



Physiologic and pathophysiologic consequences of mechanical ventilation

Author

[Kenneth Lyn-Kew, MD](#)
[Robert C Hyzy, MD](#)

Section Editor

[Polly E Parsons, MD](#)

Deputy Editor

[Kevin C Wilson, MD](#)

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INTRODUCTION — Mechanical ventilation can be performed using positive pressure or negative pressure. Positive pressure ventilation is the primary type of mechanical ventilation used today. During positive pressure ventilation, the ventilator forces air into the central airways and the resulting pressure gradient causes airflow into the small airways and alveoli. (See "[Overview of mechanical ventilation](#)", section on Types).

Physiologic and pathophysiologic consequences of positive pressure ventilation are discussed in this topic review. Two major consequences of mechanical ventilation, pulmonary barotrauma and ventilator-associated lung injury, are reviewed separately. (See "[Pulmonary barotrauma during mechanical ventilation](#)" and see "[Ventilator-associated lung injury](#)").

PULMONARY EFFECTS

Barotrauma — Pulmonary barotrauma is a well-know complication of positive pressure ventilation. Consequences include pneumothorax, subcutaneous emphysema, pneumomediastinum, pneumoperitoneum, and subcutaneous emphysema. Pulmonary barotrauma during mechanical ventilation is discussed separately. (See "[Pulmonary barotrauma during mechanical ventilation](#)").

Ventilator-associated lung injury — Ventilator-associated lung injury (VALI) refers to acute lung injury that occurs during mechanical ventilation. It is clinically indistinguishable from acute lung injury or acute respiratory distress syndrome (ALI/ARDS) due to other causes. VALI is discussed separately. (See "[Ventilator-associated lung injury](#)").

Auto-PEEP — Auto-positive end-expiratory pressure (Auto-PEEP, also called intrinsic PEEP) exists when there is positive airway pressure at the end of expiration due to incomplete exhalation [1] . In other words, inspiration is initiated before expiratory airflow from the preceding breath has ceased. (See "[Positive end-expiratory pressure \(PEEP\)](#)").

Causes — There are numerous reasons that patients receiving positive pressure ventilation are susceptible to developing auto-PEEP ([show table 1](#)) [2] :

- High minute volume — High minute volume ventilation exists when there are large tidal volumes (greater than the patient's functional residual capacity), a high respiratory rate, or both. Large tidal volumes increase the volume that must be exhaled prior to the next breath. High respiratory rates decrease the duration of expiration. In both situations, the next breath is initiated prior to completion of the last exhalation. A high minute volume may be due to patient factors (eg, fever, infection) or ventilator settings.
- Prolonged inspiratory time — When the inspiratory time is increased, there is an obligatory decrease in the expiratory time. This can lead to incomplete exhalation and auto-PEEP [3] .
- Time-constant inequality — Patients whose lung units empty heterogeneously (eg, patients

with obstructive airways disease) are particularly susceptible to developing auto-PEEP during positive pressure ventilation, even at a relatively low minute ventilation.

- Expiratory flow resistance — Resistance to airflow (eg, narrow endotracheal tube, ventilator tubing) can cause auto-PEEP by impairing exhalation.
- Expiratory flow limitation (eg, obstructive airways disease) and altered respiratory system compliance (eg, expiratory muscle activity) similarly impede exhalation, causing auto-PEEP. Altered respiratory system compliance may also interfere with accurate measurement of auto-PEEP [4] .

Detection — Auto-PEEP can be directly measured by applying an expiratory breath hold (usually 0.5 to 1 second) and determining the airway pressure during the breath hold ([show figure 1](#)). Physical examination is effective at confirming auto-PEEP (high positive predictive value), but less useful for excluding auto-PEEP (lower negative predictive value) [5] .

Consequences — Auto-PEEP exacerbates the hemodynamic effects of positive pressure ventilation (discussed below), increases the risk of pulmonary barotrauma, and makes it more difficult for the patient to trigger a ventilator-assisted breath ([show figure 2](#)). In addition, auto-PEEP can lead to incorrect estimation of the mean alveolar pressure and static lung compliance [6] .

