

### Shortening ventilator time: physiology is key



Mechanical ventilation is used to decrease work of breathing. However, because complications are axiomatic to mechanical ventilation, it should be discontinued at the earliest possible time, according to a review article published in Annals of the American Thoracic Society.

The overriding objective of mechanical ventilation is to decrease work and oxygen cost of breathing, enabling precious oxygen stores to be rerouted from the respiratory muscles to other vulnerable tissue beds.

"Achieving this goal requires that cycling of the ventilator be carefully aligned with the intrinsic rhythm of a patient's respiratory centre output," writes article author Martin J. Tobin, MD, Division of Pulmonary and Critical Care Medicine, Hines Veterans Affairs Hospital, Hines, IL.

As noted in the article, **problems** in aligning the **cycling** of a ventilator with a patient's own rhythm of breathing may arise at **three points**: cycling-on (**triggering**), **post-trigger inflation**, and cycling-off (**inspiration**<u>expiration</u><u>switchover</u>). In a study of factors contributing to ineffective triggering, **breaths** before **nontriggering** attempts had a **higher** tidal volume (**VT**) and a **shorter expiratory time** than did the breaths before triggering attempts. In addition, some patients exhibit **double triggering**, where the ventilator produces **two inflations** within a **single inspiratory effort** made by the patient.

"Some might think that these triggering peculiarities are nothing more than arcane quirks; on the contrary, they have major significance and contribute to patient mortality when they go unrecognised," Dr. Tobin points out.

Consider mechanical ventilation in patients with acute respiratory distress syndrome, where a VT of 6 ml/kg has been shown to lower mortality. This setting, the author says, is so widely accepted that it has become de rigueur in protocolised management.

"Protocol advocates, ungrounded in physiology, do not recognise that low VT is necessarily accompanied by shortening of mechanical inspiratory time. Once mechanical inspiratory time becomes less than neural inspiratory time, double triggering is inevitable," Dr. Tobin explains.

Although mechanical ventilation saves lives, the author highlights it is also responsible for many deaths. Thus, it is critical to get patients off the ventilator at the earliest possible time.

To shorten ventilator time, the critical step is to screen for weanability through use of weaning predictor tests, according to Dr. Tobin. Use of <u>T-tube trials circumvents</u> the <u>impossibility</u> of <u>estimating</u> patient <u>work</u> of breathing

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during pressure support. Before extubation, patients should demonstrate the ability to breathe successfully in the absence of pressure support and positive end-expiratory pressure.

"Over the breadth of my pulmonary and critical care practice, no area demands greater understanding of physiological principles than ventilator management. The need for physiological understanding is greatest when facilitating expeditious weaning while minimising the risk of death," the author says.

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# **NOBEL PRIZE SYMPOSIUM**

## **Physiologic Basis of Mechanical Ventilation**

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#### Abstract

The primary purpose of mechanical ventilation is to decrease work of breathing. Achieving this goal requires that cycling of the ventilator be carefully aligned with the intrinsic rhythm of a patient's respiratory center output. Problems arise at the point of ventilator triggering, post-trigger inflation, and inspiration–expiration switchover. Careful, iterative adjustments of ventilator settings are required to minimize work of breathing. Use of protocols for the selection of ventilator settings can lead to complications (including alveolar overdistention) and risk of death. Because complications are axiomatic to mechanical ventilation, it should be discontinued at the earliest possible time. To shorten ventilator time, the critical step is to screen for weanability through use of weaning predictor tests. Use of T-tube trials circumvents the impossibility of estimating patient work of breathing during pressure support. Before extubation, patients should demonstrate the ability to breathe successfully in the absence of pressure support and positive end-expiratory pressure.

**Keywords:** mechanical ventilation; control of breathing; respiratory muscles; respiratory mechanics; ventilator weaning

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The overriding objective of mechanical ventilation is to decrease work and oxygen cost of breathing, enabling precious oxygen stores to be rerouted from the respiratory muscles to other vulnerable tissue beds (1, 2). Patient work during mechanical ventilation is primarily determined by a physician's ability to align the rhythm of the machine with the rhythm of the patient's respiratory centers (3). Problems in aligning the cycling of a ventilator with a patient's own rhythm of breathing may arise at three points: cyclingon (triggering), post-trigger inflation, and cycling-off (inspiration-expiration switchover) (4).

#### Problems with Ventilator Triggering

For a given trigger sensitivity, a patient's respiratory center output determines the delay between the start of inspiratory effort and start of ventilator unloading. When a patient's respiratory center output is low, assistance may be delayed until well into the patient's inspiratory time, thereby causing the ventilator to cycle almost completely out of phase with the patient's respiratory cycle (4). When a patient's inspiratory effort opens the ventilator demand valve, the inspiratory neurons do not suddenly switch off, and a patient may expend considerable inspiratory effort throughout the remainder of inflation (5). The level of patient effort during this posttrigger phase is closely related to a patient's inspiratory motor output at the point of triggering (6).

