

Michael R. Pinsky · Laurent Brochard  
Göran Hedenstierna · Massimo Antonelli  
*Editors*

# Applied Physiology in Intensive Care Medicine 1

Physiological Notes  
Technical Notes  
Seminal Studies in Intensive Care  
*Third Edition*

 Springer

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M.R. Pinsky · L. Brochard · G. Hedenstierna · M. Antonelli (Eds.)

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Physiological Notes – Technical Notes –  
Seminal Studies in Intensive Care

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# Preface

The practice of intensive care medicine is at the very forefront of treatment and monitoring response. The substrate of this care is the critically ill patient who, by definition, is at the limits of his or her physiologic reserve. Such patients need immediate, aggressive but balanced life-altering interventions to minimize the detrimental aspects of acute illness and hasten recovery. Treatment decisions and response to therapy are usually assessed by measures of physiologic function, such as cardiorespiratory monitoring. By necessity, the treatments and monitoring are constantly evolving and require intimate knowledge of the operation of complex instruments, like echocardiography, mechanical ventilation, and hemodialysis. Furthermore, they need to be applied quickly and correctly at the bedside by the primary care intensivists. However, how one uses such information from the monitoring and guides treatment is often unclear and rarely supported by prospective clinical trials. In reality, the bedside clinician is forced to rely primarily on physiologic principals in determining the best treatments and response to therapy. However, the physiologic foundation present in practicing physicians is uneven and occasionally supported more by habit or prior training than science.

A series of short papers published in Intensive Care Medicine from 2002 until July 2011 with the rubrics Physiologic Notes and Technical Notes attempt to capture the essence of the physiologic perspectives and technical challenges that underpin both our understanding of disease and response to therapy and treatments. The present volume combines these papers with associated seminal articles addressing these central issues and published in the same time interval. This volume was created to address this fundamental unevenness in our understanding of applied physiology, to underscore what is currently known, and to illustrate how measures and monitoring interact with organ system function and response to therapy. This collection of physiologic perspectives written by some of the most respected experts in the field represent an up-to-date and invaluable compendium of practical bedside knowledge essential to the effective delivery of acute care medicine. Although this text could be read from cover to cover, the reader is encouraged to use this text as a reference source, referring to individual physiologic notes and reviews that pertain to specific clinical issues. In that way the relevant information will have immediate practical meaning and hopefully become incorporated into routine practice.

We hope that the reader finds these papers and reviews useful in their practice and enjoys reading them as much as we enjoyed editing the original articles.

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# Intrinsic (or auto-) PEEP during controlled mechanical ventilation

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## Introduction

Extrinsic positive end-expiratory pressure (PEEP) applied to the patient at the airway opening is used artificially to increase end-expiratory lung volume. Extrinsic PEEP is increased or decreased in small increments in ventilator-dependent patients because of its marked effects on cardiorespiratory status. Unintentional or unmeasured end-expiratory hyperinflation, called intrinsic or auto-PEEP, can also occur and have similarly marked profound cardiorespiratory effects in ventilator-dependent patients during controlled mechanical ventilation. Ventilatory settings can interact with the passive process of expiration and generate intrinsic or auto-PEEP [1, 2].

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## What is intrinsic (or auto-) PEEP?

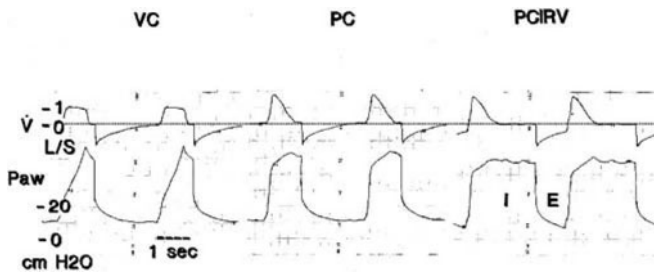
During passive expiration of the lungs the elastic forces of the respiratory system are the driving forces and can be described by the relationship between lung volume and the elastic recoil pressure of the respiratory system. The lower the elastic forces, or the higher the resistive forces, the longer will be the time needed to fully expire the inspired tidal volume. In a single-compartment model of the lung in which the lung behaves as if it has a single resistance and compliance, the volume at any given time during expiration ( $V$ ) is described by the monoexponential equation,  $V=V_o-Ve^{-kt}$ , where  $k$  is the time constant of the equation and is the product of resis-