Treatment — Immediate intervention is necessary if auto-PEEP is detected ([show table 2](#)):

- Change ventilator settings — The ventilator settings should be changed in an effort to reduce or eliminate auto-PEEP. The most helpful maneuvers are those that increase the duration of expiration: increasing the inspiratory flow rate, decreasing the respiratory rate, or both. Decreasing the tidal volume or using applied PEEP to overcome auto-PEEP may also be helpful. The use of applied PEEP in this setting is discussed separately. ([See "Positive end-expiratory pressure \(PEEP\)", section on Treatment](#)).
- Reduce ventilatory demand — Ventilatory demand can be decreased by reducing carbohydrate intake, anxiety, pain, or fever. This may decrease the minute volume, thereby reducing auto-PEEP.
- Reduce expiratory flow resistance — Reduction of expiratory flow resistance by suctioning, administration of bronchodilators, and use of a wide endotracheal tube can reduce auto-PEEP.

Heterogeneous ventilation — The distribution of positive pressure ventilation is never uniform because the amount of ventilation is a function of three factors that vary from region to region within the lungs: alveolar compliance, airway resistance, and dependency (upper versus lower lung zones). Compliant, non-dependent regions with minimal airway resistance will be best ventilated. In contrast, stiff, dependent regions with increased airway resistance will be least ventilated. The heterogeneity of ventilation is accentuated in patients who have airways disease, parenchymal lung disease, or both.

Physiologic dead space — Physiologic dead space is the alveolar area that is not involved in gas exchange because of insufficient perfusion. Positive pressure ventilation tends to increase physiologic dead space by increasing ventilation in some regions without a corresponding increase of perfusion.

Physiologic shunt — A physiologic shunt exists where there is blood flow through pulmonary parenchyma that is not involved in gas exchange because of insufficient ventilation. Patients with respiratory failure frequently have increased physiologic shunting due to focal atelectasis without a corresponding decrease in perfusion. The focal atelectasis develops because dependent lung is no longer pulled open due to decreased diaphragmatic contraction. Positive pressure ventilation can mitigate physiologic shunting by increasing the mean airway pressure, which helps maintain airway and alveolar patency. This is particularly true if positive end-expiratory pressure (PEEP) is added. ([See "Positive end-expiratory pressure \(PEEP\)"](#)).

Diaphragm — Positive pressure ventilation may lead to rapid disuse atrophy of diaphragmatic muscle

fibers. An observational study of 22 patients compared the size of diaphragmatic muscle fibers from patients who received positive pressure ventilation for more than 18 hours to those from patients who received positive pressure ventilation for fewer than three hours [7]. The mean cross sectional area of diaphragmatic muscle fibers was significantly smaller among those patients who received positive pressure ventilation for a longer duration. This relationship held for both fast twitch (1871 versus 3949 micron²) and slow twitch (4725 versus 2025 micron²) muscle fibers.

Respiratory muscles — Respiratory muscle atrophy can develop in patients undergoing positive pressure ventilation. Neuromuscular weakness in critically ill patients is discussed separately. ([See "Neuromuscular weakness related to critical illness"](#)).

Mucociliary motility — Positive pressure ventilation appears to impair mucociliary motility in the airways. In a series of 32 patients, bronchial mucus transport velocity was measured using technetium 99m-labeled albumin microspheres during the first three days of mechanical ventilation [8]. Bronchial mucus transport was frequently impaired and associated with retention of secretions and pneumonia.

SYSTEMIC EFFECTS

Hemodynamics — Positive pressure ventilation frequently decreases cardiac output, which may cause hypotension. There are several mechanisms that contribute to the fall in cardiac output:

- **Decreased venous return** — The amount of venous return is determined by the pressure gradient from the extrathoracic systemic veins to the right atrium. Intrathoracic and right atrial pressure increase during positive pressure ventilation, thereby reducing the gradient for venous return. This effect is accentuated by auto-PEEP, applied PEEP, or intravascular hypovolemia [9].
- **Reduced right ventricular output** — Alveolar inflation during positive pressure ventilation compresses the pulmonary vascular bed. This increases pulmonary vascular resistance, thereby reducing right ventricular output.
- **Reduced left ventricular output** — Increased pulmonary vascular resistance can shift the interventricular septum to the left, impair diastolic filling of the left ventricle, and reduce left ventricular output.

In contrast to these adverse effects, positive pressure ventilation may be beneficial in patients with left ventricular failure. Specifically, increased intrathoracic pressure can improve left ventricular performance by decreasing both venous return and left ventricular afterload [10].

These hemodynamic effects are the result of positive airway pressure being transmitted to the surrounding structures of the thorax. The extent to which this occurs varies according to chest wall and lung compliance. Transmission of airway pressure is greatest when there is low chest wall compliance (eg, fibrothorax) or high lung compliance (eg, emphysema); it is least when there is high chest wall compliance (eg, sternotomy) or low lung compliance (eg, ARDS, congestive heart failure).

