

Noisy Mechanical Ventilation

Listen to the Melody

BIOLOGIC systems are characterized by variability, termed “noise,” rather than monotonous patterns. For example, two cells will have different chemical compositions, despite identical gene expression. The random nature of these fluctuations improves the fitness of both subcellular processes and organismal survival, when compared to deterministic systems.¹ This phenomenon has been termed stochastic resonance, whereby noise added to a system improves the systems performance.

Traditional volume-cycled mechanical ventilation is monotonous; if the diaphragm does not participate in facilitating mechanical ventilation, then disuse atrophy occurs rapidly.² Using variability in breathing patterns during assisted spontaneous ventilation while improving lung function is not a completely new concept. It was probably first elucidated by Suki *et al.*, in *Nature* in 1998. In their study, variation of pressure during mechanical ventilation led to an increase in oxygenation and was explained by stochastic resonance, where increasing the SD of noise can amplify a weak signal and eventually increase the output.³ How might noise improve oxygenation? Because of hysteresis, more lung volume is gained when noise increases inflation pressure than is lost when the noise reduces inflation pressure. Today, there are several programs on newer generation mechanical ventilators that allow for this type of variability (Bi-level and Airway Pressure Release Ventilation). However, there is no large-scale data showing patient mortality or morbidity benefits while using these newer modalities.

In this issue of ANESTHESIOLOGY, Spieth and colleagues provide insight into novel spontaneous breathing modes of mechanical ventilation in acute lung injury (ALI).⁴ This study complements their previous work describing the importance of spontaneous breathing in acute lung injury.⁵ Using a porcine animal model, ALI was induced using surfactant depletion. When compared to more traditional modes of mechanical ventilation, noisy pressure support ventilation led to increased variability in respiratory pattern, resulting in improved ventilation/perfusion matching, lower mean airway pressures, and

improved oxygenation. In this study, Spieth *et al.* used spontaneously breathing anesthetized pigs and the concept of noisy pressure support ventilation. A target mean pressure support value was designated at the value needed to maintain a tidal volume of 6 ml/kg. From this value, variability of up to 45% over a normal distribution was introduced into the pressure support levels (no higher than 40 cm H₂O) that resulted in tidal volume variability. Looking specifically at 7.5%, 15%, 30%, and 45% variability from the mean, they determined that at moderate levels (15–30%) there was improvement in the PaO₂/Fio₂ ratio with no significant impact on hemodynamics or comfort of breathing.

Spieth and colleagues show that noisy pressure support ventilation in surfactant depleted ALI can improve oxygenation on a short-term basis. However, it has yet to be clearly illustrated that a quick improvement in this ratio can improve pulmonary function in the long run. In fact, there is no clear clinical evidence based on human trials that there is a significant improvement in patient mortality when the PaO₂/Fio₂ ratio is improved over a short period of time. The original ARDSNet low tidal volume *versus* traditional tidal volume multicenter study showed that patients who received larger tidal volumes had a statistically significant improvement in their PaO₂/Fio₂ ratio, but ultimately showed substantially increased mortality.⁶ This potential epiphenomenon has also been shown with high frequency oscillatory ventilation in adults with the acute respiratory distress syndrome (ARDS), although these studies have not been nearly as large as the ARDSNet trial.^{7,8} Therefore, rapid improvement in pulmonary function in ARDS/ALI does not necessarily translate to improvements in overall morbidity or mortality. However, improving oxygenation through increased mean airway pressure may be detrimental, whereby in the case of noisy ventilation, oxygenation is improved without concomitant increases in airway pressure.

Controlled mechanical ventilation is usually used in patients with ARDS and/or ALI. In most cases, to achieve ventilator synchrony, patients are administered sedatives and, less frequently, muscle relaxants. It is well accepted that patients on spontaneous breathing modes probably require less sedation. This sedation decrease alone can have significant beneficial effects on a patient's hospital course (fewer ventilator days, decreased intensive care unit length of stay, less delirium, etc.).^{9,10}

The majority of experimental models have examined the efficacy of noisy ventilation in the setting of ALI. What about the use of noisy ventilation in normal lungs? Could this technique protect the lungs from inflamma-

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tory injury before it occurs? Schultz *et al.* reviewed the literature supporting the use of protective mechanical ventilation, suggesting that patients without ALI/ARDS remain at risk for ventilator-associated lung injury and should be supported with lower tidal volumes.¹¹ The same group demonstrated that protective mechanical ventilation reduced the release of proinflammatory mediators into the alveolar airspaces of patients without ALI/ARDS.¹² Recent investigations have begun to identify pathways such as the Toll-like receptor, through which mechanical ventilation may stimulate inflammation. It is intriguing to speculate that, in addition to lung recruitment, noisy mechanical ventilation may limit activation of these proinflammatory processes.¹³

The importance of variability, whether referring to the respiratory system or DNA, in biologic systems should not be underemphasized. It is variability that makes each individual unique. It is genetic diversity that makes our world what it is today and what has allowed us to flourish as human beings. Removing variability may not be beneficial because variability is an essential part of normal human physiology. It allows us not only to adapt to changes in our environment, but also derangements in our bodies. Controlled mechanical ventilation provides, for the most part, a breathing pattern that is very monotonous. It is against our nature, our behavior, to sustain this for a prolonged period of time. Thus, from an evolutionary standpoint, noisy pressure support ventilation may be an important component in the future treatment of ARDS/ALI.

Over the past decade, there has been interest in whether patients with ARDS/ALI on spontaneous modes of mechanical ventilation can achieve the same improvement in pulmonary function as those on controlled mechanical ventilation. If so, could this then lead to improvements in overall morbidity and mortality? This study by Spieth and colleagues reminds us of the importance of variability in normal human physiology. Should we be trying to achieve “normal” physiology in an indi-

vidual with severe systems dysfunction? Stochastic resonance would suggest that we make a little noise; the time is here to translate these studies to the bedside.

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