tance times compliance (the reverse of elastance), and  $V_o$  is the end-inspiratory volume. In practical terms a time constant is the time required for the lungs to expire 63% of their initial volume. Thus the time needed passively to expire the inspired tidal volume is determined by the two main characteristics of the respiratory system: elastance and resistance. If expiration is interrupted before its natural end, i.e., by occurrence of the next inspiration, end-expiratory lung volume is higher than the so-called relaxation volume of the respiratory system, usually referred to as functional residual capacity. As a result the alveolar pressure at the end of expiration is higher than zero (zero being the atmospheric pressure), as predicted by the relationship between lung volume and the elastic recoil pressure of the respiratory system. This process is called dynamic hyperinflation, and the positive end-expiratory alveolar pressure associated with a higher than resting lung volume, is called intrinsic or auto-PEEP. Importantly for the clinician, this pressure is not directly measured at the airway opening and is thus not shown on the pressure dial of the ventilator. What the ventilator measures is the pressure in the ventilator circuit. Because the direction of the flow is still expiratory, the pressure measured by the ventilator at the end of expiration reflects only the relationship between flow and the resistance of the expiratory line, above the set PEEP. It does not give the clinician any information about the real alveolar pressure.

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## How one can suspect the presence of intrinsic (or auto-) PEEP

The presence of a positive alveolar pressure higher than the atmospheric pressure or higher than the external PEEP set on the ventilator (which is a new “reference pressure” for the lungs) can be identified by inspection of the expiratory flow-time curve. When the expiratory time is sufficient for lung emptying, expiratory flow de-



**Fig. 1** Tracings of flow ( $\dot{V}$ ) and airway pressure ( $P_{aw}$ ) at the airway opening during volume controlled (VC), pressure-controlled (PC), and pressure-controlled inverse ratio ventilation (PCIRV). In the first two situations the expiratory flow declines gradually to zero; in the third case inspiration is lengthened by the inverse ratio setting and expiration shortened; the expiratory flow is abruptly interrupted, indicating the presence of dynamic hyperinflation and intrinsic or auto-PEEP. (From Lessard et al. [3])

clines from a maximum to zero or to the set PEEP. An interruption in this process results in an abrupt change in the slope of this curve, immediately continued by the next inspiratory flow. In other words, the next “inspiration” starts during “expiration.” Since the ventilator, which cannot generate flow into the patient’s lungs until the pressure at the airway opening exceeds the end-expiratory alveolar pressure, one way in which to measure intrinsic or auto-PEEP is to determine the airway pressure at the exact time of inspiratory flow. One can measure the intrinsic PEEP level by simultaneously recording airway pressure and flow data using a high-speed tracing. [Figure 1](#) illustrates how shortening the expiratory phase generates such dynamic hyperinflation [3].

### Is the level of intrinsic (or auto-) PEEP predictable?

If one assumes the respiratory system to be homogeneous and behave as a single compartment, a monoexponential equation can be used. By simple mathematics it takes three time constants (one being the product of resistance and compliance) to expire 96% of the inspired tidal volume. Therefore any longer expiratory time minimizes or fully avoids incomplete emptying. For instance, a resistance of  $10 \text{ cmH}_2\text{O}\cdot\text{l}^{-1}\cdot\text{s}^{-1}$  and a compliance of  $100 \text{ ml}\cdot\text{cmH}_2\text{O}^{-1}$  ( $0.1 \text{ l}\cdot\text{cm H}_2\text{O}^{-1}$ ) results in a time constant of 1 s. Thus 3 s represents the minimal expiratory time needed to avoid intrinsic or auto-PEEP. Unfortunately, the diseased lungs are not only frequently inhomogeneous, making this calculation overly simplistic, but the presence of small airway collapse during expiration, also referred to as expiratory flow limitation, makes this even more complicated. Because of an abnormal structure of the small airways, when the pressure surrounding these conducts becomes higher than the pressure inside the airway, these small conducts collapse. The relationship between the “driving pressure” (pres-

sure in the alveoli minus pressure at the airway opening) on which is based the equation, disappears. In the setting of expiratory flow-limitation, the expiratory time required to minimize intrinsic PEEP is much longer than predicted by the time constant alone. By minimizing inspired minute ventilation the clinician can minimize intrinsic (auto-) PEEP.