Monitoring — Another consequence of positive airway pressure being transmitted to surrounding intrathoracic structures is that hemodynamic measurements may be artificially elevated. PEEP plays a particularly prominent role because most hemodynamic measurements are performed at the end of expiration when PEEP is the primary source of positive airway pressure.

The effect of positive pressure ventilation on hemodynamic measures has been best studied using the pulmonary capillary wedge pressure (PCWP). The PCWP is measured by a pulmonary artery catheter (Swan-Ganz catheter). When a patient is receiving positive pressure ventilation, the PCWP is artificially elevated and not reflective of the true transmural filling pressure.

The true transmural filling pressure can be estimated by subtracting one-half of the PEEP level from the PCWP if the lung compliance is normal, or one-quarter of the PEEP level if lung compliance is

reduced [11] . As an example, for a patient with normal lung compliance who is receiving a PEEP of 12 cmH₂O and whose PCWP is measured as 18 mmHg, the true PCWP is estimated to be 12 mmHg.

A more precise way to estimate the true transmural PCWP in patients requiring positive pressure ventilation utilizes the respiratory related variation of PCWP to estimate the transmission of alveolar pressure to the pulmonary vessels [12] . This measure is called the index of transmission:

Index of transmission =
(end inspiratory PCWP – end expiratory PCWP) / (plateau airway pressure – total PEEP)

Measurement of the plateau airway pressure is described separately. (See "[Pulmonary barotrauma during mechanical ventilation](#)", section on Prevention).

Once the index of transmission is calculated, the true PCWP can be estimated:

Transmural PCWP =
end-expiratory PCWP – (index of transmission x total PEEP)

This estimate may be unreliable if the respiratory variation of the PCWP is greater than that of the pulmonary arterial pressure tracing ([show figure 3](#)) [13] . (See "[Swan-Ganz catheterization: Interpretation of tracings](#)").

Gastrointestinal — Positive pressure ventilation for greater than 48 hours is a risk factor for clinically important GI bleeding due to stress ulceration. (See "[Stress ulcer prophylaxis in the intensive care unit](#)").

Positive airway pressure (especially PEEP) is also associated with decreased splanchnic perfusion [14] . The mechanism underlying this association is unknown, but may be related to decreased cardiac output [15] . Decreased splanchnic perfusion manifests as elevated plasma aminotransferase and lactate dehydrogenase levels.

Other gastrointestinal complications seen in patients receiving positive pressure ventilation include erosive esophagitis, diarrhea, acalculous cholecystitis, and hypomotility [16,17] . It is uncertain whether these complications are due to mechanical ventilation or the critical illness. Hypomotility usually manifests as intolerance to enteral feeding. Correction of electrolytic abnormalities and avoidance of drugs that adversely affect gastric motility (eg, opiates) can improve gastrointestinal motility.

Renal — A fall in cardiac output induced by positive pressure ventilation can stimulate the renin-angiotensin system, increase release of [antidiuretic hormone](#), and reduce secretion of atrial natriuretic peptide. The result is fluid retention and edema.

In addition, mechanical ventilation may contribute to acute renal failure. In a prospective cohort study of 29,269 critically ill patients, positive pressure ventilation was an independent risk factor for acute renal failure (OR 2.11, 95% CI, 1.58-2.82) [18] . The mechanism underlying this association is unknown, but it may also be related to decreased cardiac output.

Central nervous system — Positive pressure ventilation increases intracranial pressure (ICP). This is probably the result of elevated intrathoracic pressure impairing cerebral venous outflow.

Immune system — Positive pressure ventilation appears to induce inflammation. In a randomized trial of 44 patients, patients who received positive pressure ventilation using large tidal volumes and low PEEP had higher concentrations of inflammatory mediators in their blood and bronchoalveolar lavage fluid than patients who received a smaller tidal volumes and high PEEP [19] .

Positive pressure ventilation may also promote translocation of tracheal bacteria into the bloodstream, according to one animal study [20] . Translocation was most pronounced during ventilation with large tidal volumes and low PEEP.

