main bronchus, or rest on the carina, producing cough and bronchospasm.

Poor coordination between breathing rhythms of patient and ventilator

Shortly after mechanical ventilation begins, attempts to “fight the ventilator” are the rule in alert, awake and mildly obtunded patients [77–79]. In conventional ventilation, the triggering variable may be pressure or flow [80–82]. Patient-ventilator asynchrony during the triggering process is expressed in several forms: absence of inspiratory muscle contraction (autotriggering), delay between the beginning of inspiratory effort and ventilatory triggering (excessive triggering delay), and inability of the patient’s inspiratory effort to trigger the ventilator (ineffective efforts). Autotriggering may result from random noise or presence of leaks or water in the circuit, and cardiogenic oscillations. Autotriggering usually occurs in patients with low inspiratory drive, low breathing frequency, relatively high stroke volume, and no dynamic hyperinflation [83,84]. Autotriggering is minimized by increasing the threshold of flow or pressure triggering, augmenting the patient respiratory drive, and elimination of the leaks or water in the circuit.

Excessive triggering delay and ineffective efforts to trigger the ventilator are related to the machine’s functioning, as well as the characteristics of the respiratory system. The main patient-related factors are dynamic hyperinflation, low respiratory drive, and weak inspiratory muscles. The most important ventilator factors are related to events during the pressure delivery and termination phases, such as the maximum pressure setting and expiratory asynchrony in the form of delayed opening of the exhalation valve. The strategies for decreasing the triggering delay and the number of ineffective efforts are measures that decrease the magnitude of dynamic hyperinflation, cessation of supplemental flows (eg, continuously aerosolized prostacyclin), application of external end-expiratory pressure, decrease of the pressure and the flow thresholds for triggering, and the use of new-generation ventilators with more responsive triggers.

Patient-ventilator asynchrony during the pressure delivery and cycle off phases is due to dissociation between the patient’s respiratory effort and ventilator response in terms of timing (uncoupling between the end of
mechanical and neural inspiration), and inadequate or excessive assist. In addition, with pressure-support, the pressure rise time may influence the synchronization between the patient and the ventilator.

**Imaging of function and structural heterogeneity—the future**

To this point in the history of mechanical ventilation, the primary database from which monitored information derives has been limited to global measures of pressure and flow sampled from the airway opening. Yet it is now understood that the diseased lung, whether obstructed or acutely injured, is composed of heterogeneous subunits with behaviors and risk susceptibilities that vary considerably site to site. Poised to be introduced to clinical practice are several methodologies designed to monitor regional anatomy and function and thereby help regulate therapy and modify risk. Foremost among these are

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**Fig. 11.** Electrical impedance tomography (EIT) device for monitoring regional lung ventilation, based on the measurement of electrical voltages at the surface of the chest, resulting from repeated applications of small electrical currents to the body and transformed the collected data on two dimensional images of the distribution of electrical impedance in the chest. (Adapted from Frerichs I, Hahn G, Schroder T, et al. Electrical impedance tomography in monitoring experimental lung injury. Intensive Care Med 1998;24(8):829–36; and Frerich I, Hinz J, Herrmann P, et al. Detection of local lung air content by electrical impedance tomography compared with electron beam CT. J Appl Physiol 2002;93(2):660–6; with permission.)
electrical impedance tomography (EIT), acoustic monitoring, and pulmonary ultrasound (Figs. 11 and 12) [85–95]. Although little clinical experience has yet been accumulated, it seems clear from an expanding base of experimental and observational studies that these “real time imaging” methodologies have the potential to elevate respiratory monitoring of the critically ill onto a new plane of management better aligned with our understanding of underlying pathophysiology and treatment goals.

Summary

Many options are currently available for monitoring respiratory function in the critically ill patient. Most are obtained with little intrusion into the patterns of ongoing care. Yet, the information secured is often of vital importance in bedside decision making. To use it effectively, the clinician must take an integrative approach based on mastery of the underlying physiology and familiarity with the principles upon which these technologies are based.

Further readings


References