### Can intrinsic (or auto-) PEEP be reliably measured?

Since the reason for the presence of intrinsic PEEP is flow-dependent pressure gradients from the alveolus to the airway opening, occluding of the expiratory port of the ventilator at the exact end of expiration causes airway pressure to equilibrate rapidly with alveolar pressure and reliably measure the end-expiratory alveolar pressure. This occlusion takes place at the exact time where the next inspiration should place and is now available on most modern ventilators (“expiratory hold or pause”). If the patient is fully relaxed, this pressure measurement reflects the mean alveolar pressure at the end of expiration. Most of the time a plateau is reached after less than 1 s, but in the case of inhomogeneous lungs this pressure may require a few seconds to also reflect some very slow compartments. This airway occlusion pressure may not be homogeneously present in the whole lung but represents an average pressure of all regional levels of end-expiration alveolar pressure. Usually the difference between the expiratory pause airway pressure and the set external PEEP is called intrinsic or auto-PEEP, while the measured pressure is referred to as total PEEP.

### Can the set external PEEP influence the total PEEP in the case of dynamic hyperinflation?

A frequent confusion is the belief that external PEEP could be useful in reducing the level of dynamic hyperinflation because it helps to reduce the value of auto- or intrinsic PEEP. Obviously this is not the case. The effect of external PEEP is to minimize the difference between the alveolar and the ventilator proximal airway pressure. This difference being called intrinsic or auto-PEEP, external PEEP application results in a decreased intrinsic or auto-PEEP. The level of dynamic hyperinflation, however, depends on the level of total PEEP and is either not influenced by external PEEP when external PEEP is less than intrinsic PEEP or is even worsened if external PEEP is set higher than the minimal level of regional intrinsic PEEP.

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# **Intrinsic (or auto-) positive end-expiratory pressure during spontaneous or assisted ventilation**

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## **Introduction**

The mechanisms generating intrinsic or auto-positive end-expiratory pressure (PEEP) during controlled mechanical ventilation in a relaxed patient also occur during spontaneous breathing or when the patient triggers the ventilator during an assisted mode [1, 2]. These include an increased time constant for passive exhalation of the respiratory system, a short expiratory time resulting from a relatively high respiratory rate and/or the presence of expiratory flow limitation. Whereas dynamic hyperinflation and intrinsic or auto-PEEP may have haemodynamic consequences, this is not frequently a major concern in spontaneously breathing patients or during assisted ventilation because the spontaneous inspiratory efforts result in a less positive or more negative mean intrathoracic pressure than during controlled mechanical ventilation. The main consequence of dynamic hyperinflation during spontaneous and assisted ventilation is the patient's increased effort to breathe and work of breathing [1, 2].

---

## **To what extent does intrinsic (or auto-) positive end-expiratory pressure influence work of breathing?**

For air to enter the lungs, the pressure inside the chest has to be lower than the pressure at the mouth (spontaneous breathing) or at the airway opening (assisted ventilation). In the case of intrinsic (or auto-) PEEP, by definition, the end-expiratory alveolar pressure is higher than the pressure at the airway opening. When the patient initiates the breath, there is an inevitable need to reduce airway pressure to zero (spontaneous breathing) or to the value of end-expiratory pressure set on the ventilator (assisted ventilation) before any gas can flow into the lungs. For this reason, intrinsic or (auto-) PEEP has been described as an inspiratory threshold load. In patients with chronic obstructive pulmonary disease (COPD) this load has sometimes been measured to be the major cause of increased work of breathing [3].

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## **During assisted ventilation, is the trigger sensitivity important to reduce intrinsic (or auto-) positive end-expiratory pressure?**

Because the problem of intrinsic or (auto-) PEEP has to do with the onset of inspiration, one may reason that increasing the inspiratory trigger sensitivity to initiate a breath with a lower pressure or flow deflection should reduce the work of breathing induced by hyperinflation. These systems are based on the detection of a small pressure drop relative to baseline (pressure-triggering system) or on the presence of a small inspiratory flow (flow-triggering systems). Unfortunately, increasing the trigger sensitivity induces only a small reduction in the total work of breathing. The reason for this lack of effect relates to the need for the inspiratory trigger to sense changes in airway pressure or in inspiratory flow. Thus, intrinsic PEEP needs to be counterbalanced first by the

effort of the inspiratory muscles, in order for this effort to generate a small pressure drop (in the presence of a closed circuit) or to initiate the inspiratory flow (in an open circuit) [4]. The consequence of intrinsic or (auto-) PEEP is that the inspiratory effort starts during expiration. This is easily identified by inspection of the expiratory flow-time curve [1]. As a consequence, it cannot be detected by any of the commercially available trigger systems.