SUMMARY AND RECOMMENDATIONS

- Pulmonary effects of positive pressure ventilation include pulmonary barotrauma, ventilator-associated lung injury, intrinsic positive end expiratory pressure (auto-PEEP), heterogeneous ventilation, increased physiologic dead space, decreased physiologic shunting, diaphragmatic muscle atrophy, respiratory muscle weakness, and diminished mucociliary motility. (See "[Pulmonary effects](#)" above).
- Auto-PEEP exists when there is positive airway pressure at the end of expiration due to incomplete exhalation. It exacerbates the hemodynamic effects of positive pressure ventilation, increases the risk of pulmonary barotrauma, and makes it more difficult for the patient to trigger a ventilator-assisted breath. Detection of auto-PEEP should prompt immediate ventilator setting changes, efforts to reduce ventilatory demand, and efforts to reduce expiratory flow resistance. (See "[Auto-PEEP](#)" above).
- Positive pressure ventilation may reduce cardiac output and impair hemodynamic monitoring. In addition, it is associated with gastrointestinal stress ulceration, decreased splanchnic perfusion, gastrointestinal hypomotility, fluid retention, acute renal failure, increased intracranial pressure, and inflammation. (See "[Systemic effects](#)" above).

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GRAPHICS

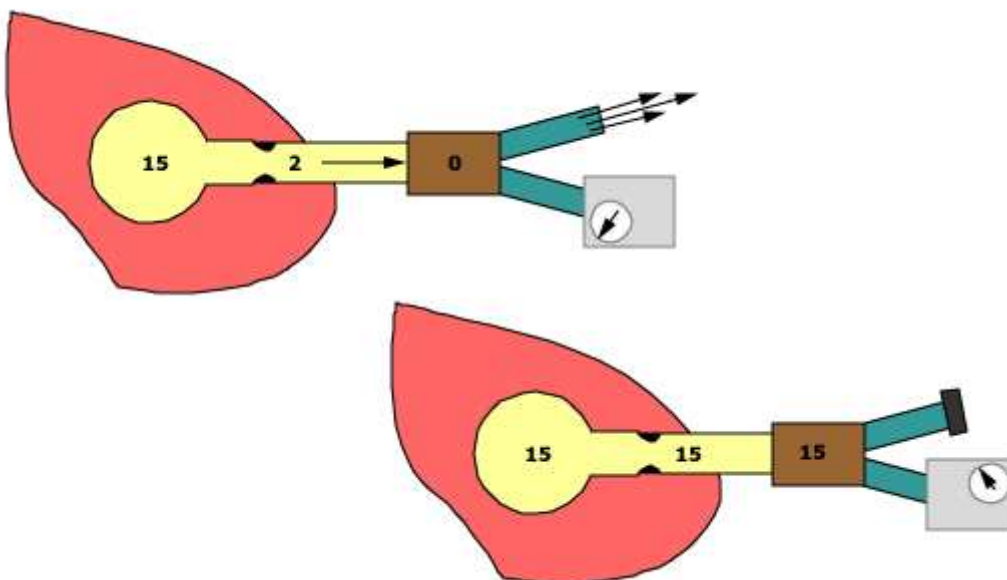
Determinants of dynamic pulmonary hyperinflation and auto-PEEP

Internal	External
Respiratory mechanics	Added flow resistance
Flow resistance	Fine bore endotracheal tube
Expiratory flow limitation	Ventilator tubing and devices
Respiratory system compliance	Ventilator setting
Breathing pattern	Frequency
Frequency of breathing	I:E ratio
T_I/T_{TOT}	Inflation volume
Tidal volume	End-inspiratory pause

T_I : inspiratory time, T_{TOT} : total cycle time.

Adapted from Rossi, A, Polese, G, Brandi, G, et al, Intensive Care Med 1995; 21:522.

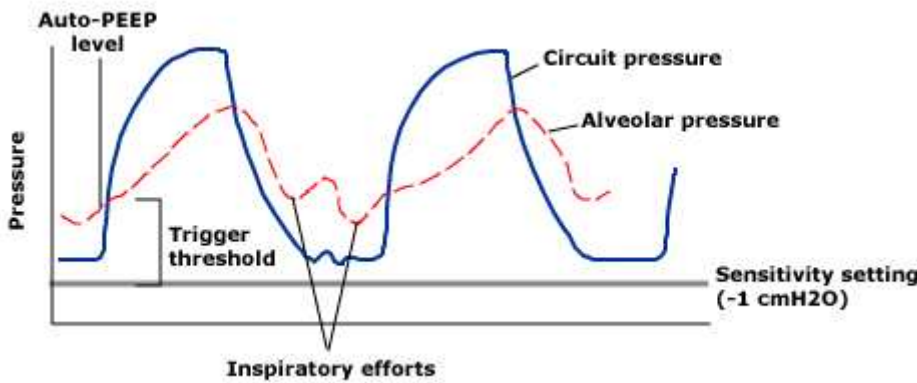
Quantification of the auto-PEEP effect



During mechanical ventilation of the patient with airflow obstruction, expiratory flow is too slow to allow complete deflation of the lung to its normal relaxed state before the ventilator delivers another breath. Slow flow continues until interrupted by the next inflation. Upper panel: Alveolar pressure remains positive at end exhalation (15 cmH₂O) but is not measured by the ventilator manometer (0 cmH₂O) located downstream from the site of increased airway resistance. Lower panel: Alveolar pressure at end-exhalation can be quantified by stopping flow transiently at the end of a set exhalation period, thereby allowing equilibration of pressures. Adapted from O'Quinn, R, Marini, JJ, Am Rev Respir Dis

1983; 128:319.