Among patients receiving a high level of ventilator assistance, a quarter to a third of a patient's inspiratory efforts may fail to trigger the machine (6). The proportion of ineffective triggering attempts increases in direct proportion to the level of ventilator assistance (6). In a study of factors contributing to ineffective triggering, breaths before nontriggering attempts had a higher tidal volume (VT) and a shorter expiratory time than did the breaths before triggering attempts (6). The combination of higher VT and abbreviated expiratory time hinders the ability of the lung to return to its relaxation volume, leading to an increase in elastic recoil pressure. This is reflected as increase in intrinsic positive end-expiratory pressure, which, in turn, raises the true pressure threshold required to trigger the ventilator.

Some patients exhibit double triggering, where the ventilator produces two inflations within a single inspiratory effort made by the patient (7). With assistcontrol ventilation, double triggering is likely when the set mechanical inspiratory time is substantially less than a patient's neural inspiratory time. In this situation, mechanical inflation terminates while the patient continues to make an inspiratory effort. After a short period, the ventilator may trigger again, resulting in a second inflation within the same neural inspiration and, thus, greater alveolar distension breath stacking—than with the delivery of a single VT (4).

Some might think that these triggering peculiarities are nothing more than arcane quirks; on the contrary, they have major significance and contribute to patient mortality when they go unrecognized. Consider mechanical ventilation in patients with acute respiratory distress syndrome, where a VT of 6 ml/kg has been shown to lower mortality (8). This setting is so widely accepted that it has become de rigueur in protocolized management. Protocol advocates, ungrounded in physiology, do not recognize that low VT is necessarily accompanied by shortening of mechanical inspiratory time. Once mechanical inspiratory time becomes less than neural inspiratory time, double triggering is inevitable (4). Protocol enthusiasts believe they are delivering a VT of 6 ml/kg, but the patient is receiving 12 ml/kg—a setting proven to increase mortality. There is no substitute for deep understanding and clinical wisdom when taking care of patients (9).

#### Setting of Inspiratory Flow

When patients are initially connected to a ventilator in the volume-control mode, inspiratory flow is typically set at some default value, such as 60 L/min (10). Many critically ill patients have elevated respirator center output, and the flow setting may not be sufficient to meet the patient's flow demands. Consequently, patients will struggle against their own respiratory impedance and that of the ventilator, with consequent increase in the work of breathing (11). This problem is usually detectable by observing a scalloped contour on the airway pressure tracing (signifying an increased level of patient work) (2). Frequently, an increase in inspiratory flow will achieve a more favorable airway pressure contour (becoming more convex or outward). In some patients, however, an increase in flow causes immediate and persistent tachypnea (12), with consequent shortening of expiratory time and increase in intrinsic positive end-expiratory pressure. The response to such adjustments is influenced by the Hering–Breuer reflex and is variable from patient to patient (13). The clinician needs to adopt a "trial-and-error" approach, adjusting ventilator flow and observing the contour of the airway pressure tracing. No algorithm can substitute for bedside iterative adjustments (11).

#### Inspiration-Expiration Switching (Cycling-Off Function)

The next point in the respiratory cycle at which problems may arise is at the switchover between inspiration and expiration (4). During pressure support, the algorithm for "cycling-off" of mechanical inflation is based on a decrease in flow to 25% of the peak value. Such algorithms can be problematic in patients with chronic obstructive pulmonary disease, because increases in resistance and compliance produce a slow time constant of the respiratory system. The longer time needed for flow to fall to the threshold value can cause mechanical inflation to persist into neural expiration (14). As a result, patients may activate their expiratory muscles while the ventilator is still inflating the thorax (15). The continuation of mechanical inflation into neural expiration is very uncomfortable, as is well recognized with use of inverse-ratio ventilation. The problem of expiratory muscle recruitment during lung inflation constitutes an underrecognized form of patient-ventilator dyssynchrony (11).

#### Interactions of Mechanical Ventilation with Sleep Quality

Behavioral factors and the wakefulness drive to breathe can interfere with patientventilator interaction and thus lead to dyssynchrony. By removing these stimuli, sleep might be expected to enhance respiratory muscle rest during mechanical ventilation (4). But again, physiological mechanisms intervene. Patients ventilated with pressure support commonly develop central apneas during sleep, which does not occur during assist-control ventilation because of the backup rate (16). The occurrence of central apneas during pressure support is not related to the size of VT. Central apneas lead to sleep fragmentation (arousals and awakenings), equivalent to that experienced by patients with obstructive sleep apnea, who have excessive daytime sleepiness and impaired cognition (17). Central apneas during pressure support occur in proportion to the difference between prevailing partial pressure of carbon dioxide and the patient's apnea threshold (16). The addition of dead space to increase prevailing partial pressure of carbon dioxide causes a decrease in the

number of central apneas and the number of arousals and awakenings. Dead space is used solely in experimental studies to elucidate physiological mechanisms and is rarely added in clinical practice. Instead, physicians suspecting this problem should ensure that patients are <u>ventilated</u> with assist-control ventilation during sleep.

#### Weaning

Although mechanical ventilation saves lives, it is also responsible for many deaths (18). Accordingly, it is critical to get patients off the ventilator at the earliest possible time. This task demands greater wisdom and cognitive skill than that required for adjusting settings on the ventilator (19).