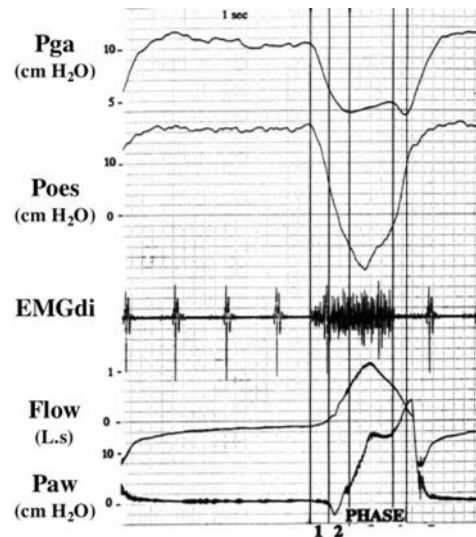
### Can the set external positive end-expiratory pressure reduce dynamic hyperinflation and work of breathing?

Responses to these two questions are the same as during controlled mechanical ventilation in a relaxed patient [1]. Their consequences are, however, very different. External PEEP reduces the difference between the alveolar and the ventilator proximal airway pressure, i.e., intrinsic (or auto-) PEEP. The inspiratory threshold load resulting from intrinsic (or auto-) PEEP is thus reduced by addition of external PEEP. Thus, the total work of breathing is reduced, especially in patients with high levels of intrinsic (or auto-) PEEP, such as those subjects with COPD [5, 6].

Although external PEEP reduces work of breathing, it does not minimise hyperinflation. The level of dynamic hyperinflation is not modified by external PEEP, unless this PEEP is set higher than the minimal level of regional intrinsic PEEP, and then hyperinflation increases. Increasing hyperinflation can aggravate the working conditions of the respiratory muscles by placing them at a mechanical disadvantage and can result in significant haemodynamic compromise by decreasing venous return and increasing right ventricular outflow resistance. Hyperinflation in excess of intrinsic (or auto-) PEEP occurs usually when the set PEEP is positioned at values above 80% of the mean "static" intrinsic PEEP [7]. For this reason, titration of external PEEP based on measuring intrinsic (or auto-) PEEP would be desirable. Unfortunately, a reliable measurement of intrinsic (or auto-) PEEP in the spontaneously breathing subject is much more difficult to obtain than in passive positive-pressure ventilation conditions.

### Can standard ventilatory settings influence intrinsic (or auto-) positive end-expiratory pressure?

During assisted ventilation, the patient is supposed to determine the respiratory rate freely, and one may suppose that he/she will govern his/her respiratory rate to control expiratory time and minimise hyperinflation. Unfortunately, most patients will not be able to counteract fully the effects of a ventilator inspiratory time longer than



**Fig. 1** Tracings of gastric ( $P_{ga}$ ), oesophageal ( $P_{oes}$ ) and airway ( $P_{aw}$ ) pressures, flow and diaphragmatic electromyographic activity ( $EMG_{di}$ ) during an assisted breath (pressure-support ventilation). The vertical lines help to delineate the different phases of the inspiratory effort. During phase 1, the flow is still expiratory: the start of  $EMG_{di}$  and the abrupt decrease in both  $P_{es}$  and  $P_{ga}$  all indicate that the patient performs an active inspiratory effort against intrinsic positive end-expiratory pressure (PEEP) at the same time that his/her expiratory muscles relax. Phase 2 is the triggering of the ventilator and occurs once intrinsic (or auto-) PEEP has been counterbalanced

their own inspiratory time [8]. Although some compensatory mechanism may exist, it will frequently be insufficient. Every setting influencing the ventilator inspiratory time may thus influence the level of dynamic hyperinflation.

### Is intrinsic (or auto-) positive end-expiratory pressure always synonymous with dynamic hyperinflation?

In patients with spontaneous respiratory activity, recruitment of the expiratory muscles frequently participates in generating intrinsic (or auto-) PEEP independently of dynamic hyperinflation. In the case of airflow obstruction, the main consequence of an activation of the expiratory muscles is to augment intrathoracic pressure, whereas their effects on expiratory flow may be very modest, especially in the case of airflow limitation, thus promoting small airways to collapse. The activation of the expiratory muscles results from an increase in respiratory drive. Many patients with COPD already have a recruitment of their expiratory muscles at rest. This expiratory muscle recruitment results in a measurable increase in alveolar pressure. However, such expiratory muscle recruitment, although creating an intrinsic (or au-