Trigger threshold for auto-PEEP



Effect of auto-PEEP on elevation of the triggering threshold in a mechanically ventilated patient with obstructive airways disease. This graphic representation shows airway pressure over time; the solid blue line demonstrates the circuit pressure as measured by the ventilator manometer, and the dashed red line is the alveolar pressure. In the absence of auto-PEEP, the sensitivity setting of -1 cm H₂O would be achieved by the patient making inspiratory efforts at the end of expiration, when airway pressure is at its minimum. In the presence of auto-PEEP, alveolar pressure remains positive. In this setting, the patient's inspiratory effort needs to decrease airway pressure not only by the -1 cm H₂O sensitivity set on the machine, but also by the amount of positive alveolar pressure (auto-PEEP). In this graph, the patient's inspiratory efforts are insufficient to trigger the ventilator and the patient is "locked out," being unable to get a breath because of an inability to overcome the elevated effective triggering threshold rendered by auto-PEEP. Adapted from Puritan-Bennett 1994, Form AA-1888.

Treatment of auto-PEEP

Changes in ventilator setting

- Increase expiratory duration
- Decrease respiratory rate
- Decrease tidal volume

Reduction in the ventilatory demand

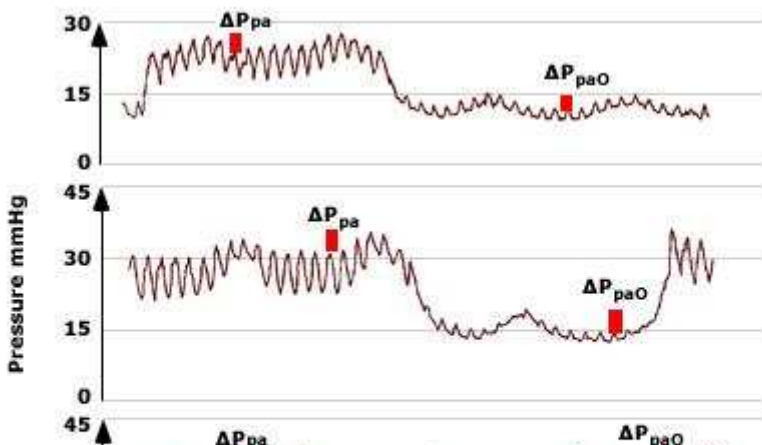
- Decrease carbohydrate intake
- Reduce dead space
- Reduce anxiety, pain, fever, shivering

Reduction of total flow resistance

- Use of large bore endotracheal tubes
- Frequent suctioning
- Bronchodilators

Application of external PEEP nearly up to the level of initial PEEP_i

Effect of PEEP on pulmonary hemodynamics





Pressure tracings from the same patient recorded at different levels of positive end-expiratory pressure (PEEP). The top panel shows 0 PEEP, the middle panel PEEP = 15 cmH₂O, and the bottom panel PEEP = 20 cmH₂O. Pulmonary artery pressure (P_{pa}) is shown at the left of the tracing. The right side of the tracing shows wedge (pulmonary artery occlusion) pressure (P_{paO}). The red bars indicate the degree of respiratory (or respirophasic) variation exhibited at each level of PEEP in pulmonary artery pressure and wedge pressure. The ratio of respiratory variation in pulmonary artery pressure divided by respiratory variation in the wedge pressure was close to 1 when PEEP = 0 or 15 cmH₂O PEEP. This increased to 2.3 at a level of 20 cmH₂O PEEP. This suggests a shift from West zone three to a non-zone three condition, where airway pressure has exceeded intravascular pressure at the balloon occluded pulmonary artery catheter tip. The end-expiratory wedge pressure value during PEEP = 20 cmH₂O is markedly higher than during PEEP = 15 cmH₂O (18 versus 10 mmHg), a change that cannot solely be explained by the increase in PEEP. *Redrawn from Teboul, JL, Besbes, M, Andrivet, P, et al, J Crit Care 1992; 7:22.*

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