Randomized controlled trials on weaning techniques reveal that physicians are inherently slow at initiating the weaning process (20, 21). Weaning predictor tests consist of physiological measurements that alert a physician that a ventilated patient might be able to come off the ventilator sooner than the physician otherwise thinks (19). The degree of rapid shallow breathing, quantified by frequency-to-VT ratio (f/VT), has been shown to be the best predictor of weaning outcome (22, 23). The accuracy of f/VT in predicting weaning outcome has been evaluated by more than 27 groups of investigators, making it the most reevaluated phenomenon in critical care. Some investigators reported that f/VT was unreliable in predicting weaning outcome. Once the "nonsupportive" data are analyzed using a Bayesian framework, however, they unwittingly confirm the reliability of f/VT (22, 23).

Weaning predictors are not done to forecast a failed weaning trial but to alert a physician that a patient might tolerate a weaning trial sooner than the physician otherwise thinks. This could move the weaning trial earlier in time and shorten the overall of duration of mechanical ventilation. If f/VT is less than 100, the physician proceeds with a weaning trial, using one of two methods: intermittent unassisted breathing (zero ventilator support, as with a T-tube trial) or gradual reduction in ventilator assistance.

The first randomized controlled trial of different weaning methods, undertaken by Brochard and colleagues in 1994, revealed that intermittent mandatory ventilation was the worst method (20).

One arm in this randomized controlled trial was T-tube trials combined with assist control, but the duration of rest between each failed T-tube trial could be as brief as 1 hour (20). At this time, Laghi and colleagues had data showing that recovery from diaphragmatic fatigue required at least 24 hours of rest (24). This was the motivation behind the incorporation of a 24-hour rest arm in a randomized controlled trial conducted by the Spanish Lung Failure Collaborative Group (25). The randomized controlled trial revealed that T-tube trials, combined with 24 hours of rest, weaned patients three times faster than did intermittent mandatory ventilation and two times faster than did pressure support (21).

The most difficult group of patients to wean is those requiring prolonged ventilation in a long-term acute care hospital. In a randomized trial, intermittent unassisted breathing (using a tracheostomy collar) resulted in 1.43 times faster removal of the ventilator than did pressure support (26).

The superior outcome with the unassisted-breathing arm (T-tube, tracheostomy collar) is best explained based on physiology (21, 26). During a tracheostomy collar or T-piece trial, the amount of respiratory work is determined solely by the patient—the ventilator cannot do any work. During pressure-support weaning, a clinician's ability to judge weanability is obscured, because the patient is receiving ventilator assistance. It may be that the ventilator is doing a moderate amount of work, a large amount of work, or very little work. During pressure support, it is extremely difficult to distinguish between how much work the patient is doing and how much work the ventilator is doing even when esophageal pressure is being monitored—and impossible without esophageal-pressure monitoring (4, 14). Because of the impossibility of guesstimating work of breathing during pressure support, clinicians are more likely to accelerate the weaning process in patients who perform unexpectedly well during a T-piece trial or tracheostomy collar challenge than when a low level of pressure support is being used (26).

Many physicians think weaning is complete when they reach pressure support of approximately 5 to 7 cm H<sub>2</sub>O, often combined with positive end-expiratory pressure of  $5 \text{ cm H}_2\text{O}$ , and extubate patients from these settings (27). When assessing a patient's readiness for extubation, a physician needs to guesstimate the patient's work of breathing. Compared with work of breathing in the extubated state, breathing through the ventilator circuit (with continuous positive airway pressure of 0 and pressure support of 0) decreases patient work by about 1%. In contrast, continuous positive airway pressure of 5 cm  $H_2O$  decreases patient work of breathing by 40% (27, 28). Pressure support of 5 cm H<sub>2</sub>O decreases patient work of breathing by <u>30 to 40%</u> (27, 28).

The vast majority of patients can cope with a 40 to 60% increase in work of breathing at the point of extubation, but a fragile patient may not. To extubate a fragile patient directly from continuous positive airway pressure of 5 cm H<sub>2</sub>O or from pressure support of 5 cm  $H_2O$  is to risk killing that patient (27). The reasoning behind this statement is the following: For decades, it has been recognized that 15 to 20% of extubated patients require reintubation and that mortality among patients requiring reintubation is 33 to 40% (29). Thus, approximately 5 to 8% of patients undergoing the first extubation will ultimately die. The dominant reason that patients fail extubation is an increase in work of breathing. Clinical estimation of work of breathing in a patient receiving assisted ventilation is impossible in the absence of esophageal-pressure monitoring. Because of the impossibility of identifying before extubation the 5 to 8% of patients who will die after extubation, it is necessary to treat all patients as vulnerable and assess their ability to breathe in the complete absence of ventilator assistance (zero pressure support and zero continuous positive airway pressure) before extubation.

#### Conclusions

Over the breadth of my pulmonary and critical care practice, no area demands greater understanding of physiological principles than ventilator management. The need for physiological understanding is greatest when facilitating expeditious weaning while minimizing the risk of death.

**Author disclosures** are available with the text of this article at www.atsjournals.org.

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